10TH EDITION

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Dear transplant colleagues

In 2019 we celebrated the 40th anniversary of the first bone marrow transplant (BMT) in our country, with the pioneering spirit of Professor Ricardo Pasquini, Eurípides Ferreira and his team, a fact that was undoubtedly a milestone and the driving force for us to arrive where we are. Today, we are 84 BMT-enabled centers in Brazil and we have seen the great success of these teams, demonstrating a process of maturation of our transplant recipients.

Our company was founded in 1996 by a group of specialists and within this same premise. Today we are prominent in the worldwide transplanting community, having entered into several partnerships with international entities, such as ASCT, LABMT, CIBMTR, FACT, among others.

We have a research group at GEDECO (Grupo de Estudo Doença Enxerto Contra o hospedeiro e complicações tardias) ,coordinated by our dear Dr. Mary Flowers and Dr Afonso Celso Vigorito. This started small as a group of studies on graft disease and because of its quality and empathy, it has now become the gateway to cooperative studies on various topics in our society. SBTMO also maintains a Pediatrics Group, a flow cytometry group, a multidisciplinary group and one of data managers. Every two years, a consensus of indications and complications of transplants is performed, which serves as a guide for the guidance of specialists and public policies.

Faced with this scenario, in a natural way, arose the need to have a journal that could disseminate the work of this scientific community, doctors and multidisciplinary professionals, thus strengthening our interaction with transplantation professionals from various countries.

It is with this spirit of joy and hope that we launched this volume of JBMCT, Journal of Bone Marrow Transplantation and Cellular Therapy, which will certainly be a periodical to publicize the work of all those who believe that science , research and caring for patients, is the best way to improve our walking.

Fernando Barroso Duarte *Nelson Hamerschlak*

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AWARDS

MARY FLOWERS AWARD BEST ABSTRACT IN CLINICAL ASPECTS OF HSCT

THE ROLE OF R-IPSS STRATIFICATION ON OUTCOMES OF BONE MARROW TRANSPLANTATION IN PATIENTS WITH MYELODYSPLASTIC SYNDROME: RESULT OF LATIN AMERICAN REGISTRY

Fernando Barroso Duarte[1], Talyta Ellen De Jesus Dos Santos Sousa[2], Vaneuza Araújo Moreira Funke[3], Virgílio Antônio Rensi Colturato[4], Nelson Hamerschlak[5], Neysimélia Costa Villela[6], Maria Cristina Martins De Almeida Macedo[7], Afonso Celso Vigorito[8], Rodolfo Daniel De Almeida Soares[9], Alessandra Paz[10], Lilian Diaz11, Mariana Stevenazzi[11], Abrahão Elias Hallack Neto[12], Gustavo Bettarello[13], Breno Moreno De Gusmão[14], Marco Aurélio Salvino[15], Rodolfo Froes Calixto[16], Maria Cláudia Rodrigues Moreira[17], Gustavo Machado Teixeira[18], Cinthya Corrêa Da Silva[5], Eduardo José De Alencar Paton[19], Vanderson Rocha[20], Alicia Enrico[21], Carmem Bonfim[22], Ricardo Chiattone[23], Anderson João Simioni[4], Celso Arrais[24], Erika Oliveira De Miranda Coelho[25].

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INTRODUCTION: The role of mutations in diagnosis, prognosis, treatment and even follow-up post HSCT in MDS has become increasingly relevant from a diagnostic point of view, especially in cases with cytopenias without blasts. The presence of mutations, epigenetic regulation or splicesseosome regulation can be of great diagnostic value. Regarding HSCT, despite being a single curative therapy, its precise indication is essential and a fundamental aspect is to select the best donor, cell source and type of conditioning, which force us to define post-HSCT goals. In view of these considerations, we decided to study the correlation of stratification with R-IPSS with overall survival, considering that we do not have molecular analysis as a tool, just like most places in Latin America.

OBJECTIVE: to evaluate the role of R-IPSS stratification on outcomes of HSCT in MDS patients.

METHODS: we analyzed data from 341 patients with MDS from the transplant registry of 32 centers in Latin America from 1989 to 2022. Statistics were performed using SPSSv.23.1, considering a significant $p<0.05$.

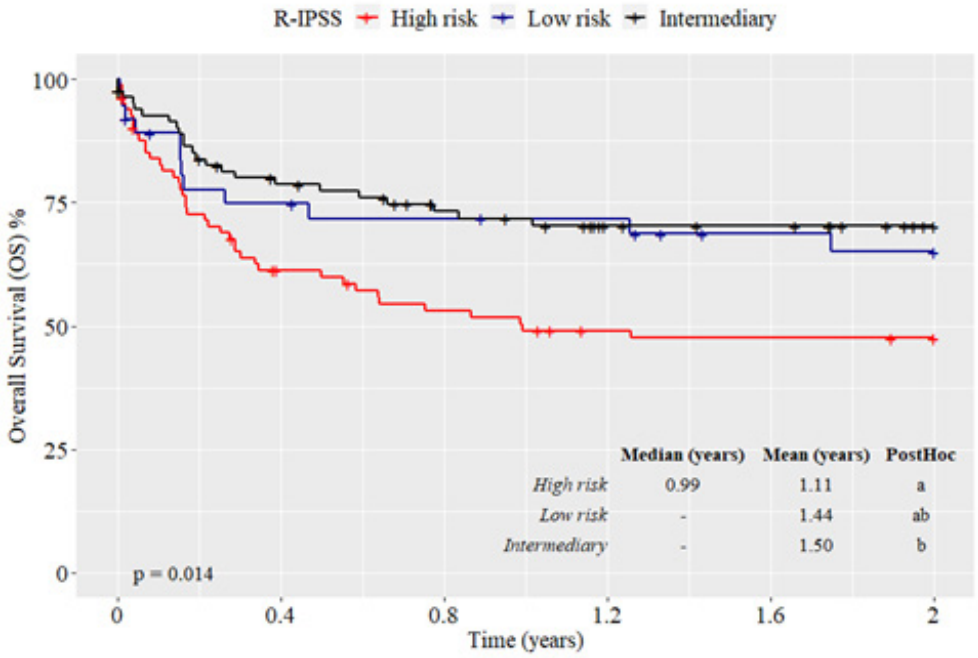
RESULTS: the mean age was 46,43 years. Most patients were ≤ 50 years (48,97%), about 21,41% were between 50 and 61 and 29,62% were > 60 years. There was a predominance of males (58,36%). Regarding to the Prognosis Scoring System (IPSS-R), patients were classified as: Very low risk (n=2; 0.59%), Low risk (n=35; 10,26%), Intermediate (n=82; 24,05%), high risk (n=63; 18,48%) and very high risk (n=19; 5,57% %). A total of 140 (41,06%) patients had no data about R-IPSS stratification. Myeloablative conditioning (MAC) was performed in 250 patients (73,96%). The predominant donor type was related 69,79% followed by non-related (22,58%) and haploidentical (7,62%). In 65,10% (n=222) of cases, a prior treatment was performed. From these patients, 61,71% used chemotherapy, 27,03% hypomethylating and 11,26% used both. The main cell source was bone marrow (BM) (53,08%). Peripheral blood (PB) was performed in 45,16% of cases and umbilical cord in 1,76%. Complications post-HSCT were observed in 260 patients (76,25%) and the most frequent was Infections (n= 212; 81,54%), followed by acute graft versus host disease (GVHD) (n=121;

46,54%) and chronic GVHD (n=98; 37,69%). The frequency of death was 40,47% (n=138). The 5-years overall survival was 56,2%. High/very high risk patients had a lower 2-years overall survival when compared to Intermediate and low/very low risk patients (p=0,014). A multivariate analyses demonstrated the association between High risk category and increase in the risk of death (p= 0,025; HR: 1,56; CI: 1,13 - 2,14).

CONCLUSION: The data presented showed that R-IPSS stratification influenced the outcomes of HSCT in patients with MDS, particularly the risk of death. The use of IPSS-R scores associated with other features as age and comorbidities can improve the management of MDS patients, especially where molecular analysis is not available.

Keywords: Hematopoietic Stem Cell Transplantation. R-IPSS Stratification. Prognosis.

FIGURE 1: 2-year Overall survival according to R-IPSS stratification.



JÚLIO VOLTARELLI AWARD BEST ABSTRACT IN CELL THERAPY AND BASIC RESEARCH

MECHANISMS INVOLVED IN THE ANTINOCICEPTIVE EFFECT OF BONE MARROW MESENCHYMAL AND BONE MARROW MONONUCLEAR STEM CELLS ON EXPERIMENTAL TRIGEMINAL NEURALGIA.

Catarina Milena Mota Costa[1], Dourivaldo Silva Santos[1], Afrânio Ferreira Evangelista[2], Géssica Sabrina de Assis Silva[1], Luiza Carolina França Opretzka[1], Milena Botelho Pereira Soares[2], Cristiane Flora Villarreal[1, 2].

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INTRODUCTION: Trigeminal neuralgia is a type of neuropathic pain that affects the trigeminal nerve. It is amongst the most common and debilitating orofacial neuropathic pain. The management of trigeminal neuralgia is still ineffective, despite the available pharmacological and surgical resources, which highlights the need to establish new therapies. The treatment with bone marrow mesenchymal stem cells (BM-MSC) and bone marrow mononuclear cells (BM-MNC) has shown great therapeutic potential for painful neuropathies. However, the mechanisms involved in these effects are still poorly understood.

AIM: To assess the mechanisms involved in the antinociceptive effect of BM-MSC and BM-MNC on a trigeminal neuralgia mice model.

METHODS: BM-MSC and BM-MNO were obtained from the bone marrow of C57Bl/6 mice, expanded in culture, and characterized by flow cytometry and cell differentiation assays. C57Bl/6 or IL10 -/- male mice machos underwent surgery for induction of the neuropathy model by partial ligation of the infraorbital nerve (CEUA 022/2015). Five days after the surgery the mice received a single intravenous administration of BM-MSC (1x106), BM-MNO (1x106) or vehicle (100µ). Nociceptive thresholds were assessed by von Frey test. The infraorbital nerve was collected 10 and 30 days after the treatment for cytokine quantification by ELISA and analysis of nerve fiber morphometric patterns by optical and transmission electron microscopy.

RESULTS: Analysis of nerve fiber morphometric patterns shows a reduction of fiber diameter and myelin sheath thickness in neuropathic mice, which characterizes the experimental trigeminal neuropathy. By contrast, in neuropathic mice treated with BM-MSC, but not with BM-MNO, the same pattern was not found. A single intravenous injection of MSC or MNO raised the levels of the anti-inflammatory cytokine IL-10 10 days after the treatment. Conversely, after 30 days elevated levels of IL-10 were found only in mice treated with BM-MSC. In IL-10 knockout animals the transplant of BM-MSC did not induce an antinociceptive effect.

CONCLUSION: The results point to a possible difference in the mechanism of action of BM-MNO and BM-MSC in trigeminal neuropathy. The effects of BM-MSC, but not of BM-MNO, on the experimental neuropathy were associated with a reduction in structural changes in the peripheral nerve. In addition, IL-10 production appears to be one of the mechanisms involved in BM-MSC-induced antinociception. These data indicate a disease-modifying profile related to BM-MSC treatment and reinforce the potential of cell therapy for the treatment of trigeminal neuralgia.

Financial Support: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001.

Keywords: trigeminal neuralgia; cell therapy; mesenchymal stem cells; mononuclear stem cells; neuropathic pain; morphometry; IL-10.

FANI JOB AWARD BEST MULTIDISCIPLINARY ABSTRACT

THE IMPACT OF THE COVID-19 PANDEMIC ON THE MENTAL HEALTH OF HEALTH CARE WORKERS (HCW) OF HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) UNITS.

Ana Claudia Ferrari Dos Santos[1], Lúcia Helena De Almeida Testa[1], Anderson João Simioni[1], Mair Pedro De Souza[1], Vergilio Antonio Rensi Colturato[1], Clarisse Martins Machado[1,2].

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BACKGROUND: The pandemic has brought to health professionals several unprecedented situations, both in relation to family life and the care provided to patients with COVID-19. In line with the recently published studies, the need to investigate feelings and the possibility of stress, suffering and even psychiatric disorders that these professionals may present during the follow-up of the study arose.

OBJECTIVE: The aim of this study was to describe the psychic suffering and the level of engagement in the work of HCW working in HSCT Units during the pandemic.

METHODS: Prospective cohort of HCW working in three related, unrelated, non-related, haploidentical and autologous Allogeneic HSCT Hospitalization Units during the hospitalization period of the transplant itself or for post-HSCT complications. The transplant center is located in an oncology hospital in the interior of the state of São Paulo. A questionnaire was elaborated to collect data, using an adaptation to the Short General Health Questionnaire (GHQ 12). The study was approved by the Ethics Committee process nº: 4.729.477.

RESULTS: We included 108 HCW, 95 female, 13 male, median age of 37(20 - 58) years and median of 5,9 years of activity in the area. The questionnaires were applied from May 13, 2020 to March 22, 2021. Table 1 describes the results obtained by the answers to the questionnaire.

DISCUSSION: Although most of the HCW did not feel uncomfortable (57%) during their stay in the work environment, and reported tranquility (52,3%) to perform their activities in the units, 52,3% of the interviewees reported anxiety at times. Surveillance for SARS-CoV2 in these units was performed weekly with nasal wash (NW) and RT-PCR testing, both of HCW and hospitalized patients. Most considered serology (61,47%) and NW (58,72%) collections adequate and uncomfortable. Regarding the risk of infection, 55,93% of the interviewees considered that there was a greater possibility of acquiring the virus in the community in daily activities than in the work environment (23%). Although the majority faced the pandemic with resilience, when asked about their weaknesses, 26,61% reported not enjoying day-to-day activities as before; 28,4% reported sleep loss because of more than before; 31,2% unhappiness or depression, and 29,3% reported sleep alteration, such as waking up several times during the night (65,63%) and insomnia (18,75%).

CONCLUSION: Despite all the challenge resulting from changes in the daily life of professionals and prolonged duration, resilience, commitment and engagement of HCW in the pandemic period were observed. These data associated with the good acceptance of periodic collections suggest that the surveillance adopted in HSCT units generated safety in the hospital environment, favoring the good performance and balance of the team during the pandemic period.

Keywords: COVID-19. Health care worker. Mental health.

TABLE 1 - HCW responses related to the pandemic period.

QUESTIONS		N	%
1. Feel anxiety during working hours	All the time	2	1,83%
	Most of the time	6	5,50%
	In some periods	57	52,29%
	No moment	36	33,03%
	They did not respond	8	7,34%
2. Feel tranquility during working	All the time	10	9,17%
	Most of the time	57	52,29%
	In some periods	32	29,36%
	No moment	2	1,83%
	They did not respond	8	7,34%
3. Feel discomfort (anguish) at work	All the time	0	0,00%
	Most of the time	5	4,59%
	In some periods	34	31,19%
	No moment	62	56,88%
	They did not respond	8	7,34%
4. Feel comfortable in working time	All the time	17	15,60%
	Most of the time	65	59,63%
	In some periods	14	12,84%
	No moment	4	3,67%
	They did not respond	9	8,26%
5. You imagined that the pandemic would last several months	No	45	41,28%
	Yes	56	51,38%
	They did not respond	8	7,34%
If so, how long?	3 months	4	7,14%
	6 months	8	14,29%
	1 year	20	35,71%
	More than 1 year	24	42,86%
6. How do you consider the periodic collection of LN	Adequate, with little discomfort	25	22,94%
	Suitable and without discomfort	64	58,72%
	Inadequate, discomfort	0	0,00%
	Inadequate, as to the periodicity	6	5,50%
	They did not respond	14	12,84%
7. How do you consider periodic peripheral blood collection	Adequate, with little discomfort	34	31,19%
	Suitable and without discomfort	67	61,47%
	Inadequate, discomfort	0	0,00%
	Inadequate, as to the periodicity	0	0,00%
	They did not respond	8	7,34%

8. Where you think there is a higher risk of acquiring corona vírus?	Work environment	25	22,94%
	Community/Everyday Life	61	55,96%
	Both	13	11,93%
	They did not respond	10	9,17%
9. During work do you use EPIs properly and follow pandemic preventive recommendations?	All the time	98	89,91%
	Most of the time	3	2,75%
	They did not respond	8	7,34%
10. During the work do you notice that your colleagues use PPE properly and follow the pandemic preventive recommendations?	All the time	80	73,39%
	Most of the time	20	18,35%
	In some periods	1	0,92%
	They did not respond	8	7,34%
11. There is material available for collective preventive measures (alcohol gel, liquid soap, etc.)	Yes	101	92,66%
	They did not respond	8	7,34%
12. Can you concentrate on what you're doing?	As normal	81	74,31%
	Better than normal	5	4,59%
	Much less than normal	4	3,67%
	usual	7	6,42%
	They did not respond	12	11,01%
13. Lost a lot of sleep because of worry?	No more than usual	46	42,20%
	Usual	9	8,26%
	A little more than usual	31	28,44%
	Much more than usual	7	6,42%
	They did not respond	16	14,68%
14. Do you feel able to enjoy your normal day-to-day activities??	Much less than usual	29	26,61%
	Usual	35	32,11%
	Much less than normal	34	31,19%
	Much more than normal	3	2,75%
	They did not respond	8	7,34%
15. Do you feel unhappy and depressed?	No more than usual	40	36,70%
	usual	11	10,09%
	A little more than usual	34	31,19%
	Much more than usual	10	9,17%
	They did not respond	14	12,84%
16. Have you had any sleep changes?	No	68	62,39%
	Yes	32	29,36%
	They did not respond	9	8,26%
If so, which one?	wake up several times in the night	21	65,63%
	Insomnia	6	18,75%
	Both	2	6,25%
	They did not respond	3	9,38%

RICARDO PASQUINI AWARD YOUNG SCIENTIST
BEST AUTHOR ABSTRACT WITH AGE EQUAL OR UNDER 35

TARGETED MARROW IRRADIATION-BASED CONDITIONING REGIMEN FOR ELDERLY PATIENTS

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2 Ohio State University, Columbus - The United States Of America.

INTRODUCTION: Hematopoietic cell transplantation for elderly patients remains a challenge. Usually non-myeloablative or reduced-intensity regimen are used, which decreases non-relapse mortality but can compromise long-term disease control. The objective of this study is to report a new targeted marrow irradiation (TMI)-based myeloablative conditioning regimen in elderly patients.

METHODS: We included patients 60 years old or older. Conditioning regimen consisted of targeted marrow irradiation (TMI, 1.5 Gy every 12h for 4 doses, total dose 6 Gy, on D-8 and D-7), fludarabine 30 mg/m2 D-6 through D-2, and phamacokinetically-guided busulfan (AUC 4,800 M*minute/day on D-5 and D-4). The goal of TMI is to include the skeleton and spleen in the irradiation field while relatively sparring critical organs like heart, lungs, liver, and bowel, among others.

RESULTS: A total of 18 patients were included, with a median follow-up of 285 days (range: 34-1365). Median age was 65.7 years; 50% were female; diseases were acute myeloid leukemia (67%), myelodysplastic syndrome (22%), chronic lymphocytic leukemia (6%) and multiple myeloma (6%); disease risk indexes were intermediate (50%), high (44%) and very high (6%); donors were matched sibling (28%), haploidentical (33%) and unrelated (39%); and graft sources were peripheral blood (83%) and bone marrow (17%). Mean infused CD34 was 6.1E6/kg (SD=4.5). All patient had neutrophil engraftment at a median of 17 days, except one (who had early disease progression and did not engraft despite achieving 67% donor chimerism on D+30). Platelet engraftment was 89% (median: 26 days) at 90 days. Of the patients who had chimerism analyses on D+100, 88% had full donor chimerism (>95%) and 12%, two patients, had mixed chimera (73% and 94%). Acute toxicities are described in table 1. One patient had very severe sinusoidal obstruction syndrome (SOS). Grades 3/4 mucositis were the main toxicity (94.4%). Eight patients had disease progression following HCT and 7 died. One patient died of acute myocardial infarction, and 1-y overall survival was 69% (95CI 47-100%). Six patients experienced grade II acute GVHD and 2, grade III.

CONCLUSIONS: Our results show encouraging 1-y survival in elderly patients who underwent targeted marrow irradiation-based myeloablative conditioning regimen. Moreover, non-relapse mortality was extremely low and only one patient died of non-relapse causes, although we had one very severe case of SOS which was successfully treated with defibrotide. Most patients engrafted and had >95% donor chimerism at D+100. Larger studies are needed to confirm these results in this population.

Project funded by PRONON and Amigo H

TABLE 1- Acute toxicities

TOXICITY	G 0	G 1/2	G 3/4
Mucositis	5,6%	55,6%	38,9%
Nausea/vomiting	11,1%	72,2%	16,7%
Diarrhea	27,8%	66,7%	5,6%
Hyperbilirubinemia	77,8%	16,7%	5,6%
AST/ALT	100,0%	0,0%	0,0%
Renal	58,8%	29,4%	11,8%
Cardiac	77,8%	22,2%	0,0%

** one patient had very severe SOS and another had hemarthrosis*

CARMEM BONFIM AWARD BEST ABSTRACT IN THE PEDIATRICS AREA

INTENSIVE MULTIMODALITY THERAPY FOR PATIENTS WITH STAGE 4 METASTATIC RETINOBLASTOMA

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1 Instituto de Oncologia Pediátrica - GRAACC/ UNIFESP, São Paulo - SP - BRAZIL; 2 Samaritano Higienópolis, São Paulo - SP - BRAZIL; 3 GPACI, Sorocaba - SP - BRAZIL.

Metastatic retinoblastoma (Rb) stage 4, including 4a (distant metastases without central nervous system-CNS-involvement) and 4b (involving the CNS/ trilateral disease) has a very poor prognosis with conventional therapy, being a highly lethal disease. Some evidence has suggested that intensification of therapy including high-dose chemotherapy (HDC) with autologous hematopoietic stem cell rescue(ASCR) might be associated with a better chance of survival.

GOAL: Report survival of stage 4 patients with intensive multimodality treatment, including HDC followed by ASCR at a single center in a developing country.

METHODS: Retrospective review from 2014 to 2021 with patients diagnosed of stage 4 retinoblastoma (according to the International retinoblastoma stage system). All of them were treated with 4 cycles of conventional intensive neoadjuvant chemotherapy. Patients with a ≥ partial response then received 1 cycle of high-dose carboplatin (AUC = 7/day, max 16.7 mg/kg/day) on days -8 to -6, thiotepa (10 mg/kg/day), etoposide (8.3 mg/kg/day) on days -5 to -3 with ASCR on day 0. Duration of overall survival and event-free survival after autologous hematopoietic stem cell rescue was calculated using the Kaplan-Meier.

RESULTS: We reported 42 patients who had stage 4 in a total of 384 children with newly diagnosed Rb. Ten of them (23.8%) had disease progression followed by death before being referred for autologous bone marrow transplantation and were excluded from the final analysis. Thirty-one were treated with 4 cycles of intensive conventional chemotherapy (vincristine, cisplatin, cyclophosphamide and etoposide) and one patient was treated with ifosfamide, carboplatin and etoposide.Twenty-seven patients were already metastatic at diagnosis, while 5 patients had relapse of intraocular disease, becoming metastatic. Eight patients were classified as stage 4a, while 24 were classified as stage 4b (6 patients had trilateral, 4 patients also had pineal disseminated, and 14 patients had disseminated disease in the CNS with or without hematogenous dissemination). The 5-year overall survival in stage 4 was 59.4%, with 50% in group 4a, 100% in trilateral and 50% in group 4b. The 5-year event-free survival was 71.9%, with 62.5% in group 4a, 100% in trilateral and 66.7% in group 4b. Three patients died from toxicity (sepsis and multiple organ failure) shortly after ASCR and 9 progressed to disease progression after auto-HSCT (mean: 6.3 months), progressing to death.

CONCLUSION: The delayed presentation seen in LMICs is a matter of concern, and there is an urgent need to create facilities for early diagnosis and timely referral of children with RB. The use of high intensity regimens like the ones discussed requires adequate supportive care that may not be available in many centers with limited resources.The only curative treatment for metastatic retinoblastoma is the use of HDC followed by ASCR.

NELSON HAMERSCHLAK AND MARCELO PASQUINI AWARD

BEST ABSTRACT IN THE DATA MANAGEMENT AREA

II DATA MANAGER (DM) TRAINING COURSE: STARTING AND UPDATING KNOWLEDGE IN HEMATOPOIETIC STEM CELL TRANSPLANTATION (HCT)

Bruna Letícia da Silva Santos Geraldo[1], Adriana Seber[1,2], Anderson João Simione[4], Livia Caroline Mariano Compte[5,6], Carmen Silvia Vieitas Vergueiro[1]

1 AMEO - Bone Marrow Association of the State of Sao Paulo – Sao Paulo/SP; 2 Samaritano Hospital - São Paulo/SP; 4 Amaral Carvalho Hospital - Jaú/SP; 5 HCFMUSP – Hospital das Clínicas da Faculdade de Medicina of University of São Paulo, São Paulo/ SP; 6 Centro Paulista de Oncologia – Oncoclinicas, São Paulo/SP

INTRODUCTION: In recent years, there has been a great effort to increase and improve the records on Hematopoietic Stem Cell Transplantation (HSCT) performed in Brazil. However, the difficulty of training and keeping the professional proficient to report HSCT data is still great. Training of a new data manager (DM) is long and there is a lack of resources to maintain it. The 1st edition of DM in HCT (2019/2020) had 60 students from 31 unrelated HSCT Centers. The 2nd edition is underway, at this time including centers that perform both allogeneic and autologous HSCT; we are making revisions and updates for already trained DMs. The formation of DM in HSCT is paramount to build and maintain a national HCT registry uptodate and accurate.

OBJECTIVE: To describe the DM training in HSCT, created to train new professionals, enabling them to understand indications and the process of HCT and the medical records; to correctly insert the data in the institutional database; to generate their institutional database; evaluate demographic data and patient survival; to be responsible for the information, in addition to consolidate the knowledge of already qualified and active DMs.

METHOD: The duration of the 2nd edition of DM training is 9 months. Requirements: to be connected to some HCT center and have 5h/week dedication to distance learning activities and online monitoring. Teachers are HCT specialists with experience in HCT. A total of 108 HSCT centers were invited and 76 signed up for the 2nd edition. Composition: 3 theoretical modules with recorded video lessons (54h) and weekly live online monitoring meetings (54h); Educational audit (online); Final work (statistical analysis of the data of each center by its DM). Evaluation methods: frequency to the video classes, post-tests and online monitoring; work and final evaluation.

RESULTS: Forty-four institutions are participating in the course, with an average of 66 students per class. Students' degrees: 75% nurses, 10% biomedicals and 15% other areas. Of the participating centers: 31 perform all types of HSCT, 6 perform autologous and allogeneic, 5 only autologous and 2 still do not perform HCT. Geographical distribution: there was an increase from 3 to 7 centers in the northeast region, from 0 to 8 centers in the midwest, the southeast maintained 24 centers, 9 new centers, and the south increased from 4 to 5 centers.

CONCLUSIONS: Despite our efforts, during the pandemic there was a loss of 30% of the DM previously trained in the 1st course and active during 2020. There is a lack of specific resources for DM in public institutions and lack of prioritization in private ones. The culture of "clinical data reporting" is still incipient in hospitals being difficult to maintain the hired GD when it is not clear to the payers the impact of this investment. Considering the relevance of knowing the data, it is necessary to encourage the institutions and the government for this professional to be included and regulated in the HCT teams.

Keywords: Data manager. Training. Hematopoietic Stem Cell Transplantation.

ALIRIO PFIFFER AWARD BEST ABSTRACT IN BONE MARROW FAILURE SYNDROMES

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN YOUNG CHILDREN WITH INHERITED AND ADQUIRED BONE MARROW FAILURES

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INTRODUCTION: Infants and young children need a differentiated approach in the diagnosis and treatment of aplastic anemia because of the higher incidence of inherited bone marrow failures syndromes (IBMFS) and the peculiarities of the disease in this age group.

OBJECTIVE: To evaluate the clinical characteristics and the outcomes of the hematopoetic stem cell transplantation (HSCT) in patients (pts) with inherited or acquired BMFS with 5yrs or less, in 3 pediatric transplantation centers between 1982 and 2020. Patient's characteristics: We described the experience of 108 pts (57% males), with a median age of 4,6yrs (range 4 to 70 months), 39 pts with Fanconi Anemia (FA), 35 with Acquired Severe Aplastic Anemia (aSAA), 15 with Diamond Blackfan Anemia (DBA), 13 with Amegakaryocytic Purpura (CAMT) and 6 with other IBMFS. The IBMFS represents 24% of pts > than 2yrs, but 60% of the group up to 2yrs.

METHODS: Retrospective, longitudinal, non-randomized, observational study. Databases and records were analyzed, and statistics performed using the EZR program.

RESULTS: Five-year overall survival (OS) was 63.2%, with a median follow-up of 4,2 years, 67.5% in the group of aSAA and 61.2% in IBMFS (FA 65%, DBA 72%, CAMT 42%) (p=0,56). Transplant related mortality (TRM) was lower in the aSAA group but it did not reach statistical significance when compared to the IBMFS (8,6% vs 19,2% p=0,56). There was a trend for lower TRM in pts transplanted after 2010 (8,6% vs 24% p=0,12). Regarding donor types, 53% (n=58) were related (4 with 1 mismatch), 16,6% (n=18) were haploidentical and 29,6% (n=32) were unrelated, with a 3-year OS, respectively, of 77.4%, 52.5% and 61.1% (p=0,04). Eighty seven percent (n=94) received bone marrow, with an OS of 67,1%, and 13% (n=14) received umbilical cord, with only 35.7% of OS (p=0.002). The conditioning regimen was myeloablative (based on busulfan or total body irradiation) in 26% of the pts, with a 5-year OS of 57%, while those who received reduced intensity conditioning had a 5-year OS of 67% (p=0.49). Eleven pts (10.3%) were retransplanted, 5 for primary graft failure. There was no difference in 5-year OS between pts transplanted below or above 2-years old (56% vs 63%; p=0,66). Median time from diagnosis to transplant was 12 months and the group of pts who underwent HSCT after 12 months had worse outcomes with a 5-year OS of 52,7% compared to 75% of the pts who were transplanted earlier (p=0,053).

CONCLUSIONS: IBMFS are more frequent in infants and young children, especially those under 2-years-old. But, despite the differences between diseases, the major impact on prognosis was the time from diagnosis to transplant and the use of bone marrow as the stem cell source. In the absence of a matched related donor, haploidentical transplants should be considered as they allow immediate donor availability and survival is comparable to those receiving unrelated donors.

Keywords: Bone marrow failure. Aplastic anemia. Young children.

JOSÉ ROBERTO MORAES AWARDW BEST ABSTRACT IN HISTOCOMPATIBILITY

HIGH-RESOLUTION HLA-A MISMATCHES ARE ASSOCIATED WITH SEVERE ACUTE GRAFT-VERSUS-HOST DISEASE AND INCREASED MORTALITY FOLLOWING UNRELATED DONOR TRANSPLANTATION FOR NONMALIGNANT DISORDERS

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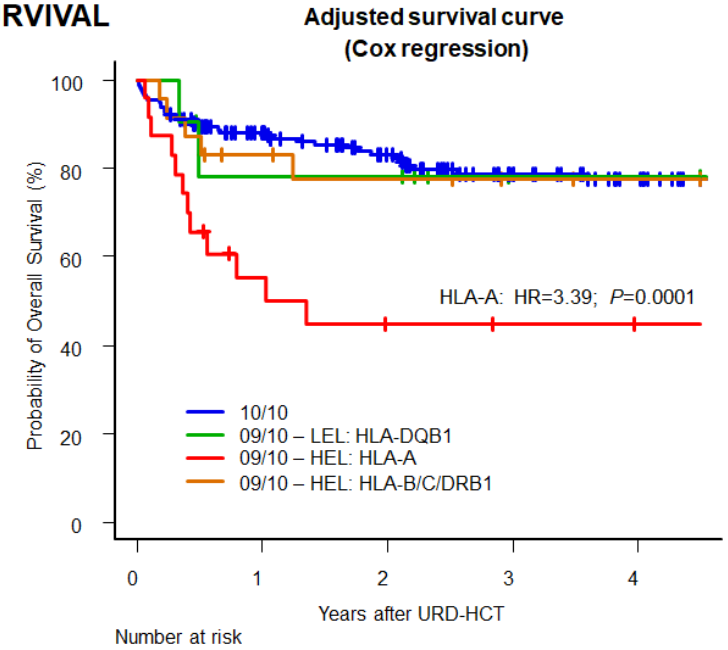
High-resolution HLA mismatches (MM) have been consistently associated with poor outcomes following unrelated donor hematopoietic cell transplantation (URD-HCT) for malignancies. Nevertheless, the role of HLA matching in URD-HCT for nonmalignant disorders (NMD) has been poorly reported, and data on the impact of specific HLA-mismatches in the NMD setting is currently unknown. To address this gap, we evaluated 224 patients with NMD who underwent 10/10 or 9/10 URD-HCT from 2007 to 2021 at our center. The primary endpoint was overall survival (OS), whereas secondary endpoints included grade II-IV and grade III-IV (severe) acute graft-versus-host disease (aGVHD). High-resolution HLA typing was performed with SBT or NGS. Multivariable analyses were performed using Cox proportional hazards regression for OS and Fine-Gray competing risk regression for aGVHD. The median age was 10 years (range, 0-52), and the main indications for URD-HCT were Fanconi anemia (n=79; 35.3%), severe aplastic anemia (n=77; 34.4%), and Wiskott-Aldrich syndrome (n=15; 6.7%). All patients received bone marrow as the graft source, 95.1% had in vivo T-cell depletion with ATG, and 80.8% received cyclosporine + methotrexate as GVHD prophylaxis. Patient-URD pairs were divided into three groups: 10/10 (n=172), high-expression loci (HEL) 9/10 (HLA-A, -B, -C, or -DRB1 MM; n=43), and low-expression loci (LEL) 9/10 (HLA-DQB1 MM, n=9). In the multivariable regression, adjusted for confounders, mismatching at a single HEL-MM was associated with poor OS (HR=2.20; 95%CI=1.25-3.86; P=0.006), higher incidence of grade II-IV aGVHD (SHR=2.16; 95%CI=1.06-4.41; P=0.035), and a trend towards more severe aGVHD (SHR=2.41; 95%CI=0.9-6.48; P=0.08) compared to 10/10 matched pairs. In contrast, LEL-MM was not predictive of worse OS (HR=1.78; 95%CI=0.55-5.79; P=0.34), grade II-IV aGVHD (SHR=1.79; 95%CI=0.51-6.34; P=0.37), and severe aGVHD (SHR=1.85; 95%CI=0.3-11.35; P=0.51). Stratifying by the distinct HEL, only HLA-A MM (n=23) was significantly associated with inferior OS (HR=3.39; 95%CI=1.81-6.33; P=0.0001), higher incidence of grade II-IV aGVHD (SHR=3.81; 95%CI=1.74-8.34; P=0.0008), and increased severe aGVHD (SHR=4.73; 95%CI=1.7-13.22; P=0.003) in the adjusted multivariable models. We performed a sensitivity analysis considering only the pediatric cohort (n=181), and HLA-A MM retained the association with increased mortality (HR=3.57; 95%CI=1.76-7.27; P=0.0004), higher occurrence of grade II-IV aGVHD (SHR=4.22; 95%CI=1.92-9.27; P=0.0003) and severe aGVHD (SHR=4.30; 95%CI=1.55-11.95; P=0.005), thus strengthening our results. This single-center study showed for the first time that HLA-A MM is highly detrimental in the URD-HCT for NMDs and should be avoided whenever possible. In addition, other HEL and LEL mismatches appear to be better tolerated and should be prioritized when a 10/10 HLA-matched URD is unavailable. Further studies with independent cohorts are warranted to validate our novel findings.

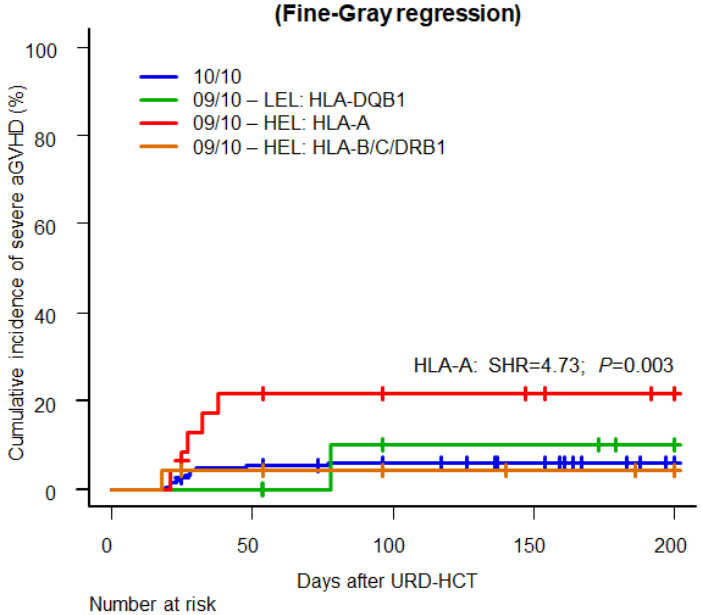
OVERALL SURVIVAL



Number at risk

10/10	172	130	103	71	55
09/10 – HLA-DQB1	9	6	6	2	2
09/10 –HLA-A	23	11	8	7	6
09/10 – HLA-B/C/DRB1	20	14	12	10	9

SEVERE ACUTE GVHD



Number at risk

10/10	167	143	135	130	122
09/10 – HLA-DQB1	8	7	6	6	4
09/10 –HLA-A	22	12	12	11	9
09/10 – HLA-B/C/DRB1	20	17	15	14	13

ORAL PRESENTATIONS

ALOGENEIC HSCT

ATG LEADS TO LOWER CHRONIC GVHD INCIDENCE WITHOUT COMPROMISING OVERALL SURVIVAL IN MATCHED-SIBLING DONOR PERIPHERAL BLOOD HEMATOPOIETIC CELL TRANSPLANTATION: A MULTICENTER RETROSPECTIVE STUDY OF BRAZILIAN PATIENTS WITH ACUTE LEUKEMIA OR MYELODYSPLASTIC SYNDROME REPORTED TO THE CIBMTR

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1 Hospital Israelita Albert Einstein; 2 Hospital Universitario Walter Cantídio – UFC; 3 Fundacao Amaral Carvalho.4 Hospital de Clinicas de Porto Alegre; 5 Hospital Sirio-Libanes; 6 UNICAMP; 7 Hospital das Clinicas da UFPR; 8 Bio Sana's; 9 CIBMTR; 10 Seattle Cancer Care Alliance; 11 Hospital Samaritano.

INTRODUCTION: Hematopoietic cell transplantation (HCT) is a curative treatment for several malignant diseases. Graft-versus-host disease, however, is the major posttransplant complication, leading to morbidity and poor quality of life.

OBJECTIVE: The objective of the current study was to compare matched-sibling donor (MSD) HCT with peripheral blood grafts with or without ATG.

PATIENTS: Patients were transplanted in 9 Brazilian centers between 2014 and 2018 and reported to the CIBMTR. All patients with acute leukemia or myelodysplastic syndrome and who underwent matched-sibling donor HCT were included. There was no exclusion criterion.

METHODS: We used the CIBMTR framework for data collection. Outcomes were overall survival (OS), relapse (REL), non-relapse mortality (NRM), and cGVHD. Survival and incidence curves were built with the Kaplan-Meier and Grey methods, respectively, and compared with the logrank and Grey test. Uni and multivariable analyses were performed with Cox models. Model selection was based on the lowest Akaike information criterion. We reported the results from multivariable analyses.

RESULTS: A total of 175 patients were included with a median follow-up of 38 months. Patients' characteristics are in table 1. In brief, there were 37 patients who received ATG and 138 who did not. Patients' characteristics were not different between the two groups. Three-years overall survival was not different between the two groups (No ATG: 48%, ATG: 56%; ATG vs No ATG: HR = 0.94, p = 0.82). Three-years relapse (No ATG: 32%, ATG: 33%; PBSC vs BM: HR = 0.91, P = 0.81) and NRM (No ATG: 24%, ATG: 14%; HR = 1.25, P = 0.49) incidences were also not different. cGVHD was significantly lower with ATG (figure 1, No ATG: 51%, ATG: 24%; ATG vs No ATG: HR = 0.32, P = 0.002).

CONCLUSIONS: Our results suggest that the results of MSD with PBSC are improved when ATG is used. OS, relapse, and NRM were not different between the groups, while cGVHD incidence was dramatically reduced. Chronic GVHD is the major source of poor quality of life posttransplant. A previous randomized trial[1] has shown the same results, but they used ATG-Fresenius, while the only brand available in Brazil is Thymoglobuline. ATG brands are different drugs and are not interchangeable. We confirmed those results with the brand available in Brazil. Taken together, ATG should be standard for MSD receiving PBSC grafts.

Keywords: Related-donor hematopoietic cell transplantation. ATG. Peripheral blood stem cells.

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DISCLAIMER

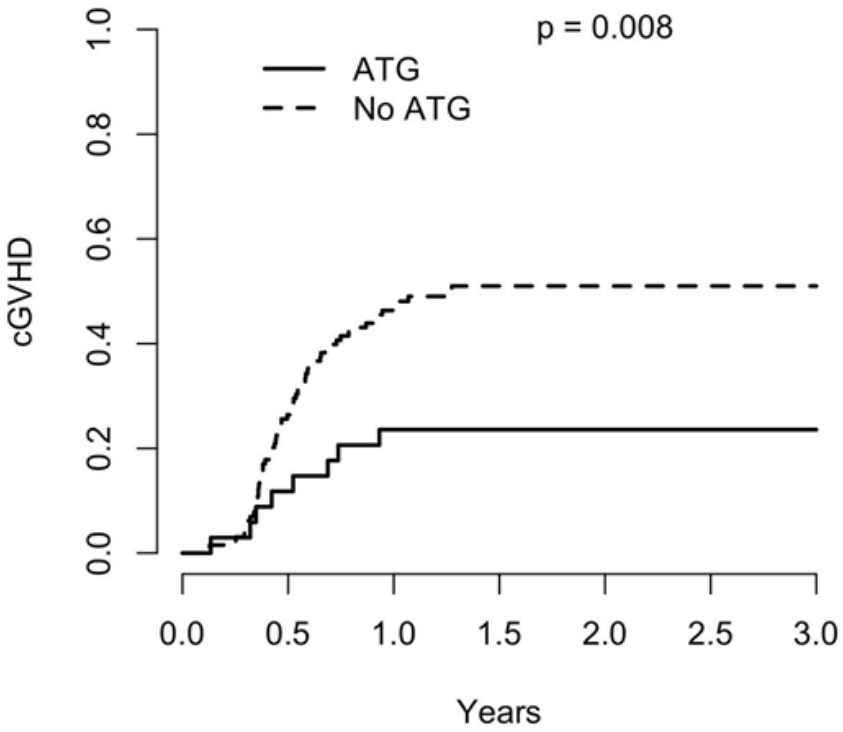
The results presented were obtained using data from the Coordinating Center of the CIBMTR. The analysis plan, result, and interpretation were not reviewed or approved by Statistical or Scientific Committees of the CIBMTR, and the CIBMTR cannot confirm their accuracy. Also, the dataset was blinded for participating center, and therefore we could not include participating centers' researchers. We thank all the participating centers.

TABLE 1. Patients' characteristics

	No ATG	ATG	P value
Total	138	37	
Median age (IQR)	47.4 (34.8,54.7)	43.5 (26.4,57.7)	0.969
Female sex	55 (39.9)	15 (40.5)	0.94
HCT-CI			0.579
0	90 (65.2)	23 (62.2)	
1	27 (19.6)	8 (21.6)	
2	4 (2.9)	1 (2.7)	
3	9 (6.5)	5 (13.5)	
4	6 (4.3)	0 (0)	
5	2 (1.4)	0 (0)	
Karnofsky			0.112
90-100	106 (77.4)	33 (89.2)	
<90	31 (22.6)	4 (10.8)	
Disease			0.23
AML	67 (48.6)	15 (40.5)	
ALL	40 (29)	9 (24.3)	
SMD	27 (19.6)	13 (35.1)	
Other AL	4 (2.9)	0 (0)	
Female donor	64 (46.4)	13 (35.1)	0.221
CMV			1
Neg/Neg	1 (0.7)	0 (0)	
Any Pos	133 (99.3)	37 (100)	
Conditioning			0.684
Myeloablative	97 (70.8)	28 (75.7)	
Non-myeloablative	9 (6.6)	3 (8.1)	
Reduced-intensity	31 (22.6)	6 (16.2)	
Median follow-up (months, IQR)	42 (23,60)	35 (25,45)	0.429

IQR, interquartile range; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome.

FIGURE 1. **Chronic GVHD**



COST ANALYSIS FOR ADULT PATIENTS WITH ACUTE MYELOID LEUKEMIA AND MYELODYSPLASTIC SYNDROME UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is a medical procedure indicated for several malignant and non-malignant diseases. Few studies have been published about costs in HSCT, despite its fundamental role in increasing efficiency in resource allocation by transplantation programs. Thus, economic evaluation studies in the transplant setting are extremely important to help better conduct the procedure worldwide.

OBJECTIVE: To analyze the cost of HSCT performed in adult patients (≥18 years) with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) as their underlying disease.

CASUISTIC: This is a single-center, retrospective cohort study that included adult patients with AML or MDS, who received their first allogeneic HSCT between 2010 and 2021.

METHODS: Cost data were extracted from the hospital system. The hospital's standard cost table was used for the cost calculations and the values in Brazilian Reais (R$) were converted into dollars at the exchange rate of R$4.90 (June 10th, 2022). To estimate the median cost, a parametric survival method with lognormal distribution was used. Costs were calculated from HSCT admission to 1 year after transplantation and patients who died or were lost to follow-up before 1 year were censored. The statistical software used was R, version 4.1.0.

RESULTS: 117 patients were included; median age was 61 years; there was a male predominance, 61% (71) and 70% (82) of the underlying disease was AML. There were 54 (46%) UD, 34 (29%) MSD, and 29 (25%) haploidentical transplants (Table 1). A summary of the multivariate analysis is in Table 2, and the distribution of costs is in Figure 1. The median cost of HSCT in the matched patients was US$123,598 (intercept). The median cost of Haplo was 2.88 times higher than MSD, US$355,963, (p=0.0001). For UD HLA 9x10 and 10x10, compared with MSD, costs were 2.84 times greater, US$351,019, (p=0.01) and 1.72 times greater, US$212,589, (p=0.02), respectively. For each 10 years of age increase, the cost increased 1.27 times (p=0.0003).

CONCLUSION: We concluded that HSCT MSD had a lower cost when compared to other subtypes such as Haplo and UD. Haploidentical and unrelated transplants use a more immunosuppressive platform, with a higher incidence of infections. In addition, there is a higher incidence of non-infectious complications from both HLA incompatibility (haploidentical) and non-HLA incompatibility (unrelated donor). Prospective studies separating the cost by type (like blood bank support and medications) are needed.

Keywords: Cost. Hematopoietic Stem Cell Transplantation. Acute Myeloid Leukemia. Myelodysplastic Syndrome.

TABLE 1. Characteristics

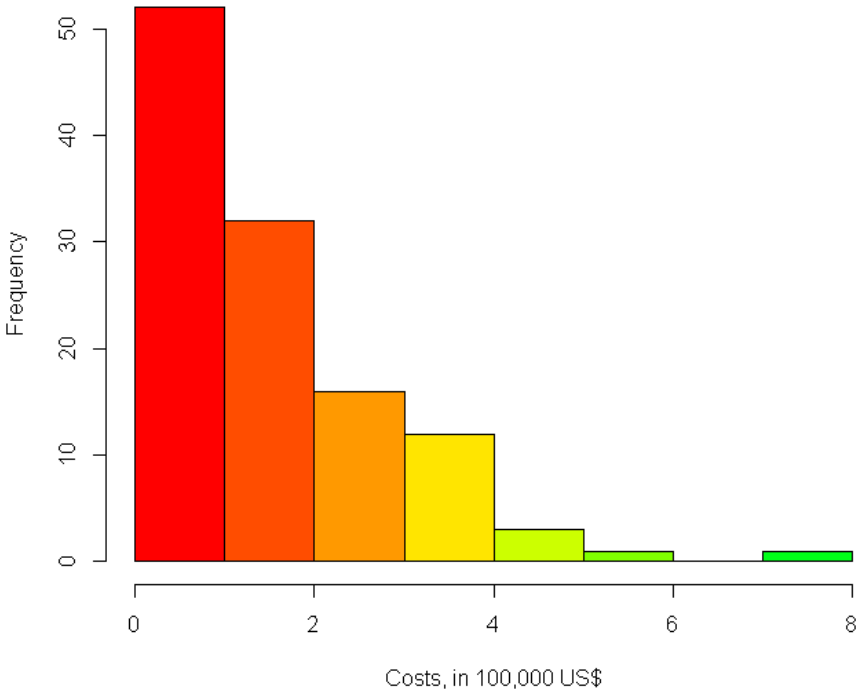
Total	**117**
Age	
Mean (SD)	56.1 (14.9)
Sex, N (%)	
Female	46 (39.3%)
Male	71 (60.7%)
Diagnosis, N (%)	
Acute myeloid leukemia	82 (70.1%)
Myelodysplasic syndrome	35 (29.9%)
HLA, N (%)	
MSD	34 (29.1%)
Haploidentical	29 (24.8%)
UD, 10x10	46 (39.3%)
UD, 9x10	8 (6.8%)
Conditioning, N (%)	
Myeloablative	47 (40.2%)
Reduced-intensity	64 (54.7%)
Non-myeloablative	6 (5.1%)
Graft, N (%)	
Peripheral blood	55 (47%)
Bone marrow	62 (53%)

TABLE 2. Multivariate analysis

	Multiplying factor	CI 95%	P
Intercept	US$ 123.598		
Donor			
MSD	Ref		
MUD	1.72	1.10-2.70	0.02
MMUD	2.84	1.26-6.41	0.01
Haplo	2.88	1.68-4.95	0.0001
Age (each 10-y older)	1.27	1.12-1.44	0.0003

MSD: matched-sibling donor; MUD: matched-unrelated donor (HLA 10x10);
MMUD: mismatched unrelated donor (HLA 9x10); Haplo: haploidentical.

FIGURE 1. **Distribution of costs**



CLINICAL IMPACT OF CYTOKINE RELEASE SYNDROME AFTER ALLOGENEIC HEMATOPOETIC STEM CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE

Nathana dos Santos Lemos[1], Lucas Freire Castelo[1], Leonardo Javier Arcuri[1], Ana Carolina Vieira de Lima[1], Ana Luisa Oliveira[1], Anna Carolinne Leal do Nacimento[1], Carolina Perrone Marques[1], Felipe Galvão Batista Chaves[1], Luana Nóbrega da Costa[1], Lucila Nassif Kerbauy[1], Mariana Nassif Kerbauy[1], Andreza Alice Feitosa Ribeiro[1], Nelson Hamerschlak[1].

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INTRODUCTION: Cytokine release syndrome (CRS) is a systemic inflammatory response resulting from high-level immune activation. CRS has been described after cellular-based therapies such as the allogeneic hematopoietic stem cell transplantation (HSCT). The use of post-transplant cyclophosphamide (PTCy) as graft-vs-host disease (GVHD) prophylaxis in haploidentical HSCT has led to the possibility of performing allogeneic HSCT to patients without HLA identical donors and thus greatly expanding the pool of donors. PTCy has also been introduced in matched unrelated donors (MUD). Even though the use of T cell replete transplantation with PTCy as GVHD prophylaxis in allogeneic HSCT has increased, the description of incidence and clinical impact of CRS in these patients is still scarce.

OBJECTIVE: We analyzed the development and characteristics of CRS in allogeneic transplant with PTCy after haploidentical and MUD HSCT. Furthermore, we analyzed the risk factors associated with its development, and the impact on overall survival (OS).

METHODS: This is a retrospective, single-center study conducted in a private hospital in Brazil from April 2018 to May 2022, including all patients who received PTCy after haploidentical or MUD HSCT. We used the published ASTCT CRS criteria to identify and grade patients who developed CRS after HSCT. OS curves were built with the Kaplan-Meier method.

RESULTS: We retrospectively analyzed 33 haploidentical and 16 MUD HSCT with PTCy from April 2018 to May 2022. The mean age was 48 years old, and AML was the most common primary disease (40,8%). Peripheral blood (PBSC) was the main stem cell source used (63,3%). CRS was significantly less frequent after MUD HSCT with only 4 cases and all grade 1, receiving symptomatic treatment. Among the 33 haploidentical patients, 45% had no CRS; 33,3% CRS grade 1; 27% grade 2; and 27% grade 3. Only one patient from the whole series had CRS grade 4, after performing haploidentical HSCT, being treated with methylprednisolone at the time. In multivariate analysis, the number of CD34 infused (OR 1,53; P = 0.01) remained as an independent risk factor. In the univariate analysis, the number of CD3 infused was significantly associated with the development of CRS grade 2-4 (OR 1,10; P = 0.009). There was no occurrence of grade 2-4 CRS when bone marrow was used as stem cell source or in MUD HSCT in the analysis. Despite that, when we excluded these categories, we still have found the number of CD3 infused as an independent factor for CRS 2-4 (OR 1,13; P = 0,05). No association was observed between CRS and other variables such as neutrophil engraftment or the development of acute GVHD grades II-IV.

CONCLUSION: In our experience, CRS 2-4 appeared more frequently in haploidentical compared to HSCT with MUD and PBSC. Patients with CRS grades 2-4 tended to have worse OS. Prospective studies involving more patients are needed to define the risk factors and prognostic implications of CRS.

Keywords: Cyclophosphamide. Cytokine release syndrome. Allogeneic hematopoietic stem cell transplantation.

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FIGURE 1. Overall survival of patients after CRS

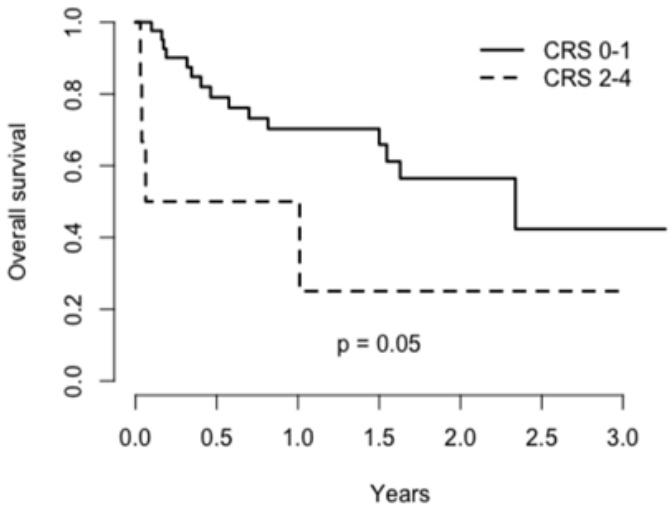

TABLE 1. Patients and transplants characteristics.

	Total
Number of patients, n	49
Mean age, years	48,1
Sex Female, n (%) Male, n (%)	 23 (46,9) 26 (53,1)
Donor Haploidentical, n (%) MUD, n (%)	 33 (67,3%) 16 (32,7%)
Primary disease, n (%) AML ALL MDS MF NHL CML Others	 20 (40,8) 8 (16,3) 4 (8,1) 2 (4,1) 6 (12,2) 3 (6,1) 6 (12,2)
Stem cell source, n (%) Bone marrow Peripheral blood	 18 (36,7) 31 (63,3)
Mean CD34+ x 10^6/kg	5,2
Mean CD3 x 10^7/kg	18,3
Mean neutrophil engraftment, n	18,6

AML (acute myeloid leukemia), ALL (acute lymphoblastic leukemia), MDS (myelodysplasic syndrome), MF (myelofibrosis), CML (chronic myeloid leukemia), NHL (non Hodgkin lymphoma)

PERIPHERAL BLOOD OR BONE MARROW YIELDS SIMILAR RESULTS IN MATCHED UNRELATED DONOR HEMATOPOIETIC CELL TRANSPLANTATION WITH ATG-BASED GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS: A MULTICENTER RETROSPECTIVE STUDY OF BRAZILIAN PATIENTS WITH ACUTE LEUKEMIA OR MYELODYSPLASTIC SYNDROME REPORTED TO THE CIBMTR

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INTRODUCTION: Hematopoietic cell transplantation (HCT) is a curative treatment for several malignant diseases. Since most patients do not have an HLA-matched sibling donor, HCT from unrelated donors are increasingly used.

OBJECTIVE: The objective of this study was to compare bone marrow (BM) with peripheral blood stem cells (PBSC) in matched-unrelated donor (MUD, HLA 8x8), in patients with acute lymphoblastic (ALL) or myeloid (AML) leukemia (or other acute leukemia), or myelodysplastic syndrome (MDS) who received ATG-based GVHD prophylaxis.

PATIENTS: Patients were transplanted in 11 Brazilian centers between 2014 and 2018 and reported to the CIBMTR. All patients with acute leukemia or myelodysplastic syndrome, who underwent MUD HCT, and received ATG-based GVHD prophylaxis were included. There was no exclusion criterion.

METHODS: We used the CIBMTR framework for data collection. Outcomes were overall survival (OS), relapse (REL), non-relapse mortality (NRM), and cGVHD. Survival and incidence curves were built with the Kaplan-Meier and Grey methods. Uni and multivariable analyses were performed with Cox models. Model selection was based on the lowest AIC. We reported the results from multivariable analyses.

RESULTS: A total of 174 patients were included with a median follow-up of 3 years. Patients' characteristics are in table 1. There were 96 BM and 78 PBSC. PBSC recipients were older, had a higher comorbidity index and more often had a reduced-intensity conditioning (RIC) regimen. The 3-year overall survival was not different (BM: 66%, PB: 58%, figure 1; PBSC vs BM: HR = 1.23, p = 0.42). The 3-year relapse rate (PBSC vs BM: HR = 0.91, P = 0.81), NRM (PBSC vs BM: HR = 1.28, P = 0.48) and cGVHD (PBSC vs BM: HR = 1.33, P = 0.32) incidences were also not different.

CONCLUSIONS: Our results suggest that the outcomes of BM and PBSC for matched unrelated HCT are comparable in terms of overall survival, relapse, non-relapse mortality, and chronic GVHD, provided that ATG is used. A previous randomized study has found superior results for BM in terms of cGVHD and quality of life1, but only a few patients had received ATG. In our study, all patients received ATG. In summary, BM and PBSC achieve the same results for URD HCT when ATG is given.

Keywords: Unrelated donor transplantation. ATG. Peripheral blood. Bone marrow. Graft source.

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DISCLAIMER

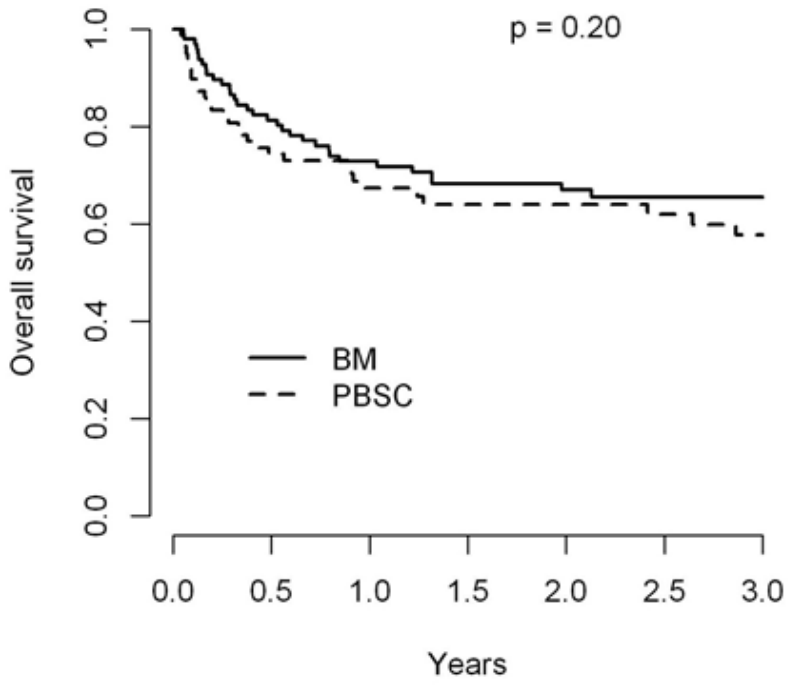
The results presented were obtained using data from the Coordinating Center of the CIBMTR. The analysis plan, result, and interpretation were not reviewed or approved by Statistical or Scientific Committees of the CIBMTR, and the CIBMTR cannot confirm their accuracy. Also, the dataset was blinded for participating center, and therefore we could not include participating centers' researchers. We thank all the participating centers.

TABLE 1. Patients' characteristics

	BM	PBSC	P value
Total	96	78	
Median age (IQR)	14.6 (8.2,33.1)	37.7 (22.4,54.6)	< 0.001
Female sex	43 (44.8%)	29 (37.2%)	0.311
HCT-CI			0.002
0	78 (81.2%)	45 (57.7%)	
1	11 (11.5%)	12 (15.4%)	
2	0 (0%)	7 (9%)	
3	4 (4.2%)	4 (5.1%)	
4	1 (1%)	4 (5.1%)	
5	2 (2.1%)	4 (5.1%)	
6	0 (0%)	2 (2.6%)	
Karnofsky			0.322
90-100	85 (88.5%)	65 (83.3%)	
<90	11 (11.5%)	13 (16.7%)	
Disease			0.018
AML	29 (30.2%)	37 (47.4%)	
ALL	52 (54.2%)	28 (35.9%)	
MDS	14 (14.6%)	9 (11.5%)	
Other AL	1 (1%)	4 (5.1%)	
Disease status			0.307
CR1	42 (43.8)	31 (39.2)	
CR2+	35 (36.5)	26 (32.9)	
Active	3 (3.1)	6 (7.6)	
Primary induction failure	1 (1)	3 (3.8)	
MDS	14 (14.6)	9 (11.4)	
Missing	1 (1)	4 (5.1)	
Female donor	30 (31.2%)	24 (31.2%)	0.991
CMV			1
Neg/Neg	2 (2.1%)	2 (2.6%)	
Any Pos	94 (97.9%)	76 (97.4%)	
Conditioning			0.018
Myeloablative	87 (90.6%)	59 (75.6%)	
Non-myeloablative	1 (1%)	2 (2.6%)	
Reduced-intensity	8 (8.3%)	17 (21.8%)	
Follow-up (IQR)	36 (24-60)	35 (12-49)	0.059

IQR, interquartile range; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome.

FIGURE 1. Overall survival



PREVALENCE OF BLACK AND BROWN PATIENTS AMONG THOSE SUBMITTED TO HEMATOPOIETIC STEM CELL TRANSPLANTATION AT THE UNIVERSITY HOSPITAL IN SOUTH OF BRAZIL

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INTRODUCTION: In centers in Brazil, most patients undergoing Hematopoietic Stem Cell Transplantation (HSCT) are white. However, the prevalence of onco-hematological diseases whose treatment involves HSCT does not follow the same proportionality. One explanation for a similar situation in the US was that non-white patients were less likely to find an unrelated donor due to a lower HLA match. In this sense, studies that analyze the racial profile of patients undergoing HSCT are essential to highlight possible disparities and search for causes to enable access to HSCT for all people who need it.

OBJECTIVES: To describe the color profile of patients undergoing HSCT at University Hospital in South of Brazil and the HSCT modalities performed. Methods: Retrospective observational study approved by the CEP-HCPA (CAAE 08762918.1.0000.5327) with data collected from electronic medical records of 138 patients with onco-hematologic diseases who underwent HSCT between 2015 and 2020. The patient's color was self-declared.

RESULTS: Of the 138 patients included in the study, 132 (95.7%) were white, 5 (3.6%) were black, and 1 (0.7%) was brown. Of the 132 whites, 54 (56.8%) received a related transplant, 21 (15.9%) received a haploidentical transplant, and 57 (43.2%) received an unrelated transplant; the 5 (100%) blacks received a related transplant, and 3 (60%) received a haploidentical transplant; the mixed-race patient received an unrelated transplant.

CONCLUSION: The data found indicate a disproportion between white and black and brown patients who underwent HSCT, similarly to the literature. This disproportionality is more significant than the difference between whites and non-whites in the population of Rio Grande do Sul, which is not an explanation. In 2019, RS had 79% of the self-declared population white, 14.3% brown, and 6.2% black. It is observed that non-white patients received more related transplants than unrelated transplants. More studies are needed to assess the causes of this disproportionate.

HYPOCELLULAR MYELODYSPLASTIC SYNDROME AND BONE MARROW TRANSPLANTATION: RESULTS OF THE LATIN AMERICAN REGISTRY

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INTRODUCTION: Most patients with myelodysplastic syndrome (MDS) presents bone marrow hypercellularity, however approximately 10 to 20% of all MDS have a Hypocellular bone marrow. Diagnosis of Hypocellular MDS can be challenging due to clinical and laboratory similarities with aplastic anemia. Some studies report a better response to treatment and a better prognosis in this group of individuals. Allogeneic HSCT is indicated for patients with high risk R-IPSS or transfusional dependence.

OBJECTIVE: to evaluate the profile of Hypocellular variant MDS patients in front of HSCT outcomes of Latin America Registry.

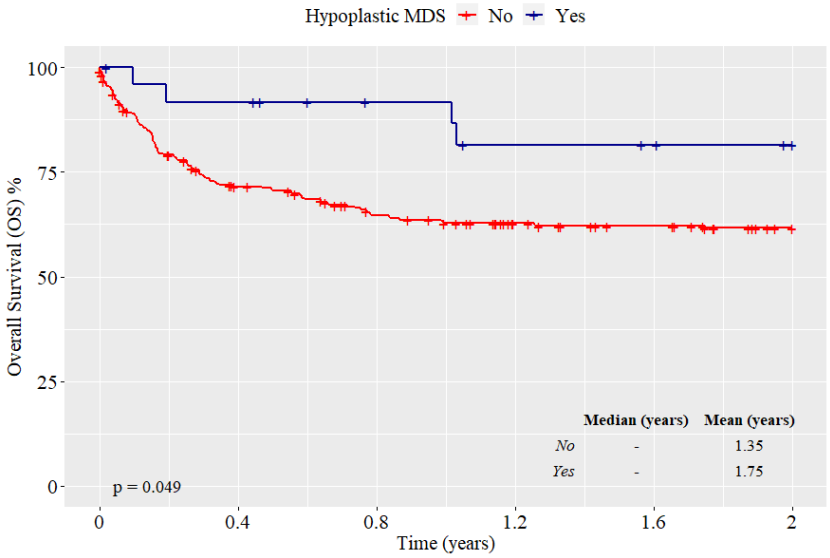
METHODS: Data of 341 patients with MDS in 32 centers of the Latin America Transplant Registry from 1989 to 2022 were analyzed. Statistics were performed using SPSSv.23.1, considering a significant $p<0.05$.

OUTCOMES: from 341 patients of Registry, prevalence of Hypocellular MDS was 7,3% (n=25). There was a predominance of male patients (n=17; 68%) and Caucasian (n= 19; 82,61 %). Regarding to R-IPSS, patients were stratified as: low /very low risk (15.38%), intermediate (69,23 %) and high/very high (15,38 %). In 48% of cases, the stratification was not possible due to missing data. Prior to HSCT treatment was performed in 13 patients (52%). Chemotherapy was the option for all cases. Normo/hypercellular patients had a higher hazard ratio to be underwent to prior treatment compared to Hypocellular patients (p=0,045; HR: 2,28; CI: 1-5,17). Myeloablative conditioning was performed in 18 cases (72%) and Reduced Intensity in 7 patients (28 %). The donor types were Related (n= 20; 80%), Non Related (n=4; 16 %) and Haploidentical (n=1; 4 %). The cell sources were bone marrow (n=12; 48 %) and peripheral blood (n=13; 52%). When compared to all patients, Hypocellular MDS group had a better 2-years OS with significant difference (p=0,049). In the multivariate analysis it was observed a higher risk of death for normo/hipercellular patients compared to hypocellular group (p=0,030; HR: 2,1; CI: 0,95-4, 66).

CONCLUSION: Patients with Hypocellular MDS presented a better OS and lower risk of death than Normo/Hypercellular group. Absence of blasts and other specific aspects as the mutational pattern may be the differential in this response to treatment. Further specific studies need to be carried out to confirm these observations.

Keywords: Hematopoietic Stem Cell Transplantation. Hypocellular variant MDS. Prognosis.

FIGURE 1: **2-year-overall survival according to bone marrow cellularity of Myelodysplastic Syndrome patients**



IMPACT OF THE KARNOFSKY PERFORMANCE STATUS SCORE IN THE COST ANALYSIS OF ADULT PATIENTS UNDERGOING AUTOLOGOUS AND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR MALIGNANT AND NON-MALIGNANT DISEASES

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INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is a medical procedure indicated for several malignant and non-malignant diseases. To better evaluate the clinical condition of the patient who will be submitted to HSCT, some tools are used such as Karnofsky PS standard way of measuring patients' ability to perform common tasks. Thus, economic evaluation studies in the transplant setting, with associated patient status performce instruments are extremely important to help better conduct the procedure worldwide.

CASUISTIC: This is a single-center, retrospective cohort study that included adult patients (≥ 18 years), who received their first autologous and allogeneic HSCT between 2010 and 2021, with malignant and non-malignant diseases.

OBJECTIVE: To assess the impact of the Karnofsky performance status (PS) score in the costs of HSCT in adult patients undergoing autologous and allogeneic transplantation, with malignant and non-malignant diseases.

METHODS: 430 cases were eligible for the analysis. Average procedure costs were calculated up to 30 and 40 days post autologous HSCT and 90 and 365 days post allogenic HSCT, with the codependent variable being Karnofsky PS. The PS ranges from 10% to 100%. A high score means that the patient is better able to perform daily activities. The 2022 standard cost table was used, and values converted to dollars (1USD = R$4.7158, May/2022). The cost correlation with the Karnofsky PS was calculated by applying the Pearson correlation coefficient method.

RESULTS: 221 patients (51%) underwent allogeneic HSCT, median age was 54 years, with a predominance of males (57%), and the main indication for the procedure was acute leukemias (49%). 209 patients underwent autologous HSCT (49%), median age was 57 years, 57% were male, and the predominant underlying disease was multiple myeloma (47%). Analyzing the Pearson correlation coefficient between the mean cost in the period of D+90 and D+365 days for allogeneic HSCT with the Karnofsky PS of patients and grouping the cases of PS <= 70% we found respectively -0.85 and -0.83 as coefficient results, which shows that the higher the Karnosfky score, the lower the costs/consumption of hospital resources. Similar results were found in the analysis of autologous transplants in the periods of D+30 and D+40 days, with correlation coefficients of -0,81 and -0,79, respectively, which also shows that the higher the Karnosfky index, the lower the costs/consumption of hospital resources. This reinforces that even analyzing a longer period after HSCT there is a correlation between the PS score and resource consumption.

CONCLUSION: It was concluded that the higher the performance status of patients undergoing autologous or allogeneic transplantation, the lower the patient costs. An estimate of transplant costs can be performed considering the type of transplant and performance status.

Keywords: Cost. Hematopoietic Stem Cell Transplantation. Pearson.

GERIATRIC ASSESSMENT AND IMPACT OF CFS IN HEMATOPOIETIC STEM CELL TRANSPLANTATION ALLOGENIC IN PATIENTS OVER 50 YEARS OF AGE: A MULTICENTRIC STUDY.

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The allogeneic hematopoietic stem cell transplant (HSTH) emerged as an important strategy in acute leukemia, lymphomas, and solid neoplasms treatment, in addition to benign disease, for example aplastic anemia. This treatment requires myeloablative chemotherapy therapy followed by the infusion of hematopoietic stem cell from the donor. Furthermore, this processing has any risks, since infections, graft versus host disease (GVHD) to death. Over the decades, the cases of hematologic disease that need allogeneic transplant are growing, requiring a comprehensive geriatric assessment as a mechanism to choose the better treatment option.

OBJECTIVE: To apply a clinical frailty score and Karnofsky score in allogeneic hematopoietic stem cell older than 50 years old for three years in two hospitals in Brazil, expecting to recognize the profile of this patients and to demonstrate the relation between the clinical frailty score and overall survived, besides to estimate the contribution of GVHD prophylaxis and relapse in overall survival.

METHODS: Multicentric, retrospective, descriptive, analytical and quantitative study, acquiring dates by means of exams and medical records from two hospitals in Brazil.

RESULTS: The study selected 252 patients, 147 males and 105 females, sort in gender, disease, HCTCI score, CFS and KPS. In three years, the overall survival in FIT score is 2,46 years, while in FRAILTY score is 1,82 years. About the prophylaxis, the combination of cyclosporine, mycophenolate mofetil, cyclophosphamide had worse results than others prophylaxis. As expected, in case of relapse, there is shorter survival.

CONCLUSION: The elderly population require a geriatric score in order to evaluate the profile of this patients once the allogeneic transplant must happen, then FIT patients has longer survival than FRAILTY patients.

FLOW CYTOMETRY MINIMAL RESIDUAL DISEASE ANALYSIS IMPACT IN HEMATOPOIETIC STEM CELL TRANSPLANT FOR ACUTE LYMPHOBLASTIC AND MYELOBLASTIC LEUKEMIAS – A PROSPECTIVE SINGLE CENTER ANALYSIS

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INTRODUCTION: Patients (pts) with high-risk leukemias have poor prognosis even with the use of allogeneic hematopoietic stem cell transplantation (allo-HSCT). Detectable Minimal Residual Disease (MRD) immediately before allo-HSCT is associated with poor survival outcomes of lymphoblastic (ALL) and myeloblastic (AML) acute leukemias. In the present study we aimed to evaluate the impact of 8-color flow cytometry MRD assessed before allo-HSCT for acute leukemias survival in a single center in Brazil.

METHODS: prospective analysis of 75 consecutive pts transplanted between 2019/Jul and 2022/May, with MRD evaluation in the month before HSCT. Statistical analyses were performed in SPSS Statistics v.20.0 software.

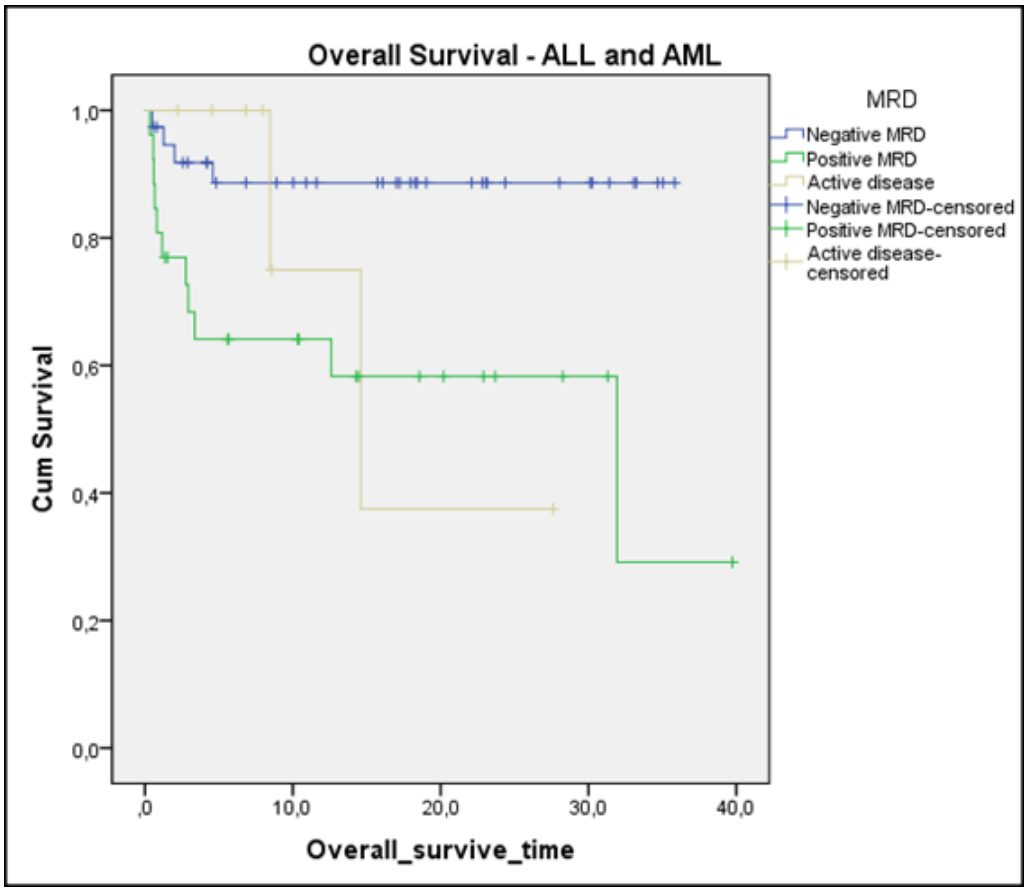
RESULTS: 34 ALL (42.6%), being 26 BCP-ALL and 8 high-risk T-ALL, and 41 AML (57.4%), median age 31.6 (4.1-62.5 years) for ALL and 42.9 (0.6-74.2 years) for AML; 45(60%) in first complete remission (CR1), 21 CR2 (28%), one CR3 and 7 active diseases. Regarding transplant-related variables: no differences in source of cells (BM 42; PB 32); median TNC 6.06±3.22x108/uL and CD34 5.96±3.47x106/uL; HLA matched 37(49.3%) MSD, 28(37.3%) MUD and 10(13.3%) Haplo-PTCy. All recipients received myeloablative conditioning regimens, but ALL received more TBI than AML (76.5%vs.12.2%). GVHD prophylaxis 86.7% MTX/CSA, 13.3% CFA/CSA/MMF. Cumulative incidence (CI) of neutrophil recovery and acute GVHD (II–IV) were 78.8% and 20.8% at d+100, respectively. Infection during conditioning in 23(56,1%) AML and 22(64,7%) ALL, with 16(21.3%) intensive care (5 AML and 11 ALL), p=0,048. Among 64 patients in morphologic remission, we found 38(59.4%) MRD negative and 26(40.6%) MRD positive before transplant. There was 7 AML MRD+ (41.4%), but 8 relapses occur, being 7MRD+ and one MRD- (false negative). Between 9 ALL MRD+ (25%), only one relapse occurs, but a higher incidence of early toxicity deaths occurs mainly in MRD positive patients. Sensibility and specificity of MRD test was 88.8% and 68.9% in this cohort. There were 20 deaths overall (26.6%), 5 in active disease; 2 ALL MRD negative and 13 (17.3%) in MRD+ (6ALL and 7AML), with significant difference in survival time (32 ±1.8 vs 22.1±3.7 months, p=0.003, 95% CI) between MRD positive and negative. Overall survival (OS) was 76.5%, 89.5% in MRD- versus 57.7% in MRD+ (p=0.031), and 82% in CR1 versus 57.1% in CR2 (p=0,064). Despite a higher incidence of early toxicity deaths in ALL (7 early sepsis, one relapse) than AML (3 early sepsis, one VOD, 4 late toxicities being two COVID-19; and three deaths in relapse), the EFS CI was not different between positive and negative MRD (2±0.77vs1.2±1.15 months, p=0,594, 95% CI).

CONCLUSION: In this cohort we observed higher relapse mortality in AML and NRM in ALL. However, in both scenarios, the pre-transplant MRD assessment allowed the identification of patients with a worse prognosis, and even positive MRD can benefit from transplantation as a form of cure.

Keywords: Measurable/minimal residual disease. Acute lymphoblastic leukemia. Acute myeloid leukemia. Allogeneic hematopoietic stem cell transplantation. Flow cytometry.

Financiamento: Programa Nacional de Apoio à Atenção Oncológica, PRONON, Ministério da Saúde, apoio Associação dos Amigos do Hospital de Clínicas.

FIGURE 1. OS negative MRD 32±1,8 months and positive MRD 22,1±3,7, p=0,003, 95% CI.



AUTOLOGOUS HSCT

LOMUSTINE IN COMBINATION WITH ETOPOSIDE AND CYCLOPHOSPHAMIDE IN CONDITIONING REGIMEN FOR LYMPHOMAS: A PHASE 1 STUDY

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The autologous hematopoietic SCT (AHSCT) is widely employed as consolidation therapy after recue chemotherapy in relapsed or refractory classic Hodgkin's lymphoma (HL) and non-Hodgkin lymphoma (NHL). However, there is no evidence regarding the best conditioning regimen to be used. In order to determine the maximum tolerated dose (MTD) of lomustine, on day -5, in association with etoposide 1 gr/m2 on day -5 and cyclophosphamide 2 gr/m2/day on day -4, -3 and -2; we develop a phase 1 study based on the traditional 3+3 design. Five lomustine cohorts were set: 200 mg/m2(L200), 300 mg/m2(L300), 400 mg/m2(L400), 500mg/m2(L500) and 600mg/m2(L600). No patient in L200 (N=3) and L300 (N=3) developed dose-limiting toxicity (DLT); one patient in the L400 cohort presented gastrointestinal grade 4 toxicity. Two of 3 patients in the L500 cohort presented grade 3 toxicity meeting criteria for DLT. There were no deaths. Fifteen patients were enrolled in this phase 1, 10 were HL and 5 NHL, 10 were in complete remission (CR) at the TIME of AHSCT. The lomustine MTD was 400 mg/m2 in association with total fixed-dose of 1 gr/m2 of etoposide and 6 gr/m2 of cyclophosphamide. LEC (lomustine/etoposide/cyclophosphamide) is an acceptable-toxicity regimen that can be used as alternative to traditional regimens, mainly in the context of the shortage of drugs, which frequently occurs in Brazil.

IMPACT OF FLUOROQUINOLONE PROPHYLAXIS IN FEBRILE NEUTROPENIA INCIDENCE IN RECIPIENTS OF AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION: Febrile Neutropenia (FN) is a frequent complication after hematopoietic stem cell transplantation (HSCT). Prophylactic fluoroquinolone can reduce FN rates, but does not reduce mortality. Autologous hematopoietic stem cell transplantation (auto-HSCT) patients are not uniformly considered as high risk for FN, because profound neutropenia lasts less than 7 days. In this population the potential benefits of fluoroquinolones (FQ), like the reduction of FN, may be surpassed by the risks, as emergence of resistance, gastrointestinal microbiota disbalance and muscle-skeletal toxicities. Because of that, universal antibiotic prophylaxis is controversial and demands further investigation.

OBJECTIVES: Evaluate FN and mortality in 2 situations: with universal prophylaxis and without universal prophylaxis with fluoroquinolones, in patients that underwent auto-HSCT.

METHODS: A retrospective descriptive study of >18 years old patients who received auto-HSCT in our institution in 2 situations: with universal prophylaxis with FQ between 2016 and 2017 and without universal prophylaxis between 2018 and 2020. We analyzed FN incidence, mortality in 30 and in 100 days, bacterial identification in cultures and clinical characteristics.

RESULTS: A total of 212 patients were included, 104 in the group without prophylaxis (NPx) and 108 in the group with prophylaxis (Px) with fluoroquinolones. Febrile neutropenia episodes significantly developed more in the NPx group than in the Px (NPx 92,3% versus Px 78,7%; p=0,009). However, no difference was identified in the occurrence of bacterial detection in cultures (NPx 29,2% versus Px 19,8%; p=0,195), mortality in 30 days (NPx 1,9% versus 0,9%; p=0,616) and mortality in 100 days (NPx 1,9% versus Px 1,9%; p=1,0). In the field of resistance emergence, there were fewer multissensitive microorganisms isolated in Px group (NPx 51,9% versus Px 18,2%; p=0,03) and higher identification of ESBL bacteria (NPx 3,7% versus Px 27,3%; p=0,03). There were no differences in length of hospital stay or in days of therapeutical antibiotic therapy.

CONCLUSION: Fluroquinolone prophylaxis in recipients of auto-TCTH reduces incidence of febrile neutropenia, however it does not reduce mortality. In the other hand, FQ prophylaxis correlates with higher identification of bacteria with some degree of resistance, as ESBL. Due to these data, in our institution we choose to do not use prophylactic fluoroquinolones. We consider that timely therapeutic antibiotic is equally effective, as it has similar mortality rates and median days of hospital stay, without the potential side effects of prophylaxis, like drug resistance and disbalance of gastrointestinal microbiota.

Keywords: HSCT autologous, fluoroquinolones, bacterial prophylaxis

HEMATOPOIETIC STEM CELL TRANSPLANTATION (AUTOLOGOUS HSCT) IN THE TREATMENT OF HIGH-RISK NEUROBLASTOMA. DO OUR CHILDREN NEED MORE?

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INTRODUCTION: Neuroblastoma is the most common extracranial solid tumor in childhood. Children with high-risk disease require multimodal treatment, including chemotherapy, radiotherapy, surgery, bone marrow transplantation, retinoic acid to treat residual disease, and immunotherapy with anti-GD2 antibodies. HSCT has been used since 1980, but immunotherapy is not yet available in our country. The European SIOPEN group reported 5-year event-free survival of 42% in 446 children with neuroblastoma without immunotherapy, compared with 57% in the 378 who received anti-GD2 antibody (p<0,001). Overall survival at 5 years was 50% without immunotherapy and 64% with immunotherapy (p<0,001). Similar results were obtained by the North American Childrens Oncology Group (COG): 2-year event-free survival of 66% with GD2 and 46% without it (p=0.01).

OBJECTIVE: To describe the survival of patients with high-risk neuroblastoma undergoing HSCT in a single Brazilian institution.

SAMPLE AND METHOD: Retrospective analysis of 128 patients who underwent autologous transplantation for high-risk neuroblastoma between October 1999 and March 2022. Most patients had stage 4 disease (88%). The source of the cells was peripheral blood stem cells in all but 2 cases, whose source was bone marrow.

RESULT: The median age was 4.9 years (1-21 years) and the median follow-up of living patients was 806 days (5-8132 days). The conditioning protocols used were Carboplatin, Etoposide and Melphalan (CEM, N=24), Busulfan and Melphalan (BuMel, N=92), Carboplatin, Etoposide and Cyclophosphamide (CECY, N=4) and, more recently, we chose to offer two autologous transplants in Tandem, following the good results obtained by the Childrens Oncology Group: 1st with Thiotepa and Cyclophosphamide (TT-Cy) and the 2nd with CEM (Tandem, N=8). Overall survival is 65%, but with 10/83 children remain alive after relapse. According to the conditioning protocol, overall survival was 29% for CEM (median follow-up of 2.8 years), 66% for BuMel (median 2.2 years) and 87,5% after Tandem (median 3.4 months of follow-up). Transplant-related mortality was 20%, related to infections, cardiotoxicity, microangiopathy, and hepatic sinusoidal obstruction syndrome. No child has had access to immunotherapy to date.

CONCLUSION: Autologous HSCT can be successfully performed in our country, however recurrence remains high. The use of immunotherapy with anti-GD2 antibodies has the potential to improve the chances of cure of these children.

Keywords: Neuroblastoma. Autologous hematopoietic stem cell transplantation. Immunotherapy.

OUTCOMES OF REFRACTORY AND RELAPSED HODGKIN LYMPHOMA PATIENTS AFTER LEAM AND LACE CONDITIONING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANT: A SINGLE INSTITUTION EXPERIENCE

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INTRODUCTION: High dose chemotherapy and autologous hematopoietic stem cell transplant (HSCT) is the standard treatment for chemosensitive refractory and relapsed (R/R) classical Hodgkin lymphoma (HL), but high-risk relapse patients still have poor outcomes. Association of anti-CD30 antibody-drug conjugates and anti-PD1 targeted T-cell checkpoint inhibitors as well as more intensive conditioning regimens have been exploited to mitigate these results.

OBJECTIVES: To assess progression-free survival (PFS), overall survival (OS) and prognostic factors related to PFS in patients with R/R HL undergoing LEAM and LACE conditioning autologous HSCT.

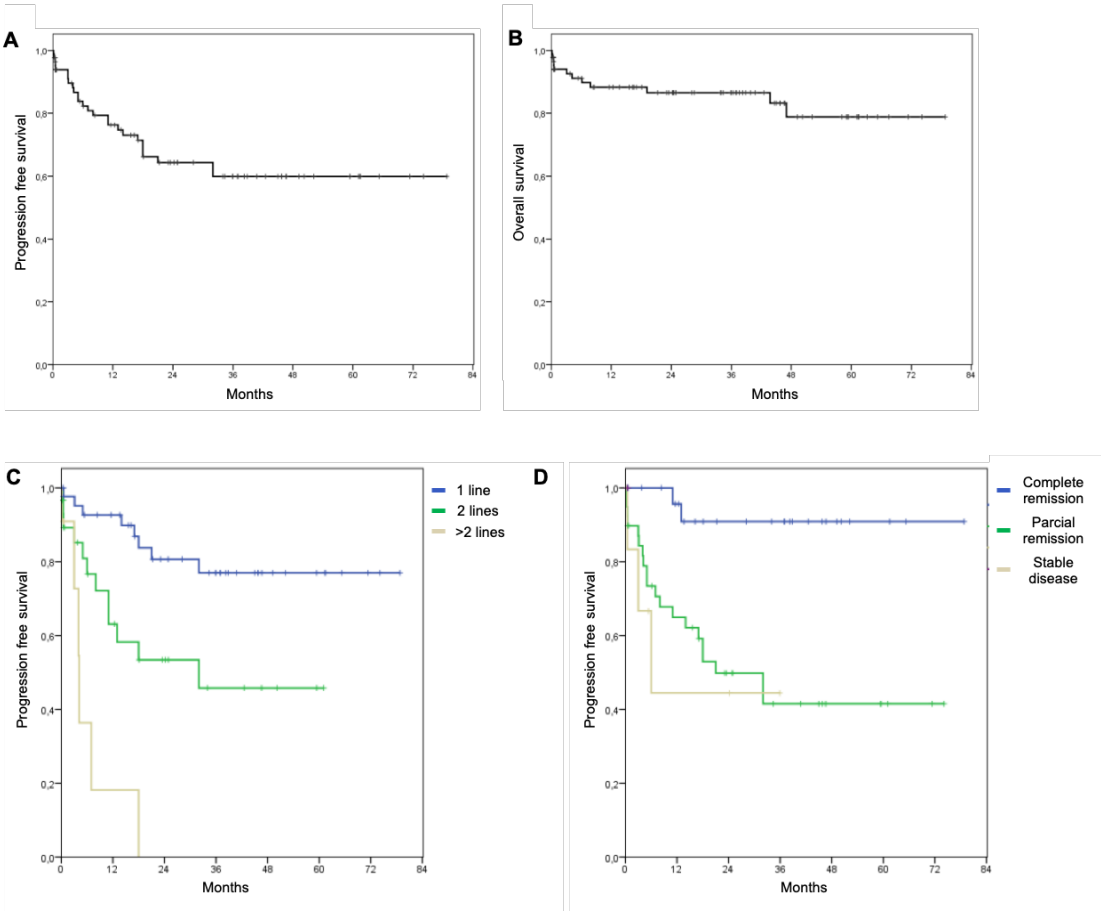
METHODS: Retrospective cohort analysis of 88 adult patients with R/R HL, who underwent LEAM or LACE conditioning autologous HSCT between 2015 and 2020, in a public south brazilian institution. High risk criteria for disease relapse after autologous HSCT were characterized as: relapse within 1 year or refractoriness to frontline therapy; extranodal extension at relapse; B symptoms at relapse; requiring more than 2 lines of salvage therapy or failure to achieve a complete remission before HSCT. The PFS and OS were estimated using the Kaplan-Meier function. Log-rank tests or Cox bivariate regression analysis and multivariate Cox multiple regression analysis identified prognostic factors associated with EFS.

RESULTS: The median age was 29 years (IQR 24.3 – 39). Eighty-four (95,3%) patients had classical HL and 4 (4,7%), nodular lymphocyte predominant HL. Most patients had a complete (41.7%) or partial (47.6%) response before HSCT, and 80 (92%) had high-risk criteria for disease relapse after HSCT. Forty-eight (54,5%) patients were treated with LACE, 39 (44,3%) with LEAM, and 1 (1,1%) with GemBuMel. Nineteen (29.7%) and 5 (7.8%) patients received brentuximab vedotin and radiotherapy, as post-HSCT consolidation therapy, respectively. After median follow-up of 24.7 months (IQR 3.9 – 45.8), the estimated 3-year PFS was 59.9% and 4-year OS was 78.9%. Twelve (13.6%) patients died, the main cause being infectious disease (6), followed by disease progression (4). Treatment-related mortality in the first 100 days post-HSCT was 4.5%. In multivariate analysis, the independent predictors for lower PFS were 2 lines or 3 or more lines of salvage chemotherapy (HR 3,16, p=0,019, and HR 9.4, p<0.001, respectively) and partial response or stable disease pre-HSCT (HR 6.7, p=0.012, and HR 10.2, p=0.013, respectively). For patients in complete response before HSCT, the presence of a bulky mass at recurrence was related to lower PFS (HR 3.8, p=0.037).

CONCLUSION: Our retrospective analysis reflects literature outcomes in a high risk relapse R/R HL patients cohort undergoing LACE and LEAM conditioning autologous HSCT. Bulky disease at relapse, number of lines of salvage therapy and disease response before transplant predicted worse outcomes. New therapy strategies must be sought to ameliorate these results.

Keywords: Hodgkin disease. Autologous Transplant. Hematopoietic Stem Cell Transplant. Treatment Outcome. Survival.

FIGURE 1. **Kaplan Meier survival estimate for (A) Progression free survival, (B) Overall survival, (C) Progression free survival according to number of lines of salvage therapy (p<0.001) and (D) Progression free survival according to status of remission disease before HSCT (p=0,013).**



FRESH VERSUS CRYOPRESERVED PERIPHERAL BLOOD STEM CELLS FOR AUTOLOGOUS TRANSPLANTATION IN MULTIPLE MYELOMA

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INTRODUCTION: Autologous stem cell transplantation is the standard procedure for multiple myeloma and the grafts are usually cryopreserved. Previous studies reported advantages in the use of fresh peripheral blood stem cells (PBSC) autotransplantation compared to cryopreservation of the grafts.

OBJECTIVE: To compare the transplant-related outcomes of two graft preservation methods: fresh storage (4°C/72h) and cryopreservation (–80°C).

INCLUSION AND EXCLUSION CRITERIA: All patients who received fresh autologous PBSC for multiple myeloma in the studied period were included in the fresh group. Patients receiving cryo transplantation at the same period were proportionately included in the cryopreserved group. The exclusion criteria were patients who received fresh and cryopreserved PBSC; infusion of fresh PBSC with TNC > 300 × 103/µL during cool storage.

METHODS: We performed an analysis of 45 patients with multiple myeloma under autotransplantation (17 fresh and 28 cryopreserved) from 2017 to 2021. Fresh PBSC were maintained in the refrigerator (4 ± 2°C) for three days in a concentration up to 300×103 TNC/µL. Cryopreserved PBSC were concentrated by plasma reduction after centrifugation (950g/10 min/4°C) and an equal volume of cryoprotection solution was added for a final concentration of 300×103 TNC/µL, 5% DMSO, 6% hydroxyethyl starch, and 3% human albumin. The patients received melphalan 200 mg/m2 or 140 mg/m2 for two consecutive days. PBSC were infused 24 h after the last dose A statistical analysis was performed with the aid of the PASW 18.0 software. P < 0.05 was considered significant.

RESULT: Both groups were similar regarding patients and transplant-related characteristics, except for the time from diagnosis to transplantation. The fresh storage time was 72 hours for all patients. The cryopreserved autografts were stored in –80°C for 86.5 days (median, range 4–483 days). Neutrophil engraftment was significantly faster with fresh PBSCs (10 versus 11.5 days, P=0.045). Adverse effects were more common in cryopreserved PBSC transplantation (75% versus 35.3% patients, P=0.013; incidence ratio [IR] = 1.46, range 1.10–1.93). Post transplantation hospital stay was 20 and 22 days for fresh and cryopreserved PBSCs, respectively (P=0.091). There was no difference in platelet engraftment time (10.5 days for both; P=0.133), number of antibiotics used after transplantation (3 for fresh and 2.5 for cryopreserved; P=0.828), days of antibiotic use after transplantation (12.2 days for fresh and 13.3 days for cryopreserved; P=0.579) and overall survival (P=0.736).

CONCLUSION: The infusion of fresh PBSC refrigerated for up to three days is effective and safe for autologous transplantation in patients with multiple myeloma, which is a useful alternative to cryopreserved PBSC.

Keywords: Hematopoietic progenitor cells. Peripheral blood stem cells. Bone marrow transplantation. Multiple myeloma. Fresh PBSC. Autologous transplantation.

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HSCT PEDIATRIC

INCIDENCE OF GENITAL GRAFT-VS-HOST DISEASE IN FEMALES 1-18 YEARS OF AGE UNDERGOING HEMATOPOEITIC STEM CELL TRANSPLANTATION FROM DECEMBER 1998 TO DECEMBER 2021.

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INTRODUCTION: Genital Graft-versus-Host Disease (GVHD) in women undergoing allogeneic Hematopoietic Stem Cell Transplantation (HSCT) remains under-diagnosed despite consequences that can severely affect post-transplantation sexuality. In pediatric patients, the issue may be even greater since genital symptoms are often unrecognized and underreported, the gynecological examination is not routinely performed, and there may exist cultural barriers to ask the patients about genital and sexual symptoms and concerns. In addition, pre- or post-HSCT gynecological assessment is not part of the children's routine follow-up.

OBJECTIVE: To evaluate the incidence and degree of GVHD in female children undergoing allogeneic HSCT.

CASUISTICS: 263 girls between 1 and 18 years of age (median 10.5 years) undergoing allogeneic stem cell transplantation.

METHODOLOGY: Data was retrospectively collected from the medical records. All girls were examined by a single gynecologist.

RESULTS: Of the 263 patients, 123 underwent related HSCT, 98 unrelated and 42 haploidentical; 53 (20%) of them were diagnosed with chronic GVHD. For this analysis, we considered 124 (47%) patients who are alive, 36 (29%) of them with chronic GVHD. Of these 36 girls, all had oral involvement, isolated in 12 (33%), and simultaneously involving other sites in 66%: skin (n=6 - 16%), eyes (n=8 - 22%) and other organs (liver, lung or gastrointestinal tract) in 10 (28%). Of the 19 girls referred to gynecological evaluation after HSCT, 12 (63%) of them were diagnosed with genital GVHD. Five patients presented with isolated vaginal involvement: one with hematocolpos due to complete obstruction of the vagina and four had vaginal sclerosis limiting sexual activity. Seven girls had vulvar involvement that prevented vaginal examination, but two of them with early diagnosis and prompt treatment, had complete resolution without sequelae. Off the remaining five, three developed inter-labial and clitoral adhesions, and two, total vulvar adhesions, obstructing the urethral meatus.

CONCLUSIONS: Almost one third of our female children and teenagers who are long-term survivors have chronic GVHD, all of them with oral involvement. Genital GVHD was observed on 12/19 girls (63%) involving the vagina and/or vulva and early diagnosis and prompt treatment may prevent long term sequelae. These results suggest the importance of routine gynecological evaluation in these patients, which has currently been incorporated into our institutional standards.

Keywords: Chronic GVHD. HSCT in childhood. Genital GVHD.

MONITORING OF RECENT THYMIC EMIGRATED T-LYMPHOCYTES (CD31+45RA+) AFTER HEMATOPOETIC STEM CELL TRANSPLANTATION

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Hematopoietic stem cell transplantation; Recent emigrated T lymphocytes from thymus; Immune recovery.

INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is potentially a curative treatment for several hematologic diseases. Post-transplant functional immune recovery may be associated with control of relapse, viral reactivations, graft-versus-host disease (GVHD) and improved survival.

OBJECTIVE: To evaluate total lymphocytes, recent thymic emigrant (RTE), and B and NK lymphocytes at D+100 in three types of grafts.

MATERIALS AND METHODS: 132 children (80M/52F), with a median age of years (0.8-17.8), 69,7% under 10 years, from two Transplant Centers from 2013 to 2020 were included. The diseases were: malignant diseases (n=49), medullary failures (n=50), primary immunodeficiencies (n=28) and inborn errors of metabolism (n=5). Type of graft, 47 patients received haploidentical transplantation (HAPLO), 17 related (MRD) and 68 unrelated (MUD). Conditioning was myeloablative in 53% and nonmyeloablative in 47%. Bone marrow 90.9% and peripheral stem sell 9.1%. Corticosteroids and methotrexate were used for GVHD prophylaxis in 65 (49.2%), cyclosporine, mycophenolate with post cyclophosphamide in 55 patients (41.6%) and corticosteroids and other drugs in 9 (9.2%). 12 patients died; one patient relapsed, one had primary failure, the others died of other causes, median overall survival was 173 days (122 - 488 days). To analyze the lymphocyte subpopulations by multiparametric flow cytometry (MFC) the markers CD3, CD4, CD8 (T lymphocytes) CD16/CD56 (NK lymphocytes), CD19 (B lymphocytes), CD31+/CD45RA+ (RTE T lymphocytes) were used, performed on D+100 posttransplant. The absolute counts of lymphocyte and T RTE lymphocytes were compared between HAPLO, MRD and MUD grafts using the non-parametricKruskal-Wallis test and Dunn's test for post-hoc multiple comparisons. Statistical analyses were performed with IBM SPSS Statistics v.20.0 software.

RESULTS: Lymphocyte recovery at D+100 in the MRD vs MUD vs HAPLO groups was as follows, CD3+CD4+ (115vs129vs141/uL p=0.994); CD3+CD8+ (247vs353vs363/uL p=0.486); CD19+ lymphocytes (64vs64vs45/uL p=0.82), and CD16+/CD56+ NK lymphocytes (132vs122vs165/uL, p=0.289), between HAPLO vs MRD vs MUD, respectively. RTE CD4+ T lymphocytes were lower in HAPLO transplantation (2.6/uL), than in MRD (7.9/uL), MUD (4.4/uL). In the comparison between MRD vs HAPLO types of BMT there was a difference for RTE T lymphocytes p=0.031 and in the analysis of GVHD prophylaxis p= <0.001.

CONCLUSION: Retrospective analysis showed no significant difference in global immunological recovery between the three types of transplantation. The recovery of RTE CD4+ T lymphocytes in the group that received HAPLO BMT was slightly lower than the MRD group, but the presence of RTE lymphocytes may indicate thymic effectiveness. Prospective studies with larger numbers of patients are needed to confirm this finding.

Keywords: Hematopoietic stem cell transplantation. Immune recovery. Recent emigrated T lymphocytes from thymus. T lymphocytes.

TABLE 1.

Variável	(coluna da planilha)	TMO			p*
		AP (n=17)	**NAP (n=68)**	**Haplo (n47)**	
		Mediana (min-max)	Mediana (min-max)	Mediana (min-max)	
WBC_d100	LEUC.	3100 (2050 - 7530)	4100 (700 - 18900)	4600 (1690 - 14680)	0,020
Lymph_d100	Linf abs	727 (129 – 1835	744 (113 - 5177)	925 (57 - 8001)	0,602
LT_d100	CD3 abs	522 (76,4 - 1301)	542 (45,1 - 4651)	594 (3,4 - 6864)	0,753
CD4_d100	CD3+CD4+ abs	115,8 (7,9 - 607)	129 (19, - 551)	141 (2,3 - 1560)	0,994
CD8_d100	CD3+CD8++ abs	247 (59,4 - 1338)	353 (7,8 - 4234)	363 (0,6 - 5152)	0,486
LB_d100	CD19+abs	64,7 (8,3 - 264)	63,9 (0 - 351)	45,2 (0 - 526)	0,820
LNK_d100	CD16+56+abs	132,8 (23,3 - 466)	122 (19,4 - 622)	165 (14,3 - 953)	0,289
RET_CD4_d100	CD4+CD31+CD45RA+(RET) abs	7,9 (0 - 69,6)	4,4 (0 - 115)	2,6 (0 - 32,2)	0,031
RET_CD8_d100	CD8+CD31+CD45RA+(RET) abs	93,1 (1,2 - 294)	63,9 (0 - 3038)	58,9 (0 - 2260)	0,819

*Teste não-paramétrico de Kruskal-Wallis, p<0,05

OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CHILDREN WITH SEVERE APLASTIC ANEMIA: EXPERIENCE OF A SINGLE CENTER.

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INTRODUCTION: Severe aplastic anemia (SAA) is a potentially fatal disorder characterized by bone marrow failure. It may be due to congenital or acquired causes. For acquired SAA in children, allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the recommended treatment when a matched sibling donor (MSD) is available. For patients without a MSD available, immunosuppressive therapy (IST) with ATG and cyclosporine (with the recent addition of eltrombopag) is still the first choice. Allo-HSCT with alternative donors is recommended for patients failing primary IST, and may be alternative for some very severe particular cases.

OBJECTIVE: To describe the outcomes of pediatric patients diagnosed with SAA treated with allo-HSCT in our institution.

METHODS: Retrospective analysis of patients' charts. Patients: From may 2011 to march 2022, 23 patients with SAA were referred for HSCT in our institution. One patient had disease progression with acute myeloid leukemia before transplantation and was excluded from this analysis. Median age was 9.5 y (1-15), 11 were male and median time from diagnosis to HSCT was 167 days (59-1627). Eleven patients had infections (eight with very severe infections) and all but one patient received more than 20 transfusions before transplantation. Five patients had a MSD and were transplanted at first intention. Six patients were transplanted with matched unrelated donors (MUD) and 11 with haploidentical donors (HAPLO). One patient with haplo donor and one with MUD were transplanted without having received previous IST, the other fifteen patients failed IST (containing ATG) before transplantation. Cell source was bone marrow in all cases. All patients, except one, received reduced intensity conditioning regimens. Detailed patients' and transplants' characteristics are showed in table 1.

RESULTS: One patient did not present neutrophil recovery and died early at day + 11 of severe infection and VOD. All other 21 patients engrafted in a median of 18 days (12-28). Three patients had acute GVHD (grades II -IV). Three patients had mild or moderate chronic GVHD. One patient had secondary graft failure, all the others engrafted with chimerism ranging from 90 to 100% at the last analysis. With a median follow up of 30 months, seventeen patients are alive. One patient has active complications (TMA). Five patients died from treatment related causes, 4 with infection (one had poor graft function) and one had a secondary graft failure and died from severe bleeding. All patients that died had severe infections before transplant and three of them died early from septic shock. Two-year overall survival was 75%; 75% with MSD, 83% with MUD and 72% with haploidentical donors.

CONCLUSION: With 75% OS, SAA may be cured by HSCT. In our analysis all patients that died had severe infections before transplant. Early referral, infectious prophylaxis and considering alternative donor transplantation earlier could improve these results.

Keywords: Severe aplastic anemia. Pediatric transplantation. Bone marrow failure.

TABLE 1 - Patients' and transplants' characteristics

		MSD	MUD	HAPLO
Total (n)		5	6	11
Median age (years)		11 (1-15)	10,5 (6-14)	8 (3-15)
Sex				
	Male	2	3	6
	Female	3	3	5
Time from diagnosis to HSCT (median - days)		64	199	213
Previous IST		-	5	10
Infections		2	2	7
Transfusions, n >20		4	6	11
Ferritin level		750 (605-2555)	1874 (786-4435)	1799 (1047-3656)
Source of stem cells, bone marrow		5	6	11
Conditioning regimen				
	Cy+ATG	5	-	-
	Flu + Cy + TBI2Gy + ATG	-	4	-
	Flu + Cy + ATG	-	1	-
	BU + Cy+ATG	-	1	-
	Flu + Cy + TBI2Gy	-	-	10
	Flu + Cy + TBI2Gy + ATG	-	-	1
GVHD prophylaxis				
	CsA + MTX	5	5	-
	CsA + MMF	-	1	-
	Post transplant Cy + CsA + MMF	-	-	11
Median time to engraftment (days)		21	20	17
Graft failure		1	1	0
Acute GVHD		-	1	2
	II	-	1	1
	III - IV	-	-	1
Chronic GVHD		-	-	3
Alive				
	yes	4	5	8
	no	1	1	3
Cause of death (n)				
	Infection	-	1	3
	Graft failure	1	-	-

ABSOLUTE LYMPHOCYTE COUNT PRECONDITIONING AND CLINICAL OUTCOMES IN PEDIATRIC PATIENTS SUBMITTED TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN USE OF ANTI-THYMOCYTE IMMUNOGLOBULIN IN A UNIVERSITY HOSPITAL

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INTRODUCTION: Rabbit anti-thymocyte immunoglobulin (ATG/thymoglobulin) is used in patients undergoing hematopoietic stem cell transplantation (HSCT) for graft versus host disease prophylaxis. The dose of thymoglobulin is based on body weight (mg/ kg), with no consensus on the most effective dose to reduce GVHD and safety. New studies have suggested that the dose of ATG should be established by considering the preconditioning absolute lymphocyte count (ALC). The ATG dose may be excessive if ALC <500/µL due to the drug's pharmacokinetic and pharmacodynamic properties.

OBJECTIVE: To evaluate the association between ALC preconditioning and clinical outcomes of transplantation.

METHODS: Retrospective cohort including pediatric patients undergoing allogeneic HSCT using ATG from 2015 through 2021.

RESULTS: Fifty patients divided into two groups were included: CAL ≥ 500/µL, 40 patients, and CAL < 500/µL, ten patients. The median age is 8.5 (P25 3,3 and P75 13) and 1.5 (P25 0,8 and P75 11,8) (p 0.91), respectively, with 60% being male in both groups. The most frequent baseline diagnoses were, respectively, acute lymphoblastic leukemia (40% and 20%); myelodysplastic syndrome (10% and 10%); primary immunodeficiency (0% and 30%); acute myeloid leukemia (0% and 10%) and aplastic anemia (2.5% and 10%). Other diagnoses, predominantly genetic diseases (20%), accounted for 47.5%. The HLA locus mismatch were 12/12 (n=1, 2%), 11/12 (n=4, 8%), 10/12 (n=2, 4%), 10/10 (n=23, 46%), 9/10 (n=6, 12%), 8/10 (n=1, 2%), and 13 (26%) patients not rercorded. The cell donor was predominantly unrelated (92.5%, ALC ≥ 500/µL and 80%, ALC < 500/µL; p 0.12). The mean dose of ATG in the groups was 9.7 mg/kg and 9.3 mg/kg (p 0.68), respectively. The source of bone marrow cells (87.5% ALC≥ 500/µL and 80% ALC< 500/µL; p 0.20). The frequency of myeloablative conditioning was 77.5% and 40% respectively; p 0.07) and RIC (10% ALC≥ 500/µL and 30% ALC< 500/µL, p 0.06) . The incidence of acute GVHD between the groups was 45% and 40% (p 0.77), in which 27.5% and 30% grade II-IV and 10% and 10% grade III-IV, respectively (p 0.94). The incidence of chronic GVHD was 22.5% and 10%, respectively (p 0.37). The median of new hospitalizations for infection in the groups was 1 (P25 0 and P75 2) and 0 (P25 0 and P75 2) (p 0.6), with a 25% incidence of sepsis in the ALC group ≥ 500/ µL and 40% in ALC < 500/µL (p 0.34). Sub-analyses using higher cut-off points (ALC 750 and 1000/µL) resulted in similar outcomes.

CONCLUSION: In the studied pediatric patients, who received thymoglobulin for lymphocyte depletion, no statistically significant association was detected between ALC and the clinical outcomes of HSCT.

Keywords: Allogeneic HSCT. GVHD. ATG. Absolute lymphocyte count.

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HCT) TO TREAT PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): HAPLOIDENTICAL DONORS WITH FLU-TBI COMPARED WITH MATCHED RELATED OR UNRELATED DONORS WITH TBI-VP16

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INTRODUCTION: Conditioning regimens in Pediatric ALL are always myeloablative and, regardless of the stem cell source and donor, total body irradiation (TBI) is widely used in children older than 4 years of age due to better overall and disease-free survival demonstrated in randomized controlled trials. The use of TBI and Etoposide (VP16) is standard of care in many Pediatric centers due to its superiority over TBI- Cyclophosphamide. The experience with haploidentical HCT for Pediatric ALL is much smaller and most Brazilian centers have adopted the conditioning regimen developed by the Atlanta adult team with TBI-Fludarabine [Solomon SR, et al. 2012*] However, these two strategies have not been compared.

OBJECTIVE: Our objective is to compare the outcomes of allogeneic transplants to treat pediatric ALL with TBI-Fludarabine-Haploidentical (Haplo) grafts versus TBI-Etoposide and matched related (MSD) and unrelated (MUD) donors.

CASUISTIC AND METHOD: This is a retrospective analysis of 90 patients with ALL undergoing allogeneic HCT between 2012 and 2022. All had TBI 1,200cGy divided in 6 doses. MSD and MUD also received Etoposide 60mg/kg single dose. Patients undergoing haplo had TBI-Fludarabine 30mg/m2/day x 3 days. GVHD prophylaxis for MSD was cyclosporine (CsA), ATG-CsA-Mtx in MUD and PT-Cy followed by CsA-MMF in haplos.

RESULT: The 43 children with Haplo-Flu/TBI (Table 1) had a median age of 9.4 years, 55% boys, most grafts were PBSC (74%); 14 of the 15 children who relapsed died due to the disease and there were 2 deaths in remission (1 venoclusive disease and 1 sepsis). The 47 children receiving TBI-VP had a median age of 9.8 years, 55% boys. Most received a bone marrow graft from MUD donors (40/47). Seven out of 47 (14%) have relapsed and died due to the disease, 9 patients (19%) died due to transplant-related complications (3 due to thrombotic microangiopathy, 2 due to sepsis and 4 related to GVHD). The median time to recurrence was 131 days. Although both strategies lead to similar overall and disease-free survival calculated by the Kaplan Meier method, they have different toxicities and chance of relapse.

CONCLUSION: It is feasible and safe to perform both Haplo and MUD for children who lack a related donor, but relapse and transplant-related mortality are real challenges when treating these children. Tight surveillance, maintenance and preemptive strategies may further improve the prognosis of these patients.

	Haplo Flu/TBI	MSD/MUD VP/TBI
N patients	43	47
Age (years, median)	9.4 (1.3 - 21)	9.8 (1.0 – 17.8)
Gender		
Male	24 (55%)	26 (55%)
Female	19 (45%)	21 (45%)
Donor		
Haploidentical	43 (100%)	0
Matched sibling donor	0	8 (17%)
Unrelated donor	0	40 (83%)
Graft		
Peripheral blood	32 (74%)	1 (2%)
Bone marrow	11 (26%)	46 (98%)
Acute lymphoblastic leukemia		
B	32 (74%)	39 (82%)
T	11 (26%)	8 (18%)
Relapsed post-transplant	15 (35%)	7 (14%)
Deaths		
In remission	2 (4%)	9 (19%)
Due to disease activity	14 (32%)	7 (15%)
Median follow up (days)	538	1007
Median time to relapse (days)	238	131

*[Solomon SR, et al. Haploidentical transplantation using T cell replete peripheral blood stem cells and myeloablative conditioning in patients with high-risk hematologic malignancies who lack conventional donors is well tolerated and produces excellent relapse-free survival: results of a prospective phase II trial. Biol Blood Marrow Transplant. 2012;18(12):1859-66.]

INFECTIOUS COMPLICATIONS

ASSESSMENT OF LETHALITY OF COVID-19 POST-HEMATOPOIETIC CELL TRANSPLANTATION IN A TRANSPLANT CENTER DURING THE PANDEMIC

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INTRODUCTION: Since December 2019, the world has been experiencing a pandemic caused by a highly contagious microorganism with a high lethality rate – SARS CoV-2, an RNA virus of the betacoronavirus genus, with a high capacity for mutation and recombination. As of June 2022, more than 500 million cases and more than 6 million deaths due to COVID-19 have been reported worldwide. In the general population, symptomatic cases have a wide presentation, ranging from mild symptoms to critical conditions, with the development of severe acute respiratory syndrome. The development of vaccines and the widespread mass vaccination have reduced the severity and lethality of COVID-19. In hematopoietic cell transplant (HCT) recipients, the clinical presentation is generally similar, but with higher mortality. Recent studies showed a lower antibody response to COVID-19 vaccines in transplant recipients compared to the general population. However, no study has evaluated the evolution of COVID-19 lethality in these patients throughout the pandemic.

OBJECTIVE: To assess the lethality of COVID-19 in patients undergoing HCT at a transplant center throughout the pandemic.

METHODS: Patients with proven COVID-19 were included. The diagnosis of COVID-19/SARS CoV-2 infection was made locally by RT-PCR on nasal wash samples.

RESULTS: We analysed 174 cases of COVID-19 in HCT recipients (68 auto, 106 allo) transplanted from April 2005 to May 2022. 112 cases (64.3%) occurred from Apr20 to May21 and 62 (35.6%) from Jun21 to May22. Of the 68 autoHCT, 27 died during the study period. COVID-19 was the cause of death in 16 patients (23.5%). Of the 106 alloHCT recipients, 15 died during the study period. COVID-19 was the main cause of death in 5 patients (4.7%), although all had other associated causes, such as relapse, GVHD or other infections (Table 1). The overall lethality rate of COVID-19 was 12.1%. Of the 21 deaths associated with COVID-19, 16 (76.2%) occurred in the period from 2020 to May 2021 and five (23.8%) occurred from June 2021 to May 2022 (Figure 1).

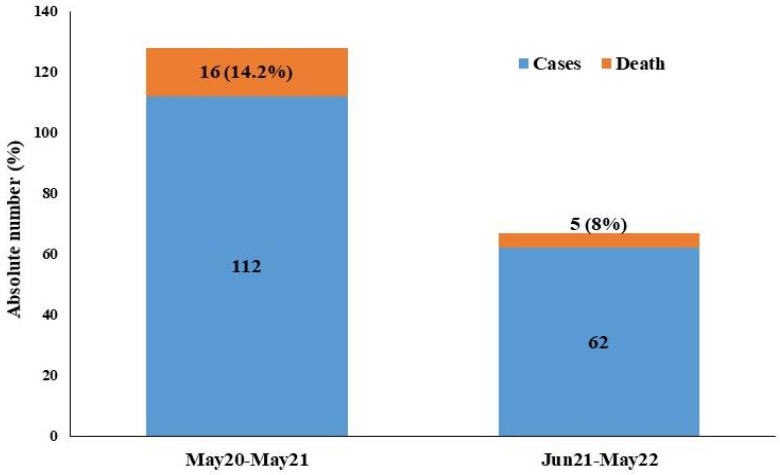
CONCLUSION: In the present series, COVID-19 lethality was higher in auto than in alloHCT recipients (23.5% vs 4.7%, p=0.0005). Older age, associated comorbidities and indolent underlying disease probably contributed to this outcome. In alloHCT patients, other factors such as relapse, GVHD or other concomitant infections may have contributed to the death. A decrease in the lethality rates of COVID-19 from 14.2% to 8% was observed after June 2021, period in which most HCT recipients have already received the second dose of vaccine. Mass vaccination probably contributed to the reduction of mortality in this population.

TABLE 1. **COVID-19 lethality according to type of HCT.**

Death by COVID-19	Autologous (%)	Allogeneic (%)	TOTAL
Yes	16 (23,5)	5 (4,7)	21 (12,1)
No	52 (76,5)	101 (95,3)	153 (87,9)
Total	68 (100)	106 (100)	174 (100)

p=0.0005

FIGURE 1. **Deaths due to COVID-19 according to the period of diagnosis**



CYTOMEGALOVIRUS (CMV) REACTIVATION OCCURS IN 93% OF BRAZILIAN CHILDREN AND ADOLESCENTS AFTER HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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INTRODUCTION: CMV reactivation occurs in 60-70% of adults undergoing HSCT, but the incidence of CMV disease has decreased mainly due to monitoring viral reactivation after HSCT and prompt preemptive treatment. Ganciclovir is the only drug available in our country for CMV, its use leads to severe pancytopenia, with other infectious complications, furthermore is not completely effective. Thus, CMV prophylaxis strategies with Letermovir have been discussed. As the cost-effectiveness of any prophylaxis depends on the incidence of the complication studied, it became essential to know the incidence of CMV reactivation in the Brazilian pediatric population.

OBJECTIVE: To describe the incidence of CMV reactivation in children undergoing allogeneic HSCT.

MATERIAL AND METHODS: Single-center retrospective cohort study from 03/01/2018 to 10/01/2021. Patients aged between 0 and 18 years, undergoing allogeneic HSCT, had weekly quantitative CMV PCR collected between neutrophilic grafting and D+100.

RESULTS: 151 patients were included, median age 9 years, 51% male, 87% with hematological malignancies. Serology (IgG) for CMV: only 13 HSCT (8%) had positive IgG donor and negative IgG recipient; in 79% (120) donor and recipient were IgG positive; 7% (11) had negative IgG recipient and positive donor; and 4% (7) negative recipient and donor. The highest chance of CMV reactivation occurred with IgG positive donor and recipient, 63% (75/120). Donor: 28 transplants were from HLA-identical donors (18%); 15 (10%) HLA-identical unrelated donors (NAP), 38 (25%) NAP with ≥ 1 mismatch, and 70 (46%) with haploidentical (Haplo) donors. CMV reactivation was higher in Haplo HSCT, 93% (65/70). Source of HSC: peripheral blood was used in 45 (30%), bone marrow (BM) in 103 (68%) and cord blood in 3 (2%). CMV reactivation occurred in 58/103 HSCT with 38% MO and 66% (30/45) with CTP. Conditioning regimen: 126 (84%) was myeloablative (MAC) and reduced intensity (RIC) in 25 (16%); 70/126 (55%) of those transplanted with MAC regimen had CMV reactivation versus 17/25 (68%) with RIC regimen. The median follow-up of patients alive until D+100 was 47 days: 43% had CMV reactivation between D+30 and D+100. 42/151 patients (28%) died, 33% with non-recurrence-related mortality. No patient died from CMV disease.

CONCLUSION: 43% of children and adolescents reactivated CMV. A higher incidence was observed when patient and donor had positive IgG pre-HSCT (63%); with MAC conditioning (55%) and, mainly, in patients who received HSC from Haplo donors (65/70 = 93%). This population should be carefully evaluated for viral reactivation prophylaxis strategies.

Keywords: Cytomegalovirus. Viral reactivation after allogeneic HSCT. Allogeneic HSCT in pediatric patients. Cytomegalovirus reactivation after pediatric allogeneic HSCT.

TABLE 1.

Pacients	151	100%
Age (Median)	9	
Sex (patients/percentage)		
Male	77	51%
Female	74	49%
Diagnosis (patients/percentage)		
Hematologic Malignancy	131	86.8%
Acute Leukemia	117	77.5%
Lymphoma	4	2.6%
MDS	8	5.3%
Myeloproliferative Neoplasms	2	1.4%
Non Hematologic Malignancy	20	13.2%
HLH	4	2.6%
AA/BMF/Immunodeficiency	16	10.6%
CMV sorological status (patients/percentage)		
D Neg/R Pos	13	8.6%
D Pos/R Pos	120	79.5%
D Pos/R Neg	11	7.3%
D Neg/R Neg	7	4.6%
DRI/CIBMTR (patients/percentage)		
Hematologic Malignancy	131	86.8%
Low	6	4%
Intermediate	43	28.4%
High	72	47.6%
Very High	10	6.6%
Non Hematologic Malignancy	20	13.2%
Donor (patients/percentage)		
HLA ID	28	18.6%
MUD	15	10%
MMUD	38	25.1%
HAPLO ID	70	46.3%
Stem Cell Source (patients/percentage)		
PBSCs	45	29.8%
BM	103	68,20%
UCB	3	2,00%
Conditioning Regimen (patients/percentage)		
Myeloablative	126	83.5%
Ruduces Intensity	25	16.5%
Follow-up Post HCT (Days, Median)	47	
Survival (patients/percentage)		
Live	109	72.1%
Death	42	27,90%

TABLE 2.

Donor	CMV Reactivation (patients/ percentage)	No reactivation (patients/ percentage)	Total (patients/percentage)
HLA ID	17/11.2%	11/7.4%	28/18,6%
MUD	10/6.7%	5/3.3%	15/10%
MMUD	18/12%	20/13.1%	38/25.1%
HAPLO	65/43%	5/3.3%	70/46.3%

TABLE 3.

Stem Cell Source (patients/ percentage)	CMV Reactivation (patients/ percentage)	No reactivation (patients/ percentage)	Total (patients/percentage)
PBSCs	30/19,8%	15/10%	45/29.8%
BM	58/38,4%	45/29.8%	103/68.2%
UCB	1/0.7%	2/1,3%	3/2%

TABLE 4.

CONDITIONING REGIMEN (PATIENTS/PERCENTAGE)	CMV REACTIVATION (PATIENTS/PERCENTAGE)	NO REACTIVATION (PATIENTS/PERCENTAGE)	TOTAL (PATIENTS/ PERCENTAGE)
MYELOABLATIVE	70/46.3%	56/37.2%	126/83.5%
RUDUCES INTENSITY	17/11.2%	8/5.3%	25/16.5%

TABLE 5.

CMV sorological status (patients/percentage)	CMV Reactivation (patients/ percentage)	No reactivation (patients/ percentage)	Total (patients/percentage)
D Neg/R Pos	5/3.3%	8/5.3%	13/8,6%
D Pos/R Pos	75/49.6%	45/29.9%	120/79,5%
D Pos/R Neg	4/2.6%	7/4.7%	11/7.3%
D Neg/R Neg	2/1.3%	5/3.3%	7/4.6%

SARS COV-2 INFECTION AND COVID-19 IN HEALTH CARE WORKERS FROM A HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) UNIT BEFORE AND AFTER VACCINATION: A PROSPECTIVE COHORT STUDY

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HSCT recipients are profoundly immunosuppressed and health care workers (HCW) of transplant units need to be tested periodically by SARS CoV-2 PCR to avoid transmission during hospitalization. We conducted a prospective cohort study with periodic serology and nasal wash (NW) sampling to estimate the cumulative incidence of COVID-19 in HCW from HSCT unit before (May/2020 to January/2021) and after COVID-19 vaccination (January to October 2021) and to evaluate the occurrence of hospital acquired COVID-19 in HSCT recipients. In addition to periodic sampling, from inclusion (dzero) onwards, HCWs were daily surveyed for the presence of symptoms (Fig 1). NW was taken if symptoms and/or exposure to a confirmed or suspected case of COVID-19. If tested positive by PCR, they were away for 14 days and returned to work with at least 1 negative PCR test. Detection of SARSCoV-2 was performed by PCR (RealStarSARSCoV-2, Altona Diagnostics/Germany) and monthly serology by ELISA (Anti-SARSCoV-2 ELISA, Euroimmun/Brazil). The incidence of SARSCoV-2/COVID-19 was estimated by cumulative incidence. Study participants received the 1st dose of COVID-19 vaccines (Sinovac/Butantan or Oxford/AstraZeneca/Covishield) between January and March 2021, and the 2nd dose between February and June 2021. Vaccine Effectiveness (VE) was identified by the formula VE = (r0-r1) / r0 (r0 = rate in unvaccinated individuals; r1= rate in vaccinated). Between May 13, 2020 and March 22, 2021, 109 HCWs were included. The median follow-up was 259 (79-309) days. Before vaccination, 29 cases of SARS CoV-2/COVID-19 were diagnosed at a median of 53 days, for a cumulative incidence of 30% (fig 2). Thirteen cases (11.9%) were detected at inclusion and 16 during follow-up. Of the 13 cases detected at inclusion, 8 (30.8%) were diagnosed by serology, showing previous infection. During follow-up, 7 individuals dropped out of the study and one was not vaccinated. Thus, 101 HCWs were included in the post-vaccine analysis. Eight PAS (8%) received chAdOx1 (Oxford/Astrazeneca/Covishield) and 93 (92%) Sinovac (Butantan). After vaccination, 76 of the 78 susceptible HCWs tested positive (97.4%), 1(1.3%) had an indeterminate result, and 1(1.3%) had a negative result after the 2nd dose. Within a median post-vaccine follow-up of 153 (91-165) days, 9 HCWs acquired COVID-19 (6 between the first and second dose) for a cumulative incidence of 9.7% (Fig 3). Three (33.35) acquired COVID-19 despite the presence of specific SARS CoV-2 antibodies. Considering only the susceptible subjects at vaccination (n=78), the rate of COVID-19 in unvaccinated (n=29) or partially vaccinated (n=6) was 44.8% (35 of 78) and the rate in those fully vaccinated was 3.8% (3 of 78), for a VE of 91.5%. In conclusion, a good serological response was observed after vaccination (97,4%), resulting in a decrease in the incidence of COVID-19 from 30% to 9,7%. The current pandemic scenario continues to represent a great challenge in HSCT units.

FIGURE 1. **Sampling algorithm**

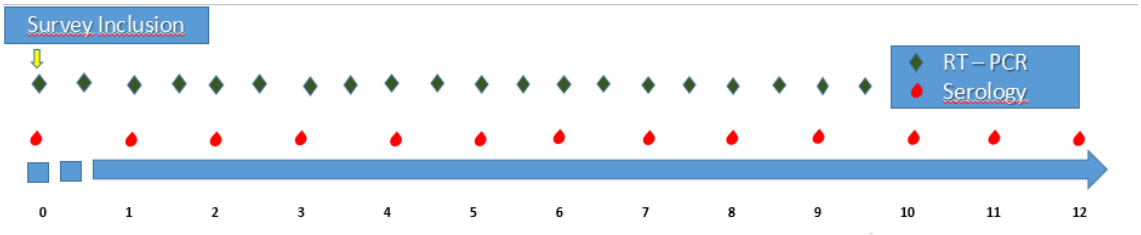


FIGURE 2. **Cumulative incidence of COVID-19 before vaccination**

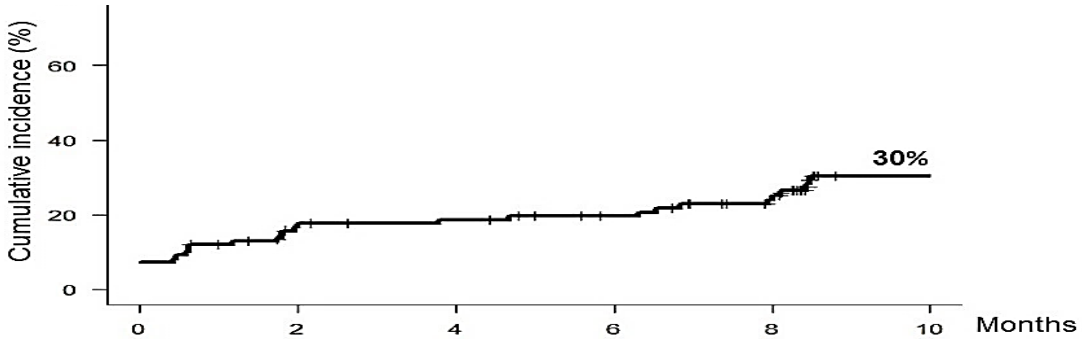
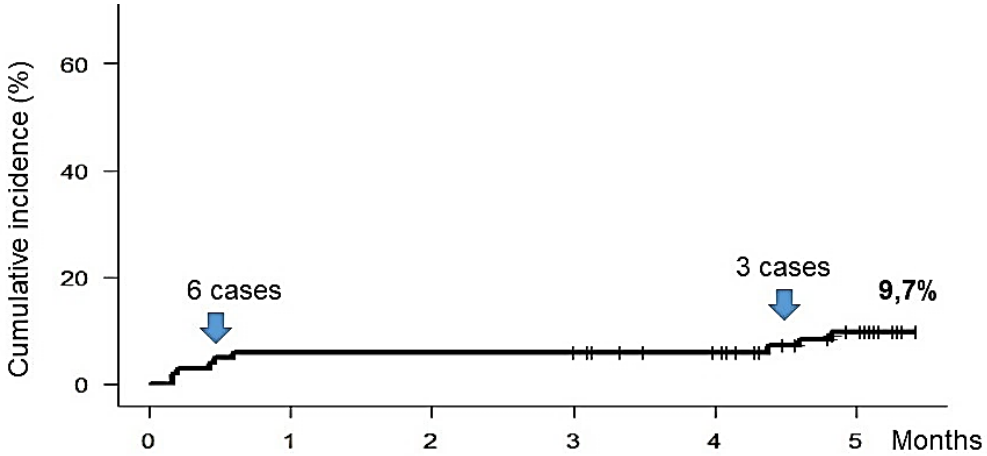


FIGURE 3. **Cumulative incidence of COVID-19 before vaccination**



EPIDEMIOLOGICAL PROFILE OF INVASIVE FUNGAL INFECTION (IFD) IN PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) AT A SINGLE INSTITUTION.

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INTRODUCTION: Among the infectious complications that occur after HSCT, IFD have high morbidity and mortality not related to recurrence. There are several risk factors: type of transplant, intensity of conditioning, duration of neutropenia, use of immunosuppressants/corticosteroids, presence of graft-versus-host disease (GVHD). Thus, in high-risk patients prophylaxis is mandatory and its use has changed the incidence of agents in this scenario.

OBJECTIVE: To assess the epidemiology of IFD in patients undergoing HSCT. To describe associated risk factors, lethality and escape from antifungal prophylaxis.

METHODS: Retrospective cohort study at a reference center for HSCT in São Paulo, with patients aged up to 21 years who underwent HSCT with a diagnosis of IFD between 2011 and 2018 according to EORTC criteria.

RESULTS: There were 33 episodes in 30 patients, 67% of whom were male and a median of 11.5 years old. Regarding the underlying disease, there was a predominance of hematological malignancies, being 30% AML, 27% ALL and 7% Hodgkin's lymphoma; 20% had non-oncological diseases and 17% had a solid tumor. 77% of HSCT were allogeneic (related in 39% and haploidentical in 17%) and 44% unrelated. In 33 episodes, 58% were neutropenic and 55% were using corticosteroids. Among the IFD identified, 64% were caused by filamentous fungi and 34% were yeasts. Among the filamentous, 71% were aspergillosis – 4 proved, 9 probable and 2 possible – 24% by Fusarium spp and 5% by Sporotrichum spp. All yeasts were Candida spp with 33% C. albicans, 25% C. parapsilosis, 8% others (tropicalis, krusei, glabrata, guilliermondii and haemulonii). Among filamentous, 33% were not on prophylaxis, 14% were using Fluconazole and 52% with prophylaxis against filamentous. Among yeasts, 42% were on prophylaxis (5/12), with 3/12 using of Voriconazole and 2/12 Fluconazole. The main sites affected were blood in 30%, lung in 27%, sinuses in 12% and disseminated infection in 9%. The death rate was 60%, and the lethality rate of Sporotrichum spp was 100% (1/1), Aspergillus spp was 67%, Fusarium spp was 60% and Candida spp was 50%.

CONCLUSIONS: The diagnosis of IFD is important due to morbidity and mortality in pediatric patients and the identification of the agent must be performed in order to guide therapy. As in the literature, the most commonly found fungi were Candida spp and Aspergillus spp, with an increase in non-albicans Candidas, which can be explained by the use of prophylaxis with Fluconazole. Most patients were neutropenic or used corticosteroids and the main site of infection was the bloodstream (associated or not with the catheter). The 60% mortality makes it urgent to identify risk factors: underlying disease (hematological malignancies are more prevalent in this and other studies), type of HSCT, use of prophylaxis and environmental control, as well as the degree of suspicion for rapid start of treatment.

CELLULAR THERAPY

BONE MARROW MESENCHYMAL CELLS FOR ADULT COVID-19 IN MECHANICAL VENTILATION DUE TO SARS: A SAFETY AND FEASIBILITY CLINICAL STUDY

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INTRODUCTION: Severe Acute Respiratory Syndrome (SARS) due to COVID-19, along with several systemic complications such as CRS and hypercoagulation, has caused millions of deaths all over the world. Some previous studies have shown that advanced therapy using Mesenchymal Stromal Cells (MSC) and its immunomodulatory properties, could be a potential therapeutic strategy to block pulmonary inflammation. This Phase I trial was elaborated to evaluate the MSC adoptive immunotherapy as adjuvant therapy for SARS caused by COVID-19.

OBJECTIVE: The primary endpoint was to define safety and feasibility of allogeneic bone marrow (BM) MSC immunotherapy in patients with SARS due to COVID-19. The secondary endpoints were to monitor treatment response by time to SARS resolution according to PaO2/FiO2 ratio (P/F ratio) variations; to verify C-reactive protein (CRP) serum variation and flow cytometric analysis of peripheral blood leukocytes immune profiling of the patients.

METHODS: BM MSC were obtained from the BM collection bag/filter cellular residues and expanded ex vivo up to the second passage. Two infusions of $1x10^6$ BM-MCS cells/kg were administered intravenously between 72 to 96 hours after mechanical ventilation was started. Patients were continuously monitored during the infusion procedure for up to two hours and for 30 days after the infusions to evaluate clinical and laboratory changes according to predetermined periodic parameters.

RESULTS: Between October 2020 and January 2021, eight patients under invasive mechanical ventilation were enrolled (Table 1). No adverse events either early or late were associated with the infusion of BM-MSC (Table 2). A total of six patients (75%) have increased clinical-laboratory parameters, being cured from SARS by reaching P/F ratio over 300 in a median of 5,5 days (Figure 1). Among the responders there was one patient with advanced liver disease and dementia that died of liver failure, after ICU discharge, as his family decided for support therapy only. Treatment was followed by a decreased tendency in CRP serum (Figure 2) and T lymphocytes increased in the responders (Figure 3).

CONCLUSION: In view of its safety and feasibility the immunotherapy using BM-MSC might be considered an alternative to COVID-19 infected patients developing SARS since it can be associated with clinical and biological improvement in some patients with severe pneumonia requiring mechanical ventilation.

Table 1. Individual patient and disease characteristics at baseline.

	Patients							
	1	2	3	4	5	6	7	8
Age (Years)	54	43	67	64	49	60	73	74
Sex	F	M	M	F	M	M	F	F
Ethnicity	Caucasian	Caucasian	Black	Caucasian	Black	Caucasian	Caucasian	Caucasian
BMI	25.65	44.08	28.01	37.95	25.85	20.70	20.34	24.44
Days from diagnosis (PCR SARS-CoV positive)	7	5	8	9	4	3	6	4
Comorbidities	Hypertension MDD Asthma	Hypertension	Dyslipidemia	Hypertension T1DM Hypothyroidism Chronic Hepatitis C	Vitiligo	Hypertension Chronic Kidney Disease	Hypertension Cardiac Insufficiency Hyperthyroidism	Hypertension T2DM
Smoking	No	No	No	No	Ex-smoker	Yes	No	No
Use of supplemental O2 before MSC infusion	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Modified NEWS score before MSC infusion	Red	Red	Red	Red	Red	Red	Red	Red
Previous therapy for COVID	No	No	No	No	No	No	No	No
Laboratory								
CRP	282	303	81	144	254.2	118.7	245	198
D-dimer	1.29	1.28	1.02	0.53	9.42	5.11	3.85	1.19
Hb	10.30	11.60	13.30	11.10	11.90	7.3	11.10	13.40
Platelets	211	357	296	282	328	42	215	197
Lymphocytes	0.22	0.82	0.43	0.68	1.11	0.15	0.57	1.25
LDH	576	594	462	505	597	472	734	470
MSC, No. doses	2	2	2	2	2	2	2	2

M: male; F: female; BMI: Body Mass Index (kg/m^2); MDD: Major Depressive Disorder; T1DM: Type 1 Diabetes Mellitus; T2DM: Type 2 Diabetes Mellitus; CRP: C-reactive protein (mg/L); D-dimer: ug/mL; Hb: hemoglobin (g/dL); Platelets: (x10^3/mcL); Lymphocytes (x10^3/mcL); LDH: lactate dehydrogenase (U/L). MSC: Mesenchymal Stromal Cell; ICU: Intensive Care Unit; Modified NEWS Score: modified version of the National Early Warning Score (NEWS) with age ≥ 65 years added as an independent risk factor.

Table 2. Adverse events.

Adverse events observed during the study	Grade	N	Related to MSC
Cardiac			
Atrial fibrillation	3	1	No
Heart failure (Cardiogenic shock)	5	1	No
Ear and labyrinth			
Vertigo	2	1	No
Gastrointestinal			
Colitis	4	1	No
Diarrhea	2	1	No
Dysphagia	3	1	No
	2	1	No
Hematological			
Anemia	3	1	No
Platelet count decreased	4	1	No
Infection			
Sepsis	4	3	No
Bronchial infection	3	1	No
Urinary tract infection	2	1	No
Herpes zoster (pre-existing)	2	1	No
Metabolism			
Hyperglycemia	2	1	No
Hypophosphatemia	2	2	No
Hypercalcemia	3	1	No
Musculoskeletal			
Rhabdomyolysis	4	1	No
Neurological			
Critical illness polyneuropathy	4	4	No
	3	2	No
Pulmonary			
Pneumonitis	4	3	No
	3	1	No
	2	1	No
Pulmonary fibrosis	3	2	No
Laryngeal edema	4	1	No
Renal			
Acute kidney injury	4	4	No
Vascular			
Thromboembolic event (pulmonary embolism)	4	4	Unlikely
Thromboembolic event (deep vein thrombosis)	2	1	Unlikely
Hypertension	4	1	No

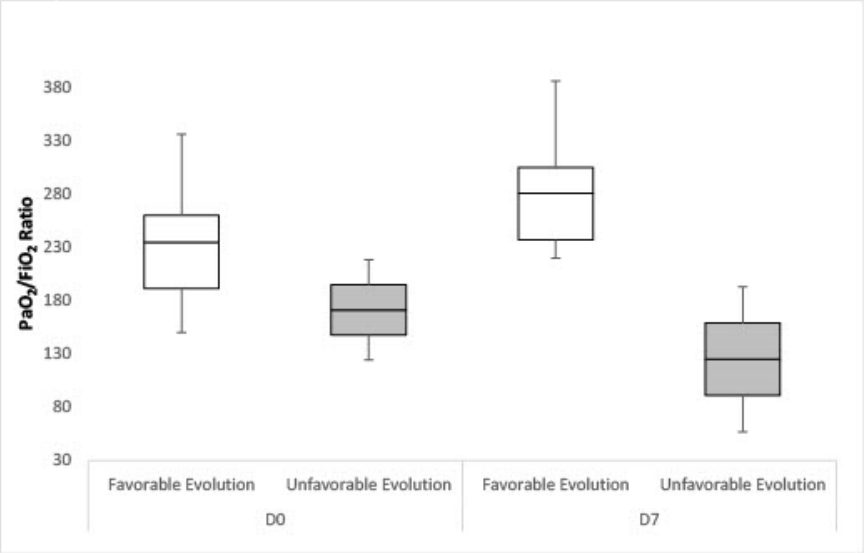

Figure 1. Differences in the oxygenation index (PaO_2/FiO_2) between patients with favorable (n=6) or unfavorable (n=2) evolution (recovered or not recovered from SARS) before BM-MSC immunotherapy (D0) and at day +7 after the second BM-MSC dose (D7).

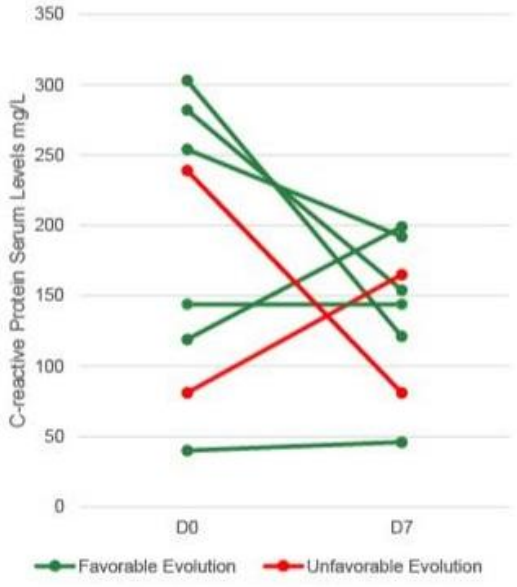

Figure 2. Changes in C-reactive protein serum levels. The concentration values are indicated by dots joined by a color line before BM-MSC immunotherapy (D0) and at day seven from the first dose (D7) for each individual and evaluable patient. Green or red colors represent patients with favorable or unfavorable evolution (recovered or not recovered from SARS).

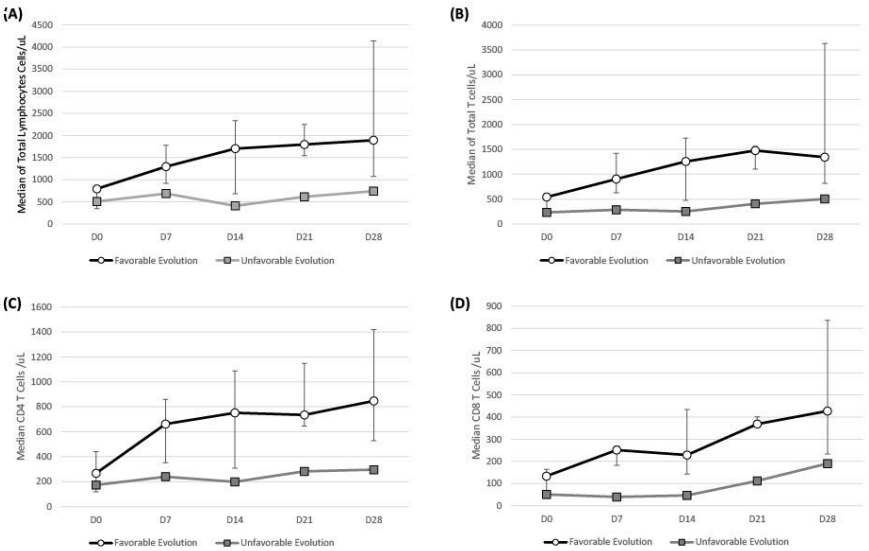

Figure 3. Changes in lymphocyte counts and lymphocyte subsets before and after BM-MSC immunotherapy. **(A)** Total Lymphocytes Cells count alterations in patients with favorable (n=6) or unfavorable (n=2) evolution (recovered or not recovered from SARS). **(B), (C), (D)** Cell counts of total T cells, and CD4+ and CD8+ T cell subsets respectively. All figures show median and interquartile range at different time points in blood from severe COVID-19 patients.

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS UNDER THREE YEARS OF AGE

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Young children have unique diseases as high-risk neuroblastoma, medulloblastoma, teratoid-rhabdoid tumors and extra-ocular retinoblastoma, that have consensus universal indications for autologous hematopoietic stem cell transplantation (HCT), tandem procedures in many protocols, but these low weight and very active patients are extremely challenging to collect and infuse autologous peripheral blood hematopoietic stem cells (PBSC). Thiotepa (TT) is the most important drug in the conditioning regimen, and not available in most centers.

OBJECTIVE: The aim of this study is to review and report the experience of autologous transplantation in children under 3 years of age.

PATIENTS AND METHODS: We reviewed the Laboratory and the electronic medical records of all patients aged 3 years or less undergoing HCT in our institution. The cryoprotectant dimethylsulfoxide (DMSO) was removed from the autologous grafts in 99 transplants of 83 patients. DMSO removal was indicated for patients under 25 kg, with renal or heart failure, and from grafts containing DMSO above 1g/kg. The removal was performed according to Rubinstein's protocol: dextrano-albumin solution 5% at 4ºC on an icy surface was slowly added to the bag in a 1:1 proportion immediately after thawing with continuous manual homogenization. An aliquot was removed for quality control and the cells were transferred to the transfer bag and centrifuged at 400g, 4°C for 20 min. The supernatant was transferred to a new bag and the buffy coat resuspended in the same solution of dextran – albumin and sent for infusion with a simple equipment. The remaining solution was centrifuged again until having <0.1x108CNT/kg. In 2018, the criterion for removal decreased to 15 kg, and from October 2021 on, the weight was no longer considered a criterion for DMSO removal.

RESULTS: From December 1999 to March 2022, 129 transplants were performed in 105 patients: 13 had 2 transplants, 9 underwent 3 and one had 4 tandem transplants. The median age was 2.1 years (0.7-3 years), median weight 11 kg (6.5 - 18 kg) and 59 were female. The diagnoses were central nervous system tumor (53), neuroblastoma (30), retinoblastoma (16), germ cell tumor (8) and teratoid-rhabdoid tumor (1). The conditioning regimens used were Bu-Mel (21), Carbo-TT (2), Carbo-VP-TT (1), CEM (12), CE-TT (58), Temodal-TT (1), TT-Carbo (6) and TT-CTX (4). After an initial severe transfusion-related adverse event, 22 years ago, no other patient had severe transfusion-related events. All patients engrafted and 71% were alive.

CONCLUSION: Autologous transplantation with hematopoietic stem cells in patients under three years of age is safe and feasible when performed in experienced pediatric HCT centers.

Bu mel= Bulsufano and Melphano
Carbo TT = Carboplatin and Thiotepa
Carbo VPTT = Carboplatin, Etoposide,Tiotepa
CEM = Carboplatin,Etoposide, Melphaline
CE TT = Carboplatin, Etoposide,Tiotepa
Temotal TT = Temodal and Tiotepa
TT-Carbo = Thiotepa and Carboplatin
TT-CTX = Thiotepa and Cyclophosphamide

THE IMPACT OF CELL CONCENTRATION, TIME OF FRESH STORAGE, AND CRYOPRESERVATION ON PERIPHERAL BLOOD STEM CELLS

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INTRODUCTION: Peripheral blood stem cells are widely used in autologous or allogeneic transplantation. The quality of the product directly impacts clinical outcomes, and the cell quality and/or functionality may be influenced by the storage conditions as time, temperature, total nucleated cells (TNC) concentration and cryopreservation requirement.

OBJECTIVE: To verify the effects of time, cell concentration, and cryopreservation/thawing in the viability and functionality of stem cells for transplantation, focusing on to determine the best storage conditions for the collected biological material to be infused into the patient.

METHODS: We evaluated TNC (hematology analyzer; ABX Micros ES60, Horiba); CD45+ viable cells, CD34+ viable cells, and cell viability (flow cytometry; ISHAGE protocol; FACS Canto II, BD Biosciences); sterility (BacT/ALERT; bioMérieux SA) and functionality (colony-forming units [CFU] assay) of 11 samples. Measurements were performed immediately and 24 h, 48 h, 72 h, and 96 h after sample collection at high (WBC 570–600 x 103/uL) and low (270–300 x 103/uL) TNC concentrations. The same parameters were also evaluated after cryopreservation (5% DMSO, 6% hydroxyethylstarch, and 3% human albumin; -80 °C, uncontrolled freezing) and thawing of the samples (37–40°C water bath).

RESULTS: Duration of storage and TNC concentration exhibited a negative effect on cell quality (CD45+ viable cells, CD34+ viable cells and functionality) (Table 1 and Figure 1). Moreover, the association of these parameters increased the negative effect on graft quality. Cryopreservation and thawing also negatively affected the collected sample regarding viable CD34+ cells (recovery 66.2%), viable CD45+ cells (recovery 56.8%), and 7AAD viability (Table 2). No significant losses in viable CD45+/CD34+ cells and functionality were observed in the first 24 h in both TNC conditions. The percentage of cell debris in the samples also revealed an increase considering the effects of storage cool time, TNC concentration and cryo/thaw process ($P<0.001$) when compared with post collection PBSC samples. These results significantly agree with CD45+ and CD34+ cell losses (negative correlation, $P<0.001$). No microbiological or fungal contamination was observed in the fresh samples stored for up to 96 h.

CONCLUSION: These results emphasize the importance to consider carefully the storage conditions until transplantation, measuring TNC/uL until 24 h after collection (diluting the product when TNC>300 x 103/uL) and infusing fresh graft as soon as possible.

Keywords: Hematopoietic progenitor cells. Peripheral blood stem cells. Bone marrow transplantation. Cryopreservation. Cell concentration. Fresh storage.

Funding: This work was supported by Fundo de Incentivo à Pesquisa e Eventos (FIPE) – Hospital de Clínicas de Porto Alegre (GPPG-2018-0410).

TABLE 1. Mean loss of 7-aminoactinomycin D (7-AAD) viability (%) and mean recovery (%) of total nucleated cells (TNC), viable $CD45^+$ cells, viable $CD34^+$ cells, and colony-forming units (CFU) relative to T0 peripheral blood stem cell samples.

	LC	p-value	HC	p-value
Total nucleated cells				
T24	98.2 (1.00)	0.699	98.9 (0.93)	>0.999
T48	98.9 (0.97)	>0.999	98.3 (1.01)	0.876
T72	98.8 (0.74)	>0.999	98.2 (1.69)	>0.999
T96	97.5 (0.67)	0.052	96.5 (1.53)	0.234
Viable CD45+ cells				
T24	98.5 (2.02)	>0.999	95.8 (1.25)	0.007
T48	97.1 (3.09)	>0.999	89,3 (2.64)	<0.001
T72	95.7 (2.99)	>0.999	78,6 (3.32)	<0.001
T96	87.2 (2.59)	<0.001	69,7 (4.23)	<0.001
Viable CD34+ cells				
T24	100 (4.04)	>0.999	92.9 (3.00)	0.187
T48	100 (4.92)	>0.999	87.1 (3.72)	0.005
T72	97.2 (4.17)	>0.999	77.9 (4.82)	<0.001
T96	90.1 (4.53)	0.281	67.3 (5.10)	<0.001
Viable cells (7-AAD)				
T24	0.4 (0.95)	<0.001	1.0 (0.32)	0.025
T48	1.1 (0.22)	<0.001	4.3 (1.20)	0.003
T72	3.1 (1.00)	0.021	9.9 (3.09)	0.015
T96	7.0 (2.00)	0.005	19.1 (5.18)	0.002
Colony-Forming Units				
T24	90.7 (9.17)	>0.999	96.2 (12.44)	>0.999
T48	88.8 (8.65)	>0.999	73.0 (8.75)	0.021
T72	71.1 (6.78)	<0.001	48.1 (6.09)	<0.001
T96	66.9 (9.76)	0.007	31.6 (6.95)	<0.001

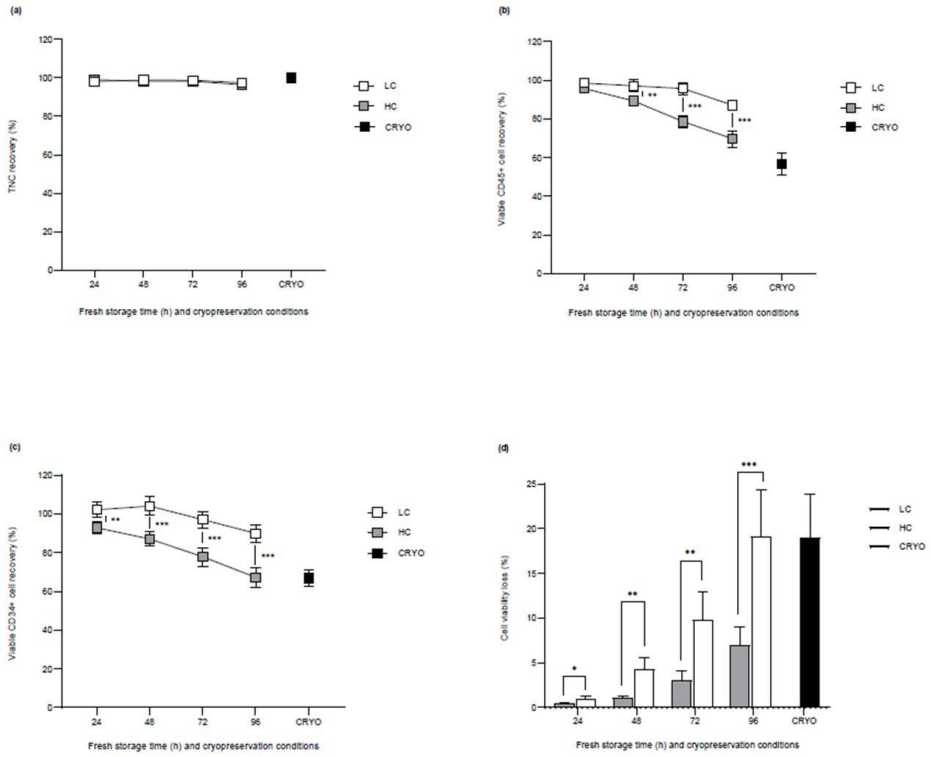
Data are reported as estimated mean and standard error of mean; p-value: GEE with Bonferroni correction; LC – low concentration (WBC 270–300 x 10^3/uL); HC – high concentration (WBC > 570 x 10^3); T24 – 24 h after collection; T48 – 48 h after collection; T72 – 72 h after collection; T96 – 96 h after collection.

TABLE 2. Mean loss of 7-aminoactinomycin D (7-AAD) viability (%) and mean recovery (%) of total nucleated cells (TNC), viable CD45+ cells, viable CD34+ cells, and colony-forming units (CFU) of cryo/thawed samples relative to T0 peripheral blood stem cell samples.

	Estimated mean (%)	SE	p-value
Total nucleated cells	103.9	2.03	0.054
Viable CD45+ cells	56.8	5.85	<0.001
Viable CD34+ cells	66.9	4.04	<0.001
Viable cells (7-AAD)	19*	4.77	0.001
Colony-Forming Units	83.8**	6.7	0.156

SE: standard error; p-value: GEE with Bonferroni correction.
* Viability report of whole cells and not considers cells wasted in cellular debris.
** This result represents the ability of Trypan blue viable cells and should not be assessed separately because not consider the cellular loss observed in post-thaw samples.

FIGURE 1. Impact of cryopreservation/thawing (CRYO) and time of refrigerated storage in peripheral blood cells at low (LC) and high (HC) total nucleated cell (TNC) concentrations. (A) TNC recovery, (B) viable CD45+ cells, (C) viable CD34+ cells, and (D) loss of viability (CD45+7-AAD+ cells). Results are presented as means and standard errors. *, **, and ***: statistically significant differences (*P < 0.05; **P < 0.01; ***P < 0.001; GEE with Bonferroni correction) when comparing fresh LC and HC samples at the same time of storage (n = 11 samples). The comparison between cryopreserved and fresh samples is described in the Results section.



CONTINGENCY PLAN FOR THE STORAGE OF CRYOPRESERVED PRODUCTS: HOW TO PROCEED IF THE N2 TANK COLLAPSES

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INTRODUCTION: The proper storage of hematopoietic progenitor cells (HPCs) is essential to ensure the viability of the product and, therefore, the success of the bone marrow transplantation. Due to the absence of a backup tank, a contingency plan was implemented in case of collapse of the current tank (rupture or leakage of the cylinder).

OBJECTIVE: To validate the contingency plan which consists of immediately transferring of the products from the liquid N2 tank to ultra-freezers at -80˚C on a temporary basis, until another liquid N2 container is available.

MATERIALS: We used products from patients (or allogeneic donors), which would be discarded after the patient's authorization or after the patient's death. A total of 56 samples (31 bags and 25 segments) were studied from 10 collections of 6 patients.

METHODS: On D0, all racks containing the products were removed from the liquid N2 and immediately stored in a -80oC freezer. These samples were gradually removed from the freezer on days 0, 6, 14, 21, 30, 61, 90, 120, 150 and 180, thawed in a water bath (37oC), tested by the Trypan Blue (TB) viability test by optical microscopy, and also tested for viable CD34+ cells with 7AAD by flow cytometry.

RESULTS: The viability analysis by TB showed no significant difference between the days analyzed ($p>0.05$), with a mean of 78.8 ± 5.5%. The only difference ($p=0.002$) was observed between D0 and D180, however we only had 2 samples available on D180. Greater variability, however, was noted by 7AAD between the samples (10 samples/day) of days 6, 30 and 90 (mean ± sd: 87.5 ± 0.9%; 84.4 ± 13.6%; 86.1 ± 13%, respectively). When comparing both methodologies, there was a significant difference only on D0 (mean 87.2 ± 5.3 by TB; 76.5 ± 12.5 by 7AAD), but both presented similar averages after D6 (mean 84.2 ± 6 by TB, 87.5 ± 10.9 by 7AAD). In the 10 samples analyzed on D0 - an average recovery of 72% of viable CD34+ was observed by TB and 76% by 7AAD, when compared to the pre-freezing dosage.

CONCLUSIONS: Although some authors[1,2,3] mention that it is common cell viability in thawed samples to reach values below 70% using the TB test, in our study all samples showed acceptable viability (above 70%). During the analysis with the 7AAD test, the results were also above those found by other authors. Thus, in an emergency situation, it is feasible to use ultra freezers at -80oC to store cryopreserved products until another liquid N2 container is obtained. Due to the criticality of the product, this storage should be done for the shortest period possible, only as a palliative solution, until another N2 container is provided, preferably not exceeding a period of 15 days.

Keywords: Hematopoietic stem cells. Freezing. Validation study.

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OTHER TOPICS

10 YEARS OF FACT ACCREDITATION: THE IMPACT IN A HEMATOPOIETIC CELL TRANSPLANT PROGRAM IN LATIN AMERICA

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Hematopoietic Progenitor Cell Transplantation (HPCT) is a highly complex process associated with substantial morbidity and mortality risks. The FACT (Foundation for the Accreditation of Cellular Therapy) accreditation evidences excellence in patient care undergoing Cellular Therapy, through compliance with international standards, covering the three areas of activity: Clinical Program, Collection and Processing. In 2009 the studied center started a series of actions focused on quality and safety, achieving in 2012, the first FACT accreditation in Latin America. The aim of this study was to evaluate the impact of FACT accreditation on the clinical outcomes of patients undergoing HTC in our center. Patients undergoing allogeneic HTCH between 2009- 2020 were included, totaling 444 transplants and 416 patients, grouped by triennium (2009-2011; 2012-2014; 2015-2017; 2018-2020). Analyses were performed with Bayesian lognormal models and weakly prior with STAN. There has been an increase in the median age throughout time as well as an increase in alternative donor usage. Non-relapse mortality (NRM) was significantly lower in recent trienniums (β=0.41 for each later triennium; 95CI 0.09 to 0.75), and NRM was higher with unrelated donors (β=-1.05; 95CI -1.96 to -0.19), in multivariable analysis (Figure1). There was a trend towards higher NRM in haploidentical, compared with related transplants (β=-0.98; 95CI -2.02 to 0.02). This lower NRM translated into higher Overal Survival (OS) in most recent trienniums (β=0.29 for each triennium; 95CI 0.03 to 0.56). Older age (β=-0.03; 95CI -0.042 to -0.018) and alternative donors (β=-0.90; 95CI -1.64 to -0.22 for unrelated donors and β=-0.90; 95CI -1.70 to -0.07 for haploidentical transplants) were associated with poorer OS (Figure 2 and 3). Over these 10 years we can highlight the implementation of a specific quality program in Cellular Therapy, with actions such as: mapping and standardization of processes, management of operational policies, data management, specific indicators, audits, critical analysis discussions, clinical discussions, training, and changes in the infrastructure of the unit. According to the results presented, it is possible to evidence that the accreditation process can continuously improve the results of the HPCT. Few pharmacological advances have been achieved in the last 20 years and it is unlikely that they could have influenced our results, given the date of publication of these advances and the date of approval in Brazil. A highly qualified team, with standardized processes and a consistent system of risk assessment, performance analysis, instrumented by data and the direction of actions collaborate for better results. The certification program enables continuous and progressive improvements; at each cycle we have the opportunity to challenge ourselves in the search for high care reliability.

FIGURE 1. **Multivariable analysis**

	Mean	SD	2.5%	97.5%
Non-relapse mortality				
β_0	3,076	0,452	2,244	4,011
Triennium (each)	0,409	0,168	0,090	0,747
Age (each year)	-0,018	0,007	-0,033	-0,004
Donor				
Related	Ref	Ref	Ref	Ref
Haploidentical	-0,980	0,529	-2,018	0,017
Unrelated	-1,047	0,451	-1,959	-0,189
$\sigma_{lognormal}$	1,406	0,351	0,860	2,199
$\sigma_{random\text{-}effects}$	2,398	0,320	1,725	2,993
Overall survival				
β_0	2,472	0,351	1,803	3,198
Triennium (each)	0,289	0,136	0,031	0,556
Age (each year)	-0,030	0,006	-0,042	-0,018
Donor				
Related	Ref		Ref	Ref
Haploidentical	-0,897	0,417	-1,704	-0,069
Unrelated	-0,897	0,366	-1,640	-0,216
$\sigma_{lognormal}$	1,185	0,198	0,847	1,623
$\sigma_{random\text{-}effects}$	2,323	0,207	1,936	2,727

FIGURE 2. **Non-relapse mortality**

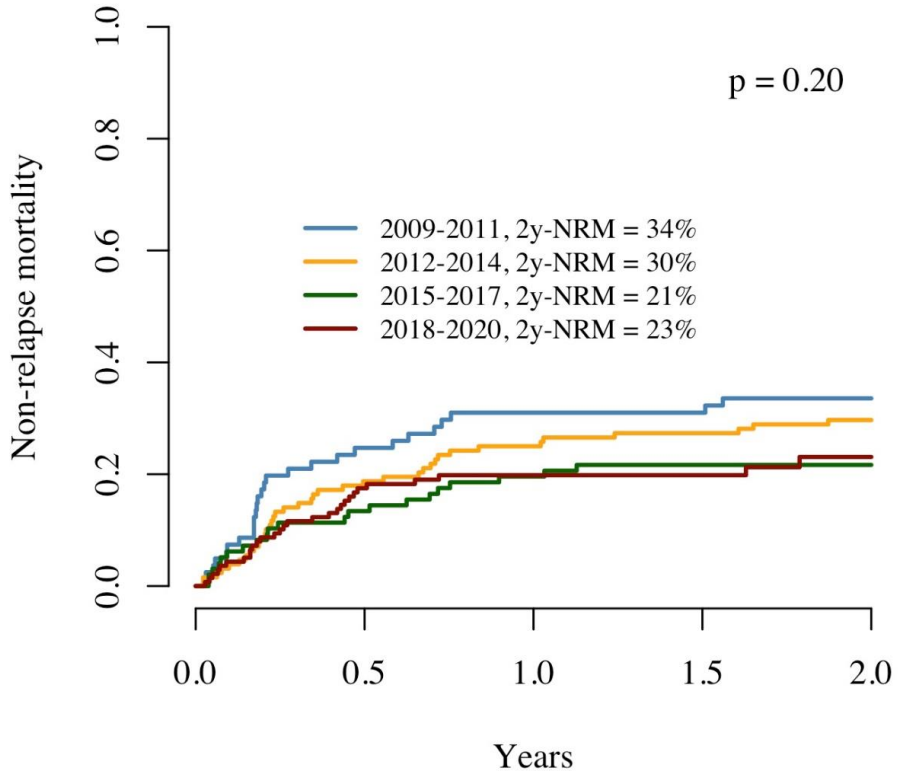
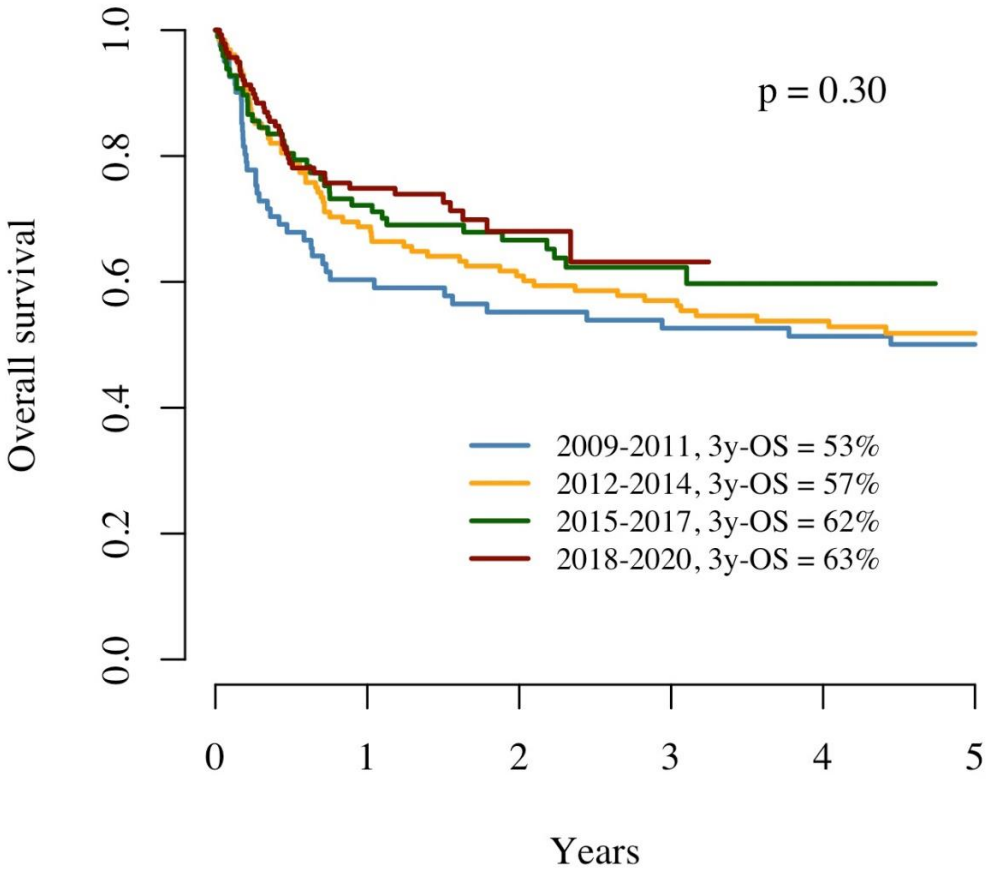


FIGURE 3. **Overall Survival**



POST-TRANSPLANT FOLLOW-UP FLOW TO ASSIST IN THE ACTIVE SEARCH FOR PATIENTS IN LONG-TERM FOLLOW-UP AFTER HSCT

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INTRODUCTION: Hematopoietic Stem Cell Transplantation (HSCT) is a therapy with significant potential for cure for many malignant and non-malignant hematological diseases, knowing the outcomes of this modality is important for planning public policies aimed at improving results bringing benefits to the patients. One of the main outcome analyses in HSCT is overall survival (OS), to the analysis of reliable OS indicators, it is very important to update follow-up data of post-HSCT patients, which is a challenge in a country of continental size such as Brazil. The service performed on average over the last 10 years about 200 transplants/year, more than 50% of these patients were referred for HSCT from other Brazilian states, which can be a barrier to keeping update follow-up data.

OBJECTIVE: Develop a flow to maintain contact with patients who post-HSCT follow-up in another center, maintaining the long-term follow-up of patients that performed HSCT at the institution, thus enabling the reliability of the data, allowed report in national and international registries and performed post-HSCT outcomes analyses.

METHOD: The Transplant center has been sending data to the Center for International Bone Marrow Transplant Research (CIBMTR) since 2009, this data makes up the HSCT Brazilian registry, in this period it has been developing actions and tools to enable the report of all transplants performed and maintenance of the follow-up data of this patients. Post-transplant follow-up updates are periodic, 100 days, 6 months, annually from the first to the sixth year after HSCT and every 2 years thereafter. Cases without updated information in any of these periods should be reported as lost of follow-up. Patients are divided into two groups: (1) Patients who follow-up at the transplant center, in this group the forms are filled out using the data available in the medical records, and (2) those who return for follow-up in the state of origin. For the group 2, that returns for follow-up in other center, a post-HSCT follow-up flow was created (Figure 1), this flow begins before the transplant, when the patient fills out a data registration form and authorizes the use of social networks for future contacts, in the post-HSCT periods, initial contact attempts are made directly with the patient referral service, by email and telephone, when we do not get a response, we try to contact the patient or relatives by telephone and social medias, we also use websites of CPF consultation, send a letter to the registered addresses and contacting the health department of the patient's municipality of residence, this flow is repeated for up to 3 months of the deadlines for sending data.

RESULTS: After the development of the post-HSCT follow-up flow, in the period between January/2018 and April/2022, 2 (0.11%) lost follow-up forms were completed, 1 patient in the one year update, with contact recovery in the following year and 1 patient in the 10-year follow-up, still without success in the update.

CONCLUSION: The development of a post-HSCT follow-up flow to accompany patients who returned to the service of origin, allows us to keep the database updated, fill out the CIBMTR follow-up forms within the deadlines established by the registry, guaranteeing the reliability of the data and enabling post-HSCT outcome analyzes.

FIGURE 1. **Post-HSCT follow-up flow**

PROGNOSTIC FACTORS FOR CRITICALLY ILL HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS

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INTRODUCTION: The prognosis of hematopoietic stem cell transplant (HCT) recipients admitted to the intensive care unit (ICU) has improved over the last decades. However, reports of patients who need to be admitted in the ICU during the peri-transplant period are scarce. The absence of information is even more notable regarding the South Hemisphere's population. To know the profile of patients who become critically ill during the transplantation process is essential to understand causes of mortality better and improve outcomes.[1, 2, 3].

OBJECTIVE: We investigated the main causes and the prognostic factors associated with being admitted to the UCI in the first one hundred days after HCT.

METHODS: This is a single-center retrospective study. We included patients who underwent HCT between 2019 and 2020. The assessed variables included in the Acute Physiology and Chronic Health Evaluation (APACHE) and the Sequential Organ Failure Assessment (SOFA) scores. The analysis period was restricted to the first 100 days. Risk factors for UCI admission was performed with Cox model.

RESULTS: Ninety-eight patients were included. Fifty four percent were male, mean age was 50.9 years and 61% underwent allogeneic HCT. Of the allogeneic HCT, thirty-seven patients received cells from unrelated donor, fourteen from related donor and nine were haploidentical. Graft sources of the cells were: peripheral blood (74%), bone marrow (23%), and umbilical cord (2%). The mean quantity of CD34+ cells infused was 5.2x106/kg (SD3.2). Conditioning regimens were myeloablative (58%), reduced-intensity (35%), and non-myeloablative (5%). Twenty-four patients were admitted to the ICU and 80% were neutropenic. The causes for ICU admission were sepsis, respiratory failure, veno-occlusive disease, arrhythmia, decreased consciousness, and acute hemolytic syndrome after blood cell infusion. Twenty-five percent of patients undergoing any type of HCT went to the ICU. The cumulative incidence in three months was 17,3%. The factors most strongly associated with ICU admission were the type of transplant (haploidentical – HR:010.2; p:0.03) and Karnofsky performance status. Each 10% lower Karnofsky/Lansky score represented the increased risk (HR:1.51; p:0.04) of being admitted to the ICU.

CONCLUSION: Minimizing neutropenia duration may avoid the cumulative incidence of ICU admission during the first one hundred days after HCT. Future studies with larger sample sizes would provide better understand the causes and risk factors associated with becoming critically ill during HCT.

Keywords: Hematopoietic stem cell transplantation. Intensive Care Unit. Hematological Neoplasms.

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FIGURE 1. **Cumulative incidence in three months: 17,3% (95CI 11.3-26.7)**

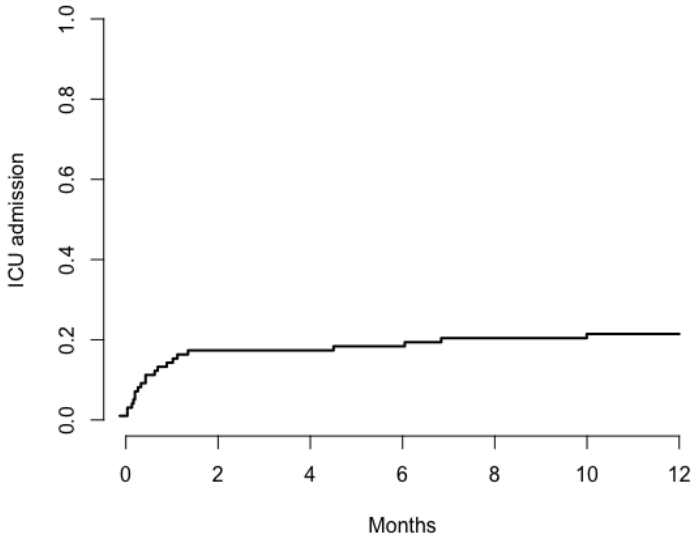

TABLE 1. **Risk Factors associated with ICU admission (multivariable analysis)**

Variable	HR	P
Type of transplant		
Related donor	Ref	
Haploidentical	10.2	0.03*
Non-related donor	4.67	0.14
Autologous	1.35	0.79
Karnofsky/Lansky (each 10%)	0.66	0.04*

RISK FACTORS FOR INFECTION IN FEVER AFTER HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION USING POST-INFUSION CYCLOPHOSPHAMIDE AS GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS

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INTRODUCTION: The infusion of haploidentical stem cells (HSC) is frequently followed by a cytokine release syndrome, where the most common manifestation is fever of non-infectious origin. Although there are few data in the literature about the occurrence of infection in this period, discernment about the etiology of fever in this context is essential.

OBJECTIVES: To determine the incidence of fever and infection between D0 and D+5 on HSC transplantation at our institution. Identify risk factors for the development of fever of infectious origin and determine its impact on neutrophil and platelet engraftment outcomes, 30-day and 100-day mortality.

MATERIAL AND METHOD: A retrospective and observational study was performed including all patients who underwent HSC transplantation from 2012 to 2020. 119 patients were evaluated, of which 7 were excluded because they did not have fever in this period. Descriptive analysis of the variables of interest was performed. To assess overall survival (OS), Kaplan-Meier curves were constructed. Multiple logistic regression was performed for the variables that showed statistical relevance in the simple regression.

RESULTS: Patients were evaluated in relation to epidemiological, clinical and therapeutic characteristics, and compared regarding the occurrence or not of fever of infectious origin. The mean HCT-CI score in the group with infection was 1.97, compared with 1.00 in the group without infection (p=0.003). The maximum C-reactive protein (CRP) value in patients with infection was 26.33, compared with 21.13 in the group without infection (p=0.007). The median of neutrophilic engraftment for the group that presented infection was 18 days and for the group that did not present infection it was 17 days. The median platelet engraftment for both groups was 22.50 days. OS at 30 and 100 days for the group that presented infection was 66% and 50%. For the group without infection, OS at 30 and 100 days was 93% and 78.8%, respectively. The occurrence of infection increased the risk of death by 5.87 times in 30 days (95%CI:2.07-16.69, p=0.001), and by 3.13 times in 100 days (95%CI:1.59-6.15, p=0.001). The main risk factor for infection was pre-transplant disease status, where the lack of complete response increased the risk of the patient having infection in the period between D0-D+5 by 3.22 times (95%CI: 1.416-7.352; p=0.005), being an important death predictor.

CONCLUSIONS: In this present study the incidence of fever was 94.11% and the prevalence of infection was 32.1%. The factors that were related to a higher risk of infection were pre-transplant disease status, HCT-CI score and CRP value. The occurrence of infection had no statistically significant impact on neutrophil and platelet engraftment time, however correlated with worse OS outcomes at 30 and 100 days. The main risk factor found was the lack of complete response, which we believe is related to a worse immunological status of the patient.

Keywords: Infection. Fever. Haploidentical hematopoietic stem cell transplantation.

MULTIDISCIPLINARY

SUITABILITY OF THE DOSAGE FORMS TO MAKE THE TREATMENT OF PEDIATRIC ONCOLOGICAL PATIENTS FEASIBLE

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INTRODUCTION: The limitations of oral Dosage Forms (DF) developed for children, the use of DF developed for adults is necessary. However, adherence rates are variable (11 – 93%) and are related to the characteristics of these DF. To meet the needs of different pediatric age groups, their different dosages, swallowing capacity and palatability, it is necessary to adapt the DF in order to provide safe and effective treatment for this population. Crushing tablets, fractionation to allow the correct dosage, preparation of extemporaneous formulations, addition of excipients such as sweeteners and flavoring agents, co-administration with food are ways to promote adherence to drug treatment for this population.

OBJECTIVE: To report the strategies of adequacy of pharmaceutical forms to enable the treatment of pediatric cancer patients.

METHODOLOGY: Retrospective, descriptive study with a quantitative approach carried out between March/2022 - May/2022. Was performed an analysis of the medical prescription of the oncology clinic, considering the presentation, frequency, dose and route of administration. The medication was manipulated from its primary DF, the identification and elaboration of a label containing general guidelines for the medication to be delivered to the patient, enabling the treatment.

RESULTS: Ten drugs need dose variation and palatability, adjustments according to age (1-6 years). Among the classes of drugs that were adapted, we had: 5 antineoplastic, 2 antimicrobial, 1 corticosteroid, 1 non-steroidal anti-inflammatory and 1 retinoid. Regarding the adaptations, 6 fractionations were carried out (voriconazole, fludrocortisone, mercaptopurine, mitotane, celecoxib, imatinib) 4 dilutions for dose adjustment (voriconazole, vancomycin, isotretinoin, mercaptopurine), 2 adjustments of injectable forms for oral solution through reconstitution and dilution (etoposide, vancomycin), 3 combinations with food to optimize palatability (imatinib, mitotane, isotretinoin, calcium polystyrenesulfonate). After the adjustments, the drugs were dispensed to the patients through guidelines, such as: correct administration (via, dose, times, ingestion with food), proper storage and disposal, as well as supply of kit with materials necessary for administration and disposal of the drug.

CONCLUSION: In this work we present some adjustments of dosage forms that made possible the safety and acceptance of the treatment of pediatric patients. Strategy that was consolidated with the guidelines provided by the pharmacist at the time of dispensing considering the individual need of each patient.

Keywords: Dosage form. Treatment. Pediatrics.

MONITORING OF PLASMATIC VORICONAZOLE LEVELS IN ONCOLOGIC AND SUBMITTED HEMATOPOIETIC STEM CELL TRANSPLANTATION PEDIATRIC PATIENTS FOR TREATMENT OPTIMIZATION

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INTRODUCTION: Pediatric, immunosuppressed, transplant and onco-hematology unit patients are at significant risk of invasive fungal infections (IFI). Among the available treatments, there is Voriconazole (VCZ), a broad-spectrum triazole antifungal agent against filamentous fungi. This drug has non-linear pharmacokinetics, generating variable dosage, effectiveness and safety of treatment. In this way, frequent monitoring of VCZ plasma levels can optimize treatment. Objective: Monitor of plasma VCZ levels in pediatric patients from hematopoietic stem cell transplantation and onco-hematology units in order to optimize treatment.

METHODOLOGY: Retrospective cohort from January/2021 to May/2022 included 14 patients who used VCZ (CAAE: 56983322.9.0000.0097). Whole blood samples were collected 4 to 7 days from the start of treatment, 15 minutes before VCZ ingestion. From these samples, plasmas were obtained, which were analyzed by means of high-performance liquid chromatography (HPLC) to obtain the serum concentration of VCZ. Values between 1-6 µg/mL were considered therapeutic levels. RESULTS: The 14 patients included in the study, 50% did not reach the therapeutic serum level of VCZ at the initial dose, 42.9% reached the therapeutic levels and only 7.1% had levels above the recommended. Among the majority of patients who did not reach therapeutic level, doses were adjusted, however 28.6% of patients still did not reach therapeutic levels. Regarding treatment optimization after dosing, 37.5% of patients underwent only 1 dose adjustment to reach therapeutic level compared to 62.5% who required 2 or more dose adjustments. Total of the 53 samples were collected, ranging from 1 - 6 collections per patient, aged 2 - 17 years, who received median doses of 4mg/kg - 10mg/kg twice a day. Elevated liver enzymes and drug interactions were the most frequent adverse events.

CONCLUSION: Since many patients do not reach therapeutic levels of VCZ at the first dose and there is also significant variability in serum levels between the pediatric age group. We highlight the need for frequent monitoring of VCZ concentrations throughout treatment so that the treatment is effective and safe.

Keywords: Voriconazole. Pediatrics. Serum Level.

EVALUATION OF ORAL MUCOSITIS PROPHYLAXIS AFTER SUPPLEMENTATION WITH MILK PROTEIN CONCENTRATE.

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BACKGROUND: Transforming growth factor beta (TGF-β) present in whey is associated with the control of intestinal inflammation and mucositis. It was previously published by our research group that whey protein concentrate (WPC) reduces the severity and duration of oral mucositis (OM).

OBJECTIVE: In order to prove these findings, we performed a randomized study with WPC supplementation in patients undergoing Hematopoietic Stem Cell Transplantation (HSCT).

METHODS: A blind randomized study was conducted with patients undergoing HSCT at the UFJF University Hospital between January 2018 and June 2019. Patients received WPC (treatment group) or milk powder (control group) daily starting on the first day of conditioning chemotherapy until the end of neutropenia. The World Health Organization oral toxicity scale was used to assess the degree of oral mucositis, and adverse events were graded according to the National Cancer Institute criteria. All patients underwent mucositis prevention protocols using low-intensity laser therapy (1J / cm2).

RESULTS: Forty patients were randomized, with no difference between treatment and control groups for the main factors that may influence the occurrence of mucositis. The overall incidence of OM was 52.5% (n = 21). Of these 21 patients 40% (n = 8) were supplemented with WPC, and 65% (n = 13) were not (p = 0.2). Although without significant statistical difference (p = 0.179), there was three time more severe oral mucositis in the control group (60%, n = 6) in comparison to the patients receiving WPC (10%, n = 2).

CONCLUSIONS: Patients supplemented with WPC had three time less severe OM than who did not receive WPC.

Keywords: Mucositis. Whey protein concentrate. Hematopoietic stem cell transplantation.

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COGNITIVE ASPECTS AND QUALITY OF LIFE OF CHILDREN AND ADOLESCENTS WITH SICKLE CELL ANEMIA UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION: A LONGITUDINAL STUDY

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INTRODUCTION: Studies point to the need for research on the impact of treatments involving chemotherapy on cognitive aspects and quality of life of non-adult patients.

OBJECTIVE: To evaluate the quality of life and cognitive aspects of children and adolescents before and one year after Hematopoietic Stem Cell Transplantation (HSCT).

METHOD: This is a clinical research with a prospective longitudinal design. Collection was performed over a four-year period (considering the first evaluation). In this interval, 15 transplants were performed in patients in this age group, with three refusals to participate in the research. The sample then consisted of 12 patients, aged between 10 and 15 years (X=12.5, dp=1.9), seven males. The instruments used were: a questionnaire for socio-familiar and clinical characterization, a specific Quality of Life scale for children and adolescents (Pediatric Quality of Life: PedsQL) and cognitive assessment tests (Raven). Quality of life is measured from 0-100, and the closer to 100 the more preserved is the domain evaluated. Data were collected at the hospitalization for transplantation and then at the outpatient clinic. Data were quoted according to the recommendations of each technique, analyzed quantitatively and submitted to statistical treatment.

RESULTS: The results of the intellectual evaluation show that three participants have below average cognitive performance (and were behind in school schedule) and the others had average performance (five lower medians, four medians and three upper medians). Despite these indicators of intellectual difficulty, the school domain is not impaired, having scores close to those of the others. Regarding quality of life, the domains presented similar values pre-HCT, being the social one with the highest score. After the procedure all these domains showed significant improvement. The increased score for the physical domain (29.2 points) and the satisfaction expressed with social functioning (90.4) draw our attention, as can be seen in Table 1:

TABLE 1. Results of Quality of life domains before and after HSCT

Domain	Pré-HSCT		Pós-HSCT		
	M	SD	M	SD	P
Physical functioning	52,4	15,3	81,6	16,4	0,01
Emotional functioning	61,4	22,2	80,0	10,0	0,04
Social functioning	66,6	23,0	90,4	13,9	0,01
School functioning	59,0	14,2	79,9	8,4	0,01
General	59,8	26,4	82,9	18,3	-

CONCLUSION: The data show that most participants had average cognitive performance before HSCT and even those with impairment expressed contentment with school functioning. Quality of life improved after the procedure in all aspects. These data indicate that the gains from HSCT for children and adolescents with sickle cell anemia go beyond the recovery of physical health, reinforcing the relevance of this therapy for these patients.

Keywords: Quality of life. Sickle cell anemia. Hematopoietic stem cell transplantation.

SAFETY HUDDLE: EVALUATION OF THE IMPLEMENTATION OF A TOOL TO IMPROVE THE QUALITY OF ASSISTANCE IN A HEMATOPOIETIC STEM CELL TRANSPLANTATION INPATIENT UNIT

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INTRODUCTION: In 2017 the Institute for Healthcare Improvement proposed nine tools to increase patient's safety, one of them is the huddle tool which is a daily quick meeting aiming to recognize situations that may interfere with the healthcare quality and to prevent possible adverse events. The hematopoietic stem cell transplant (HSCT) inpatient unit is a complex environment of specialized assistance. The huddle tool can be an effective strategy to improve the quality of assistance, stimulating better interactions between the multidisciplinary team.

OBJECTIVES: To evaluate the implementation of the safety huddle tool (figure 1) in an HSCT inpatient unit.

METHODS: Prospective, observational, transversal, descriptive study, in an adult HSCT inpatient unit, from July-2021 to May-2022. Daily morning meetings were held from Monday to Friday following specific questions script about the last 24 hours events.

RESULTS: One hundred and fifty meetings were held, with average length of 5.19 minutes. At least a nurse and a doctor took part in 100% and 94% of the meetings, respectively; at least a nursing technician, a physiotherapist and a nutritionist in more than 70% of the meetings; a pharmacist in 60%; a psychologist and a dentist in 37% of meetings. In 100% of the meetings, it was found that the fall, phlebitis, and pressure injury risk management protocols were updated and implemented; no warning signs were observed in 93% of the days. Regarding the clinical aspects, 89% of the days, at least one patient was considered potentially critical, in 77% of the days there were one or more (≥1) febrile neutropenic with antibiotic, in 54% were ≥1 neutropenic without fever, in 38% ≥1 had fluid retention and weight gain, in 35% ≥1 hypertensive, in 16% ≥1 hypotensive and in 12% ≥1 hypoxemic using oxygen. Regarding therapies, procedures or protocols, in 72% of the days there were ≥1 transfusion, in 55% ≥1 premedication, and in 53% ≥1 received medications exclusively via central venous catheter. Regarding psychosocial aspects and mobility, 52% of the days ≥1 patient had some psychosocial problem, in 21% ≥1 had behavioral disturbance and in 29% ≥1 had some mobility deficit. In 29% of the meetings, some type of adverse event was identified, of those, in 25% of the days at least in one patient a device injury was observed and some medication error in ≥1 patient in 22% of the days. All adverse events were reported, contributing to failures identification and the implementation of assistance quality improvements.

CONCLUSION: The HSCT inpatient unit is an environment that requires a lot of attention and caution. With the presented results, it is possible to note that the tool has been effective to promptly identify and may mitigate possible faults, as well as cooperate for the techniques, processes, and institutional protocols improvements.

Keywords: HSCT. Nursing care. Prevention. Safety. Quality. Adverse events.

SAFETY HUDDLE		
Unidade: Unidade Internação TCTH	**Data: ____/____/_____**	**Tempo gasto: _____min**

• Equipe do Huddle: Nº Enfermeiros ____ Nº Técnicos de enfermagem: ____ Nº Fisioterapeutas: ____ Nº Nutricionistas: ____
Nº Médicos: ____ Nº Farmacêuticos: ____Nº Psicologo _____ Nº Odonto_____ Nº Residentes: Médicos ____ Enfermeiros _____ Fisio_____
• Número de leitos ocupados: • Número de leitos interditados: • Número de previsões de alta:

Questionamentos da equipe do huddle:	**Não**	**Sim**	**Quais?**
1. Paciente com gerenciamento de risco atualizado e implementado?			
2. Algum sinal de alerta?			
3.Pacientes para iniciar protocolo estão com alguma pendência, exame ou medicações pré?			( ) Pré TMO ( ) Outros ( ) Exames ( ) Medicações pré ( ) Problemas sociais
4. Pacientes críticos ou instáveis? Alguma conduta proposta?			
5. Alta			( ) Previsão de alta ( ) Plano de alta iniciado
6. Terapias, procedimentos, protocolos ou dispositivos de alto risco ou não habituais? (Listar o que precisa de intervenção)			( ) Transfusão ( ) História Alergia ( ) Med. Exclusiva CVC ( ) ATG ( ) Pré Medicação ( ) Reconst e diluições especiais ( ) VP - Puro ( ) Restrição hídrica ( ) CPH congeladas ( ) Outros _____
7. Insuficiência Renal e/ou hepática necessitando de ajuste de doses de medicações? Ajuste de dose pós diálise?			( ) Renal _____ ( ) Hepática _____
8. Alterações de comportamento, dependência, mobilidade prejudicada, funções mentais alteradas e/ou problemas sociais?			( ) Alterações de comportamento _____ ( ) Alta dependência _____ ( ) Deficit Mobilidade _____ ( ) Funções mentais alteradas _____ ( ) Problemas Sociais _____
9. Higiene oral			( ) Higiêne oral prejudicada ( ) Laserterapia prófilática ( ) Neutropênicos sem clorexedine prescrito ( ) Laserterapia tratamento ( ) Neutropênicos com clorexedine no quarto ( ) Mucosite ( ) OUTROS_____
10. Eventos adversos? Notificações? Total:_____ Notificados:_____			( ) Perda de dispositivo_____ ( ) Lesão _____ ( ) Erro de medicação_____ ( ) Flebite _____ ( ) Lesão por dispositivo_____ ( ) Queda_____ ( ) Atraso de tratamento_____ ( ) Dietas _____ ( ) Outros _____ _____
11. Problemas com infraestrutura , equipamentos, materiais ou medicamentos? Total:_____ Notificados:_____			( ) Bombas de infusão_____ ( ) Farmácia_____ ( ) Bombas de seringa_____ ( ) Hotelaria_____ ( ) Monitor_____ ( ) Ar_____ ( ) PC_____ ( ) Régua_____ ( ) Impressora_____ ( ) Sistemas_____ ( ) Outros_____ _____
12. Dieta			( ) Dificuldades de aceitação de dieta ( ) Má adesão suplementos ( ) Necessidade de alteração de dieta ( ) Progressão ( ) Desmame
13. Dispositivos invasivos			( ) Sinais flógisticos _____ ( ) Hemocultura _____ ( ) Risco de de flebite _____ ( ) Retirada de Cateter_____

OBSERVAÇÕES:

POTENTIAL APPLICATION OF ADDUCTOR POLLICIS MUSCLE THICKNESS IN PATIENTS WITH SKIN GRAFT VERSUS HOST DISEASE: INITIAL RESULTS

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INTRODUCTION: The adductor pollicis muscle is the only one that allows an adequate assessment of its thickness in a direct way, as it has a well-defined anatomical reference, with the potential to be reproduced by trained evaluators. It is an indicator of low cost and represents a sign of malnutrition, loss of working life as a result of various clinical and surgical conditions. Measurement values are considered suitable above 12 mm. Graft-versus-host disease (GVHD) is a frequent complication in patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT), affecting between 40 and 60% of transplant recipients. The skin is an organ frequently affected by GVHD, being characterized by several clinical manifestations that can progress to scarring, with significant impairment of movements and joints. In long-term follow-ups, indicators of nutritional status, such as adductor pollicis muscle thickness (APMT), and functionality, such as the handgrip strength (HAND) test are used, however, its application in patients with these characteristics needs to be further explored, considering the extent of skin involvement.

OBJECTIVE: to evaluate the behavior of functionality measures in patients who underwent allo-HSCT, comparing the groups with and without skin GVHD (sDEHC).

METHODOLOGY: a retrospective cross-sectional study, using data from electronic medical records such as: sex, age, diagnosis, APMT and HAND with CAAE approval: 28359220.9.0000.5440. The data showed normal distribution, were analyzed in the Minitab statistical software, with the application of T tests to compare the groups (patients with sGVHD and patients without GVHD) and a significance level of $p \leq 0.005$ was adopted.

RESULTS: Of the 37 patients evaluated, 22 had malignant disease and 12 patients developed sGVHD, 51% of the sample was female (n=19) and the mean age was 37 years (sd±11.7). The mean values of APMT and HAND in the sGVHD group were 16.3mm and 22kg and in the group without GVHD they were 15.0mm and 25.3kg, respectively. There was no statistical difference between the groups with sGVHD and without GVHD in terms of HAND (p=0.61) and APMT (p=0.33) measurements.

CONCLUSION: The APMT values without significant changes in the group with sGVHD indicate that this measure can be applied in patients with cutaneous involvement, without prejudice to its interpretation and correspondence with nutritional status. These findings can be reinforced through the application of the handgrip strength test, which does not suffer interference from the evaluators. The study suggests that APMT, an important indicator of functionality and nutritional status, can be safely applied in patients with GVHD skin involvement.

Keywords: Nutrition. Nutritional assessment. Graft versus host disease. Handgrip strength. Adductor pollicis muscle thickness.

PERIPHERALLY INSERTED CENTRAL VENOUS CATHETERS FOR HAEMATOPOIETIC STEM CELL TRANSPLANTATION: PRELIMINARY EXPERIENCE OF A TREATMENT CENTRE IN BRAZIL

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INTRODUCTION: The insertion of the peripherally inserted central catheters using the modified Seldinger technique and ultrasound technology, allows for safe central venous access for anti-cancer therapy, with a reduction in complications related to infection, and adverse events, as well as lower cost, greater device durability and ease of insertion.

OBJECTIVE: To report the experience of a bone marrow transplant unit with the use of a peripherally inserted central venous catheter for the infusion of hematopoietic stem cells.

METHODS: observational and descriptive study carried out in a teaching hospital in Campinas, Brazil, by consulting the database on the infusion of hematopoietic stem cells through the peripherally inserted central venous catheter. The database includes variables such as diagnosis, type and source of hematopoietic stem cells, number of bags prescribed, infusion time, catheter insertion date, insertion site characteristics, catheter patency, and flushing with saline during stem cell infusion. Results were presented using descriptive statistics, with absolute values and relative frequency for categorical variables, and mean, median and dispersion measures for numerical variables.

RESULTS: From November 9, 2020 to May 25, 2022, 69 infusions of hematopoietic stem cells were performed, of which 41 (59.4%) were autologous transplants, 18 (26.1%) were allogeneic and 10 (14.5%) transplants were haploidentical. Indications for transplantation were multiple myeloma (n=29, 42.0%), acute myeloid leukemia (n=13, 18.8%), Hodgkin's lymphoma (n=9, 13.1%), non-Hodgkin's lymphoma (n=4, 5.8%), acute lymphocytic leukemia (n=3, 4.3%), myelodysplastic syndromes (n=1, 1.5%) and others (n=10, 14.5%). Of the total infusions, 47 (68.1%) were performed through the peripherally inserted central venous catheter, 27 (57.4%) of them with a 5Fr calibre and double lumen, 19 (40.5%) with a 6Fr calibre double lumen and 1 (2.1%) single-lumen 5Fr. Peripherally inserted central catheters have inserted an average of 21.43 days (SD 52.07) before hematopoietic stem cell infusion, none of the patients had inflammatory signs at the insertion site, catheter flow was unchanged in 43 of them and reflux was present in all catheters. During infusion, 44 (93.6%) catheters did not show changes in flow and for 8 (17.4%) catheters, between one and three flushes with the saline solution were necessary to maintain catheter permeability. One hundred bags of hematopoietic stem cells were infused, 98 CPP cryopreserved, 1 CPP fresh and 1 bone marrow cryopreserved, with an mean volume of 196.8 ml (61 to 582 ml). The mean infusion time of the bags were 28,0 minutes (first bag), 24,7 minutes (second bag), 21,2 minutes (third bag), and 24,9 minutes (fourth bag).

CONCLUSION: The peripherally inserted central venous catheter appears to be an effective and safe device for the infusion of hematopoietic stem cells in the transplantation of patients with haematological diseases.

Keywords: Peripherally inserted central catheter. Haematopoietic Stem Cell Transplantation. Haematologic Diseases.

Financing: Nothing to declare.

EDUCATIONAL TECHNOLOGY: VIDEO USE AND DIDACTIC GAME ON PULSATILE FLUSHING AS A PERMANENT EDUCATION STRATEGY FOR NURSES OF THE BONE MARROW TRANSPLANT UNIT

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INTRODUCTION: Central venous catheter (CVC) is implanted in all patients undergoing Bone Marrow Transplantation (BMT). Post-implantation complications such as phlebitis, infiltrations, obstructions and infections result in its early removal(1). Flushing with pulsatile technique promotes whirling inside CVCs prevents mixing of incompatible medications, obstructions and biofilm formation in these devices[1]. This is a simple, low-cost technique with recognized effectiveness, but its implementation is not routine in many institutions and there is no standardization among professionals. Although flushing with 0.9% sodium chloride solution is recommended, transplant services still use 4,000 IU heparin solution to maintain the permeability of CVCs. The effectiveness of this solution is questioned and can cause coagulation disorders in patients[2].

OBJECTIVE: Produce teaching material and to describe the preliminary results of the standardization of the pulsatil flushing technique and the use of 0.9% sodium chloride for the maintenance of CVC permeability in BMT patients.

METHOD: Digital educational material on pulsatile flushing with 0.9% sodium chloride was elaborated contemplating six stages: conversation with nurses and identification of the main doubts related to the procedure; preparation of the script of the videos according to the technical work instruction of the institution[3]; authorization of the patient, by signing a Free and Informed Consent Form, for filming actual scenes of the procedure, in accordance with resolution 466/12[4]; recording and editing of videos; creation of a quiz on a digital platform, with 10 closed questions; validation of the material by nursing professionals who assist patients of BMT.

RESULTS: Three videos were produced, with an average duration of 2 minutes. The topics covered were: pulsatile flushing: technique, indications, volume and specificities; Pulsatile flushing after change of CVC connectors and after CVC fluid collection. Nurses and nursing technicians were trained using videos and online game, with space for discussion of questions in twenty minutes. The materials were made available for professionals to access later. The professionals were instructed to report the occurrence of CVC obstructions in patients with BMT. During thirty days after the educational action obstructions of CVCs did not occur and an economy was obtained in 824 reais with the non-use of heparin to maintain the CVC.

CONCLUSION: The use of videos and the quiz for the training of the nursing team resulted in the absence of obstruction of CVCs of patients of B,T and reduction of institutional costs. The maintenance of CVCs is the responsibility of nurses and nursing technicians, and adequate knowledge about the pulsatile flushing technique is relevant, given the impacts of device-related complications in patients undergoing BMT.

Keywords: Bone Marrow Transplant. Educational Technology. Catheter-Related Infections.

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HISTOCOMPATIBILITY

THE HOMOZYGOSIS CHALLENGE IN NGS: RISKS AND PROPOSED SOLUTIONS.

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2 CareDx Pty Ltd , Fremantle, Australia.

INTRODUCTION: One of histocompatibility labs' challenges is distinguishing between true and false HLA homozygosity. It may be due to an allelic dropout (PCR artefact) or an immune escape mechanism in hematologic cancers. Strategies to avoid mistyping include confirming results on patient buccal swabs, retesting with another methodology or using a linkage disequilibrium approach. Hybrid capture (HC) is a complementary target-enrichment strategy for Next Generation Sequencing (NGS) library preparation that promises to reduce allele dropout. HC also allows the assessment of gene copy number using Assign CopyNumber tool, whereby individual samples were normalized for the read count and per locus read allocation compared to expected mean values.

OBJECTIVE: To calculate the frequency of homozygous samples in our lab, confirm the absence of dropouts in HC assay and validate a new copy number tool.

METHODS: We typed 521 samples from January to May of 2022 using AlloSeq Tx17 kit (CareDx Inc., AU) and genotypes were assigned with AlloSeq Assign software v.1.0.2 (CareDx). Homozygosity at HLA-A, -B or -DRB1 were confirmed using PCR-SSO (One Lambda Inc., California). Hemizygosity and nullizygosity were assessed using HLA-DRB3,-DRB4 and -DRB5 genes.

RESULTS: A rate of 10,2% of homozygosity was detected in HLA-A, 4,6% in HLA-B and 6,9% in HLA-DRB1, all of them (100%) were confirmed using PCR-SSO and copy number tool (mean predicted gene dose: 1,96, 1,98 and 2,05 respectively). HLA-C, -DQB1 and -DPB1 had 6,5%, 11,5% and 14,6% of homozygosity respectively, also confirmed by Assing CopyNumber tool (1,96, 2,02 and 1,99 respectively). The mean gene copy number and standard deviation (SD) were similar between homozygous and heterozygous samples as exemplified in HLA-A (1,96, SD 0,1 x 1,98, SD 0,1), HLA-B (1,98, SD 0,09 x 1,98, SD 0,11) and HLA-DRB1 (2,05, SD 0,14 x 2,00, S.D. 0,14). The accuracy to identify hemizygosity was confirmed in 301 samples that express only one copy of HLA-DRB3 (1,00, SD 0,1), -DRB4 (1,01, SD 0,04) and –DRB5 (0,99, SD 0,02) and in 14 nullizygous samples (0,05, SD 0,13). Interestingly, the predicted gene dose boxplot showed 19 outliers in hemizygous DRB3 group and 18 of them were positive to DRB1*08 genotype. Therefore, the DRB3 allocation in those samples is due to sequence homology between those genes/alleles.

CONCLUSION: No allelic dropout was detected, which validates both the tool to confirm zygosity and the success of the enrichment strategy with biotinylated probes. Combination of HC with copy number tool makes retyping required only on samples with read counts outside the normal range, which reduces costs and turnaround-time of the test. In patients with active disease, erroneous homozygosity occurs by duplication of a chromosomal segment originate from one parent, so retesting with buccal swab or typing parents are still mandatory. The accuracy of HLA homozygosity is essential to avoid transplants with unknown mismatched donor.

FIGURE 1. **Homozygosity prevalence in HLA-A, -B, and -DRB1 loci in a cohort of 521 samples.**

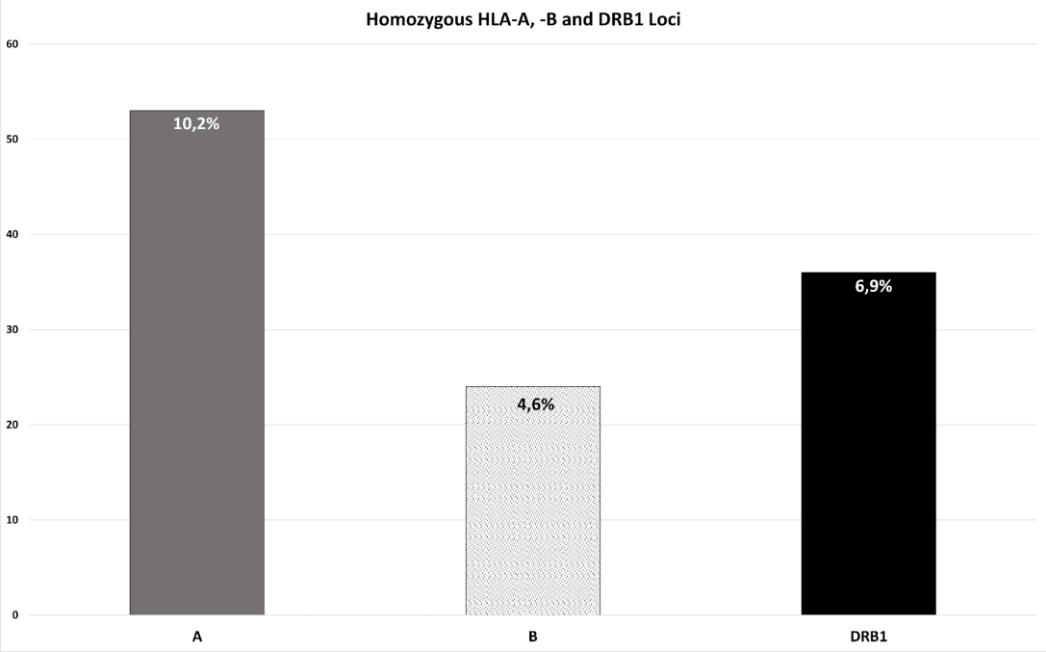


FIGURE 2. **Homozygosity prevalence in HLA-C, -DQB1, and -DPB1 loci in a cohort of 521 samples.**

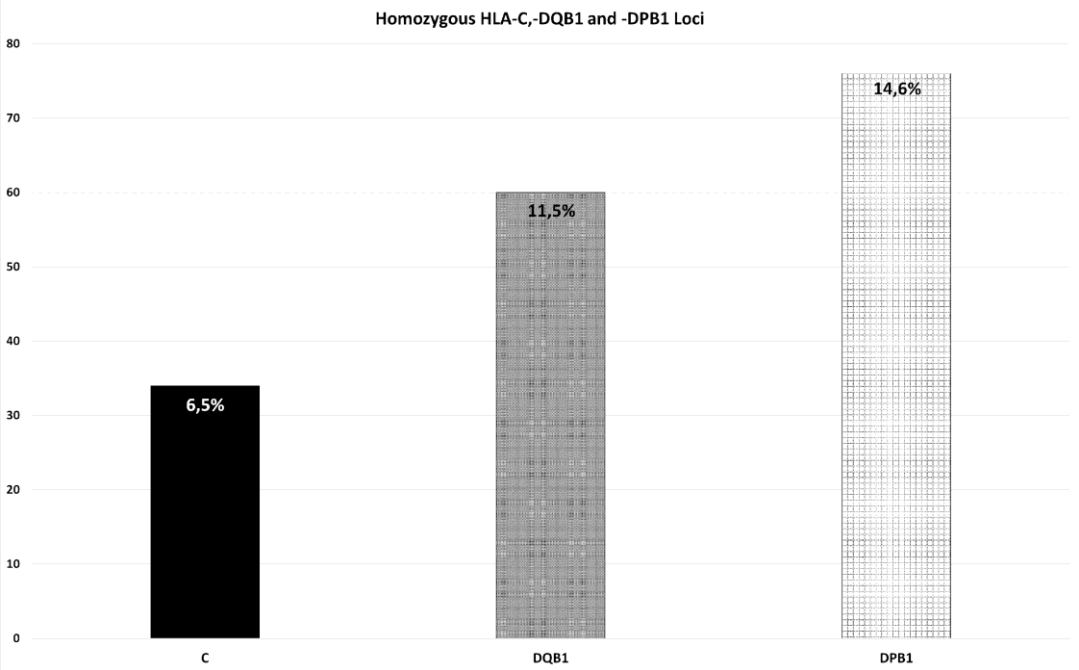


FIGURE 3. Copy number gene plot (all samples): HLA-A, -B and -DRB1 gene zygosity (expected allele zygosity, x-axis) versus predicted copy number (calculated from hybrid capture read allocation (y-axis)). Calculated gene dosage of homozygous and heterozygous samples were not distinctly different.

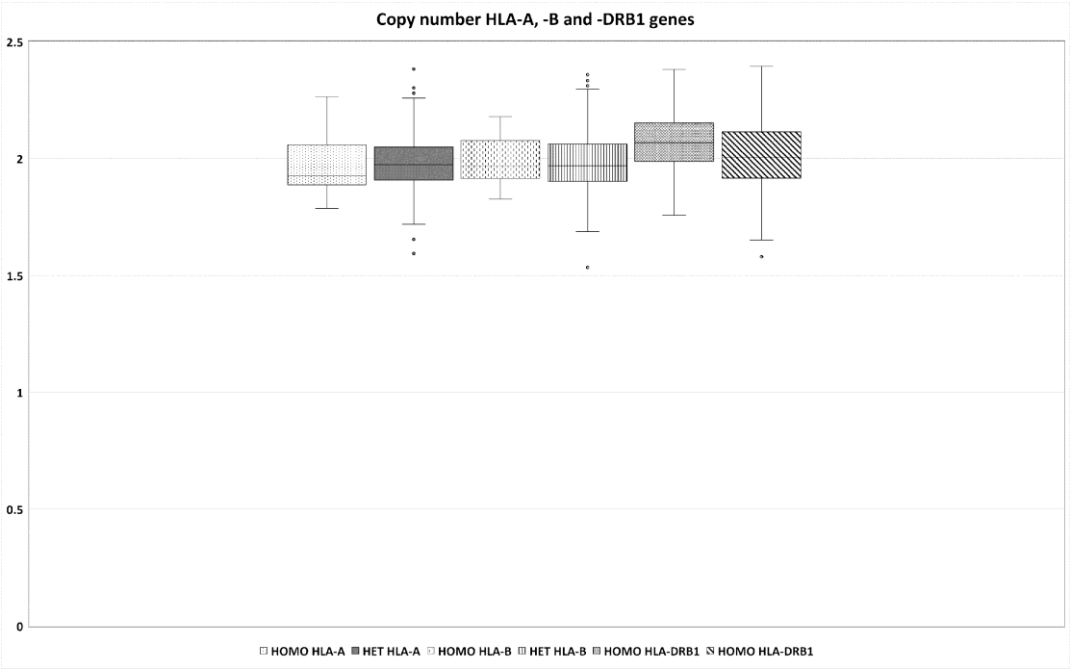


FIGURE 4. Copy number gene plot (all samples): HLA-C, -DQB1 and -DPB1 gene zygosity (expected allele zygosity, x-axis) versus predicted copy number (calculated from hybrid capture read allocation (y-axis)). Calculated gene dosage of homozygous and heterozygous samples were not distinctly different.

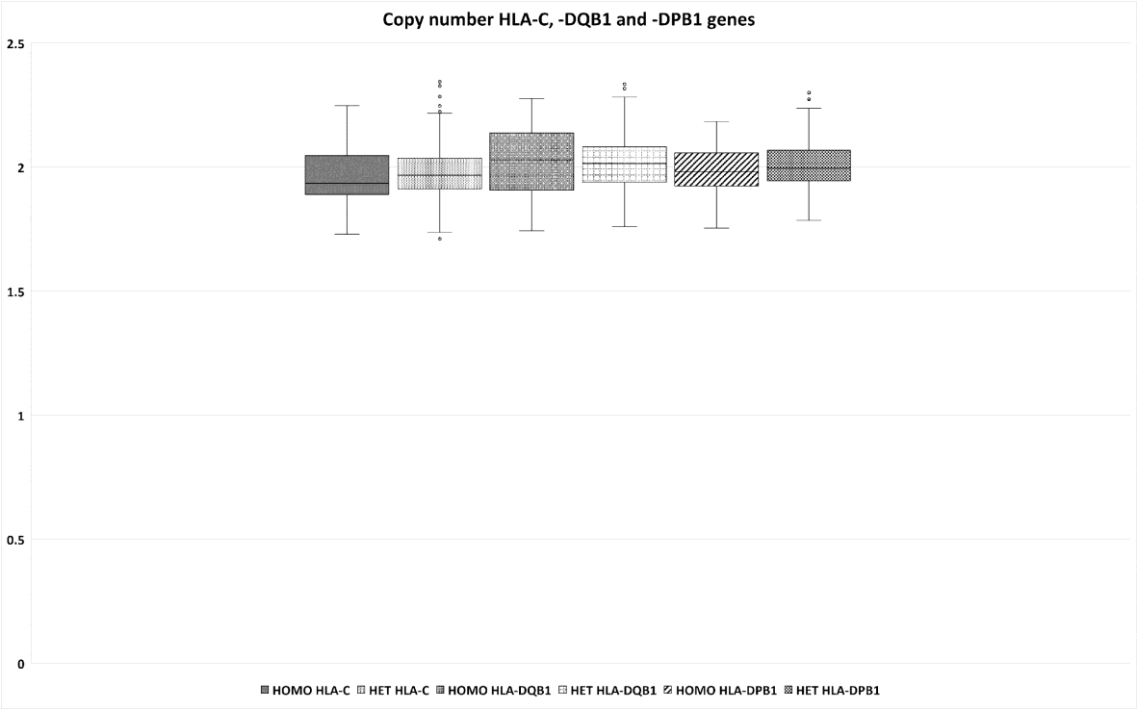
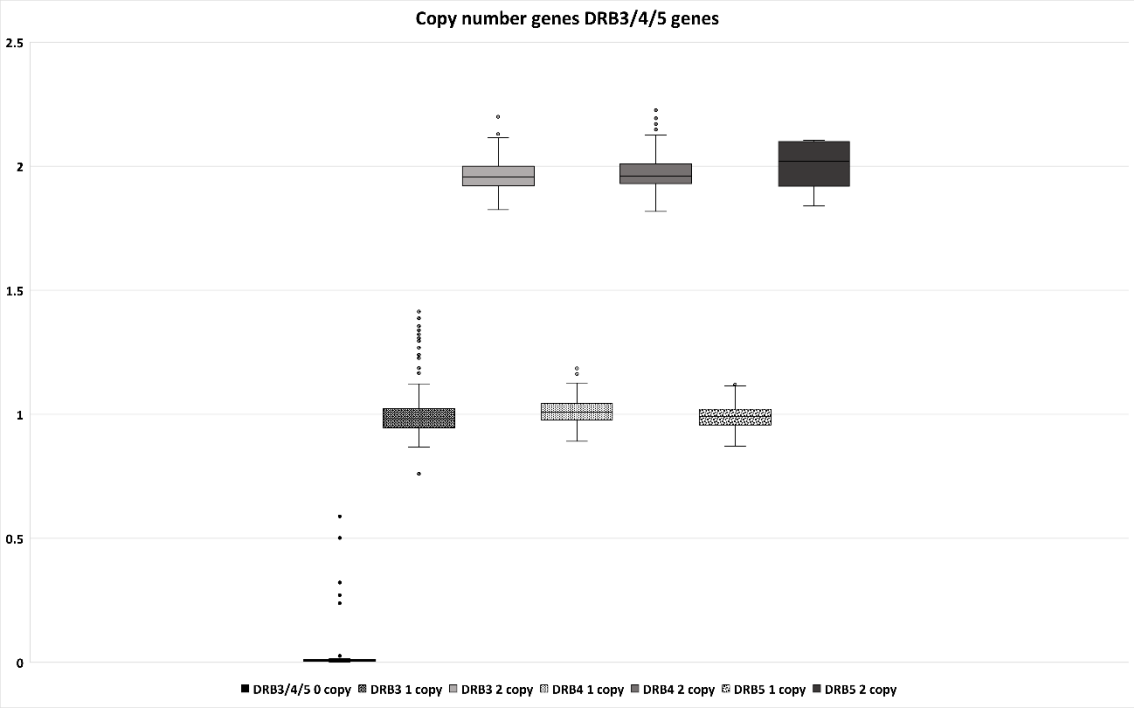


FIGURE 5. **Gene dosage plot (all samples): DRB3/4/5 Genotype zygosity (expected allele zygosity, x-axis) versus predicted gene dose (calculated from hybrid capture read allocation (y-axis)). Homozygous and hemizygous samples did not overlap.**



HLA LOSS DETECTION WITH NGS: A CASE REPORT

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INTRODUCTION: HLA loss has been described as a de novo genomic loss of the human leukocyte antigen (HLA) haplotype, mismatched between patient and donor. Pathogenesis is described replacing the "lost" haplotype with a corresponding region from the homologous chromosome, known as acquired partial uniparental disomy, and therefore, there is no copy-number variation. Chromossome abnormalities can complicate analysis of microsatellite chimerism by reducing informative loci, so checking cytogenetics studies can help to select markers unaffected by copy number changes. The detection of the HLA loss can alter therapeutic decisions, because DLI (donor leukocyte infusions) may not be effective. If HLA loss is demonstrated, a second transplant from a donor that has the other family haplotype, mismatched to the blasts, may provide the desired graft-versus-leukemia (GVL) effect and a realistic chance of curing these patients.

AIM: To report a case of HLA loss detected by Next Generation Sequencing (NGS) assay.

METHODS: HLA typing was performed by NGS using AlloSeq Tx17® kit (CareDx Inc.). Genotypes were assigned with AlloSeq Assing ®software v.1.0.2 (CareDx). Gene copy number was evaluated by Assing Copy Number tool®(CareDx). Chimerism detection was performed by PCR–STR (Polymerase Chain Reaction – Short Tandem Repeats) using the GlobalFiler Amplification Kit (Thermo-Fisher), followed by capillary electrophoresis and automated analyzes were performed with Chimer Marker Software (Softgenetics).

CASE REPORT: A 12-year-old girl diagnosed with high-risk acute lymphocytic leukemia in September 2017, underwent HCT from her haplo brother in March 2021 in first refractory relapse. She relapsed again one year later with 98% marrow blasts and complex karyotype. We first performed chimerism analysis which showed absence of donor genetic material and loss of one pre-transplant allele in 13 of 24 loci analysed (chromossome regions: 3p21.31, 12p13.31, 5q33.3-34, 18q21.33, 19q12, 4q28, 22q12.3, 13q22-31, 7q11.21-22, 10q26.3, 1q42.2, 12p13.2 and 2q35). HLA typing by NGS confirmed HLA loss and it showed homozygosity of haplotype shared with her donor (HLA-A*11:01, -B*08:01, -C*07:01, -DRB1*03:01, -DQB1*02:01, -DPB1*104:01) and loss of mismatched haplotype (HLA-A*11:01, -B*40:01-C*03:04, -DRB1*04:04, -DQB1*03:02, -DPB1*06:01). As expected, read count toll confirmed maintenance of predicted mean gene dose of the sample without deletions on HLA region. The patient underwent a second HCT from her father and was just discharged in remission one month post-HCT.

CONCLUSION: The detection of HLA loss in the reported case allowed a better donor selection for retransplantation and avoided possible ineffective treatments. Assing copy number tool® was essential to exclude allelic dropout as the mechanism of homozigosity.

Finally, further studies testing more samples with variable chimeras are essential to validate an algorithm with NGS methodology for HLA loss testing.

FIGURE 1. PCR-STR: Electropherogram of pre- and post-relapse blue dye markers showing loss of an allele on several chromosomes.

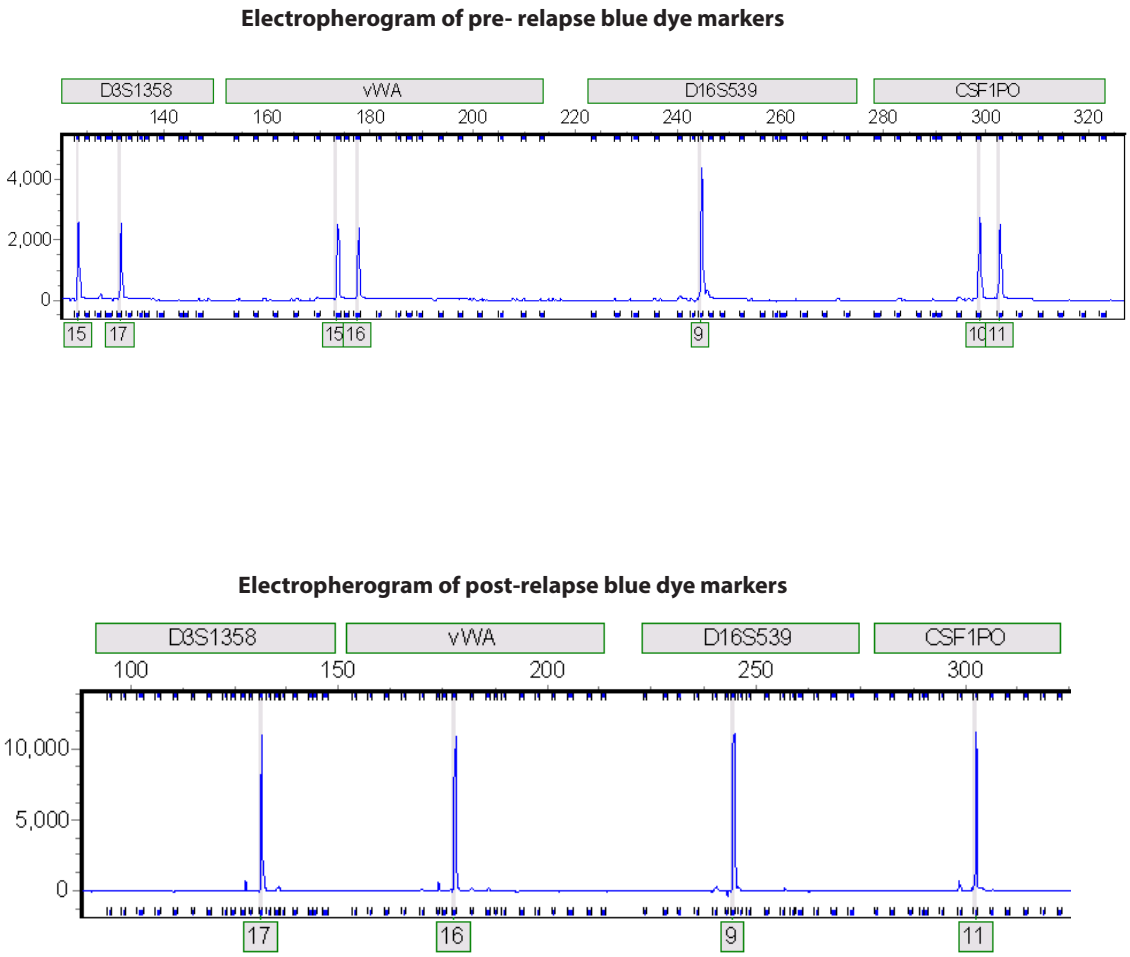


FIGURE 2. Assing copy number tool® confirming homozigosity across HLA-A, -B, -C, - DQB1, -DRB1 and -DPB1 loci in the loss HLA sample without predicted gene dose reduction.

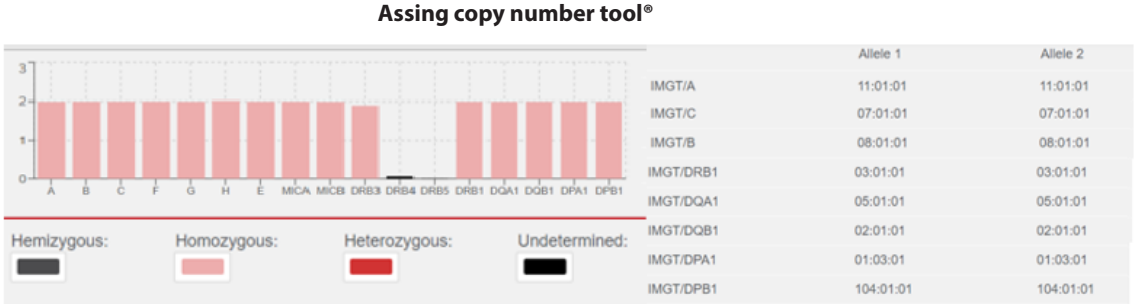
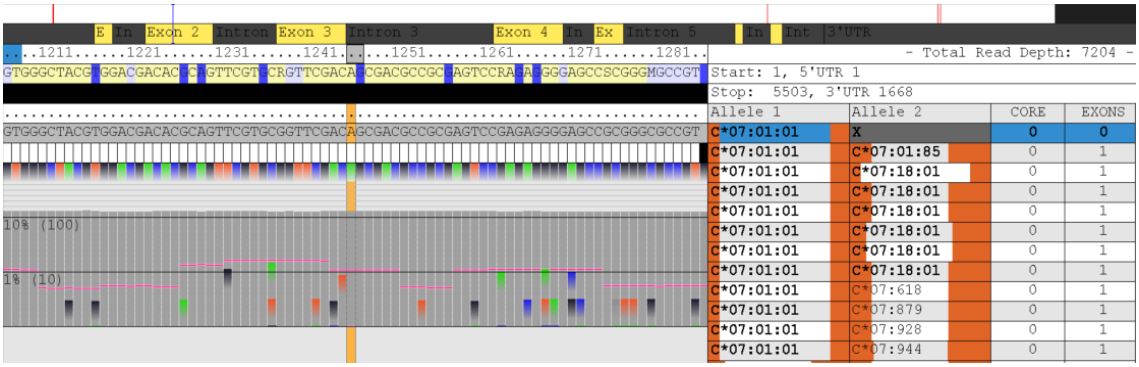


FIGURE 3. **AlloSeq Assing ® result showing no background or noises on homozygous results in post relapse sample.**

AlloSeq Assing ®software



VALIDATION OF HLA GENES COPY NUMBER DETERMINATION FROM NEXT GENERATION SEQUENCING HYBRID CAPTURE TARGET ENRICHMENT DATA

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2 Laboratório de Imunologia dos Transplantes, Hospital de Amor, Barretos, Brasil

INTRODUCTION: Next generation sequencing (NGS) platforms have taken Sanger sequencing's place as the choice methodology to perform clinical high-resolution HLA genotyping. However, NGS have brought new challenges to laboratory staff like allele dropouts, easily misinterpreted as homozygous calls, increasing the risk of HLA mismatching and poor transplant prognosis. Established classical HLA allele linkage information is a valuable tool to detect dropouts but relies on observations from different populations, often with typing resolution lower than that obtained by NGS. A reliable tool to investigate the number of copies sequenced for each HLA gene might reduce the risk of undetected allele dropouts. We propose an approach to distinguish hemizygous and homozygous calls on NGS data.

OBJECTIVE: Validate HLA genes copy number detection through read balance calculation from hybrid capture NGS data.

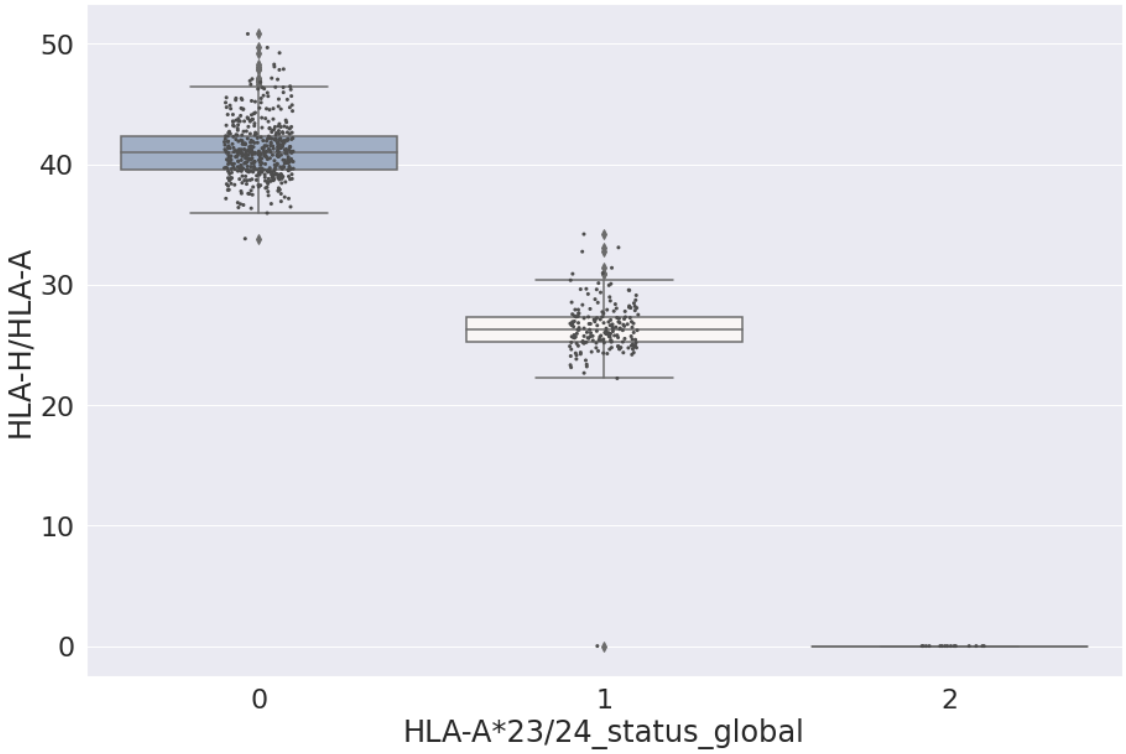
CASUISTIC: 815 bone marrow donor and recipient candidates.

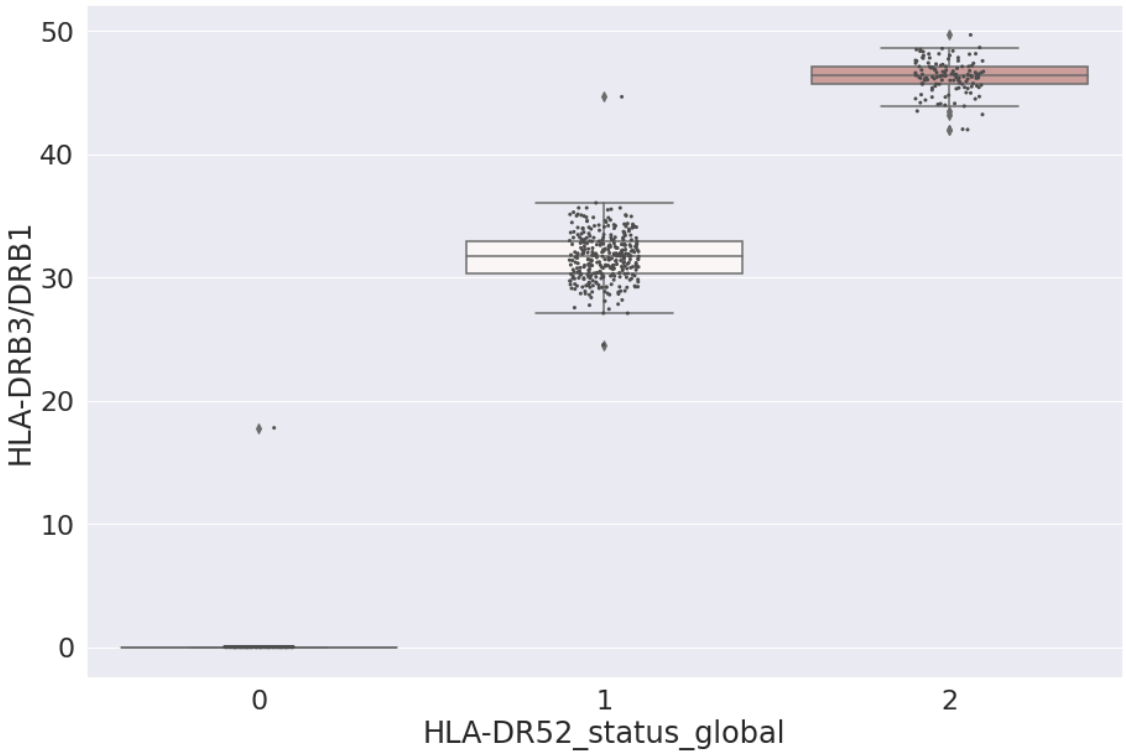
METHODS: DNA sample isolation and hybrid capture target enrichment/library preparation for 17 HLA genes was performed according to manufacturer instructions (Maxwell Blood, Promega; AlloSeq, Caredx®). FastQ files were analyzed using custom protocol on HLA Twin software (Omixon®, Budapeste) to obtain HLA genotyping and read count for each gene. Samples with total read count lower than 150k were excluded. To investigate read count-based metrics able to distinguish HLA genes copy number variations, already described zygosity variation on class I (HLA-H) and II (-DRB3,4,5) regions were analyzed through read balance ratios calculation. For HLA-H and -DRB3,4,5 copy number estimation, samples were divided in 03 groups according to the number of allele copies (0,1,2) for HLA-A*23/24 allele or HLA-DR51/52/53 haplotypes.

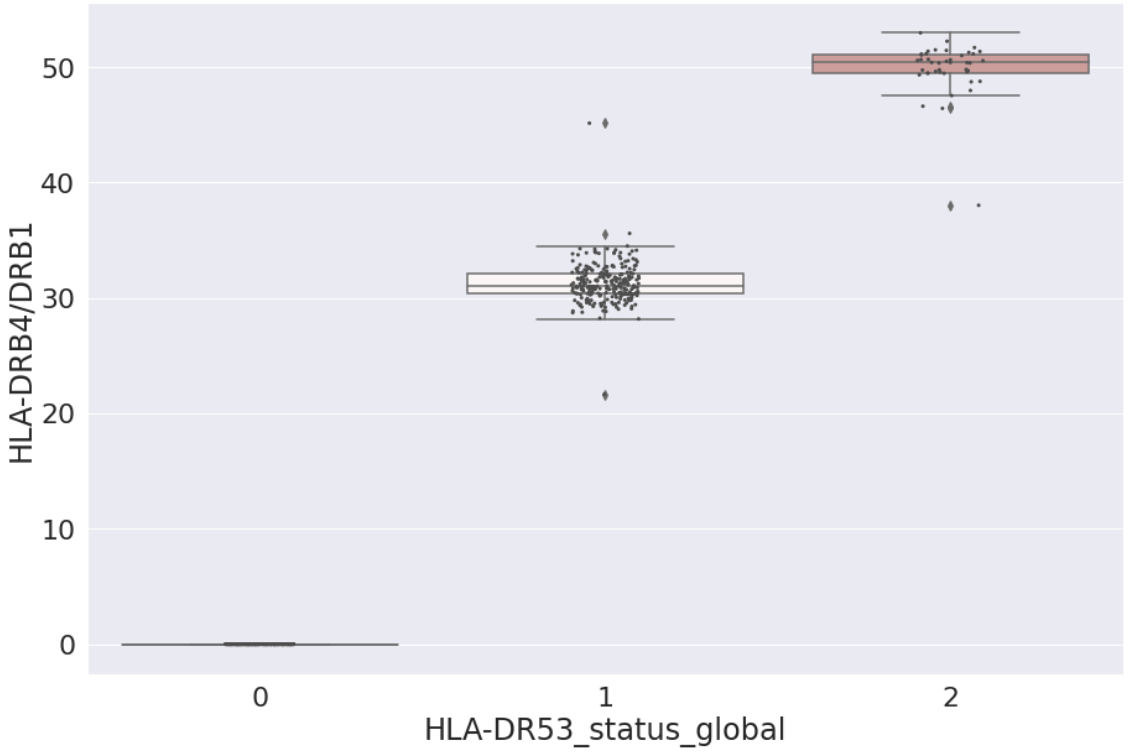
RESULTS: Sample groups showing none (485), only 1(193), or 2 HLA-A*23/24 allele copies (15) could be separated by H/A ratio cutoffs >35%, 20-35%, 0, confirming expected sequenced HLA-H allele copy counts 02, 01 and none, respectively. DR51, DR52 and DR53 respective groups cutoffs were determined (DRB3 [0]: 0, [1]: 24-33%, [2]: >42%; DRB4 [0]: 0, [1]: 30-33%, [2]: >45%; DRB5 [0]: 0, [1]: 24-33%, [2]: >42%). For 14 out of 693 samples (1%) unexpected typing-ratio correspondence was detected, being 09 samples associated to low quality data and 05 were rare DRB1-DRB5 associations. For one of the unexpected associations, DRB5/DRB1 ratio was compatible to DR51 one-copy only group (34.6%). However, associated HLA genoytpe for this sample is DRB1*15:03:01, DRB5*01:01:01 suggestive of possible DRB1 homozygous and unexpected DRB5 hemizygosity, only detectable by DRB5/DRB1 lower than normal ratio.

CONCLUSIONS: Our data sugests that read count ratios H/A and DRB3-4-5/DRB1 can be applied to confirm common and detect rare HLA allele copy number variations for HLA-H, -DRB3/4/5 genes. Further investigations are needed to study possible impacts on transplant matching and application on clinical typing challenging scenarios.

Keywords: High-Throughput Nucleotide Sequencing. HLA Antigens. Data analysis. Homozygote, Hemizygote. HLA-DR beta-Chains. HLA-A Antigens. HLA-H


HLA-H/HLA-A
50
40
30
20
10
0
0
1
2
HLA-A*23/24_status_global


HLA-DRB3/DRB1
50
40
30
20
10
0
0
1
2
HLA-DR52_status_global


HLA-DRB4/DRB1
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40
30
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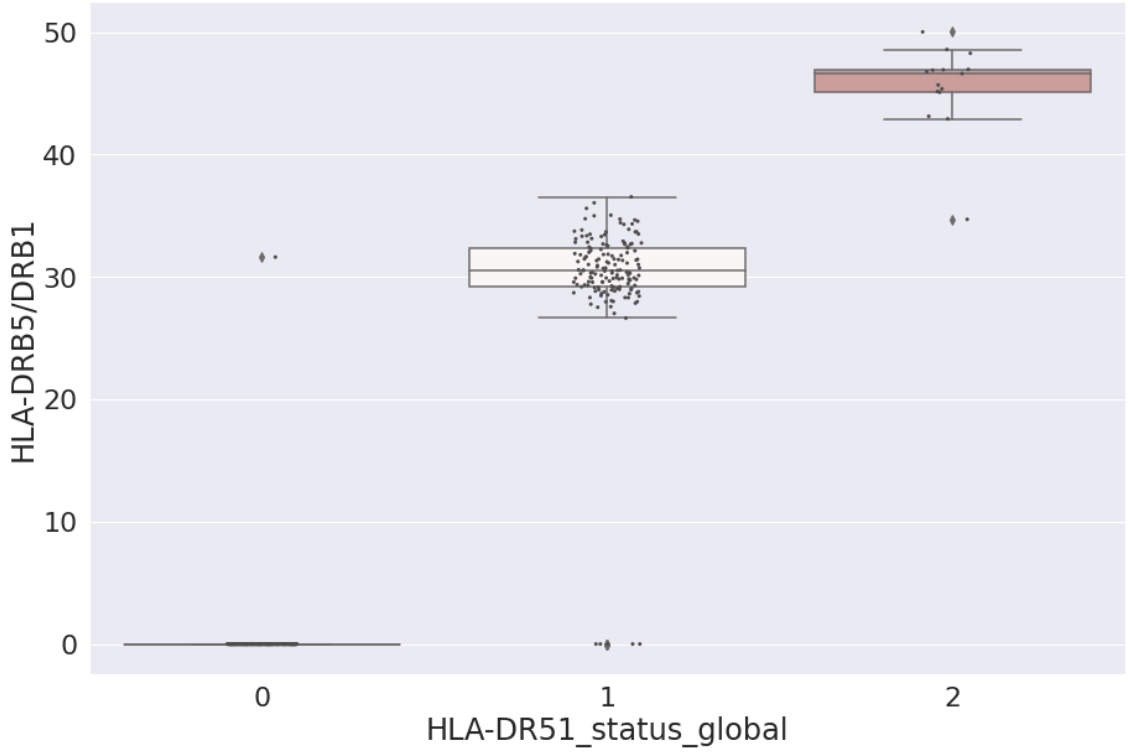
HLA-DR53_status_global


HLA-DRB5/DRB1
50
40
30
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2
HLA-DR51_status_global

CHROMOSOMAL DELETION REVEALED BY SHORT TANDEM REPEATS MARKERS AFTER BONE MARROW TRANSPLANTATION IN ACUTE MYELOID LEUKEMIA PATIENT

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Post-transplant chimerism analysis using short tandem repeats (STR) is a useful tool to monitor patient and donor cell levels after hematopoietic stem cells (HSCs) but demands careful analysis. Among the challenges of the analysis is the suppression of STR alleles already known from an individual, observed in post-transplant samples, which may be related to chromosomal deletions. This work aimed to investigate a case of changes in the STR alleles pattern in a post-transplant peripheral blood sample during relapse. In this report, a 61-year-old male patient diagnosed with acute myeloid leukemia underwent haploidentical transplantation with his daughter in 2021 after fludarabine 150 mg/mm2 + busulfan 9.6 mg/kg conditioning. The analysis of 15 STR loci was performed by multiplex PCR, followed by capillary electrophoresis and interpretation using GeneMapper (v. 6.0) software. The pre-transplant sample was collected in December 2021 and showed alleles 12 and 13 at marker D5S818 and alleles 10 and 11 at marker CSF1PO. The first post-transplant analysis was performed on D+31 and showed 98% donor cells. As expected, the electropherogram of STR markers showed alleles and balanced height peaks for donor cell engraftment. A new evaluation was performed on D+59 and showed autologous recovery, with only 1% of the donor cells. This sample showed an imbalance in the height peak between alleles 12 (RFU = 4,018) and 13 (RFU = 310) of marker D5S818, as well as alleles 10 (RFU = 258) and 11 (RFU = 2,874) of marker CSF1PO. Immunophenotypic analysis by flow cytometry of bone marrow and peripheral blood on D+59 showed 7% and 14.3% of blast cells with an altered myeloid lineage maturation pattern, respectively. In the bone marrow karyotype, 14 metaphases were analyzed, and several cytogenetic alterations were observed: 42~46,XY-,inv(2)(p24q21),add(3)(q29),del(5)(q?21),-6,del(9)(q2?),-12,-17,+mar1,+mar2,+mar3,inc[cp14], including the deletion of the long arm of chromosome 5, where markers D5S818 and CSF1PO are found. In this context, it was possible to conclude that the low detection of allele 13 in D5S818 and allele 10 in CSF1PO was due to the deletion of the long arm of chromosome 5, which is present in relapse cells. Deletion in 5q is one of the most frequent chromosomal alterations found in myeloid malignancies. The careful evaluation of chimerism analysis using STR markers allows the recognition of evidence that leads to the investigation of possible chromosomal deletions and consequently alerts to disease relapse.

Keywords: STR markers.Post-transplant chimerism. Chromosomal deletion.

POSTER

ALOGENEIC HSCT

ADDITION OF GDP CHEMOTHERAPY TO NIVOLUMAB AFTER NIVOLUMAB MONOTHERAPY FAILURE AS A BRIDGE TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT IN PATIENTS WITH CLASSIC HODGKIN LYMPHOMA: THREE CASE REPORTS

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INTRODUCTION: Treatment of patients with refractory and relapsed (R/R) classic Hodgkin lymphoma (HL) who fail anti-PD-1 targeted T-cell checkpoint inhibitors' monotherapy is challenging. The addition of conventional chemotherapy to anti-PD-1 drugs has been studied as an option in these cases, with promising results. There are no relevant published scientific data about the concomitant use of GDP (gemcitabine, cisplatin and dexamethasone) and nivolumab as a bridge to allogeneic hematopoietic stem cell transplant (HSCT).

OBJECTIVE: To report 3 clinical cases of GDP pretreated R/R classic HL patients who lost response to nivolumab monotherapy and were rescued by the addition of GDP to nivolumab as a bridge to allogeneic HSCT.

METHODS: Retrospective review of the patient's medical records.

RESULTS: P1: Female, 33 years, clinical staging (CS) IVB, obtained complete response (CR) after 8 ABVD. Patient's disease relapsed 4 months after the end of first-line therapy and was treated with 6 GDP, being achieved partial response (PR). Afterwards, the patient sustained the same response after 5 MINE and was submitted to autologous HSCT, followed by brentuximab vedotin (BV) consolidation. The disease progressed 4 months after HSCT and was rescued by nivolumab monotherapy, evolving with new progression 28 months later. Subsequently, the patient achieved CR to 4 GDP in addition to nivolumab. Then, she underwent reduced intensity conditioning (RIC) haploidentical allogeneic HSCT, but died 14 days later, due to septic and cardiogenic shock.

P2: Female, 26 years, CS IIA, obtained CR after 6 ABVD. Patient's disease relapsed 18 months later, achieving PR to 3 ICE, followed by autologous HSCT. New recurrence was identified 17 months later and was unsuccessfully treated with BV for 8 months. Then, the patient was treated for 13 months with nivolumab monotherapy, when the disease progressed again. Afterwards, she underwent 6 GDP in addition to nivolumab, achieving a PR and was submitted to RIC HLA-identical sibling allogeneic HSCT. She is in remission 10 months after transplant.

P3: Male, 25 years, CS IIB, was primarily refractory to 6 AVD and persisted refractory to 2 DHAP, 3 GDP and 2 ICE. Then, the patient was treated with BV during 8 months, evolving with new disease progression. Subsequently, he has no response to nivolumab monotherapy, during 3 months, but achieved CR after 2 GDP plus Nivolumab. Afterwards, he performed RIC allogeneic HLA-identical sibling HSCT and persists in remission 2 months after transplant.

CONCLUSION: Our report suggests a synergistic effect of concomitant nivolumab and GDP therapies to the treatment of R/R HL patients previously exposed to both regimens separately. All 3 patients obtained favorable disease status remission allowing allogeneic HSCT. Clinical trials are needed to corroborate the benefit of this association, as well as to determine which chemotherapy regimen and anti-PD1 drug combination would provide better outcomes.

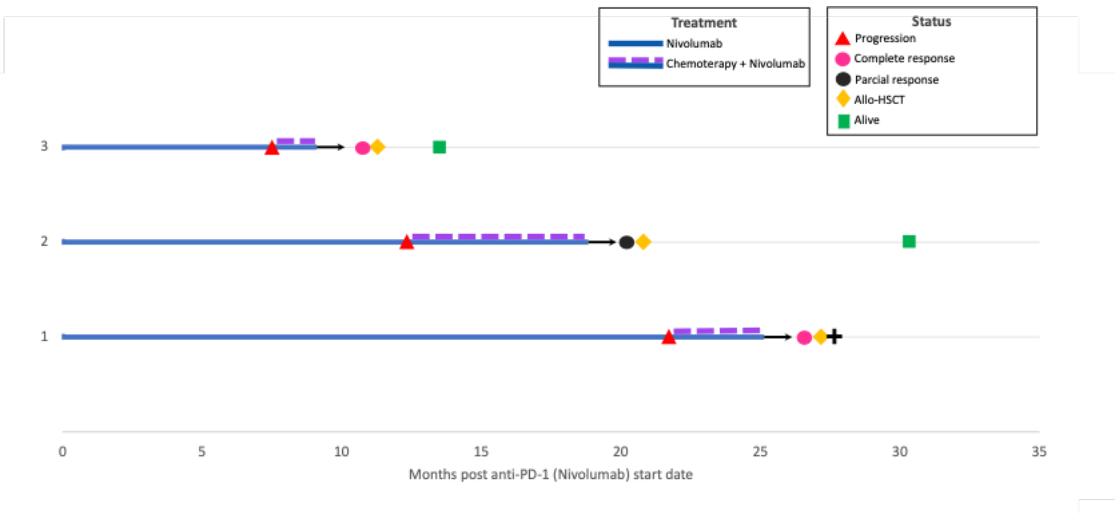
Keywords: Hodgkin Lymphoma. Immune Checkpoint Inhibitors. Nivolumab. Chemotherapy. Hematopoietic Stem Transplantation.

TABLE 1. Patient characteristics and treatments performed.

Feature	Case 1	Case 2	Case 3
Age	33 years	26 years	25 years
Sex	Female	Female	Male
Staging at diagnosis	IVB	IIA	IIBx
1st Line CT	8 x ABVD	6 x ABVD	6 x AVD
Status After 1st line	CR	CR	Refractory
Time to relapse	4 months	18 months	-
Staging at recurrence	IIB	ND	-
2nd Line CT	6 x GDP	3 x ICE	2 x DHAP
Status	PR	PR	Refractory
Subsequent Lines	5 x MINE	-	3 x GDP + 2 x ICE
Status	SD	-	Progression
Brentuximab	ND	ND	12 cycles
ASCT	Yes	Yes	No
Status before ASCT	SD	PR	-
Consolidation with BV	Yes	No	-
Time of disease's progression after ASCT	4 months	17 months	Refractory
BV in relapse after ASCT	4 cycles	12 cycles	-
Nivolumab in monotherapy			
Time of use	28 months	13 months	3 months
Time to recurrence after Nivolumab	28 months	13 months	Refractory
Complications	No	No	No
	Nivolumab + GDP		
Dose	480mg every 4 weeks	3mg/kg every 2 weeks	3mg/kg every 2 weeks
Cycles	4x Nivo + GDP	6x Nivo + GDP	2x Nivo + GDP
Complications	No	No	Pulmonary sepsis
Status	CR	PR	CR
	Allogeneic HSCT		
Age	38	33	29
Donor	HLA-haploidentical sibling	HLA-identical sibling	HLA-identical sibling
Source of stem cells	PB	PB	PB
Conditioning regimen	Flu160Mel100TBI4	Flu120Bu6,4TBI4	Flu120Mel140
GVHD prophylaxis	PTCy, CSA e MMF	PTCy, CSA e MMF	PTCy, CSA e MMF
Complications	Septic and cardiogenic shock	Parotitis	G2 cutaneous GVHD
Last follow-up (months after alloSCT) and response	Dead D+14	10 months, Remission	2 months, Remission

ABVD: Doxorubicin + Bleomycin + Vinblastine and Dacarbazine, AVD: Doxorubicin + Vinblastine and Dacarbazine, GDP: Gemcitabine + Cisplatin + Dexamethasone, ICE: Ifosfamide + Carboplatin + Etoposide, DHAP: Cisplatin + Cytarabine + Dexamethasone, MINE: Mitoxantrone + Ifosfamide + Etoposide, FluMelTBI: Fludarabine + Melphalan + Total Body Irradiation, FluBuTBI: Fludarabine + Busulfan + Total Body Irradiation, FluMel: Fludarabine + Melphalan, PTCy: post-transplant-cyclophosphamide, CSA: cyclosporine, MMF: mycophenolate mofetil, CT: chemotherapy, ASCT: autologous stem cell transplantation, PB: peripheral blood, HSCT: allogeneic hematopoietic stem cell transplantation, PR: Partial Response, CR: complete response, SD: Stable Disease, ND: not done.

FIGURE 1. **Swimmer plot. Patient response to GDP plus nivolumab, after nivolumab monotherapy. Each line represents one patient.**



CLINICAL-DEMOGRAPHIC PROFILE OF PATIENTS WITH ACUTE MYELOID LEUKEMIA AND RELAPSED MYELODYSPLASTIC SYNDROME AFTER ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION.

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INTRODUCTION: Allogeneic hematopoietic stem cell transplantation (HSCT) is the therapy with the best curative potential for patients with intermediate/high-risk acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS)[1]. Post-transplant recurrence occurs in a considerable number of cases, around 30% of patients relapse 3 to 6 months after allogeneic HSCT, and the mortality rate is 70% for relapsed AML patients [2]. These data reflect the difficulty in the management of relapsed AML after HSCT. Treatment options for post-transplant relapse include chemotherapy, hypomethylanting agents, donor lymphocyte infusion (DLI), and second allogeneic HSCT. Despite this, the prognosis is still unfavorable, especially in patients with early relapse[3]. It is estimated that the overall survival at 2 years post-HSCT relapsed AML is less than 20%, regardless of the rescue therapy instituted[3].

OBJECTIVE: The study aimed to evaluate the clinical-demographic profile and outcome of patients with disease recurrence treated with allogeneic HSCT for high-risk MDS and intermediate/high-risk AML. METHODS: This is a retrospective, single-center study conducted in a private institution in Brazil from January 2016 to May 2022. All patients who relapsed after HSCT for high-risk MDS and intermediate/high-risk AML were included. Overall survival curves were built with the Kaplan-Meier method.

RESULTS: Twenty-four patients relapsed after HSCT during this period, 79% were AML patients. There was a slight predominance in males (54%) and a mean age of 55 years at the diagnosis of relapse. Forty-one percent had undergone related transplantation, 25% haploidentical donor HSCT; 79% received reduced-intensity conditioning; and 66% of the grafts were peripheral blood progenitor cells. The median relapse time after HSCT was 137 days, and the median chimerism at the diagnosis of relapse was 78%. The most instituted treatments were hypomethylating agents (62%) and DLI (45%), with or without other associated therapy. The rate of chronic graft-versus-host disease (GVHD) at relapse was 20%. The extramedullary disease was 20%, and the most prevalent site was the central nervous system. Survival one year after the diagnosis of recurrence was 33.5% (CI 17.6–63.6%).

CONCLUSION: It is known that patients with recurrence of disease after allogeneic HSCT for AML or MDS have a poor prognosis with high mortality rates. Our study had similar results to that of the literature, which describes 20% of survival after recurrence of the disease, despite the rescue therapies instituted. This fact reflects the need for further studies involving treatment and prevention of this occurrence.

Keywords: Allogeneic hematopoietic stem cell transplantation. Myelodysplastic Syndromes. Acute Myeloid Leukemia. Relapsed.

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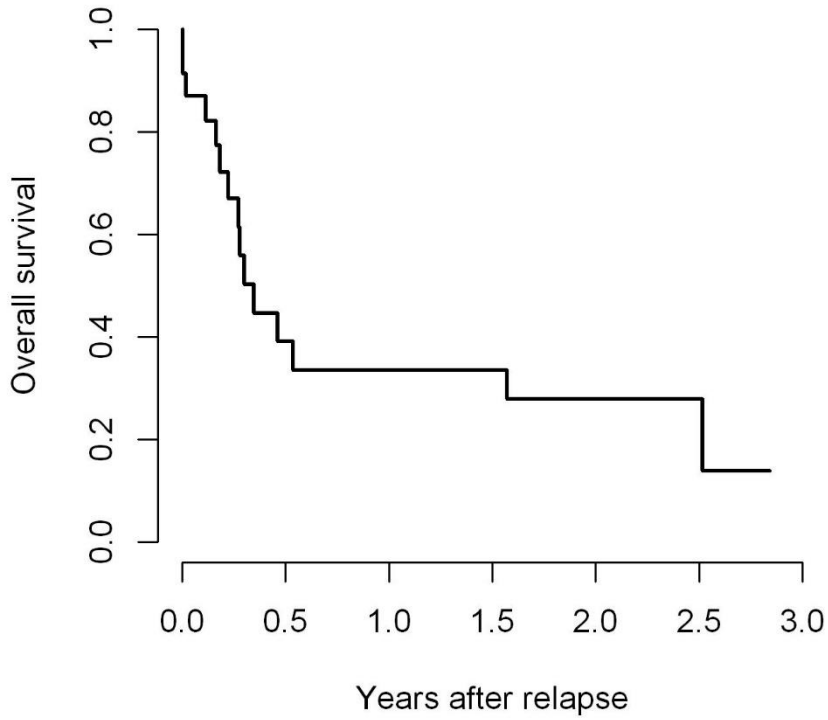
FIGURE 1. **Overall survival of patients after diagnosis of disease recurrence.**



COMPARISON BETWEEN POST-TRANSPLANT CYCLOPHOSPHAMIDE AND OTHER T DEPLETION STRATEGIES FOR BONE MARROW TRANSPLANTATION

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INTRODUCTION: Allogeneic Bone Marrow Transplantation (BMT) is the only curative therapy for several malignant and benign diseases. One of the main complications is graft-versus-host disease (GVHD). One of the strategies to reduce the risk of GVHD is the depletion of T cells in vivo, using alemtuzumab, antithymocyte globulin (ATG) and post-transplant cyclophosphamide (CyPT).

OBJECTIVE: To assess the impact of alemtuzumab, ATG, and CyPT use on HLA-identical (AP) and unrelated (NAP) allogeneic related BMT outcomes.

CASUISTRY: 31 participants, followed up for 10 months.

METHODS: Retrospective, unicentric and longitudinal cohort. Transplants performed between Jan/19 and Nov/21 were evaluated.

RESULTS: A total of 96 BMTs were performed in the period, 57 haploidentical and 8 benign cases were excluded. Thirty-one patients were analyzed, the median follow-up was 10 months. Overall survival was 72% for patients receiving CyPT and 64% for ATG/Alemtuzumab (A/A) (p=0.43). The cumulative incidence of grade III and IV acute GVHD was 5% for CyPT versus 9 % A/A (p=0.64).. Extensive chronic GVHD was 24% in patients who received CyPT versus 19% in the A/A group (p=0.63). Mortality not related to relapse of 27% for CyPT versus 22% for A/A (p=1). Relapse 20% versus 17% for CyPT versus A/A, respectively (p=0.82).

CONCLUSION: The data observed in our study suggest that the use of CyPT in the context of BMT AP and NAP is a safe strategy and comparable to other T-depletion strategies in vivo.

Keywords: Cyclophosphamide. Haploidentical. Allogeneic hematopoietic stem cell transplantation.

COMPARISON OF CLINICAL OUTCOMES BETWEEN IMMUNOSUPPRESSIVE THERAPY AND BONE MARROW TRANSPLANTATION IN PATIENTS WITH APLASTIC ANEMIA

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INTRODUCTION: Aplastic anemia (AA) is a rare disease that presents with cytopenias and a markedly hypocellular bone marrow. Its pathophysiology involves several factors not yet fully understood, but the immune destruction of hematopoietic precursors is an important factor. The treatment of AA consists of Immunosuppressive Therapy (IST) or Hematopoietic Stem Cell Transplantation (HSCT), and the choice depends on the patient's age and the availability of an HLA-identical donor among other criteria.

OBJECTIVE: to evaluate and compare the clinical outcome of patients undergoing IST and HSCT.

PATIENTS: patients with Aplastic Anemia (>15 years) and indication of treatment from January 2012 to August 2021.

METHOD: analysis, with data collection in electronic medical records, calculation of means, Standard Deviation and Kaplan-Meier curve, with analysis by log-rank test; and non-parametric statistics, using the t-test and log-rank test. Calculations performed using the program R-Studio version 1.3.959.

RESULTS: Fifty-two patients were analyzed, nine undergoing first-line HSCT (1LHSCT), and 43 undergoing first-line IST; of these, 14 underwent HSCT in a subsequent line. The median age at diagnosis was 32 (15-79) years. The mean time from diagnosis to treatment was 30 days for IST and 100 days for HSCT. The Overall Response (OR) rate to the first-line IST was 44.2% (39.5% PR), and of the non-responders, 25% died before new therapy. HSCT had 24% of Transplant-related Mortality (TRM), with no case of post-transplant relapse. The rate of acute Graft-versus-Host Disease (GVHD) was 23%, with no Grade III-IV aGVHD cases. The rate of chronic GVHD was 11%, with no cases of extensive cGVHD. Neutrophil engraftment occurred in 77% and platelet engraftment in 72%. Comparison of 1LHSCT versus IST showed Failure-Free Survival of 88% versus 38% (p=0.064) and Overall Survival (OS) of 88% versus 73% (p=0.48), and mean OS of 75%.

CONCLUSIONS: The choice of first-line treatment in AA is still complex and must be individualized. HSCT continues to have a better outcome when indicated in the 1st line of treatment than in subsequent lines. HSCT in AA has low levels of GVHD but still suffers from relatively high levels of graft failure and early mortality. The results with IST and HSCT have evolved substantially in the last few decades, especially using alternative donors. It is necessary to advance in the understanding of the pathophysiology of AA to the point of understanding the value and the most appropriate form of immunosuppression therapies. It is also necessary to carry out new studies considering the evolution of general HSCT and new IST treatments.

Keywords: Aplastic Anemia. Immunosuppressive therapy. Hematopoietic stem cell transplantation.

CURRENT TREATMENT OF APLASTIC ANEMIA: A MODERN BRAZILIAN COHORT STUDY FROM THE PAST 10 YEARS

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INTRODUCTION: Aplastic anemia (AA) is a potentially fatal bone marrow (BM) failure syndrome characterized by a paucity of hematopoietic stem cells and progenitor cells, with varying degrees of cytopenia and fatty infiltration of the BM space. Etiologies are varied, from iatrogeny, genetic lesions or immune-mediated processes. The course of AA can be complicated by the development of clonal disorders such as paroxysmal nocturnal hemoglobinuria (PNH), myelodysplastic syndrome (MDS) or acute myeloid leukemia. Diagnosis of AA requires a comprehensive approach with prompt evaluation for inherited and secondary causes of BM aplasia, while providing aggressive supportive care. The choice of frontline therapy is determined by several factors. The gold standard treatment is the hematopoietic stem cells transplantation (HSCT) with a match sibling donor (MSD). However, the therapy in older adult patients and in all patients lacking an MSD involves immunosuppressive therapy (IST). In the refractory setting of acquired AA, several therapeutic options exist, with improving outcomes of matched unrelated donor and haploidentical HSCT as well as the addition of eltrombopag.

OBJECTIVE: The goal of this study was to assess the clinical profile of patients with AA attended in our service, their treatment, response, and survival.

METHODS: Retrospective cohort study that included all patients with a diagnosis of AA at a Brazilian tertiary hospital, who were attended between January 2009 and December 2019. Demographics, exams at diagnosis, clinical features, treatment and evolution were analyzed through medical records analysis. A Kaplan-Meyer survival analysis was performed.

RESULTS: A total of 50 patients with acquired AA were diagnosed during the study period. Most of them had no known risk factor associated. The mean age of diagnosis was 30 years, there were no significant differences in gender prevalence. Only 1 patient had a previous diagnosis of PNH. Most patients were classified as having non severe AA. As frontline treatment, 37 patients were treated with IST and 9 underwent HSCT. At 6 months, 51% had a partial response with IST and the median time of use of cyclosporine was 11 months. All patients who underwent HSCT had at least a partial response and just one (2%) died of infectious complications. The most common complications at the HSCT group were graft versus host disease, fungal and cytomegalovirus infections. Of all patients studied, 16 died from central nervous system bleeding or serious infection. Conclusion: patients treated with HSCT had a shorter time of transfusion dependency compared to IST. Patients who were treated with HSCT as any line had a better survival than those who did not (P 0.021). AA, previously known as a fatal condition, is now much more understood and has a greater therapeutic arsenal; HSCT remains the only cure alternative with less risk of clonal evolution, but we can get great result with IST and alternatives donnors.

TABLE 1. **Criteria for response to IST in AA**

SAA/VSAA	
None	Still fulfill severe disease criteria
Partial	Transfusion independence No longer meet criteria for severe disease
Complete	Hemoglobin normal for age and gender Neutrophil count > 1500 micro/L Platelet count > 150 000 micro/L
NSAA	
None	Blood counts are worse, or do not meet criteria below:
Partial	Transfusion independence (if previously dependent) Doubling or normalization of at least one cell line Increase of baseline - Hemoglobin > 3 g/dL (if initially < 6) - Neutrophils > 500/microL (if initially < 500) - Platelets > 20 000/microL (if initially < 20 000)
Complete	Same criteria as for severe disease

Legends: IST immunosuppressive therapy; AA aplastic anemia; SAA severe aplastic anemia; VSAA very severe aplastic anemia; NSAA non-severe aplastic anemia.

TABLE 2. **Characteristics of patients at baseline with AA and the correlation with death and response ratio**

Characteristics	N = 50	Death	Response
Age – yr Median	30.7 ± 18.3	-	-
Age distribution – no. (%) < 20 20-40 > 40	 18 (36%) 20 (40%) 12 (24%)	P 0.011 P 0.003	P 0.026 P 0.012
Gender – no. (%) Female Male	 28 (56%) 22 (44%)	P 0.213	P 0.362
Race – no. (%) Caucasian Pardo Black Indian	 40 (80%) 4 (8%) 5 (10%) 1 (2%)	P 0.192	P 0.456

Comorbidities – no. (%) Cardiovascular disease Endocrinologic disease Neurologic disease Psychiatric disease Rheumatologic disease Non-hematological malignancy Gastrointestinal disease	 4 (8%) 3 (6%) 2 (4%) 2 (4%) 1 (2%) 1 (2%) 1 (2%)	-	-
Known risks factors Viral hepatitis Pregnancy Autoimmune hepatitis Use of anticonvulsants	5 (10%) 2 (4%) 1 (2%) 1 (2%) 1 (2%)	-	-
Severity of AA at diagnosis NSAA – no. (%) SAA – no. (%) VSAA – no. (%) Not classified – no. (%)	 22 (44%) 10 (20%) 11 (22%) 7 (14%)	P 0.185	P 0.181

The response was defined according to the treatment (IST or HSCT) and its severity, and it was considered having a positive response if it was partial or complete. The P value is for testing through Pearson Chi-Square the correlation between the patient's characteristics and evolution to death or response to the treatment.

Legends: NSAA non severe aplastic anemia; SAA severe aplastic anemia; VSAA very severe aplastic anemia.

TABLE 3. Exams at diagnosis of patients with aplastic anemia

Exam	N = 43
Hemoglobin Mean	 6.6 g/dL ± 2.1
Leucocytes count Mean	 2 266/microL ± 1211
Neutrophils count Median	 420/microL (800-870)
Platelets count Median	 14 000/microL (900-27 000)
Reticulocytes Mean	 31 687/microL ± 24 318
Reticulocytes distribution – no. (%) < 20 000 20 000-50 000 > 50 000	 16 (37%) 20 (46%) 7 (16%)
Size of PNH clone at diagnosis Neutrophil Median	 8.7% (2.6-18.7)
Monocyte Median	 9.9% (4.7-17.1)
Erythrocyte Mean	 3.4% ± 10.72

Legends: PNH paroxysmal nocturnal haemoglobinuria; FC flow cytometry

TABLE 4. **Treatment of patients with aplastic anemia**

First line	N = 46
CsA alone – no. (%) CsA + ATG – no. (%) MSD HSCT – no. (%) MUD HSCT – no. (%)	19 (41%) 18 (39%) 8 (17%) 1 (2%)
Second line	**N = 14**
CsA + ATG – no. (%) MSD HSCT – no. (%) MUD HSCT – no. (%) Haploidentical – no. (%) Eltrombopag – no. (%)	5 (35%) 2 (14%) 3 (21%) 2 (14%) 2 (14%)
Third line	**N = 4**
MSD HSCT – no. (%) MUD HSCT – no. (%) Haploidentical – no. (%) Eltrombopag – no. (%)	1 (25%) 1 (25%) 1 (25%) 1 (25%)

Legends: CsA cyclosporine A; ATG anti-thymocyte globulin; MSD match sibling donor; MUD match unrelated donor; HSCT hematopoietic stem cell transplant.

TABLE 5. **Death ratio and response to IST treatment in frontline or HCST at any point**

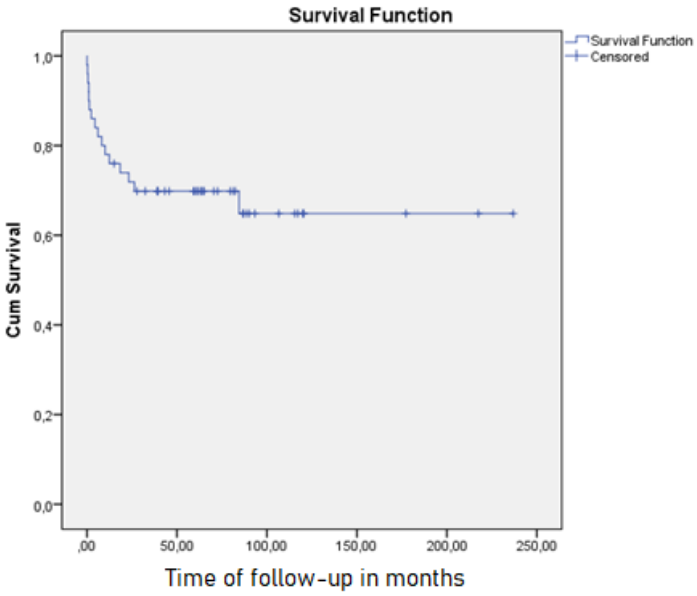
IST	N = 37	Death	Response
CsA alone CsA + ATG No response in 6 months – no. (%) Partial response in 6 months – no. (%) Complete response in 6 months – no. (%) Necessity of second line therapy – no. (%) Complications – no. (%)	 18 (48%) 19 (51%) 1 (2%) 12 (32%) 2 (5%)		
HSCT	**N = 18**		
MSD HSCT – no. (%) MUD HSCT – no. (%) Haploidentical HSCT – no. (%) Syngeneic HSCT – no. (%)	10 (55%) 5 (27%) 3 (16%) 1 (5%)		
Response in 30 days No response – no. (%) Partial response – no. (%) Complete response – no. (%)	 0 2 (11%) 16 (88%)		
Response in 6 months No response – no. (%) Partial response – no. (%) Complete response – no. (%)	 0 2 (18%) 9 (81%)		
Response in 12 months No response – no. (%) Partial response – no. (%) Complete response – no. (%)	 0 6 (35%) 11 (64%)		
Response in 5 years No response – no. (%) Partial response – no. (%) Complete response – no. (%)	 0 2 (18%) 9 (81%)		

The response was defined according to Table 2.
Legends: IST immunosuppressive treatment; CsA cyclosporine A; ATG anti-thymocyte globulin.

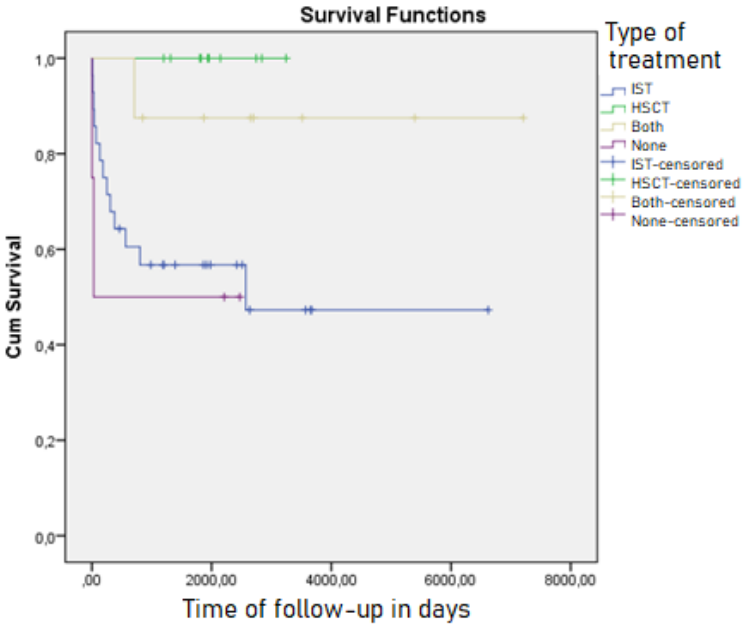
FIGURE 1. **Mean for survival time**

Mean[a]			
		95% Confidence Interval	
Estimate	Std. Error	Lower Bound	Upper Bound
160,190	15,996	128,838	191,542

a. Estimation is limited to the largest survival time if it is censored.

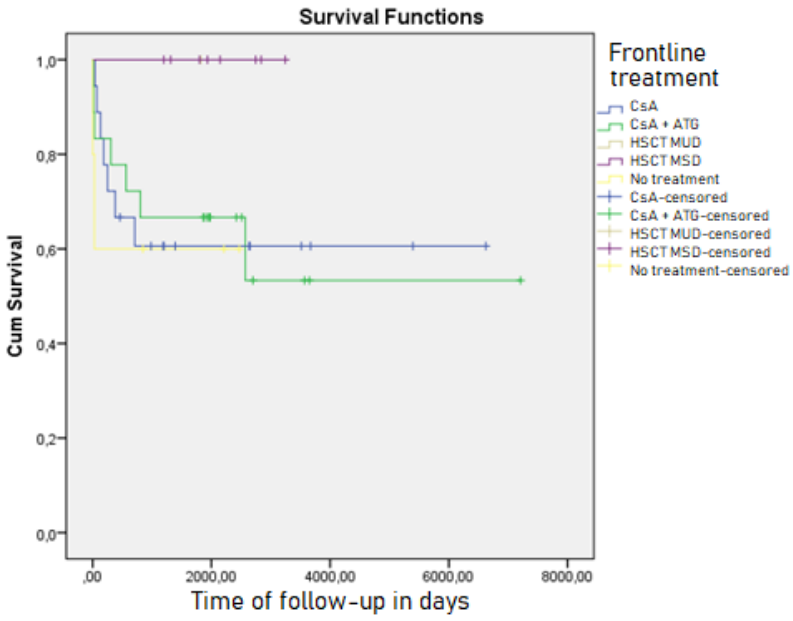


GRAPH 2. **Survival relation to treatment: IST, HSCT, both or none P value (Chi-Square) 0.021**



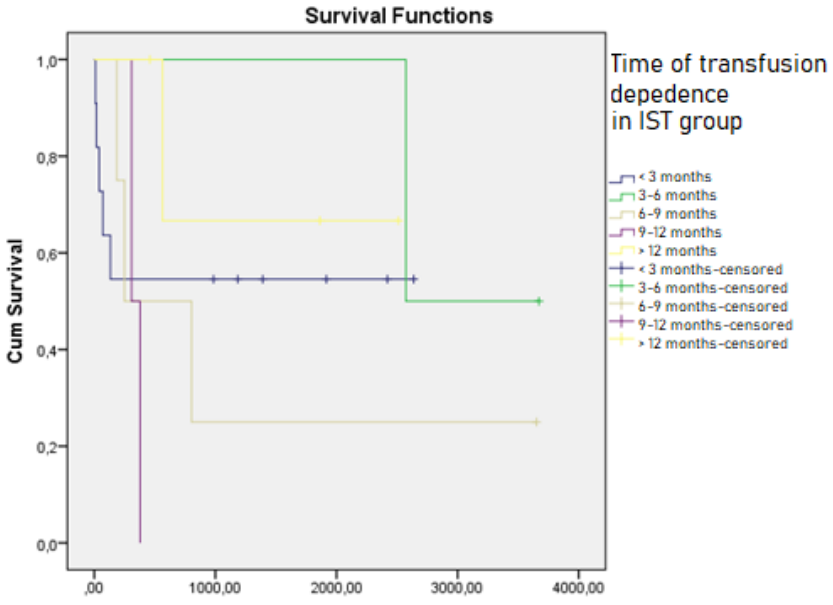
Legends: IST immunosuppressive treatment, HSCT hematopoietic stem cell transplant.

GRAPH 3. **Survival relation to the specific treatments P value (Chi-Square) 0.334**



Legends: CsA cyclosporine A; ATG anti-thymocyte globulin; HSCT hematopoietic stem cell transplant; MSD match sibling donor; MUD match unrelated donor.

GRAPH 4. **Survival and time (divided in months) of transfusion dependence on IST group P (Chi-Square) 0.587**



Legends: IST immunosuppressive treatment.

EARLY CARDIAC EVENTS FOLLOWING POST-TRANSPLANT CYCLOPHOSPHAMIDE IN ALLOGENEIC HEMATOPOEITIC STEM CELL TRANSPLANTATION.

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INTRODUCTION: The allogeneic hematopoietic stem cell transplantaition (HSCT) is still essential for many hematologic diseases. In the last decades, the incorporation of post-transplant cyclophosphamide (PTCy) has changed the field, facilitating haploidentical transplantation[1,2]. However, there is an association between PTCy and early cardiac events (ECE), those that happen within the first hundred days. A recent data showed cumulative incidences of 19% of ECE in the PTCy group versus 6% in control group[2], however, it may not increase in matched HSCT3. Then, risk factors and outcomes need to be more understood.

OBJECTIVE: This study aimed to understand incidence, risk factors, clinical features, and the impact in outcomes of cardiac events associated with PTCy.

METHODS: This is a retrospective single-center study of patients received PTCy, from April 2018 to May 2022, conducted in a private hospital in Brazil, including haploidentical and unrelated donors (UD) HSCT. Overall survival curves were built with the Kaplan-Meier method.

RESULTS: With a median follow-up of 1.3 years, 49 patients received PTCy (67.3% haploidentical and 32.7% MUD). The most prevalent hematological disease was acute myeloid leukemia (AML, 40.8%), followed by acute lymphoblastic leukemia (ALL, 16.3%). Seventy-one percent were males, and the mean age of patients was 48 years. Fifty-three percent received reduced-intensity conditioning; 63,3% received graft from peripheral blood stem cells. The incidence of cardiac events in the first year was 22.6% (95% CI 0.134-0.38), which had no impact in overall survival (OS). The most common ECE was arrythmia, followed by systolic disfunction, with 12.2% and 10.2% respectively. The only two risk factors found for ECE were previous allogeneic (HR 4.9, p=0.05) and autologous HSCT (HR 4.12, p=0.03). There was also a statistically significant but clinically irrelevant 3-point drop in the median of left ventricular ejection fraction after HSCT (p=0.03).

CONCLUSION: Our study showed an incidence of cardiac events in patients undergone PT-Cy similar to that already reported, but without impact in OS. Classical cardiovascular comorbidities and total body irradiation were not associated with an increased risk of cardiac events in our cohort. These results may corroborate the safety of PTCy and help to improve the selection of patients to HSCT with that strategy.

Keywords: Allogeneic stem cell transplantation. Cyclophosphamide. Cardiotoxicity.

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FIGURE 1. **Overall survival**

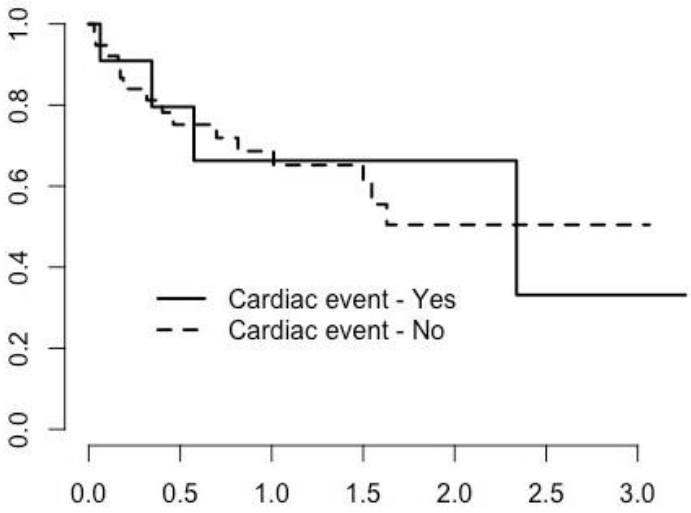
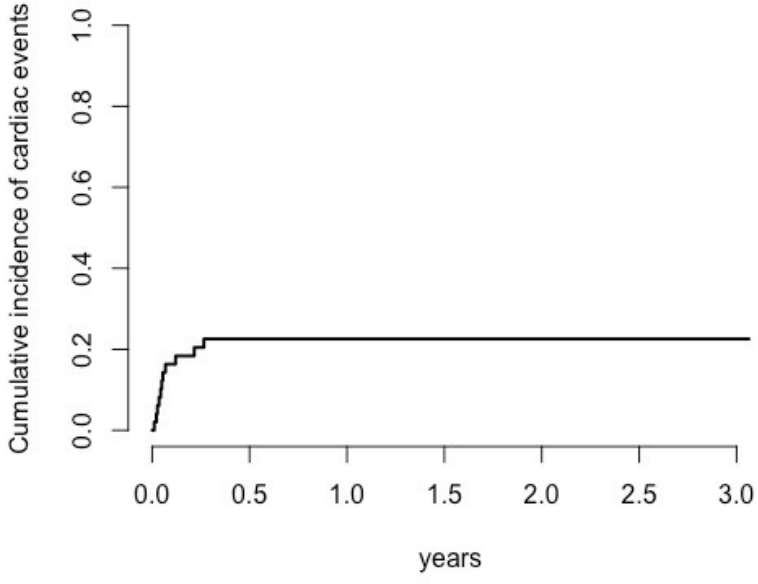


FIGURE 2. **Incidence of cardiac events**



ELTROMBOPAG FOR PRIMARY GRAFT FAILURE AFTER HAPLOIDENTICAL STEM CELL TRANSPLANTATION – A CASE REPORT

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INTRODUCTION: Primary graft failure (PGF) occurs in less than 3% of allogeneic HLA-matched stem cell transplantation. In haploidentical transplants, this rate reaches 10%. The overall survival of patients with PGF is less than 20% at 5 years. Once PGF is diagnosed, a second transplant is considered. After the second infusion, the engraftment rate is 70%, and the overall survival in 3 years is 30%. Eltrombopag emerged as an alternative treatment for poor graft function. It is believed that the drug has a stimulatory role on residual stem cells, promoting hematopoiesis recovery.

OBJECTIVE: To report a case of PGF in an elderly patient who underwent haploidentical transplantation and presented late grafting after the introduction of eltrombopag.

CASE REPORT: Male patient, 74 years old, previously treated with chemotherapy for colorectal adenocarcinoma, was diagnosed with myelodysplastic syndrome with excess blasts. He received treatment with azacitidine with a reduction OF transfusion requirement, but maintenance of cytopenias. He underwent a haploidentical stem cell graft from his 43-year-old daughter. The HLA antibodies were negative. The conditioning regimen was FluCyTBI (RIC), and 8.6x10e6 CD34 cells/kg from peripheral blood were infused. GVHD prophylaxis with cyclophosphamide on D+3 and +4, and with tacrolimus and mycophenolate from D+5 onwards was made. He received filgrastim from D+5 onwards, as well. On D+28, the neutrophils count was below 500 cells/mcL and the patient was requiring frequent platelets and red blood cells transfusions. A bone marrow study was performed on D+28 and showed hemodiluted myelogram, karyotype without metaphases, immunophenotyping without abnormalities, hypocellular bone marrow biopsy, chimerism with 100% allogeneic cells and the HLA antibodies remained negative. The PCR for Cytomegalovirus (CMV) was undetectable. These findings confirmed PGF. Then, the patient was listed for a public search of an unrelated stem cell donor. During this process, rescue therapy with eltrombopag was proposed to the patient and family, starting at a dose of 50mg/day (D+28) and progressively increasing to 100mg/day (D+31) and 150mg/day (D +34). At D+49, the neutrophils reached a count above 500 cells/mcL. New chimerism was performed, showing 100% of allogeneic DNA. On D+58, the patient received the last platelet transfusion, reaching platelet engraftment on D+65. The patient had CMV reactivation and started ganciclovir treatment on D+61. He was discharged on D+69 and finished treatment with ganciclovir at home. At the last follow-up evaluation on D+74, he had hemoglobin 7.4 g/dL, neutrophils 3610 cells/mcL and platelets 44000/mcL; he was tolerating ganciclovir therapy well with no need for blood transfusion.

CONCLUSION: This case shows the late grafting after the introduction of eltrombopag. This strategy can avoid morbidity and mortality associated with a second transplant by reducing the period of bone marrow aplasia and its inherent risks.

Keywords: Primary graft failure. Allogeneic transplantation. Haploidentical transplantation. Eltrombopag.

GRAFT-VERSUS-LEUKEMIA EFFECT INDUCES SPONTANEOUS COMPLETE REMISSION AFTER BONE MARROW TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA

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INTRODUCTION: In acute leukemias treated with hematopoietic stem cell transplantation (HSCT), spontaneous remission is quite rare and usually of short duration, and may be accompanied by restoration of donor hematopoiesis. It occurs mainly in the context of immune reactivation reflecting the graft-versus-leukemia (GVL) effect amidst a complex graft-versus-disease (GVHD) relationship. GVL has been previously described in retrospective studies as the disappearance of leukemic relapse after transplantation in the context of abrupt cyclosporine withdrawal or after donor leukocyte infusions (DLI). There are few published cases linking GVL to natural remission of acute myeloid leukemia (AML).

OBJECTIVE(S): to describe an AML-MDS patient who progressed with spontaneous complete remission during the development of moderate GVHD, despite not having restarted chemotherapy or other treatment.

CASE REPORT: AML-MDS 62-year-old patient with complex karyotype (44~49, XY, +8[11], +12[10], +19[3][CP15]) was treated with AraC+Danorrubicin (7+3), consolidation and FLAG, after which the patient presented prolonged neutropenia and infectious complications. Despite presence of 15.3% blasts at pre-HSCT evaluation, he received a HLA-matched sibling donor bone marrow, conditioning Bussulfan and Fludarabine. At D+44 he developed grade IV acute GVHD in skin and intestine, requiring systemic corticotherapy and Basiliximab. He also had cytomegalovirus reactivation treated with ganciclovir, C.difficile infection, and K.pneumoniae urinary infection. After treatment, the gastrointestinal symptoms and acute GVHD improved and D+100 chimerism was 99% donor cells. After 9 months he presented with pancytopenia, relapse of the disease (29.1% blasts) and complex karyotype (46~50, XY, +5, +8, +12, +15, +19, +21[CP22]). Cyclosporine was discontinued, but the patient developed chronic GVHD, and a lower limb deep venous thrombosis. Due to the severity of the skin and liver chronic GVHD and the persistence of blasts and dysplasia, we decided to maintain only palliative care at home. About six months after discharge, he surprisingly began to show improvement in the hematological counts, despite worsening disease in the liver, gastrointestinal tract, skin and eyes. Bone marrow re-evaluation at this time showed no blasts or dysplasia in morphology, normal cytogenetics, and chimerism 100% donor, establishing complete remission of the leukemia. Unfortunately, the patient developed respiratory failure and death due to coronavirus B19 infection. Bone marrow and hematologic evaluation remained normal.

CONCLUSION: Discontinuation of immunosuppression has been related to long-term complete remissions accompanied by chronic GVHD, suggesting the importance of the concomitant effect of GVL. A better understanding of the mechanisms of GVHD and GVL may be helpful in maximizing the benefits of HSCT in myeloid leukemias.

Keywords: Acute myeloid leukemia. Spontaneous remission. Bone marrow transplantation. Graft-versus-leukemia effect.

HEALTH EDUCATION IN A HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT: EXPERIENCE REPORT

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INTRODUCTION: Health education is a potential tool that makes visible the approach to health promotion, care, rehabilitation, and follow-up of patients with chronic health conditions in long-term treatments or that require outpatient follow-up. Thus, such actions aimed at patients undergoing Hematopoietic Stem Cell Transplantation and at their caregivers become essential to make them able to make decisions with a critical analysis of their reality and encourage them to seek of viable solutions regarding their treatment, as well as creating ties with the team to report doubts and clarifications.

OBJECTIVE: To describe the experience of planning and executing health education actions within an inpatient unit for Hematopoietic Stem Cell Transplantation.

METHOD: Experience report, with a descriptive qualitative approach, about health education actions carried out by nurses at a bone marrow transplant center in the State of Rio de Janeiro, Brazil. The actions are aimed at post-Hematopoietic Stem Cell Transplantation patients and their caregivers and have taken place since 2014. Due to the COVID-19 pandemic, there was an interruption of actions, resuming in April 2022. Prior to these, meetings are held with the nursing's management and team to plan activities and carry out a literature review about the care directed to the target population; elaboration of a roadmap for actions, in addition to complementary materials with guidelines for the non-hospital environment. Materials from official health agencies and references are used, such as: World Health Organization; Ministry of Health of Brazil; Center for Disease Control and Prevention; European Society for Blood and Marrow Transplantation; and Brazilian Bone Marrow Transplantation Society. The actions take place weekly for two hours and are mediated by a nurse, using educational technologies such as booklets and verbal and expository guidelines; the target population is previously invited by the team.

RESULTS: During the actions, prior knowledge about living with the illness, prognoses, and the meaning of HSCT linked to various obstacles is perceived. Some themes are recurrent: HSCT severity; reconstitution of the immune system; return to work activities; personal and home care; receiving visits; medications; food; revaccination and vaccination of the caregiver and family members; and sexuality.

CONCLUSIONS: Recognition of the knowledge brought by patients and caregivers is essential for carrying out educational actions, given that the demands of the target population also direct guided actions. In addition, the exchange of experiences is characterized as a mechanism for creating interpersonal relationships that consequently will focus on effective measures to be incorporated into the target population's daily routines.

Keywords: Hematopoietic stem cell transplantation. Educational technology. Nursing.

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA AND MYELODYSPLASTIC SYNDROME: A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Acute myeloid leukemia (AML) is a malignancy of stem cell precursors of the myeloid lineage, characterized by the infiltration of immature, proliferative and abnormally differentiated cells in the bone marrow, peripheral blood and other tissues. Myelodysplastic syndrome (MDS) is a disease with a heterogeneous clinical profile, characterized by clonal, dysplastic and ineffective hematopoiesis, with one or more cytopenias in peripheral blood. Hematopoietic stem cell transplantation (HSCT) is the only potentially curative treatment, when indicated, for these diseases.

OBJECTIVES: To evaluate the clinical-epidemiological profile of patients with AML and MDS who underwent HSCT in a single Brazilian center.

METHODS: Descriptive retrospective study, with data collection through patient charts. The population studied consisted of all patients who underwent HSCT, in a single Brazilian center, from February 2019 to February 2022.

RESULTS: In the proposed period, 71 HSCT were performed, 13 for MDS and 59 for AML. Among the HSCT for AML, three autologous and 56 allogeneic were performed. For patients with MDS, all HSCT performed were allogeneic. The median patients age at the time of transplant was 40 years. Of the patients with AML, 22 (37.3%) were in the first complete remission, and 37 (62.7%) were in the condition of greater than or equal to the second complete remission. Of the total allogeneic HSCT performed, 32 (47%) were matched related, 20 (29.4%) were haplo-identical and 16 (23.6%) were unrelated. The source of stem cells used was mostly obtained from peripheral blood, in 68 (95.7%) of the cases. Regarding the intensity of conditioning used, 27 (38%) were myeloablative, 37 (52%) were of reduced intensity conditioning (RIC) and 7 (10%) were non-myeloablative. As of May 2022, 28 (39.5%) patients had died, with 13/32 (40.6%) matched related, 7/20 (35%) haplo-identical and 7/16 (43.7%) unrelated. In addition, up to May 2022, 10 (14%) patients had relapsed of the underlying disease, with 6/32 (18.7%) matched related, 1/20 (5%) haplo-identical and 1/16 (6%) unrelated. Only 2 primary graft failures were identified, 1 in the context of haplo-identical HSCT and 1 in the autologous one.

CONCLUSIONS: It is observed, therefore, that the greatest demand for HSCT was for adult patients with AML, in most cases in second or greater complete remission. The majority of allogeneic cases performed were from identical related donors, followed by haplo-identical related and, finally, unrelated, reflecting the global growth of haplo-identical HSCT in recent years, in addition to the impacts of the COVID-19 pandemic on donor selection. The source of stem cells used was peripheral blood in almost all cases, with 14% of relapses and 39.5% of deaths identified up to May 2022. The highest rates of deaths occurred in the context of unrelated allogeneic HSCT and the highest relapse rates recorded in the context of identical related allogeneic HSCT.

Keywords: Hematopoietic stem cell transplantation. Acute myeloid leukemia. Myelodysplastic syndrome.

HOW AGE INFLUENCES THE OUTCOMES OF BONE MARROW TRANSPLANTATION IN PATIENTS FROM LATIN AMERICAN REGISTRY: RESULTS OF A MULTICENTRIC STUDY

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INTRODUCTION: Several issues can interfer the viability of hematopoietic stem cell transplantation (HSCT) for patients with Myelodysplastic Syndromes (MDS). For years, aging was a limitant factor. However, changes in conditioning regimen and other tools in the management of older patients is modifying this scenario. Objective: to investigate the influence of age on outcomes of HSCT in MDS patients.

METHODS: data of 341 patients in 32 centers of the Latin American Transplant Registry from 1989 to 2022 were analyzed. Subjects were stratified according to the age in to groups: < 50 years (1) and ≥ 50 years (2). Statistics were performed using SPSSv.23.1, considering a significant p<0.05.

RESULTS: most patients were ≥ 50 years (53,07%). In both groups, there was a predominance of males and Caucasians. Regarding to the Prognosis Scoring System (IPSS-R), in group 1 most patients were intermediate (n= 38; 41,3 %). In group 2 the predominance was high/very high risk (n= 51; 46,79 %). The frequency of high/very high risk in group 2 was significantly higher when compared to group 1 (p= 0,047; OR: 2,7; CI: 1,21 - 6,02). Myeloablative conditioning (MAC) was performed in 140 patients (85%) of group 1 and in 110 patients (61,45 %) of group 2. Reduced intensity/non-myeloablative regimen was the main regimen performed in group 2 (n=69; 38.5%); in group 1 it represented 11,9% of cases (n=19). This conditioning regime was significantly associated to group 2 (p< 0,001; OR: 4,62; CI: 2,62 - 8,14). In both groups Related donor type was predominant: (group1- n=95; 59,38 %; group 2- n=143;79,01 %). Group 2 presented a higher probability undergo to HSCT with a Related donor (p< 0,001;OR: 3,53; CI:2,03 - 6,14). The main cell source in group 1 was bone marrow (BM) (n=95; 59,38 %)) and in group 2 was peripheral blood (PB) (n= 95; 52,49 %). There was an association between the age and peripheral blood as cell source (p=0,009; OR: 1,78; CI: 1,15 - 2,75). The analysis of all patients showed post-HSCT complications in 260 (76,25%) and the most frequent was Infections (n= 212; 81,54%), followed by acute

graft versus host disease (GVHD) (n=121; 46,54%) and chronic GVHD (n=98; 37,69%). The frequency of death was 40,47% (n=138). There was no significant difference in 2 and 5 years overall survival for groups 1 and 2. Nonetheless, according to Cox regression patients aged > 50 years had 1.55 times risk of death than patients ≤ 50 years (HR:1.55; p=0,026).

CONCLUSION: the better management of individual's fitness through tools as Comprehensive Geriatrics Assesments, the knowledge of disease characteristics and the improvement of treatment patterns have improved the outcomes of HSCT over the years. However, despite all this context aging is still a risk factor for HSCT success and as it was observed it influenced the risk of mortality.

Keywords: Hematopoietic Stem Cell Transplantation. Myelodysplastic Syndrome. Age.

INCIDENCE OF GVHD AMONG CALCINEURIN INHIBITORS IN PATIENTS UNDERGOING ALLOGENEIC HSCT IN A UNIVERSITY HOSPITAL

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INTRODUCTION: Allogeneic hematopoietic stem cell transplantation (HSCT) requires the prevention of graft-versus-host disease (GVHD), a serious complication of transplantation. Prophylaxis strategies include using calcineurin inhibitors, Cyclosporine (CsA), and Tacrolimus, depending on the type of conditioning and the donor. In unrelated transplants, a clinical trial showed a greater benefit of the Tacrolimus + Methotrexate (MTX) regimen in terms of survival and reduction of acute GVHD. In related transplants, CsA +MTX was more effective in the prophylaxis of acute GVHD. At our transplantation center, the regimens used are: CsA + MTX (HSCT related to myeloablative conditioning); CsA + mycophenolate mofetil (HSCT related to reduced- intensity or non-myeloablative conditioning); CsA (HSCT related to cord cell source); CsA, in children, or Tacrolimus (unrelated cord HSCT); Tacrolimus + MTX + ATG (unrelated HSCT).

OBJECTIVES: To describe the incidence of GVHD among calcineurin inhibitors used in prophylaxis. Methods: This is an observational study with data collection performed on medical records.

RESULTS: 164 patients with onco-hematological diseases who underwent HSCT from 2015 to 2021 were included. One hundred four patients used CsA, 53 (50.9%) had acute GVHD (14 grade I; 22 grade II; 8 grade III; 2 grade IV; 7 without information on severity), and 27 (25.9%) had chronic GVHD (15 mild; 8 moderate, two severe and two without information on severity). Seventy-three patients used Tacrolimus, 36 (49.3%) had acute GVHD (12 grade I; 12 grade II; 7 grade III; 3 grade IV, and two without severity information), and 16 (21.9%) had chronic GVHD (7 mild; 6 moderate, one severe and one without information on severity). Of the patients included, 13 used CsA +Tacrolimus, and 11 used sirolimus. Considering patients who used only one calcineurin inhibitor (CsA or Tacrolimus), the incidence of acute GVHD was 50.5% and 49.3%, respectively (p 0.87), and chronic GVHD was 25.3% and 21.9%, respectively (p 0.61).

CONCLUSION: The incidence of acute and chronic GVHD in the sample is similar between CsA in related HSCT and Tacrolimus in unrelated ones, with a percentage similar to that reported in the literature.

Keywords: Allogeneic HSCT. GVHD. Calcineurin inhibitors.

NURSING CARE INTERFACES IN A HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT: EXPERIENCE REPORT

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INTRODUCTION: Patients undergoing cancer treatments, as well as those who underwent hematopoietic stem cell transplantation (HSCT) experience long periods of hospitalization, associated with complications of the disease, aggressive antineoplastic therapy and even immunosuppression, where assessments related to biopsychosocial aspects are necessary. Such aspects are widely discussed in the literature and are guided by disorders such as anxiety, depression, irritability, loss of control, yearnings for death, the search for compatible donors, self-image dysfunctions, among others. Therefore, the context of hospital admission in the HSCT sector is characterized by a high level of practical-assistance complexity and specific care demands performed by the multiprofessional team, requiring dedication and hours of workload from the nursing team to meet the needs of patients. patients, donors, family members and caregivers. In addition, this context is surrounded by the experiences and preoccupations of patients and families, which can cause stress and emotional exhaustion for the team, especially the nursing team, that spend most of their time with the assisted clientele.

OBJECTIVE: To describe the experiences of the nursing team of an inpatient unit for HSCT.

METHODS: This is an experience report with a qualitative and descriptive approach, about the care actions and experiences of assistant nurses from a public inpatient unit for HSCT in a bone marrow transplant center in the State of Rio de Janeiro.

RESULTS: It is noticed that nurses who provide care to patients after HSCT are involved in the practice of sensitive listening, close contact and direct observation of the treated person, to deal with pain, suffering, struggle for life and mourning the loss of the patient. Such situations show the feeling of loss as a constant element in professional practice, in which healing is not always possible, but the task of caring is always present. Although these constant experiences can lead to the emergence of personal difficulties in these professionals, they learn to deal with their own problems and conflicts with patients, family members and the multiprofessional team, which serves as support in the face of stressful situations that directly impact the performance of assignments.

CONCLUSION: The experiences demonstrate the importance of health institutions considering the particularities of a sector such as HSCT, and the situation of anticipatory grief in the nursing professional, requiring the implementation of stress relief strategies, with greater investment in activities aimed at the team, with the use of light care technologies, so that these professionals can perform their tasks effectively. It is also evident the need for research on this topic, to reveal the real needs of professionals.

Keywords: Hematopoietic Stem Cell Transplantation. Oncology Nursing. Psychological Anxiety.

PERIPHERAL BLOOD STEM CELLS AND FEMALE DONOR INCREASES THE RISK OF CHRONIC GVHD IN HAPLOIDENTICAL TRANSPLANTATION WITH PTCY WITHOUT DECREASING RELAPSE RATE: A MULTICENTER RETROSPECTIVE STUDY OF BRAZILIAN PATIENTS WITH ACUTE LEUKEMIA OR MYELODYSPLASTIC SYNDROME REPORTED TO THE CIBMTR

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INTRODUCTION: Only about 30% of the patients will have a matched-sibling donor for hematopoietic cell transplantation and not all patients will find a matched donor in donor registries. Haploidentical transplantation with posttransplant cyclophosphamide (PTCy) has nearly revolutionized the field, greatly expanding the pool of donors.

OBJECTIVE: The objective of the current study was to identify risk factors for adverse outcomes in patients who underwent haploidentical transplantation with PTCy.

PATIENTS: Patients were transplanted in 12 Brazilian centers between 2014 and 2018 and reported to the CIBMTR. All patients with acute leukemia or myelodysplastic syndrome and who underwent haploidentical HCT with PTCy were included. There was no exclusion criterion.

METHODS: We used the CIBMTR framework for data collection. Outcomes were overall survival (OS), relapse (REL), non-relapse mortality (NRM), and cGVHD. Survival and incidence curves were built with the Kaplan-Meier and Grey methods, respectively, and compared with the logrank and Grey test. Uni and multivariable analyses were performed with Cox models. Model selection was based on the lowest Akaike information criterion. We reported the results from multivariable analyses.

RESULTS: A total of 163 patients were included with a median follow-up of 32 months. Patients' characteristics are in table 1. The 3-y overall survival was 43% (95CI 35-52%). Risk factors for poorer OS were age (HR = 1.18, p = 0.004 for each 10-y older) and disease status (CR2: HR = 1.94, p = 0.02; active disease: HR = 3.04, p = 0.02; primary induction failure: HR = 2.90; p = 0.01; compared with CR1). Only disease status was associated with relapse risk (CR2: HR = 2.20, p = 0.03; active disease: HR = 9.64, p < 0.001; primary induction failure: HR = 3.94; p = 0.02; compared with CR1). Only age was associated with NRM (HR = 1.29 for each 10-y older, p < 0.001). Chronic GVHD was higher with peripheral blood stem cell (HR = 2.87, p = 0.003, compared with bone marrow) and female donors (HR = 2.96, p = 0.001, compared with male).

CONCLUSIONS: Our results shows that the main factors impacting overall survival are age (because of higher NRM) and disease status (because of higher relapse rates). Moreover, peripheral blood stem cells and female donors increase the risk of chronic GVHD without any beneficial effect in the relapse rate. In the haploidentical setting, peripheral blood stem cells and female donors should be avoided.

Disclaimer: The results presented were obtained using data from the Coordinating Center of the CIBMTR. The analysis plan, result, and interpretation were not reviewed or approved by Statistical or Scientific Committees of the CIBMTR, and the CIBMTR cannot confirm their accuracy. Also, the dataset was blinded for participating center, and therefore we could not include participating centers' researchers. We thank all the participating centers.

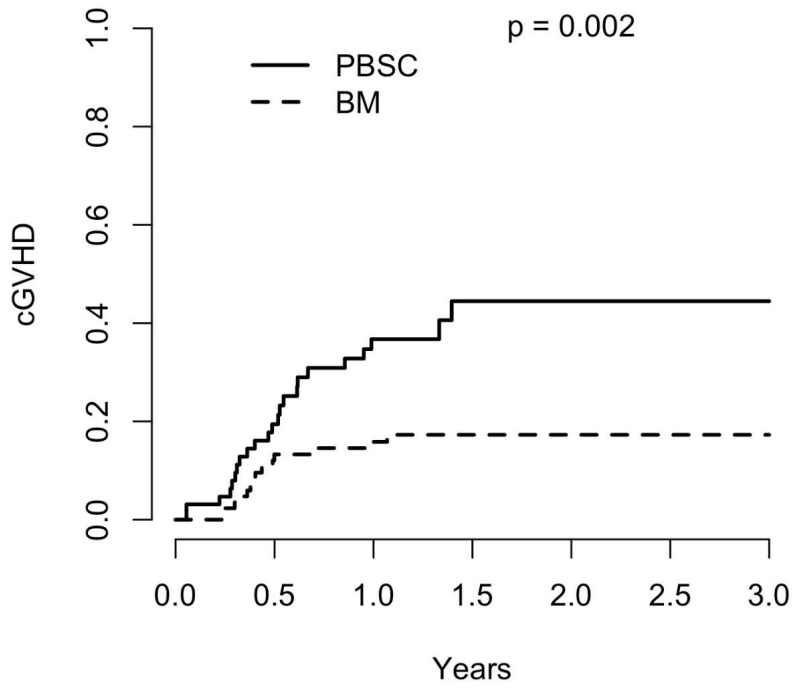
Keywords: Haploidentical transplantation. Risk factors. Posttransplant cyclophosphamide.

TABLE 1. Patients' characteristics

TOTAL	
TOTAL	163
MEAN AGE (SD)	30.8 (21.7)
SEX	
FEMALE	72 (45.6%)
MALE	86 (54.4%)
HCT-CI	
0	104 (66.2%)
1	28 (17.8%)
2	6 (3.8%)
3	13 (8.3%)
4	3 (1.9%)
5	1 (0.6%)
6	2 (1.3%)
KARNOFSKY	
90-100	130 (82.8%)
<90	27 (17.2%)
DISEASE	
ACUTE MYELOID LEUKEMIA	74 (46.8%)
ACUTE LYMPHOBLASTIC LEUKEMIA	61 (38.6%)
MYELODYSPLASTIC SYNDROME	21 (13.3%)
OTHER ACUTE LEUKEMIA	2 (1.3%)
STATUS AT TRANSPLANT	
CR1	61 (38.6%)
CR2+	57 (36.1%)
ACTIVE	8 (5.1%)
PIF	9 (5.7%)
MDS	21 (13.3%)
MISSING	2 (1.3%)
GRAFT	
BM	91 (57.6%)
PBSC	67 (42.4%)
DONOR SEX	
MALE	100 (63.3%)
FEMALE	58 (36.7%)
CMV	
NEG/NEG	8 (5.2%)
ANY POS	146 (94.8%)
CONDITIONING	
MYELOABLATIVE	98 (62.4%)
NON-MYELOABLATIVE	16 (10.2%)
REDUCED-INTENSITY	43 (27.4%)

SD, STANDARD DEVIATION; HCT-CI, HEMATOPOIETIC CELL TRANSPLANTATION-SPECIFIC COMORBIDITY INDEX.

FIGURE 1. **Chronic GVHD**



STEM CELL TRANSPLANTATION AS A SUCCESSFUL TREATMENT FOR THROMBOCYTOPENIA ASSOCIATED WITH THE ETV6 GENE (THROMBOCYTOPENIA 5)

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INTRODUCTION: Thrombocytopenia 5 (THC5) is an autosomal dominant disorder that leads to low platelet counts and variable bleeding tendencies related to germline mutations in the ETV6 gene. Affected individuals have a moderate risk of developing a hematologic malignancy such as B-cell acute lymphoblastic leukemia. Management of this condition is based on treatment or prevention of excessive bleeding and eventual treatment for the development of hematologic malignancies with specific standard therapy, including the possibility of allogeneic stem cell transplantation (allo-SCT).

OBJECTIVE: Report a successful treatment of THC5 with identical allo-SCT and perform a literature review.

CASE REPORT: We report a case of a 26-yo male patient with a history of known thrombocytopenia since 2017, with a mean platelet count of 12,000/mm3 and recurrent infections due to associated neutropenia with a mean count of 250/mm3. He underwent bone marrow (BM) investigation in 2020, with a myelogram without any dysplasia and showing 2.4% of blasts with no abnormalities at immunophenotyping; conventional cytogenetics with 46,XY; a BM biopsy with global hypocellularity; and fluorescence in situ hybridization without chromosomal abnormalities. A Next-Generation Sequencing (NGS) panel was performed and showed ETV6 Exon 8 gene mutation confirming the diagnosis of THC5. Due to the history of multiple hospitalizations for infectious conditions requiring prolonged treatment with antibiotics, severe thrombocytopenia refractory to corticosteroid and concerning the risk of developing a hematologic malignancy it was decided to submit the patient to an allo-SCT. The patient received SCT from identical related donor (sister - heterozygous for the ETV6 gene) in 2021 without prior therapy and with myeloablative conditioning with Fludarabine and Busulfan. He presented neutrophilic graft on D+15, without intercurrences. He underwent graft versus host disease (GVHD) prophylaxis with cyclosporine, anti-thymocyte globulin and methotrexate. In the subsequent evaluation of the transplant on D+30, the myelogram showed no dysplasia and had a 100% chimerism. He evolved with acute GVHD of the skin and gastrointestinal tract and was treated with corticosteroid. He maintains clinical follow-up (last in March 2022) without signs of thrombocytopenia. To our concern no similar report has been made to date, only reports regarding patients with other familial thrombocytopenia and current hematologic malignancy have been described.

CONCLUSION: We report a case of a patient diagnosed with THC5 without current hematologic malignancy who underwent successful allo-SCT. Considering this is a rare disease there is much work to be done to improve the understanding of ETV6-related thrombocytopenia. The current recommendation is that these patients should be referred to a center with experience in managing of patients with leukemia predisposition syndromes.

Keywords: Stem Cell Transplantation. ETV6-Linked Leukemia. Thrombocytopenia 5.

TARGETED MARROW IRRADIATION-BASED CONDITIONING REGIMEN FOR HAPLOIDENTICAL TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA

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INTRODUCTION: Haploidentical hematopoietic cell transplantation with posttransplant cyclophosphamide (PTCy) is a relatively new procedure. A recent meta-analysis demonstrated that myeloablative conditioning regimen can achieve better results. However, optimal myeloablative regimen for haploidentical transplantation with PTCy has not been defined yet. The objective of this study is to report a new targeted marrow irradiation (TMI)-based myeloablative conditioning regimen.

METHODS: We included patients with acute myeloid leukemia who underwent haploidentical hematopoietic cell transplantation. Conditioning regimen consisted of targeted marrow irradiation (TMI, 1.5 Gy every 12h for 4 doses, total dose 6 Gy, on D-8 and D-7), fludarabine 30 mg/m2 D-6 through D-2, and phamacokinetically-guided busulfan (AUC 4,800 M*minute/day on D-5 and D-4). The goal of TMI is to include the skeleton and spleen in the irradiation field while relatively sparring critical organs like heart, lungs, liver, and bowel, among others. GVHD prophylaxis was posttransplant cyclophosphamide (50 mg/kg on D+3 and D+4) combined with tacrolimus and mycophenolate mofetil, both starting on D+5.

RESULTS: A total of 8 patients were included, with a median follow-up of 453 days (range: 97-783). Median age was 57.4 years, 75% were female, disease risk indexes were intermediate (50%) and high (50%), and graft sources were peripheral blood (87.5%) and bone marrow (12.5%). All patients underwent first allogeneic transplantation except one patient, who had been previously treated with an autologous and a cord-blood transplantation. Mean infused CD34 was 5.7E6/kg (SD=1.6). All patients had neutrophil engraftment at a median of 20 days and all but one had platelet engraftment (median: 31 days). All patients achieved >95% donor chimerism at D+100. Acute toxicities are described in table 1. Grades 3/4 mucositis were the main toxicity (62.5%). One patient had very severe sinusoidal obstruction syndrome (SOS). Three patients had disease progression following HCT and died. No patient died of non-relapse cause, and 1-y overall survival was 86% (95CI 63-100%). Three patients experienced grade II acute GVHD.

CONCLUSIONS: Our results show encouraging 1-y survival in patients with acute myeloid leukemia who underwent targeted marrow irradiation-based myeloablative conditioning regimen. Moreover, non-relapse mortality was extremely low and no patient died of non-relapse causes, although we had one very severe case of sinusoidal obstruction syndrome which was successfully treated with defibrotide. All patients engrafted and had >95% donor chimerism at D+100. Larger studies are needed to confirm these results.

Project funded by PRONON and Amigo H

TABLE 1. **Acute toxicities**

TOXICITY	G 0	G 1/2	G 3/4
MUCOSITIS	0,0%	37,5%	62,5%
NAUSEA/VOMITING	12,5%	50,0%	37,5%
DIARRHEA	37,5%	62,5%	0,0%
HYPERBILIRUBINEMIA	75,0%	25,0%	0,0%
AST/ALT	100,0%	0,0%	0,0%
RENAL	42,9%	42,9%	14,3%
CARDIAC	50,0%	50,0%	0,0%

* ONE PATIENT HAD VERY SEVERE SOS AND ANOTHER HAD HEMARTHROSIS

TELEMEDICINE AS A VIABLE MEANS OF EVALUATION OF RELATED BONE MARROW DONORS

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INTRODUCTION: The pandemic of COVID-19 has had a major impact on bone marrow transplant services worldwide. In allogeneic transplants, there was a risk that the donor would be diagnosed with COVID-19 during the conditioning regimen, even after epidemiological analysis for the presence of clinical evidence of infection and guidance on home isolation and hygiene measures. In these cases, the stem cell collection would have to be postponed and a new donor would have to be recalled. Therefore, one of the recommendations from the Ministry of Health was that the cells to be cryopreserved, ensuring the collection of the cell therapy product before the start of the conditioning regimen. Another measure that our service implemented was the telemedicine donor evaluation. During Telemedicine, guidance was provided on the hematopoietic progenitor cell (HPC) collection procedure, risks, adverse events, and clinical interview. This strategy was used mainly when the donor lived in another city/state, to avoid unnecessary travel of donors with clinical unsuitable and to accelerate the first orientation and performance of tests.

OBJECTIVE: To evaluate the feasibility of telemedicine in the orientation of allogeneic bone marrow donors.

METHODS: The evaluation by videoconference was scheduled according to the potential donor's availability. The donor could be accompanied during the initial orientation but was instructed to be alone during the clinical interview. After the telemedicine, if the donor agreed to the donation, a request for medical tests and HLA confirmation test was sent. The donor could choose to have the tests performed at our service. After the tests or the initial evaluation were performed, the in-person evaluation was scheduled, with the HPC donation already scheduled for the same time.

RESULTS: From June 2020 to June 2022, 50 evaluations of potential bone marrow related donors were performed, 9 of which with the initial evaluation being performed by telemedicine. Of the 9 candidates, 8 were from another state and one was from São Paulo state, but a resident of another city. Only one of the donors evaluated by telemedicine was unsuitable. The completion of the potential donor evaluation was done in person due to the need for physical examination, collection of infectious disease markers from the blood bank (including NAT), and evaluation of the peripheral access for apheresis collection. The reduction in length of stay in São Paulo (where the hospital is located) could not be objectively measured, but within 2 days the donor was ready to start mobilization. The telemedicine guidance does not formalize the signing of the Consent Form and does not authorize the start of the conditioning regimen in the recipient. However, it speeds up the donor evaluation process. And with this, we can reduce the length of stay in the city of São Paulo and avoid unnecessary trips of unsuitable donors.

CONCLUSION: Evaluation by telemedicine of related bone marrow donors is a viable strategy.

THE ROLE OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CHRONIC MYELOID LEUKEMIA PATIENTS IN THE TKI ERA

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BACKGROUND: The management of chronic myeloid leukaemia (CML) has changed over the last two decades after the introduction of tyrosine kinase inhibitors (TKI). The majority of patients treated with TKIs achieve excellent responses. However, a portion of patients do not achieve molecular response due to treatment failure. The definition of treatment failure is characterized by both resistance to medication and intolerance to side effects. For patients who fail to use ITKs, a change in treatment is considered essential to limit the risk of progression and death. In this context, stem-hematopoietic cell transplantation (HSCT) continues to be considered an effective and potentially curative therapy and should be indicated for these patients resistant or intolerant to two or more ITKs and also for patients progressing to the accelerated phase.

AIM: this study aim to investigated clinical characteristics, disease phase, presence of mutations, criteria for indication and variables related to TCTH.

METHODS: We analyzed 62 patients resistant to TKIs transplanted at the BMT Center of Federal University of Paraná, from January 2001 to May 2019. The study is retrospective, observational and analytical, held from data record in either STMO database or medical chart.

THE ROLE OF CELL SOURCE ON OUTCOMES OF BONE MARROW TRANSPLANTATION IN PATIENTS WITH MYELODYSPLASTIC SYNDROME: RESULTS OF MULTICENTRIC STUDY (LATIN AMERICAN REGISTRY)

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INTRODUCTION: Hematopoietic stem cell transplant (HSCT) is known as the only curative therapy for Myelodysplastic Syndrome. This procedure is increasing in recent years and there are important features to be observed that may influence the outcomes of the HSCT.

OBJECTIVE: To evaluate the role of cell source on the outcomes of HSCT in MDS patients from Latin America.

METHODS: data of 341 patients with MDS of 32 centers from the Latin American Transplant Registry were analyzed. The period of the study was 1989 to 2022. Statistics were performed using SPSSv.23.1, considering a significant $p<0.05$.

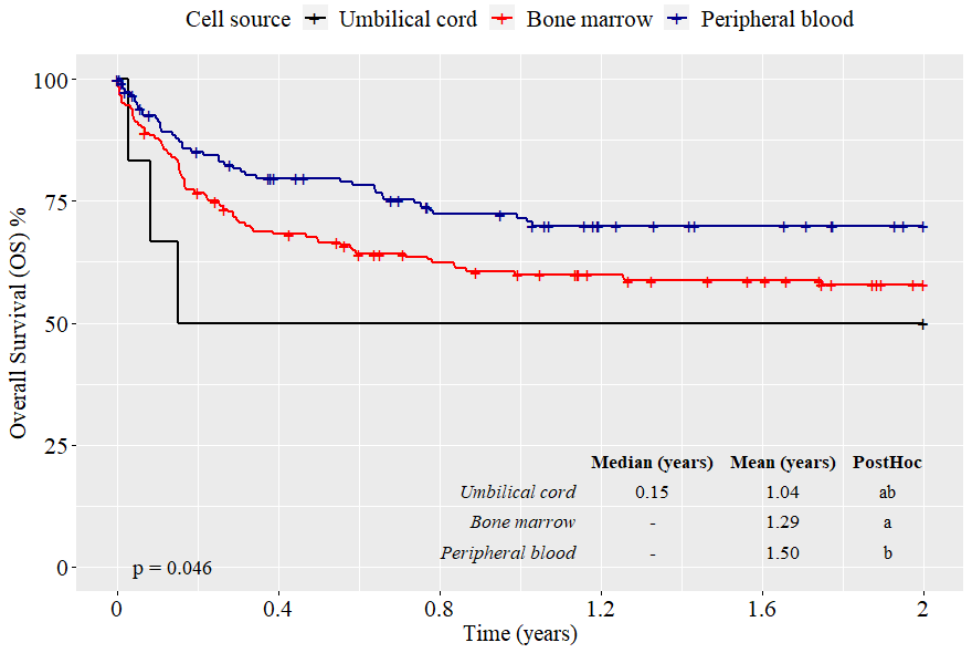
OUTCOMES: the mean age was 46,43 years. Most patients were ≤ 50 years (48,97%), about 21,41% were between 50 and 61 and 29,62% were > 60 years. There was a predominance of males (58,36%) and Caucasian (86%) . Patients were stratified according to the Prognosis Scoring System (IPSS-R as: Very low risk (n=2; 0.59%), Low risk (n=35; 10,26%), Intermediate (n=82; 24,05%), high risk (n=63; 18,48%) and very high risk (n=19; 5,57% %). A total of 140 (41,06%) patients had no data about R-IPSS. The cell sources were bone marrow (BM) (181; 53,08%), peripheral blood (PB) (154; 45,16%) and cord blood (6; 1,76%). The main conditioning regimen was Myeloablative (MAC) (250; 73,96%). The predominant donor type was related (239; 69,79%) followed by non-related (77; 22,58%) and haploidentical (26; 7,62%). In 65,10% (n=222) of cases, a prior treatment was performed. From these patients, 61,71% used chemotherapy, 27,03% hypomethylating and 11,26% used both. The main cell source was bone marrow (BM) (53,08%). Peripheral blood (PB) was performed in 45,16% of cases and umbilical cord in 1,76%. Complications post-HSCT were observed in 260 (76,25%) and the most frequent was Infections (n= 212; 81,54%), followed by acute graft versus host disease (GVHD) (n=121; 46,54%) and chronic GVHD (n=98; 37,69%). The frequency of death was 40,47% (n=138). The 5-years overall survival was 56,2%. When stratified according to cell source, the 2-years OS was significantly lower with bone mar-

row (p=0.046). A multivariate analyses demonstrated the association between BM and the risk of death (p=0,025; HR= 1,36 (CI95%:1,03 - 1,78).

CONCLUSION: The results obtained showed an influence of bone marrow as cell source in the risk of death, through the frequency of death and multivariate analysis. These findings are relevant to better management of entire process of HSCT in MDS patients.

Keywords: Hematopoietic Stem Cell Transplantation. Myelodysplastic Syndrome. Cell Source.

FIGURE1. 2-year-overall survival according to cell source in MDS patients



TREATMENT OF POOR GRAFT FUNCTION USING SELECTED CD34+ CELL BOOST: A CASE REPORT

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CASE REPORT: 64-years-old male patient, diagnosed in 2021 with AML secondary to MDS. Bone marrow study showed 21% of blasts, normal karyotype and NGS myeloid panel with SRSF2 and RUNX1 mutations. He underwent 1 cycle of induction with 3+7 and consolidation with 2 cycles of Cytarabine, reaching negative MRD. It was followed in May/2021 with unrelated allogeneic HSCT, identical ABO, with non-myeloablative conditioning (BuFluATG) obtaining neutrophilic engraftment on D+18 and chimera of 98% on D+30. In August/2021, due to the maintenance of pancytopenia and the need for transfusional support of red blood cells and platelets, a new chimerism was obtained, with a result of 72%. Cyclosporine was suspended, GCSF and Eltrombopag were started, and DLI was performed, with chimera dropping to 32% despite the measurements. Secondary graft failure was diagnosed, not associated with disease relapse. In October/2021, he received a second haploidentical HSCT, minor ABO incompatibility (O+ donor and A+ patient), with evaluation of bone marrow chimerism on D+30, D+100 and D+180 of 98%, > 98% and 100% respectively. Due to the maintenance of bicytopenia and transfusion dependence of red blood cells and platelets, despite complete donor chimerism, it was concluded that it was a poor graft and it was decided to perform a boost with CD34+ cells from the donor. The patient received 1 bag with 12.04 x 10^6/kg of selected CD34+ cells with total cell viability of 98% in February/2022. After infusion of stem cells, the patient evolved with transfusion independence (last red blood cell and platelet transfusions on D+28 and D+8 after the boost, respectively).

DISCUSSION: Allogeneic hematopoietic cell transplantation (AHCT) represents a potential cure option for malignant and non-malignant diseases. The conditioning strategies with chemotherapy and/or radiotherapy aim to prepare the medullary environment by eliminating both healthy and diseased cells; they also lead to the destruction of recipient lymphocytes, reducing the risk of graft rejection, and of donor lymphocytes, reducing the risk of GVHD[1]. Such strategies can result in delay in bone marrow and/or immune system recovery mediated mainly by T lymphocytes, which ends up conferring greater morbidity and mortality associated with transplantation[2]. Bone marrow and immune recovery in these patients depends on numerous variables, such as donor and recipient characteristics (e.g., ABO compatibility, CMV infection status), underlying disease, source of stem cells, degree of HLA compatibility, regimen of conditioning, pre- and post-transplant immunosuppressive therapy, presence of GVHD and occurrence of complications related to the phase before bone marrow recovery, and it is not possible to predict the impact of these conditions on the engraftment of donor cells process. When compared with alternative donors, HLA-matched related donor confers a higher success rate in engraftment and immune recovery[3]. Bone marrow engraftment after stem cell transplantation is defined as neutrophils > 500/L on the first day of 3 consecutive days and platelets > 20,000/L on the first day of 7 consecutive days without the need for transfusion support. We can have several situations depending on the degree of donor chimerism associated with the criteria for grafting and the transfusion dependence of the recipient[4]:

- Primary graft failure: dono cells < 95%, neutrophils < 500/L on D+28 after AHCT using a peripheral source and D+42 after AHCT using an umbilical cord source.

- Secondary graft failure: loss of donor cells with neutrophils < 500/L after initial engraftment.

- Poor graft function: severe cytopenias of at least 2 cell lines and/or transfusion requirements associated with hypoplastic/aplastic bone marrow with total donor chimerism.

Poor graft function occurs in 5-27% of patients and is associated with considerable infectious and hemorrhagic complications[4], and also to low survival rates. In a study of unmanipulated haploidentical stem cell transplantation, overall survival was lower in patients with poor engraftment compared with patients with functional engraftment (34.6 vs. 82.7%, $p < 0.001$)[5].

The pathophysiological mechanism of poor engraftment has not yet been fully elucidated, but it is described that immune and medullary microenvironment alterations inherent to the conditioning process and prophylaxis of GVHD and graft rejection, contribute to this condition. Situations often associated with poor graft function are numerous, including HLA-mismatch and ABO incompatibility, as well as inadequate dose of infused progenitor cells and infectious complications[6]. The treatment of poor graft function aims at hematological recovery associated with the maintenance of total donor chimerism, and independence from transfusion support and from hematopoietic growth factors reducing serious complications and risk of death[7]. Boost infusion of selected CD34+ cells (poor or absent of CD3+ cells) without performing a prior conditioning regimen is well described in the literature as a therapeutic strategy leading to a long-lasting results with satisfactory safety profile[8]. Our clinical case shows the evolution of a patient with poor graft function after underwent a second hematopoietic stem cell transplant using hoploidentical stem cells and ABO incompatibility, who was dependent on transfusion and hematopoietic growth factors, that showed medullary recovery after a boost of CD34+ cells and a functional engraftment. The importance of knowing well the factors involved in poor grafting in order to adopt pre- and post-transplantation strategies, aimed at minimizing the risks of poor graft function, is necessary and indispensable to reduce the risks and increase the chances of successful transplantation.

Keywords: Cell transplantation. Poor graft function. Hematopoietic recovery.

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AUTOLOGOUS HSCT

AUTOLOGOUS HEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION: RESULTS OBTAINED IN TEN YEARS OF EXPERIENCE AT PROCÉLULA – TERAPIA CELULAR, RJ, BRAZIL

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1 Procélula – Terapia Celular

The demand for autologous hematopoietic progenitor cell transplants has been increasing over a ten-year period in the state of Rio de Janeiro. Procélula has been collaborating to meet this demand in the private sector, increasing technical and infrastructure investments. We present below the results of our work in this period and the technical characteristics used for its development. From December 2011 to April 2022, 1051 patients were treated (590 myelomas, 417 lymphomas and 44 other diseases) with a median age of 56 years (18 pediatric patients aged between 7 months and 14 years; 1033 adults aged between 15 and 76 years). For the collection of HPC, apheresis started on the first day in which patients had more than 10 CD34+/mm3 cells in peripheral blood. An average of four blood volume per apheresis was collected for mononuclear cells in CobeSpectra or Spectra Optia and leukocyte quantification was performed in an ABX Micros ES60 automatic counter. The products were cryopreserved in hydroxyethyl starch (HES) solution at a concentration of 5.83%, human albumin at 4% and dimethyl sulfoxide at 5% of the final volume, divided into fractions from 60 to 115mL, with a target cell concentration of 2-3 x108 total leukocytes/ml. These fractions were stored in a freezer at -80°C and kept at constant temperature until the date of transplantation. Cell viability was defined by light microscopy and trypan blue exclusion. For the quantification of HPC, we used flow cytometry for CD34+/CD45low cells, according to the methodology defined by ISHAGE, in a BD FACSCalibur cytometer. We performed clonogenic assay with MACSTM HSC-CFU Media system (Miltenyi Biotec) of methylcellulose culture with recombinant factors for the growth of colony forming units of granulocytes and monocytes (CFU-GM) that were observed in inverted light microscopy 14 to 16 days after the incubation at 37oC. The 1051 patients analyzed performed 1142 mobilizations with G-CSF (53 associated with chemotherapy, 355 with Plerixafor and 13 with chemotherapy and Plerixafor; 1080 with apheresis and 62 mobilization failures without apheresis) and a total of 1594 apheresis. The mean circulating HPC before the first apheresis was 23 CD34+/mm3 (0-410), with a mean of 4.05x106 CD34+/Kg (0.11-50.50) collected by apheresis. The frozen products had an average cell concentration of 2.56x108/mL (0.23-6.61) with a recovery of 109.44% upon thawing (52.40-283.33). They showed cell viability >99% before cryopreservation and recovered on average 92.03% (68.05-99.76) of viability and 79.86% (5.5-830.5) of CFU-GM on thawing. A total of 3186 functional assays were performed, and the ratio between them (CD34/CFU-GM) was 2.57 (0.7-88.9) in the fresh sample and 3.34 (0.7-91.1) in the thawed sample. Transplants were performed in 983 of these patients, with mean of 3.64x106 CD34+/Kg (1.20-19.79) and 1.66x106 CFU-GM/Kg (0.04-10.60) infused in each patient. The time to engraftment granulocytes averaged 10 (8-18) days. The data presented in this series corroborate those presented previously, reinforcing that cryopreservation in a mechanical freezer - 80°C with HES and low concentration of DMSO results in excellent clinical outcomes for autologous HPC transplantation.

Keywords: Hematopoietic Progenitor Cells (HPC). Cryopreservation and Autologous Transplantation.

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: INITIAL EXPERIENCE IN A PRIVATE HOSPITAL IN BRAZIL

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INTRODUCTION: Autologous hematopoietic stem cell transplantation (HSCT) refers to the use of a patient's own hematopoietic progenitor cells to reconstitute bone marrow after high-intensity chemotherapy. Some diseases have an indication for performing HSCT as first-line consolidation and in others only when there is relapse or disease progression. The decision to perform the transplant or not is always individualized, considering the risks and benefits, considering the patients' comorbidities, pre-transplant disease status, alternative therapeutic approaches and the patient's individual needs and preferences. Currently, with greater and better knowledge of apheresis techniques, conditioning and supportive care, several centers have been enabled to perform HSCT. For a patient undergoing chemotherapy with an indication for HSCT, it is important that there is a close communication between the team that follows the patient and the transplant team for no discontinuity in care.

OBJECTIVE: The present study aims to report the initial clinical experience of a private tertiary hospital with autologous HSCT.

METHODS: Retrospective cohort study that included all at a Brazilian tertiary hospital, who underwent HSCT between January 2009 and December 2019. Demographics, exams at diagnosis, clinical features, treatments and evolution were analyzed through medical records analysis. A Kaplan-Meyer survival analysis was performed.

RESULTS: Of 41 transplanted patients, the main underlying diseases were the plasma cell neoplasms and lymphomas, with a median age of 59 years old, being 78% men. 34 patients survived the first 100 days post-transplantation and had a median follow-up of 19 months. The variables that were related to overall survival were clinical staging in lymphomas and the number of lines of treatment in multiple myeloma. There were 7 deaths and the main causes of death were hemorrhage and infection, with only 2 dying due to disease progression, probably due to the short follow-up.

CONCLUSION: HSCT is a highly complex procedure where the continuous monitoring of clinical outcomes and those reported by patients allows improving the care process. Close communication and early referral allow the patient to perform the procedure in a timely manner and without discontinuities in care. The results obtained in the present study are very consistent with similar studies already reported and allow a better understanding of the main factors that interfere in the success of autologous transplants. However, Brazilian studies are still scarce and should be encouraged, as well as the expansion of services, aiming to increase the chance of cure for patients.

TABLE 1. **Frequency analysis according to normality test**

Variable	Mean	Median
Age at diagnosis (years)	-	59 (50-62)
Time to neutrophilic engraftment (days)	11.29 (±3.5)	-
Time between diagnosis and HSCT (months)	-	12 (8-25)
Time between diagnosis and first appointment with the transplant center (months)	-	9 (5-21,5)
Time between the first appointment at the transplant center and the HSCT (months)	-	3 (1-4)
Time between diagnosis and relapse/progression (months)	-	15.5 (7.75-26.25)
Time between relapse/progression to HSCT (months)	-	6.5 (3.75-12)
Time between HSCT and death (days)	-	17 (10-63)
Number of stem cells infused (x10^6 CD34 cells/kg of recipient)	-	4.8 (2.9-6.5)
Number of treatment lines	1.73 (±1)	-

Legends: HSCT autologous hematopoietic stem cell transplantation.

TABLE 2. **Baseline disease of patients who underwent hsct**

Baseline disease	Frequency	Percentage
Multiple myeloma	23	56,1
Classic Hodgkin's Lymphoma	3	7,3
DLBCL	4	9,8
Follicular lymphoma	1	2,4
Adult T-cell leukemia/lymphoma	1	2,4
POEMS syndrome	1	2,4
Plasmacytoma	1	2,4
Peripheral T lymphoma NOS	1	2,4
Mantle cell lymphoma	3	7,3
Plasmablastic lymphoma	1	2,4
Intravascular large B-cell lymphoma	1	2,4
Testicular choriocarcinoma	1	2,4

Legends: DLC; Diffuse large B-cell non-Hodgkin's lymphoma; POEMS polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes; NOS no other specifications.

TABLE 3. **Evaluation of pre-transplant plasma cell disease**

Degree of response	Frequency	Percentage
Partial response	8	32,0
VGPR	7	28,0
Complete response	3	12,0
Stringent complete response	2	8,0
Progression	2	8,0
Minimal response	1	4,0
No data	2	8,0

Legends: VGPR Very good partial response.

CRYOTHERAPY WITH CHAMOMILE ICE MITIGATED THE DEVELOPMENT OF ORAL MUCOSITIS IN PATIENTS TREATED WITH MELPHALAN

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INTRODUCTION: Melphalan cancer therapy prevents cancer cell division by alkylating and cross-linking DNA strands. Once apoptosis of these cells is induced, the intense inflammatory reaction begins, from which the side effects of the treatment originate. In multiple myeloma (MM) and Hodgkin's (LH) and non-Hodgkin's lymphomas (NHL), including transplanted patients, there is inflammation of the mucous membranes, mucositis. Oral mucositis occurs within two weeks of treatment, and although it is self-limiting, it takes about six weeks after the end of cancer treatment to resolve. In the meantime, the patient presents with lesions ranging from grade 0 to grade III with ulceration, and difficulty eating due to pain from the lesion. Articles report that there are remedies that can reduce or mitigate the occurrence of oral mucositis, provided they have an anti-inflammatory, healing, analgesic effect and correct the oral pH, which should be between 6.5 and 7. Chamomile is known for its beneficial effects in combating this disease. Pain, inflammation and its nociceptive action. Its extract is rich in terpenes, flavonoids and coumarins, known anti-inflammatory chemical compounds.

OBJECTIVE: In this context, the chamomile used, regardless of the species, has potential for the treatment of oral mucositis. The low toxicity of its preparations, high patient tolerance and easy access support the inclusion of chamomile-based treatments.

METHODS: Thirty-five patients diagnosed with MM, HL, and NHL were treated with a melphalan protocol within a 1-year period to evaluate the effects of cryotherapy with chamomile infusion. Prepared with 450 ml of hot water and 3 sachets of chamomile tea, which, after infusion, is placed in an ice cube tray with a lid and stored in the freezer. Patients were divided into those who used cryotherapy (n=8) or not (n=27). If they used the ice cubes, they were offered more during 30 minutes before and during the 1-hour melphalan infusion two doses in a row.

RESULTS: All patients who underwent cryotherapy had grade 0 mucositis (100%) and of those who did not use cryotherapy, 29% (n=8) had grade 0 mucositis. Grade I mucositis occurred in 55% (n=15) of patients and grade II in 14% (n=4).

CONCLUSION: It should be noted that most patients develop some degree of damage without treatment with chamomile. Follow-up of chemotherapy patients should be constant and daily. Even though this was a short experiment, the benefits of using chamomile affect a better quality of life for patients with MM, HL and NHL treated with melphalan. Research with chamomile should be expanded and deepened to standardize the use of its properties. Moreover, a prophylactic and therapeutic protocol can be established to obtain the best results, along with the use of chemotherapy.

LACE CONDITIONING IN RELAPSED AND REFRACTORY LYMPHOMA TRANSPLANT: RETROSPECTIVE ANALYSIS OF TOXICITY AND EFFICACY IN A NORTHEAST PUBLIC CENTER

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INTRODUCTION: The autologus bone marrow transplantation (BMT) is an important treatment in relapsed and refractory lymphoma diseases. With the shortage of carmustine, other available, safe and efficient conditioning was necessary. Based on KHATTRY et al, LACE versus BEAM conditioning in relapsed and refractory lymphoma transplant: retrospective multicenter analysis of toxicity and efficacy. Int J Hematol (2016) 103:292–298 and others articles was started the LACE condiotining in our service.

OBJECTIVE: Describe the patients characteristic, toxicities, neutrophilic and platelets grafts and survival outcomes of patients realized BMT used LACE.

METHODS: We included all the patients realized BMT used LACE (lomustine 200 mg/m 2 day-7, etoposide 1000 mg/m 2 day-7, cytarabine 2000 mg/m 2 day-6 to day-5, and cyclophosphamide 1800 mg/m 2 day-4 to day-2) conditioning between September/2018 and May/2022 at University Hospital Walter Cantidio at Fortaleza, Ceará. Patients were followed up for development of transplant-related toxicities and survival outcomes. The datas were collected in the REDCAP, the database of our service.

RESULTS: Fifty-five patients had BMT used LACE between September/2018 and May/2022. The oldest patient was 69 years old and the youngest 14 years old. 58% had Hodgkin disease and 20% Mantle cell disease. 65,5% had complete response before BMT and 34,5% with partial response. The Table 1 had others characteristics. The toxicities during the BMT were low, according the Table 2. None death related therapy. One patient had hemorrhagic cystitis. The medium Neutrophilic graft was D+10 and the medium platelets graft was D+15. 76,4% had complete response in D+90. 87,5% had complete response in D+360, into the patients evaluated.

CONCLUSION: We concluded that LACE is effective and well-tolerated conditioning regimen. We need a long term follow-up to better evaluation.

Keywords: Conditioning regimen. Hodgkin lymphoma. Hematopoietic stem cell transplantation. Non-Hodgkin lymphoma.

TABLE 1. Patients Characteristic.

	N:55
Age	Under 20: 8
	21-30 y: 8
	31-40 y: 11
	41-50 y:10
	51-60 y:12
	61-70 y: 6
Sex	Male: 26
	Female: 29
Race	White:20
	Black: 5
	White and Black: 30

Karnofsky	100:39
	90:17
	80:1
Comorbidity	HAS:12
	Diabetes: 3
	Psiquiatric disease: 9
Disease	Hodgkin disease: 32
	B cell Lymphoma: 5
	Follicular lymphoma: 3
	Mantle cell: 11
	T cell Lymphoma: 4
Time of BMT	First line: 10
	Refractory or early relapse:28
	Late relapse:17
Response before BMT	Complete response: 36
	Partial response: 19

TABLE 2. Results of LACE conditioning.

		N=55
Toxicity (CTCAE)	Mucositis	Grade 1: 25 Grade 2: 27 Grade 3: 3
	Vomits and nauseas	Grade 1: 32 Grade 2:21 Grade 3: 2
	Diarrhea	Grade 1: 37 Grade 2:16 Grade 3: 2
	Hepatic toxicity	Grade 1: 47 Grade 2: 8
	Renal toxicity	Grade 1: 52 Grade 2:2 Grade 3: 1
Febrile neutropenia	Yes	44
	No	11
Hemodynamic instability	Yes	4
	No	51
Graft syndrome	Yes	10
	No	45
Neutrophilic graft	Minimum	+8
	Medium	+10
	maximum	+22

Platelet graft	Minimum	+10
	Medium	+15
	maximum	+31
Inpatient time	Minimum	18
	Medium	22
	maximum	39
D+90 response	Complete	42
	Partial	3
	Refractory	7
	Under D+90	3
D+360 response	Complete	21
	Partial	1
	Refractory	2
	Not evaluated/ not information	18
	Under D+360	16

LEAM VERSUS LACE CONDITIONING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANT FOR RELAPSE AND REFRACTORY HODGKIN LYMPHOMA: RETROSPECTIVE SINGLE CENTER ANALYSIS OF EFFICACY

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INTRODUCTION: BEAM (carmustine, etoposide, cytarabine and melphalan) chemotherapy is the most widely adopted conditioning regimen for autologous hematopoietic stem cell transplant (auto-HSCT) in refractory and relapsed (R/R) Hodgkin lymphoma (HL) patients. Owing to carmustine and melphalan shortages in undeveloped countries in the last decade, many transplant centers have substituted BEAM for LEAM (lomustine, etoposide, cytarabine and melphalan) or LACE (lomustine, etoposide, cytarabine and cyclophosphamide), although efficacy and comparative data about these alternative regimens are scarce.

OBJECTIVE: To compare LEAM versus LACE conditioning auto-HSCT progression free survival (PFS) and overall survival (OS) in a R/R-HL-patient cohort.

METHODS: Retrospective analysis of 87 adult patients with R/R HL, who underwent LEAM or LACE conditioning auto-HSCT between 2015 and 2020, in a public south brazilian institution. A minimal of 2x106/kg cryopreserved CD34+ cells were infused per patient. High risk criteria for disease relapse after auto-HSCT were characterized as: relapse within 1 year or refractoriness to frontline therapy; extranodal extension and/or B symptoms at relapse; requiring >2 lines of salvage therapy or failure to achieve a complete remission before HSCT. The PFS and OS were estimated using the Kaplan-Meier function. Patient characteristics and early post-HSCT outcomes were compared using Chi-square test, Fisher's exact test, Student's t-test and likelihood ratio test.

RESULTS: Thirty-nine patients (44,3%) were treated with LEAM and 48 (54,5%) with LACE. The median age was 33.7 and 31.6 years (p=0,43), and 94,9% and 89,4% of the patients had high risk criteria for disease relapse after auto-HSCT (p=0,45), respectively. Other clinical features were similar between the groups, except for extranodal extension at diagnosis (LEAM: 39,5%; LACE: 12,8%; p=0,005), BEACOPP first-line treatment (LEAM: 10,3%; LACE: 0%; p=0,036), B symptoms at relapse (LEAM: 47,8%; LACE: 13%; p=0,01) and disease status before transplant (LEAM versus LACE: complete response, 37,8 and 43,5%; partial response, 62,2 and 37%; stable disease, 0 and 15,2%; disease at progression, 0 and 4,3%, respectively; p=0,004). Median inpatient hospital stay (22 days) and time to neutrophil engrafment (10 days) were similar between the groups. After median follow-up of 24.7 months (IQR 3,9 - 45,8), the 3-year estimated PFS and OS were 52,7% and 63,9% (p=0,623) and 78,2% and 84,9% (p=0,945), for LEAM and LACE groups, respectively. Six patients in each group died, the main cause being infectious disease, followed by disease progression.

CONCLUSION: Our retrospective analysis demonstrated similar outcomes for PFS, OS and early mortality between LEAM and LACE auto-HSCT, in a single center R/R-HL-patient cohort. Also, these results are comparable to BEAM conditioning historical data, and support the use of LEAM and LACE as low-cost and accessible conditioning regimens for R/R HL patients.

Keywords: Hodgkin disease. Autologous Transplant. Hematopoietic Stem Cell Transplantation. Transplant Conditioning. Treatment Outcome.

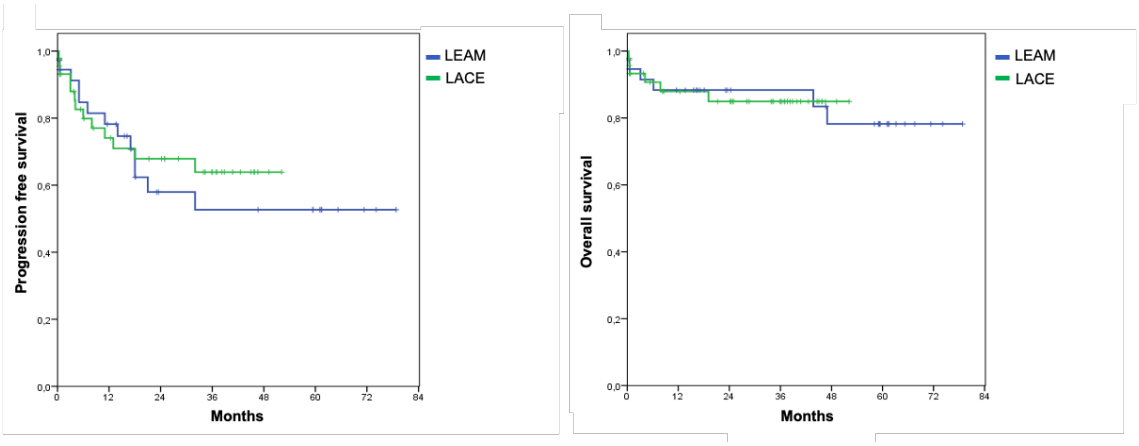
TABLE 1. Clinical characteristics of patients with R/R HL who underwent autologous HSCT, according to LEAM or LACE conditioning regimen.

	Total	Conditioning regimen		p
		LEAM	LACE	
Age (years)				0,431**
median (p25; p75)	29 (24,3; 39)	29 (25; 42)	29,5 (23; 36,8)	
Sex, n (%)				0,627
Female	41 (47,7)	17 (44,7)	24 (50)	
Male	45 (52,3)	21 (55,3)	24 (50)	
Stage at diagnosis, n (%)				0,218#
Favorable	10 (11,9)	2 (5,4)	8 (17)	
Unfavorable	25 (29,8)	11 (29,7)	14 (29,8)	
Advanced	49 (58,3)	24 (64,9)	25 (53,2)	
B symptoms at diagnosis, n (%)				0,170
Yes	59 (68,6)	29 (76,3)	30 (62,5)	
No	27 (31,4)	9 (23,7)	18 (37,5)	
Extranodal extension at diagnosis, n (%)				0,005
Yes	21 (24,7)	15 (39,5)	6 (12,8)	
No	64 (75,3)	23 (60,5)	41 (87,2)	
Bulky disease at diagnosis, n (%)				0,227
Yes	31 (36,9)	11 (29,7)	20 (42,6)	
No	53 (63,1)	26 (70,3)	27 (57,4)	
Frontline therapy, n (%)				0,036#
ABVD	78 (89,7)	33 (84,6)	45 (93,8)	
BEACOPP	4 (4,6)	4 (10,3)	0 (0)	
Other&	5 (5,7)	2 (5,1)	3 (6,3)	
Prior radiotherapy, n (%)				0,709
Yes	26 (30,2)	11 (28,2)	15 (31,9)	
No	60 (69,8)	28 (71,8)	32 (68,1)	
Status after frontline therapy, n (%)				0,554
Complete response	43 (50)	22 (56,4)	21 (44,7)	
Partial response	13 (15,1)	5 (12,8)	8 (17)	
Refractory	30 (34,9)	12 (30,8)	18 (38,3)	
Relapse, n (%)				0,773
< 12 months	23 (47,9)	11 (45,8)	12 (50)	
≥ 12 months	25 (52,1)	13 (54,2)	12 (50)	
Stage of relapse, n (%)				0,302
Favorable/unfavorable	22 (46,8)	9 (39,1)	13 (54,2)	
Advanced	25 (53,2)	14 (60,9)	11 (45,8)	
B symptons at relapse, n (%)				0,010
Yes	14 (30,4)	11 (47,8)	3 (13)	
No	32 (69,6)	12 (52,2)	20 (87)	

Extranodal extension at relapse, n (%)				0,250
Yes	15 (32,6)	9 (40,9)	6 (25)	
No	31 (67,4)	13 (59,1)	18 (75)	
Bulky disease at relapse, n (%)				0,694*
Yes	7 (15,2)	4 (18,2)	3 (12,5)	
No	39 (84,8)	18 (81,8)	21 (87,5)	
Status before auto-HSCT, n (%)				0,004#
Complete response	34 (41)	14 (37,8)	20 (43,5)	
Partial response	40 (48,2)	23 (62,2)	17 (37)	
Stable disease	7 (8,4)	0 (0)	7 (15,2)	
Progressive disease	2 (2,4)	0 (0)	2 (4,3)	
Risk factors for progression after auto-HSCT, n (%)				0,448*
High risk	79 (91,9)	37 (94,9)	42 (89,4)	
Low risk	7 (8,1)	2 (5,1)	5 (10,6)	
Number of previous salvage therapies, n (%)				0,332
1	46 (52,9)	24 (61,5)	22 (45,8)	
2	29 (33,3)	11 (28,2)	18 (37,5)	
3 or more lines	12 (13,8)	4 (10,3)	8 (16,7)	

Chi-square test; *Fisher's exact test; #Likelihood ratio test; **Student's t-test.
&Stanford V, VAMP, ICE e R-DA-EPOCH.

FIGURE 1. Kaplan Meier survival estimate for (a) Progression free survival, (b) Overall survival, according to type of conditioning (p=0,623 and p=0,945, respectively).



MEDULLOBLASTOMA IN CHILDREN LESS THAN FIVE YEARS OLD: A PROSPECTIVE ANALYSIS OF OUTCOME WITH INTENSIVE MYELOABLATIVE CHEMOTHERAPY AND AUTOLOGOUS BONE MARROW TRANSPLANT.

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INTRODUCTION: Medulloblastoma (MB) is the most common malignant brain tumor in children less than three-five years. Histological variants consist of classic, MB with extensive nodularity (MBEN), desmoplastic/nodular (MBDN), large-cell/anaplastic and are staged based on extent of resection, dissemination and more recently, molecular stratification.

OBJECTIVE: The aim of this study is to evaluate the outcome of children less then 5 years of age treated with intensive myeloablative chemotherapy and autologous bone marrow transplant (IMC/ABMT).

METHODS: A prospective study was performed between 2016-2019. Twenty patients were treated according to a modified Head Start backbone (HS) protocol followed by ABMT. Radiogenomics/ Immunohistochemical correlation was used to stratify into molecular subgroups: MB with wingless (WNT) activation, sonic hedgehog (SHH) activation and non-WNT/non-SHH MB.

RESULTS: Mean age 2.6 years (1.5-4.8y), 12 males. Mean time to initial symptoms to diagnosis was 3.9 months (0.2-12months). Sixteen had complete resection, thirteen no metastasis. Fourteen were classified as MB-SHH, four with P53 protein >50% and six as non-WNT/non-SHH. All twenty patients proceeded to ABMT after 3-5 cycles of modified HS. The most common toxicities were gastrointestinal and fever with all patients presenting with mucositis/ typhlitis and febrile neutropenia. Two patients also presented with veno-occlusive disease and five with bloodstream infection. The Progression-free survival (PFS) and overall survival (OS) across the entire cohort was 46.2% and 72% at a median follow-up of 27.5 months. According to histology, PFS and OS for MBDN was 68.6% and 90%, for classic-MB 35% and 67.5%, respectively. Two MBDN patients relapsed, both with M+ disease and radiogenomics/ immunohistochemical correlation with SHH-activation and possible Tp53 mutation (p53>50%); One patient died without disease due to Coronavirus + and meningitis four months after ABMT. Among relapsed classic-MB, one had M+ disease and SHH characteristics and the other three were classified as non-WNT/ non-SHH: two also had M+, one with MYCC+ on histology. Both MBDN and two/four relapsed classic-MB are alive after salvage therapy with craniospinal irradiation. Thirteen patients (65%) are alive without RT.

CONCLUSION: We report the outcome of children with medulloblastoma less than 5 years of age, treated with IMC/ABMT, showing a very acceptable outcome despite difficulties in referral and in performing properly the molecular evaluation on a routine basis.

PLERIXAFOR USE IN POOR MOBILIZERS FOR AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Autologous hematopoietic stem cell transplantation is a modality of cell therapy in which cells mobilized from the patient himself are used as a rescue of the damaged hematopoiesis due to the infusion of high dose chemotherapy used in the treatment. In the mobilization process using only high doses of G-CSF, up to 40% of patients do not reach the minimum of 2x106/kg of collected CD34+ cells and in a second attempt, this rate can reach 77%, making transplantation impossible. Among the risk factors for poor mobilization are advanced age, diagnosis of lymphoma, bone marrow infiltration, radiotherapy, ≥3 treatment chemotherapy protocols, use of alkylating agents, thalidomide and lenalidomide. Plerixafor is a selective inhibitor of CXCR4, resulting in increased release of stromal cells from bone marrow to peripheral blood. Due to its high cost, it is reserved for patients who cannot mobilize an adequate number of CD34+ cells.

OBJECTIVE: To evaluate the epidemiology and results of the use of plerixafor in patients with poor mobilization at a Brazilian HSCT center.

METHODS: Retrospective study of data from medical records of patients who received the association of G-CSF and plerixafor in the mobilization strategy, from 2014 to April 2022. We analyzed parameters of sex, age, funding, underlying disease, quantification of CD34+ pre-collection and on the product. Data will be presented using descriptive statistics. Consent terms were collected for data sharing, which were anonymized.

RESULTS: Twenty-six patients who used plerixafor were identified, 38% male and 62% female, with a median age of 55.5 years (18-73), with 65% and 35% of care, respectively, with public or private funding. The underlying diseases under treatment were: plasma cell neoplasms (N=10), lymphomas (N=15) and germ cell tumor (N=1). The mean pre-collection of peripheral CD34+ cell count was 35/mm3 (6.5-124.46) and in the final product it was 3.7x106/kg of patient weight (0.84-9.53). All patients underwent a collection attempt on day 5 of mobilization, with plerixafor infusion 6-8h before initiation. Six patients (23%) did not reach the collection goal, five diagnosed with lymphoma and one with multiple myeloma.

CONCLUSIONS: Local data show that most treated patients reach an adequate number of cells to proceed with autologous transplantation with the use of G-CSF and plerixafor in mobilization. There was no barrier to accessibility to plerixafor among users of the public health system in this study. Lymphoma patients had more collection failures. More real-life data on the use of plerixafor, including economic studies, are needed to assess cost savings due to fewer collection procedures required, better graft quality with reduced costs for complications and blood transfusions, besides assessment of overall and progression-free survival of this patient population.

Keywords: Plerixafor. Hematopoietic stem cell mobilization. Peripheral blood stem cell transplantation.

RETROSPECTIVE STUDY OF PATIENTS WITH HODGKIN'S LYMPHOMA WHO HAD HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM 2009 TO 2020 IN A REFERENCE HOSPITAL IN THE STATE OF CEARÁ

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INTRODUCTION: Autologous hematopoietic stem cell transplantation preceded by chemotherapy that allows disease reduction and mobilization of stem cells in peripheral blood is considered standard treatment for patients who relapse after first-line therapy. Profile evaluation of patients with relapsed/refractory Hodgkin's Lymphoma is essential for defining the rate of relapse after HSCT, in addition to the prognosis and therapy to be instituted after transplantation.

OBJECTIVE: To evaluate the profile of patients with Hodgkin's Lymphoma who underwent hematopoietic stem cell transplantation from 2009 to 2020 at the Bone Marrow Transplantation Service of the Reference Hospital of the State of Ceará.Casuistry. We analyzed autologous and allogeneic transplants performed between 2009 and 2020, in patients over 18 years of age diagnosed with refractory/recurring Hodgkin's Lymphoma after previous therapy. Methods. This is a retrospective, descriptive, analytical study with data collection through the analysis of exams and medical records. A collection form was used, and the data were entered in an Excel spreadsheet for quantitative analysis. Variables related to the patient and the therapy instituted before and after transplantation were analyzed. The outcomes correspond to the assessment of prognosis and the need for post-transplant therapy.

RESULTS: 91 patients were included in the study, 44 female patients and 47 male patients, divided into two age groups: patients between 18 and 35 years old with a total of 70 patients (76.92%) and 36 to 55 years old, 21 patients (23.07%). In the evaluation of the patients' profile, 31 of them (34.06%) had had three or more lines of treatment. In histological evaluation, 74 (81.3%) were of the Nodular Sclerosis subtype. The staging shows the prevalence of patients with B symptoms at diagnosis, in addition to a bulky mass, totaling 42%. The pre-transplant response assessment showed that 49 patients (53.84%) had a complete response and 42 (46.1%) had a partial response. On D+90, the patients were reassessed and 57 (62.6%) were in complete response, while 20 (21.9%) had active disease. The need for post-transplant therapy was evaluated, with a record of 21 patients (23%) having had radiotherapy, 11 (12%) had radiotherapy and Brentuximab and 16 (17.5%) had undergone Brentuximab.

CONCLUSIONS: The importance of this assessment is essential to define the impact on the prognosis of post-transplant patients, such as: number of chemotherapy lines performed, presence of a bulky mass at diagnosis, advanced staging, presence of B symptoms and chemosensitivity. The standard therapy for patients with relapsed/refractory Hodgkin's Lymphoma remains high-dose chemotherapy followed by autologous HSCT. About 40-50% of patients will relapse even after HSCT, but despite this chance of relapse, the use of therapies such as radiotherapy, anti-CD30 or second HSCT, increases the survival of these patients.

START OF THE HEMATOPOIETIC STEM CELL TRANSPLANTATION PROGRAM AT HOSPITAL NOSSA SENHORA DA CONCEIÇÃO IN PORTO ALEGRE / RS.

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INTRODUCTION: hematopoietic stem cell transplantation (HSCT) is a potentially curative treatment modality for a wide variety of hematologic diseases. It is a high complexity procedure, the success of which directly involves the performance of a specialized multidisciplinary team, which implies overcoming several barriers to its implementation, especially in public institutions. The Nossa Senhora da Conceição Hospital (HNSC), linked to the Ministry of Health, has 800 beds for 100% SUS care. It has a long tradition in the care of onco-hematological diseases and still did not have an HSCT program. The Hematology unit has 25 exclusive beds (2 with HEPA filter), and a medical and multiprofessional fellowship program. In its conclusion phase, the new Hematology and Oncology Center will expand access to the population, with 98 beds (48 with HEPA filter) and a complete structure for day hospital and radiotherapy.

OBJECTIVE: to characterize the first patients who underwent autologous HSCT at the HNSC.

METHODOLOGY: descriptive study that presents data from the first patients undergoing HSCT. The protocol used includes pre-BMT multidisciplinary assessment, mobilization with outpatient/home filgrastim, CD34 count before collection and before catheter insertion.

RESULTS: six autologous HSCT were performed since December 2021. All patients were diagnosed with multiple myeloma. The mean age was 61 years (43-70 years). All patients were evaluated as normal weight according to ASGPPP and the mean BMI was 30.68kg/m^2. In the assessment of muscle strength, performed by dynamometry, the average for the dominant limb in women (n=2) was 19KgF and for men (n=4) it was 49KgF. (normal 27.05KgF for women and 47.9KgF for men), with all patients with dominance in the right limb. Hypertension was the most frequent comorbidity (n=3). All patients had ECOG 1 pre-transplantation. Five of these patients reached the target of 2x106 CD34+cells/kg in just one day of collection, and the mean infused CD34+ cells was 3.6x106/kg (2.4 - 5.6x106/kg). Half of the patients used conditioning with Melphalan 200mg/m2, while the rest used 140mg/m2, due to age. Fresh infusion occurred within 48 h of cell collection in all patients except one. The mean length of hospital stay was 16.6 days, and the bone marrow engrafment took place in an average of 10.4 days. The most frequent complications resulting from the procedure were mucositis (grade 1, n= 1; grade 2, n= 3; grade 3, n= 1; CTCAE v5.0), febrile neutropenia (grade 3, n= 6; CTCAE v5 .0) and diarrhea (grade 2, n=3; CTCAE v5.0). One patient developed septic shock and was transferred to the intensive care unit, with recovery within 4 days.

CONCLUSION: the initial data demonstrate the adequacy of the protocol used and the importance of engaging the entire institution in the implementation of a program of this nature.

HSCT PEDIATRIC

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT IN PEDIATRICS: A SINGLE-CENTER UNIT EXPERIENCE

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INTRODUCTION: Allogeneic hematopoietic stem cell transplantation (allo-SCT) can be a curative treatment for pediatric patients with hematologic malignancies and non-malignant disorders, such as bone marrow failure syndromes. It is known that the main obstacles for a successful allo-SCT are relapse of the underlying disease, GvHD and infection, and it is essential to assess results and patients' profile to improve the center's efficiency.

OBJECTIVE: The present study aimed to analyze the results of 40 patients, including survival rate and transplant complications, performed in a single pediatric center.

METHODS: Retrospective study of data medical records of pediatric patients from graft allo-SCT from August 2019 to May 2022. We analyzed parameters of donor, graft source and survival. Data will be presented using descriptive statistics. Consent terms were collected for data sharing, which were anonymized.

RESULTS: In total, 40 allo-SCT procedures were performed from August 2019 to May 2022. Of those, 5% undergoing 2nd allo-SCT. Most of the patients were treated for ALL (65%), followed by AML (15%) and SAA (15%). Bone marrow was the major stem cell source (62,5%). Twenty-five patients (62,5%) underwent haploidentical transplant, 9 patients (22,5%) received matched unrelated donor (MUD) source, 5 patients (12,5%) matched related donor (MRD) and 1 patient (2,5%) mismatched unrelated donor (MMUD). We identified 7 patients who relapsed after all-SCT, most children (n=5) presented with ALL. Relapse was grater in MRD–SCT (40%), followed by haplo-SCT (16%) and MUD-SCT (10%). The 33-months overall survival was 75%. Among the causes of death, relapse occurred in 5 patients (12,5%) and transplant-related mortality (TRM) in 4 patients (10%), due to infection (n=3) and grade IV acute GvHD (n=1).

CONCLUSION: Allo-SCT plays an important role in the management of pediatric patients. Despite the limitations related to its retrospective nature and small cohort, our study shows primary disease as one of the main causes of death, similar to what was found in the literature. There was a higher occurrence of haplo-SCT and this donor source was not associated with a higher relapse rate. Despite bone marrow being the main source of cells, we observed a reduction in its use during the pandemic period. We believe that the careful and continuous analysis of our data will help to achieve continuous improvement of the services provided.

Keywords: Allogeneic Hematopoietic Stem Cell Transplant. Data analyses. Pediatrics.

COVID-19 IN CHILDREN UNDERGOING BONE MARROW TRANSPLANTATION: CLINICAL CHARACTERISTICS AND ASSOCIATION WITH GRAFT-VS-HOST DISEASE.

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INTRODUCTION: Infectious complications are an important cause of morbidity and mortality for hematopoietic stem cell transplant (HSCT) recipients and, associated with graft-versus-host disease (GVHD), represent important obstacles to therapeutic success. In the current context of a pandemic, COVID-19 represents another threat to these patients. Most children have mild COVID, even after HSCT, but the prevalence of complications and the impact of GVHD are unknown.

OBJECTIVE: To describe the characteristics of SARS-CoV-2 infections in children undergoing HSCT and their association with GVHD.

METHODS: Retrospective observational study carried out at a reference center for Pediatric Oncology in the State of São Paulo. Patients up to 21 years of age undergoing HSCT between 1/1/20 and 3/6/22 with positive RT-PCR for SARS-CoV-2 were included.

RESULTS: During the study period, 198 patients underwent HSCT. Sixteen (8%) had SARS-CoV-2 infection at a median of 94.5 days after HSCT (5-681 days). Of these, 14 had received allogeneic HSCT, of which 11/71 (15%) were haploidentical, 3/19 (16%) were related and 2/86 (2%) were autologous. Nine had neutrophils < 1,500/mm3, three of them < 500/mm3. Half were using some immunosuppressant, but only one with corticosteroids. The clinical presentation of COVID-19 was mild in 87% and 13% progressed to a severe condition. One patient developed diabetes insipidus 6 days after the diagnosis of COVID, with the need to continue using desmopressin afterwards. Only one patient required intensive care, with mechanical ventilation, dialysis and died from "Multisystem Inflammatory Syndrome in Children" (MIS-C). Viral clearance occurred in a median of 20 days after diagnosis (10 to 40 days). Five patients already had a diagnosis of GVHD when they were infected with SARS-CoV-2, four of them showed significant clinical worsening of acute GVHD and three progressed to overlap syndrome. Three additional patients developed acute GVHD of the skin (3/3), liver (1/3), and intestine (1/3) 27 to 104 days after infection. Three patients had a palmoplantar rash typical of serum sickness, with marked intersection between healthy and diseased skin, as well as rapid progression to overlap syndrome and significant intestinal involvement.

CONCLUSION: Most patients with SARS-CoV-2 infection had a mild condition, but we observed complications never before described in HSCT, such as diabetes insipidus and a rash similar to serum sickness. MIS-C and death occurred in only one patient with mild acute GVHD before infection: case fatality in the study was 6% (1/16). COVID after allogeneic HSCT presented significant morbidity and unfavorable evolution in the presence of GVHD. Larger studies are needed to study the impact of the COVID-19 pandemic on the clinical outcome of post-HSCT patients.

Keywords: Bone marrow transplant. COVID-19. Hematopoietic stem cells.

FIGURE 1. **Plantar rash typical of serum sickness, with marked intersection between healthy and diseased skin seen in patients with GVHD and covid.**

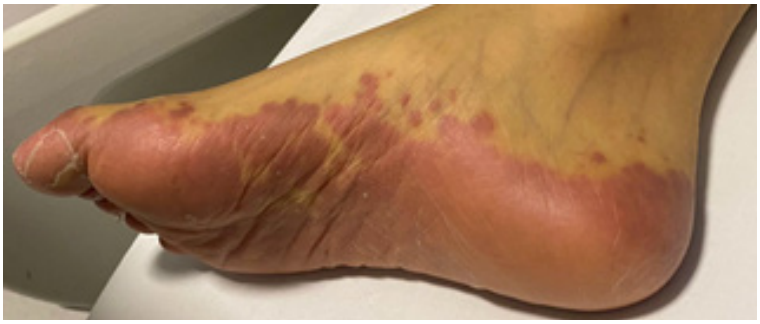
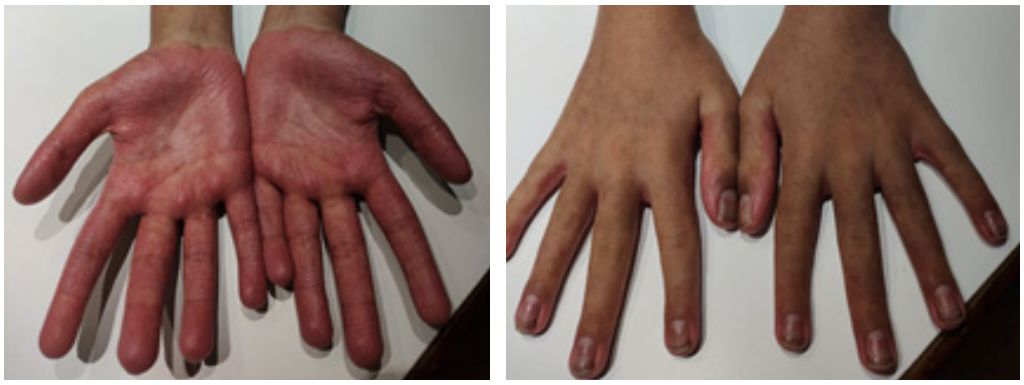


FIGURE 2. **Palmar rash typical of serum sickness, with marked intersection between healthy and diseased skin seen in patients with GVHD and COVID.**



FECAL MICROBIOTA TRANSPLANTATION IN CHILDREN AFTER HEMATOPOIETIC STEM-CELL TRANSPLANT: A CENTER EXPERIENCE

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BACKGROUND: Intestinal microbiota imbalance after hematopoietic stem cell transplant is associated with worse outcomes. There is plenty of evidence that microbiota influences the immune system, suppresses pathogenic bacteria, and promotes regeneration of the gastrointestinal (GI) mucosa. Fecal microbiota transplantation (FMT) is directed to recovery of recipient microflora. Our aim is to present two cases treated by FMT.

CASES: Three-year-old boy, treating a juvenile myelomonocytic leukemia relapse underwent his second HSCT, with a match unrelated donor 12/12. No history of infection or colonization by multiresistant bacteria prior to transplant. Conditioning regimen included Bussulfan AUC 3600 um/min, Fludarabine 120 mg/m2 Melphalan 140 mg/m2. GVHD prophylaxis consisted of methotrexate with cyclosporine (CSA). Graft source was bone marrow with TNC/kg 5,89x10*8 and neutrophil engraftment at day +28. He had countless infectious episodes. Positive Blood culture for Candida krusei, Candida tropicalis, Enterococcus faecalis and Klebsiella pneumoniae ESBL. On day +84, patient presented with grade III lower GI GVHD, progressing to severe GVHD, confirmed by biopsy. Diarrhea persisted even though he was on immunosuppression (CSA) and steroids. Eight months post HSCT patient was submitted to a FMT, with no complications. His GI symptoms resolved and no new episodes of infection occurred. Currently well and 18 months post-transplant. The second case was a 3-year-old girl, with pre-B-acute lymphoblastic leukemia and early bone marrow and CNS relapse, who underwent HSCT with her mother as the haploidentical donor. Conditioning consisted of Cy 100 mg/Kg and total body irradiation (12 Gy). GVHD prophylaxis with Cy 100mg/Kg, CSA and MMF. Graft source was peripheral stem cell with CD34/kg 7,5x10*6. Neutrophil engraftment at day +15. Previous to HSCT she was already colonized by Klebsiella Pneumoniae Carbapenemas (KPC) and had recurrent infections by Clostridium difficile (C.dif). On day +25 initiated with diarrhea and C.dif test positive. At the time she also had skin and gut grade III GVHD. Her symptoms did not improve despite steroids and immunosuppressive therapy. On day +31 she was submitted to FMT, with no complications. Diarrhea was resolved, no new episodes of C.dif. infection, and vigilance swabs were negative 30 days after the procedure. Currently 1-year post HSCT and well. The protocol for FMT followed the North American and European Society Guidelines, with fresh material, performed by colonoscopy, single infusion with 50 ml, and stool preparation, infused liquid. Donors underwent serological and infectious screening before the procedure.

CONCLUSION: The role of FMT is yet unclear, but it has been described as a successful treatment for C.dif., decolonization by multiresistant bacteria and GVHD. FMT was safely performed in our patients and might offer a novel therapeutic option for aGVHD.

Keywords: Transplantation of fecal microbiota; multiresistant bacteria; graft versus host disease.

INDIVIDUALIZED DOSE OF ANTITHYMOCYTE GLOBULIN(ATG) IN PEDIATRIC PATIENTS WITH MALIGNANT AND NON MALIGNANT DISEASES: SAFETY AND OUTCOMES

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BACKGROUND: Anti Thymocyte Globulin (ATG) is used extensively during conditioning as GvHD prophylaxis in children and adults. Recent data (Aadmiral et al, Lancet Hematology 2022) has shown that individualized dosing based on weight and absolute lymphocyte count (ALC) is associated with a high rate of immune reconstitution in chidren , measured by CD4 counts at day 100 post-transplant.

OBJECTIVE: Report our experience with individual ATG dosing in children and analyze the rate of engraftment, immune reconstitution, GvHD, CMV reactivation, non-relapse mortality and overall survival.

PATIENTS AND METHODS: Patients transplanted from 2015 through 2021 were included in the analysis. dose was adjusted to weight and ALC as described previously and started on day -9. Conditioning regimens are shown in table 1. GvHD prophylaxis included a calcineurin inhibitor plus methotrexate for recipients of MSD or URD donors or prednisone for UCB donors. Engraftment was defined as >95% chimerism on day +30. CD4 counts were performed at day +90 and a direct comparison was done between malignant and nonmalignant patients (paired T test). CMV viral load was monitored weekly. Non-relapse mortality (NRM) and overall survival (OS)were analyzed by Kaplan Meyer.

RESULTS: 93 children were included in the study. Median age was 7 yrs., range 9 months-17 yrs. 52 had hematological malignancy and 41 nonmalignant diseases (Table 1). The average ATG dose administered was 6 mg/kg(range 4 to 10)Engraftment rate was 94 %. Mean day 90 CD4 count was 171 per µL (range 18-1985) and it was > 50 per µL in 82% pts. No difference was seen between malignant and nonmalignant pts: 155 per µL vs 198 per µL (p=0.17, fig 1). 24% pts had CMV reactivation. Grade 2-4 aGvH incidence was 30% pts and grade 3-4 21%. cGvH incidence was 8% and extensive cGvH 4%. No pt developed lung cGvH. With a median time of follow up for pts at risks, overall survival is 85.2 % (CI 78%-93%), 79.8 % for malignant and 90.7% for nonmalignant pts (p=0.14). NRM was 11% (CI 5% - 18%, fig 3)) ? No difference was seen in OS or NRM regarding the donor source (matched sibling donor vs unrelated).

CONCLUSION: Individualized dosing using weight and ALC in pediatric patient is safe and correlates with almost universal engraftment, low rates of cGvH and NRM and good overall survival. Longer follow up of patients with malignancies is needed to demonstrate the impact on relapse rates.

TABLE 1. Patient´s diagnosis and preferred conditioning regimens

Diagnosis	Stage of disease	n	Preferred conditioning
ALL	CR1, CR2	22	TBI, cyclo
ALL	>CR2	10	TBI, cyclo, thiotepa
AML, MDS, CML		16	Treo Cy (flu) Mel
Lymphoma		4	Treo Cy (TTP)
Severe aplastic anemia		15	Cy Flu +/- TBI 2Gy
Congenital hematological (Blackfan, agranulocytosis, Chediak, FHL)		7	Treo Flu +/- Thiotepa
Congenital immunodeficiencies (SCID, WAS, CD40 def, APDS1, GOF STAT1, CGD, LAD, IPEX, XLP EBV)		16	Treo flu +/- Thiotepa
Inborn errors (XALD, MPS1)		3	Treo flu Thiotepa

FIGURE 1.

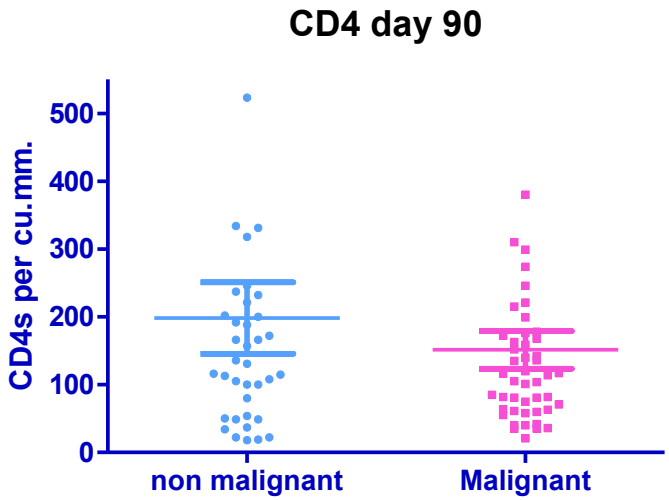


FIGURE 2.

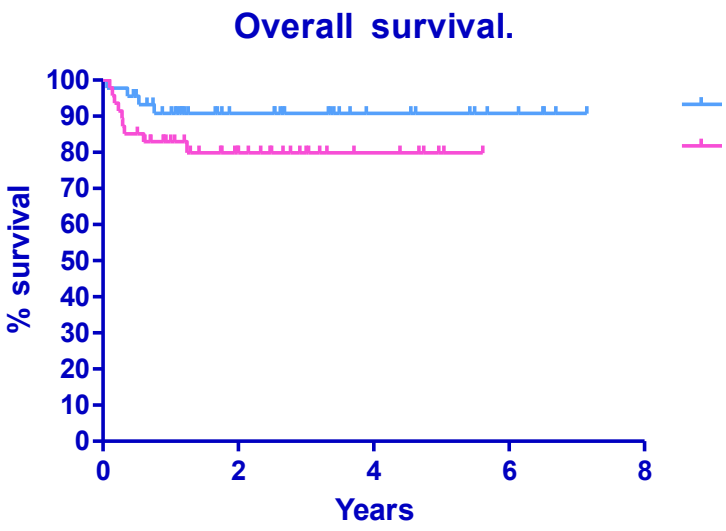
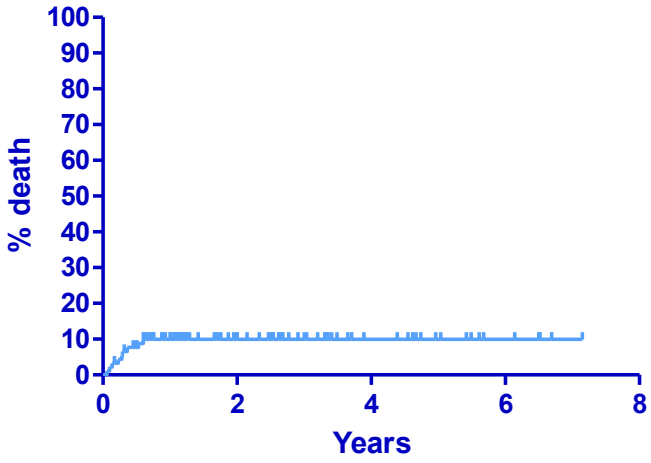


FIGURE 3.



MANAGEMENT PRE AND POST-STEM CELL TRANSPLANTATION OF A CHALLENGING CASE OF A CHILD WITH MYELOID/LYMPHOID NEOPLASM WITH FGFR1 REARRANGMENT

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INTRODUCTION: Myeloid/lymphoid neoplasms with eosinophilia and FGFR1 rearrangement (MLN-eo FGFR1) is rare. Allogenic stem cell transplantation (SCT) is the best choice for long-term survival, but early relapses are frequent.

OBJETIVE: We reported the management pre and post-allogeneic SCT in a child presenting MLN-eo with FGFR1 rearrangement.

CASE REPORT: An 11-year-old girl was admitted in Nov/2019 with marked leukocytosis, eosinophilia, lymphadenomegaly and splenomegaly. Myelogram showed hypercellular marrow infiltrated by small lymphocytes, granulocytic hyperplasia, eosinophilia. Flow cytometry (FC) showed dysplasia in myeloid sector and eosinophilia. Bone marrow (BM) and cervical lymphnode (LN) biopsy were compatible with the diagnosis of T lymphoblastic Leukemia/Lymphoma (T-NHL/L). Cytogenetic study was normal (27 metaphases). Molecular analyses were negative for bcr-abl, CBFb-MyH11, RUNX1-RUNX1T1, JAK2 mutation and PDGF . BFM protocol 2009 was initiated in Dec/2019. Ten months later, recurrence of splenomegaly, lymphadenomegaly, leukocytosis with marked eosinophilia occurred. FC was suggestive of myeloproliferative disease/myelodysplasia. BM showed predominance of granulocytic series, eosinophilia with delayed maturation, without excess blasts; histology within the context of MLN-eo. Biopsy of inguinal LN was compatible with T-NHL. FISH analyses on BM and LN with FGFR1 breakapart probe showed FGFR1 rearrangement. Due to relapse, BFM 2002 REZ protocol was started, with initial response until new progression on Mar/21, treated with one cycle of FLAG-IDA. She underwent allogeneic HLA-matched SCT from her ABO-matched, with standard CYTBI conditioning (12 Gy) and short methotrexate with tacrolimus (FK) for graft-versus-host disease prophylaxis (GVHD). Engraftment occurred at D+16. Monthly chimerism tests in BM and PB were all complete chimerism (CC). Marrow FC at D+30 and +60 showed dysplastic monocytic population and maturation asynchrony. Karyotype at D+60 was 46,XX-[1]/46,XY[22]. Due to the high risk of relapse, FK was discontinued on D+55, prophylactic azacytidine (AZA) was started (five cycles of 36 mg/m2/day for 5 day/monthly until Dec/21) with donor lymphocytes infusions (DLI). She received two prophylactic DLIs on D+83 and +113 and one preemptive on Feb/22. On D+90 and +120, had dysplastic changes with negative MRD, 100% male karyotype. BM evaluation on Jan/22 showed positive MRD (0.23%). Increased AZA dose to 75mg/m2/day (5 cycles from Jan to Jun/22). At the last evaluation, 13 months post-SCT, she was in molecular remission, without GVHD.

CONCLUSIONS: Aza combined with DLI and early tapering of FK sustained the response for 7 months after SCT. Frequent monitoring of MRD enabled us to increase the dose of AZA and DLI in time for enhance the GVL effect with mild toxicity. Clinical trials are necessary to define the best strategy for maintenance therapy after SCT for MLN-eo FGFR1 patients.

Supported by: FAPERJ, Ministério da Saúde-INCA.

Keywords: Myeloid. Lymphoid Neoplasm with FGFR1 rearrangement. Stem cell transplantation. Azacitidine. Donor lymphocyte infusion

SHOULD HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT)BE PURSUED AS UPFRONT THERAPY IN CHILDREN WITH SEVERE APLASTIC ANEMIA? A SINGLE CENTER TALE OF TWO PERIODS.

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BACKGROUND: Current guidelines for childhood severe aplastic anemia (SAA) recommend matched sibling donor (MSD) HSCT as therapy of choice followed by the use if immunosuppressant therapy (IST) for 3 to 6 months for pts lacking an MSD. An unrelated (URD) or haploidentical donor (haplo) HSCT is considered only in non-responders to IST. Improved results with URD or haplo transplants in SAA have challenged this guideline (Dufour et al, BJH 2015; Marsh et al BBMT 2019). Upfront HSCT from any donor may be a better option due to IST´s relatively high rate of failure, the increased risk of clonal abnormalities in long term survivors, the high risk of severe opportunistic infections with prolonged immunosuppression and the risk of graft rejection should the patient finally receive a HSCT. Nevertheless, these potential benefits have to be weighed against the risk of extensive cGvH.

OBJECTIVE: Analyze the outcome of childhood severe aplastic anemia in a single center in two time periods comparing IST versus upfront URD or haplo HSCT in children lacking a MSD.

PATIENTS AND METHODS: children with SAA treated at our institution form 1993 though 2021 were included in the analysis. From 1993 through 2009 (period A) patients were treated with upfront HSCT for those with a MSD, or a combination of prednisone, ATG and cyclosporine for the rest. Patients not responding to IST received a second course of ATG, a URD or haplo transplant or continued supportive care. From 2010 through 2021 (period B) all children with a MSD, fully matched or 1 antigen mismatched URD received upfront HSCT. The conditioning regimen included ATG, fludarabine and cyclophosphamide +/- 2Gy TBI. We analyzed: a) response rates to IST; b)5 year overall survival (OS) and a comparison of both periods. Survival was analyzed by Kaplan Meier and compared by Mantel Cox test.

RESULTS: 44 pts were included in the study, 23 in period A and 21 in period B. Median age was 9,7 years (range 1,8 – 19). 7 had very severe disease, 3 post hepatitis. During period A, 8 children received HSCT from a MSD and 15 IST. During period B, 19 children received an upfront HSCT: 7 from a MSD, 11 from an URD and 1 from a haplo donor. The median time from search to transplant with an URD was 67 days (range 14-139). 8/16 patients responded to IST (7 complete, 1 partial). 2 non-responding pts received a second course of ATG and 4 a HSCT with an URD or haplo donor. Median time to follow up was 8.9 and 2.5 tears for period A and B. 5 year OS for the whole group was 86.7% (CI 70.1 - 94.3%), 77.7% for period A and 100% for period B (Chi2 3.72, p=0.05, figure 1). 5 yrs OS for all pts transplanted upfront was 96% (CI 75 to 99.4%).

CONCLUSION: Upfront HSCT with MSD, URD and haplo donors confer an excellent outcome for children with SAA. Only 50% of patients responded to IST. Our study is limited for the long period of observation. GRFS data are needed to complete the analysis.

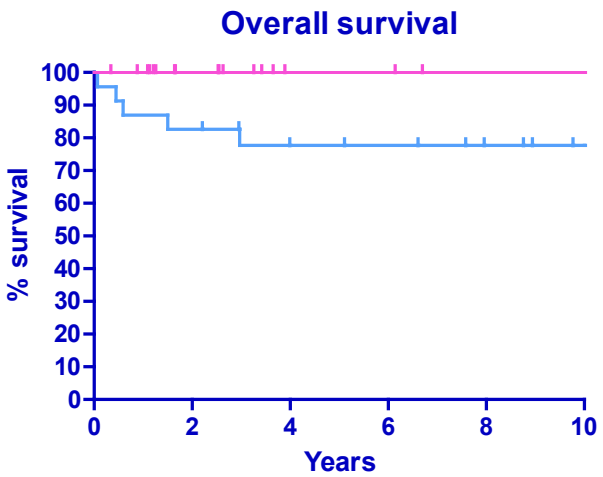

FIGURE 1. Overall survival for period a and B

INFECTIOUS COMPLICATIONS

COVID-19 INFECTION MIMICKING HODGKIN'S LYMPHOMA RELAPSE AFTER BONE MARROW TRANSPLANT

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INTRODUCTION: Since the emergence of COVID-19, there has been a global effort to unravel the effects of this new viral infection on the population. There are several publications on the impact of this infection in hematological patients and even postulations about the effect of the virus and the vaccine on immune regulation.

OBJECTIVE: To describe a clinical case of a patient after allogeneic bone marrow transplantation who acquired COVID-19 and mimicked a relapse of lymphoproliferative disease on PET/CT.

CASE REPORT: 25 years old male, diagnosed with classic Hodgkin's lymphoma refractory to several therapeutic lines and autologous transplantation. In 2021, he underwent a haploidentical bone marrow transplant. In the follow-up exams after transplantation, he always maintained complete chimerism and PET/CT without hypermetabolic lesions - Deauville classification 2 and 3. After 1 year of the transplant, he was asymptomatic in a routine clinical evaluation, but with a history of viral infection by COVID-19 one month ago. The blood count showed bicytopenia (Hb: 6.5g/dL, leukocytes 6190/mm3, neutrophils 1150/mm3, lymphocytes 3000/mm3, platelets 37,000/mm3), lactic dehydrogenase 422U/L, negative direct Coombs test, 5% reticulocyte count and PET-CT with hypermetabolism in cervical, thoracic and abdominal lymph nodes, in addition to diffuse uptake of bone marrow and spleen, which report did not confirm whether the lesions were neoplastic, inflammatory or infectious. To elucidate these findings, a tonsil biopsy was performed that found reactive and nonspecific follicular lymphoid hyperplasia, and the bone marrow biopsy revealed hypercellularity of the erythroblastic series with a maturative shift to the left, a hypocellular granulocytic series, with maturation and few young cells, and a markedly hypocellular megakaryocytic series, with no evidence of neoplasia. We repeat the PET/CT after three months of infection and there was complete remission of the lesions without any treatment. Discussion: The pandemic generated an incessant need for information about the pathophysiology, treatment, and clinical behavior of SARS-CoV-2 virus in individuals. Several publications appeared in different medical specialties to describe unusual cases during the pandemic. There are publications reporting cases in which COVID-19 infection induced remission of lymphoproliferative diseases. Others in which vaccination against COVID-19 induced the appearance of lymph node enlargement with FDG uptake on PET/CT, suggesting a mistaken progression of the lymphoma.

CONCLUSION: In the present study, we highlight a case in which COVID-19 infection simulated lymphoma relapse with metabolic uptake on imaging. Biopsies ruled out relapse and we concluded that it was a reactional effect to viral infection with spontaneous remission of the PET/CT findings.

Keywords: Hematopoietic stem cell transplantation. Hodgkin's Lymphoma. COVID-19.

CYTOMEGALOVIRUS ENCEPHALITIS: A RARE BUT FATAL COMPLICATION OF ALLO HSCT – CASE REPORT AND LITERATURE REVIEW

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INTRODUCTION: Cytomegalovirus (CMV) encephalitis is a rare but often fatal complication associated with allogeneic hematopoietic stem cell transplantation (allo HSCT). There is currently few data on the outcomes of CMV encephalitis in this settings. We describe a case report and literature review to address this lack of knowledge.

CASE REPORT: We report the case of a 15 yo, female, diagnosed with Philadelphia positive acute lymphoblast leukemic (ALL) at the age of nine. She was treated with IC BFM-2009 chemotherapy regimen and remained in complete response (CR) for six years. Relapse occurred after this period and was salvaged, followed by an HLA-identical sibling HSCT while on CR and negative MRD with a myeloablative conditioning regimen (CyTBI). Both donor and recipient were CMV seropositive and graft vs host disease prophylaxis consisted of methotrexate plus cyclosporine. Neutrophil and platelet engrafting occurred up to day +11. Full donor chimerism was confirmed. On day +44, the patient presented with ataxic gait and low grade fever. Cytological analysis of cerebrospinal fluid (CSF) revealed 13 cells/mm3 with 10% thought to be blasts, although immunophenotyping was negative for malignancy. Neurological status deteriorated with generalized tonic-clonic seizures. Following 45 days of her admission and empiric treatment for paraneoplastic encephalomyelitis with no improvement, a new CSF was performed including CMV PCR, revealing a low count of 35,7 UI/mL. Serum CMV was low (102 UI/mL).Treatment was promptly initiated with IV ganciclovir for 21 days and tapering of cyclosporine. Shortly after, an improved clinical status was noted with CMV PCR control indetectable on CSF and serum.

DISCUSSION: Fifteen cases were raised between 2010 and 2022 and a high mortality was identified (13 out of 15). To our knowledge, ours is the third successfully treated patient with CMV encephalitis in the context of allo HSCT. The preemptive therapy approach reduces the incidence of early systemic disease but is also associated with non-relapse mortality and potential resistance and refractory CMV infection. Most cases of CMV encephalitis are associated with multidrug resistant CMV (10 out of 11 tested; with 14 out of 15 with previous preemptive therapy), and usually occurs after D+100 (13 of 15). Other additional risk factors for reduced T-cell activity are T cell graft depletion, anti-thymocyte globulin, umbilical cord blood transplantation (9 of 15). CD 4 count was underreported, but levels below 100 cells/mm3 seems to be associated with infection (8 of 10). Our case is an unusual presentation one, since it occurred early after allo HCST, with no previous CMV reactivation. Diagnosis was delayed because cytological analysis of CSF suggested malignancy. It is important to highlight to all physicians the differential diagnosis of other causes other than the relapse of underlying disease even in the context of low/negative CMV on peripheral blood.

Keywords: bone marrow transplantation; encephalitis; cytomegalovirus; ganciclovir resistance; central nervous system; immunosuppression

EVALUATION OF THYMOGLOBULIN AND POST-TRANSPLANT CYCLOPHOSPHAMIDE AND THE INCIDENCE OF CYTOMEGALOVIRUS REACTIVATION FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION. A SINGLE-CENTER EXPERIENCE.

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INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is a curative therapeutic strategy for several oncohematological and benign diseases. However, the arsenal of drugs used and the inherent transplantation immunosuppression are associated with infectious complications. Viral reactivations, especially cytomegalovirus, are very common and have important consequences in terms of morbidity and mortality in this setting.

OBJECTIVE: The objective of this analysis is to evaluate the incidence of cytomegalovirus reactivation in patients undergoing allogeneic HSCT and who used thymoglobulin or post-transplant cyclophosphamide (PTCy) as an in vivo lymphocyte depleting agent.

METHODS: A retrospective evaluation of electronic medical records of patients who have undergone allogeneic HSCT in a single center was performed. Patients with a follow-up of more than 30 days after HSCT and who used thymoglobulin or PTCy during the transplant procedure between August 2019 and May 2022 were included. The primary endpoint was the incidence of cytomegalovirus reactivation, while the secondary endpoint was the incidence of II to IV acute graft-versus-host disease (aGVHD) among these patients.

RESULTS: 36 allogeneic HSTCs involving PTCy or thymoglobulin were identified (patient's characteristics are demonstrated in table 1). In this population, the platform of PTCy was only used for mismatched related donors, and thymoglobulin was used for all bone marrow failure disorders and polytransfused patients with a matched related donor or matched unrelated donor, and for all patients with onco-hematological diseases undergoing matched related and matched unrelated transplant (all these patients received peripheral blood stem cells as a source of stem cells). Among the 36 patients, the rate of cytomegalovirus reactivation was 63,8% (23/36 patients), with 61,1% using a PTCy strategy (11/18) and 66,7% (12/18) in the group that used thymoglobulin. The median follow-up was 218,5 days (range 34-927 days). Prophylaxis to prevent cytomegalovirus reactivation was not used. The incidence of II to IV aGVHD among patients who had cytomegalovirus reactivation was 36,3% for who received PTCy (4/11) and 25.0% for patients who underwent transplantation after using thymoglobulin (3/12).

CONCLUSION: The rate of cytomegalovirus reactivation was similar between the two groups, however, prospective studies with a larger number of participants in a population with a high prevalence of cytomegalovirus are needed to better elucidate these results and evaluate the impact of either the use of thymoglobulin or PTCy in the reactivation of cytomegalovirus. The reactivation rate was above 60,0% in both groups, and demonstrates the high incidence of viral reactivation in our clinical practice, and is higher than that reported in the literature. Given the impacts associated with cytomegalovirus reactivations, it is important to adopt pharmacological strategies to prevent this important complication.

Table 1		N=36
Characteristic	Thymoglobulin (N=18)	PTCy (N=18)
Gender		
Female sex — no. (%	7 (38.9)	11 (61.1)
Male sex — no. (%)	11(61.1)	7(38.9)
Age		
Median (range) — yr	41(1-64y)	39y(9m-71y)
Stem cell donors		
MRD	10(55.5)	0
MMRD	0	18(100)
MUD	7(38.8)	0
MMUD	1(5.5)	0
Stem cell sourcce		
Bone marrow — no. (%)	4(22.2)	4(22.2)
Peripheral blood stem cells — no. (%)	14(77.7)	14(77.7)

FEBRILE NEUTROPENIA IN PATIENTS SUBMITTED TO BONE MARROW TRANSPLANTATION: PROFILE OF BLOOD CULTURE RESULTS

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INTRODUCTION: The development of fever in neutropenic patients induced by myeloablative chemotherapy is a challenging clinical situation for bone marrow transplant units worldwide. Febrile neutropenia remains an important cause of morbidity, mortality, and cost burden in cancer patient care.

OBJECTIVE: This study addresses a relevant and current issue in oncology and has the objective to determine the incidence of febrile neutropenia in patients at a referral BMT (Bone Marrow Transplant) Unit for patients from the North and Northeast of the private health care network, who has undergone autologous bone marrow transplant therapy. It is also fitting here in the study to portray the main pathogens identified in the microbial screenings.

METHODS: A cross-sectional, retrospective and analytical study was carried out in a population of 35 patients admitted to a hospital in the capital city of Fortaleza in the State of Ceará -Brazil, between the months of April 2021 to June 2022. The definition of neutropenia was adopted as neutrophil count less than 1000 cells/microliters with predicted pre-transplant chemotherapy-induced decrease or neutrophil count less than 500 cells/microliters. The neutropenic patient was diagnosed with febrile neutropenia when the axillary temperature was higher than 37.8°C for more than 1 hour. The unit's protocol recommended, soon after the diagnosis of NF (Neutropenia Febrile), the collection of blood cultures from at least 2 and ideally 4 distinct sites followed by the administration of a broad spectrum antimicrobial.

RESULTS: Febrile neutropenia affected 71% (25) of the patients in the study group, 37% (13) with negative blood cultures and 34% (12) with positive blood cultures. Timely microbiological screening enabled the identification of the probable causative agents of NF (Neutropenia Febrile). The pathogens isolated in blood cultures of patients with febrile neutropenia were: Staphylococcus epidermidis (5); Klebsiella pneumoniae (2); Escherichia coli (2); Staphylococcus hemolytic (1); Pseudomonas aeruginosa (1) and Streptococcus mitis (1). The results revealed a higher incidence of Gram-positive bacilli (20%). However, the patients who progressed to clinical instability and were classified as high risk, were those who had positive blood cultures for Gram negative (11%), versus Gram positive (5%).

CONCLUSION: It is of extreme importance to analyze the incidence profile and microbial prevalence of the health institution, as a sector, for an adequate therapeutic choice and success in facing NF (Neutropenia Febrile).

IMMUNOGENICITY AND SAFETY OF A HETEROLOGOUS COVID-19 VACCINE REGIMEN IN HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS.

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INTRODUCTION: Vaccination is the main strategy for COVID-19 prevention. However, its benefit is inferior in immunosuppressed individuals, such as hematopoietic stem cell transplant (HSCT) recipients. There is no literature evidence for Coronavac.

OBJECTIVE: To assess immunogenicity and safety of COVID vaccine in HSCT recipients.

METHODS: Open-label, non-randomized, phase IV clinical trial. HSCT recipients who had not received COVID vaccine were eligible for the study. Vaccination was performed at least 1 month after autologous HSCT. Exclusion criteria included active cancer, acute illness, and fever. Participants received 2 doses of inactivated vaccine (Coronavac) with an interval of 28 days between doses. A 3rd dose (mRNA vaccine, Pfizer) was administered at least 28 days after the 2nd dose. Participants were monitored for SARS-CoV-2 infection by monthly telephone contact. Nasal swab for viral detection by PCR was done in symptomatic cases. Vaccine immunogenicity was assessed by measuring total immunoglobulin (Ig) against nucleocapsid (N) and IgG against S1 and S2 portions of the spike protein and the receptor binding domain (RBD) of SARS-CoV-2 at baseline and 28 days after the 1st, 2nd and 3rd doses.

RESULTS: From 34 eligible HSCT recipients, 30 were included in the study. Median age was 38 years (20 to 66), and 9 (30%) were female. The most frequent underlying diseases were Hodgkin's lymphoma (n=6), acute myeloid leukemia (5) and non-Hodgkin's lymphoma (4). Sixteen (53%) subjects underwent autologous HSCT. The time between HSCT and the first vaccine dose ranged from 1 to 212 months (median, 5 months). Median follow-up after the 1st dose was 9 months. Among 14 allogeneic HSCT recipients, 10 (71%) were on immunosuppressive agents, including systemic steroids (>0.5 mg/kg/day of prednisone), cyclosporine or sirolimus. In the whole cohort, 11 participants reported previous COVID-19 infection prior to vaccination, while 4 were diagnosed with it during the study (no hospitalization required), with sore throat, nasal congestion, and fever being the predominant symptoms. Before the 1st dose, 15 (50%) patients had reactive total Ig, and 20 (69%) had reactive IgG (only 9 had reported previous COVID-19 infection). After the 2nd dose, 16 (53%) had reactive total Ig, and 25 (83%) had reactive IgG. After the 3rd dose, 22 (73%) had reactive total Ig, and 30 (100%) had reactive IgG. After 3 vaccine doses, 27 patients presented with at least 1 adverse event, with a total of 263 events. Pain at the injection site, headache and myalgia were the most frequent events. There were no serious adverse events related to vaccination.

CONCLUSION: Vaccines were shown to be safe in this group. After a heterologous vaccination regimen (2 doses of Coronavac + 1 dose of mRNA vaccine), all participants had reactive IgG. Four participants were diagnosed with mild COVID-19 after receiving at least one vaccine dose.

Funding: Instituto Butantan

Keywords: Coronavac. hematopoietic stem cell transplant. COVID-19.

LETERMOVIR FOR CYTOMEGALOVIRUS (CMV) PROPHYLAXIS IN ALLOGENEIC PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HCT)

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Letermovir has proven efficiency and tolerance when used to prevent CMV reactivation, but little is known about its use in our country and in the pediatric age group.

OBJECTIVE: To evaluate the institutional experience with letermovir in children undergoing HCT.

SAMPLE: Between December 2021 and April 2022, six children received letermovir prophylaxis and were included in this retrospective analysis.

METHOD: Letermovir was requested to the insurance companies for children and adolescents with positive serology for CMV and undergoing haploidentical HCT, with CMV-negative donors, or with an early CMV reactivation as primary or secondary prophylaxis, respectively. The dose varied according to the weight: <20Kg - 120mg/day (or 240 mg every other day), 21-30Kg - 240mg, and >31Kg – 480mg. The dose of letermovir was not modified in patients using antifungal prophylaxis with azoles, we only adjusted the dose of voriconazole and immunosuppressors according to through levels. Prophylaxis with acyclovir for herpes simplex reactivation was maintained. Weekly quantitative CMV-PCR was performed in all patients up to D+100. The limit of detection is 34.5 IU CMV copies/mL. The use of letermovir was discontinued when ganciclovir was required due to Herpesvirus 6 (HHV6) reactivation, restarting it upon completion of the therapy. Possible adverse events related to letermovir were carefully monitored.

RESULTS: The characteristics of the patients and transplants are described in Table 1. Five of the six patients received letermovir by nasoenteral tube. Patients <20Kg received 240mg every other day. Four patients received primary and two, secondary prophylaxis: one after CMV hepatitis on D+14 (prophylaxis initiated after the treatment on D+38) and another, after an early CMV reactivation while off letermovir on D+18 (prophylaxis initiated on D+51). The median day to start letermovir in primary prophylaxis was D+5. Three of the four patients who underwent primary prophylaxis had letermovir discontinued to treat an HHV6 reactivation with ganciclovir for at least 21 days. Three patients had grade II acute GVHD requiring corticosteroids 2mg/kg/dia. One patient has chronic GVHD. The median follow-up time is 70 days. Only one patient has completed the expected 100 days of prophylaxis after transplantation so far. There was no interruption of the letermovir use by adverse events. One patient presented with important nausea that resolved after the treatment of HHV6 demonstrated by PCR in the gastrointestinal tract biopsy. There was no increase in transaminases > 3x the upper reference value. No patient who received primary or secondary prophylaxis with letermovir had more than 250 IU/ml of CMV on therapy.

CONCLUSIONS: Letermovir was effective and well tolerated for CMV prophylaxis. The frequent interruption of its use due to HHV6 reactivation and the need of ganciclovir should be studied since it may impact the real benefit of using letermovir in our population.

TABLE 1. **Characteristics of pediatric patients receiving letermovir**

N	Age (yr)	Weight (Kg)	Dose (mg/ day)	NG tube	Type of HCT	CMV IgG	Prophylaxis	GVHD	HHV6 Reactivation	CMV reactivation post letermovir	Ganciclovir treatment (days)	Days post HCT
1	6	22	240	Y	MUD	R+/D+	Secondary	A+C	N	N	N	172
2	16	48	480	N	Haplo	R+/D+	Secondary	A	Y*	N	N	87
4	4	18	120	Y	MUD	R+/D-	Primary	N	N	N	N	53
5	20	53	480	Y	Haplo	R+/D+	Primary	A	Y	N	15	46
6	5	15	120	Y	Haplo	R+/D+	Primary	A	Y	N	15	43

NG- nasogastric or nasoenteral; HCT - hematopoietic stem cell transplantation; CMV- cytomegalovirus; HHV6- herpesvirus 6; Y-yes; N- no; MUD- unrelated donor; Haplo- haploidentical donor; R- recipient; D- donor; A- acute; C- chronic. *Prior to the letermovir use

MULTIRESISTANT BACTERIA AND BONE MARROW TRANSPLANTATION: HOW I TREAT. THE EXPERIENCE IN FORTALEZA.

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INTRODUCTION: The mulitresistant bacteria(MRB) is a big challenge in a bone marrow transplantation (BMT) unit. The colonization of Gram negatives resistant for carbapenem or gram positive resistant for vancomicine previous BMT increases the risk of septic shock and dead in the early phases. It is important to investigate previous infections and colonization to isolation into the unit and determined the use of antibiotic in the febrile neutropenia. In University Hospital Walter Cantidio, the preemptive diagnosis of colonization into the hospitalization, through once a week rectal swab to Klebsiella pneumonia carbapenamase (KPC) and Vancomycin resistant enterococci (VRE) has made. We reduced the intensity of conditioning in patients with previous infections or colonization to MRB gram-negative and the patient assigned consent term about the major risk of complication related. The VRE patient, in the last year, has not isolated or reduced conditioning. We just change the antibiotic in the hemodynamic instability.

OBJECTIVE: described the protocol of the Walter Cantidio Hospital in patient of MRB. Described the results in early phase of BMT in patient colonization of MRB.

METHODS: We included datas of BMT realized in University Hospital Walter Cantidio, Fortaleza, Ceará, in 2020 until May 2022 with colonization or previous infections of MRB and all the patients with blood culture (BC) positive of MRB in BMT.

RESULTS: All the patients the 103 autologus had KPC and VRE negative before BMT, three patients had febrile neutropenia with BC positive: 1 to KPC and 2 to Pseudomonas MR. They recovered. 60 allogeneic BMT were realized. Ten patients had colonization or infection previous BMT (16,7%), 4 of them with multiple colonization or infection. Two patients (20%) with previous infection had febrile neutropenia and BC positive, KPC and P. aeruginosas. 20% did not had fever, 30% had just febrile neutropenia and 30% had BC positive to MRB. The patient with KPC died with septic shock and febrile neutropenia. After BMT: 13 with colonization for KPC (21,7%) and 6 with VRE (10%), four of them had both colonization. Four patients had febrile neutropenia without previous infection/ colonization with MRB (2 Pseudomonas and 2 KPC). The mortality In allogeneic of KPC was 33% and P. aeruginosas was 66%.

CONCLUSIONS: VRE positive is not associate to infection and mortality. In autologous the MRB infections is not associated to mortality. The increase of colonization is considerable. The reduced conditioning became feasible BMT in patient with MRB previous, but specific care was necessary.

Keywords: Multiresistant bacteria. Bone marrow transplantation.

TABLE 1. **Autologus BMT and MRB.**

	Previou BMT colonization or infections	BMT Colonization	Infections	Death
KPC	0	7	1	0
VRE	0	5	0	0
Other MRB	0	-	2	0

TABLE 2. **Allogeneic BMT and MRB.**

	Previou BMT colonization or infections	BMT Colonization	Infections	Death
KPC	7	17	KPC previous:1	1
			KPC post: 2	0
VRE	6	10	0	0
Other MRB	2 Acinetobacter MR and P. aeruginosas MR	-	Previous: 1	0
			Post: 2 P.aeruginosas MR	2

NOSOCOMIAL COVID-19 INFECTIONS IN A PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT.

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INTRODUCTION: Patients undergoing hematopoietic stem cell transplantation (HSCT) have a high risk of infectious complications due to myelosuppression of the conditioning protocol, and the immunosuppression used after transplantation to avoid graft rejection and control graft-versus-host disease. Due to the widespread of the SARS-CoV2, healthcare providers in direct contact with HSCT patients have been diagnosed with COVID-19 immediately after taking care of those patients. Despite continuous use of face masks, the real risk of transmitting the disease to the patients is unknown.

OBJECTIVE: Determine the risk of SARS-CoV-2 transmission to the patients or family members when a healthcare professional is diagnosed with the disease and establish containment measures, like isolation and closure of the HSCT unit to new patients or not.

METHODS: Retrospective observational study of the incidence of positive RT-PCR (real time polymerase chain reaction) for SARS-CoV-2 among inpatients at the time attending physicians were proven to have COVID-19 disease on the day after directly taking care of the patients. All healthcare providers had been vaccinated and used face masks at all times inside the unit, even outside the patients' rooms. All patients and caregivers were asymtomatic and COVID-19 free as demonstrated by routine nasopharyngeal RT-PCR prior to admission. The unit was closed to the admission, all patients were started on aerosol and contact precautions, the central hepafilter was turned off and portable hepafilters were added to each room. All asymptomatic patients and caregivers were screened on the 3rd day of contact if febrile or with respiratory symptoms, or on the 5th day if asymptomatic.

RESULTS: During three different periods within the pandemic we had attending physicians diagnosed with COVID-19 immediately after taking care of the HSCT patients: April 04-30, 2020, January 02-21, 2022 and May 09-28, 2022. A total of 30 patients and their caregivers were hospitalized at these times, and 23 of them had direct contact with the pre-symptomatic professionals, whose were always using face masks. Two of the 23 patients and one of their caregivers developed positive RT-PCR for SARS-CoV-2, one in each of the 2022 periods. The latter presented symptoms (fever) and neither developed pneumonia or require d intensive care

CONCLUSION: Despite the COVID-19 rigorous preventive measures, there is a real possibility of spreading the virus to HSCT patients by pre-symptomatic professionals. The continuous use of N-95 respirators in the HSCT unit has been reinforced, as well as adherence to vaccinations. Unfortunately, our experience shows that isolating and closing the HSCT unit is appropriate when a healthcare worker taking care of the patients is diagnosed with COVID-19 infection, avoiding larger outbreaks and casualties.

SEVERE ATYPICAL FUNGAL INFECTIONS: THREE CASE REPORTS

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INTRODUCTION: Allogeneic hematopoietic stem cell transplantation (HSCT) is indicated for the treatment of some onco-hematological diseases. This procedure results in profound immunosuppression, especially in the period of aplasia after conditioning and stem cell infusion, and may result in atypical and severe infections. Emerging non-candida and non-cryptococcal yeasts are increasingly recognized causes of invasive fungal infections in this population.

OBJECTIVE: To report three cases of post-allogeneic bone marrow transplant patients with rare fungal infections.

DESCRIPTION: Case 1 - male, 17 years old, unrelated 10x10 allogeneic HSCT due to T-lymphoblastic leukemia in 3rd complete remission (CR), conditioning FluMel-TBI 600cGy + ATG 6. In day+18, he presented with dyspnea and desaturation, using meropenem and amikacin. Blood cultures with growth of Geotricum sp. Treatment with voriconazole and anidulafungin was started. Engraftment on day+22. Echocardiogram without vegetations, chest tomography with micronodules and abdomen ultrasound with hepatosplenic nodular lesions. Antifungal treatment was performed for 8 weeks. He evolved with acute grade IV intestinal graft-versus-host disease, with death on day+116. Case 2 - male, 40 years old, rescue haploidentical HSCT after primary graft failure, FluMel + PTCy conditioning, initial diagnosis B-ALL in CR2. On day+17, he was admitted to the ICU due to cardiotoxicity after cyclophosphamide, using meropenem, polymyxin E, amikacin, ganciclovir and anidulafungin. He had febrile neutropenia with identification of Trichosporon asahii in blood cultures. Echocardiogram and CT without identification of focal lesion. Neutrophilic engraftment on day+26. Despite the use of voriconazole and amphotericin, death occurred on day+56 due to bloodstream infection by T. asahhi and Klebsiella sp. Case 3 - male, 33 years old, haploidentical HSCT for relapsed acute myelomonocytic leukemia in CR2, FluBu12 + PTCy conditioning. On day+10, he presented with arthralgia, edema and movement restriction in the left knee, which resulted in a positive arthrodesis culture for T. asahii, present in concomitant urine culture. Negative blood cultures. Treated with voriconazole and amphotericin lipid complex. Engraftment on day+16. Echocardiogram and CT scans without focal lesions. Death occurred by day+61 with associated bacterial infection.

CONCLUSIONS: Although the most frequent fungal infections in patients undergoing HSCT are mucormycosis, candidemia and aspergillosis, the occurrence of rare fungal infections cannot be mitigated for correct diagnosis and treatment. As illustrated in the cases above, the outcome can be dismal, emphasizing the need for prophylactic drug antifungal measures, aggressive therapies, environmental control and, if possible, a shorter time for immunosuppression tapering.

Keywords: Hematopoietic stem cell transplantation. Immunosuppression. Fungal infection.

UNUSUAL LATE MANIFESTATION OF INFECTION BY CYTOMEGALOVIRUS: CASE REPORT

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BACKGROUND: Cytomegalovirus (CMV) is one of the most common infectious complications following hematopoietic stem cell transplant (HSCT), having a high morbidity and mortality rate. Although vastly studied, pediatric literature on CMV is sparse. It is poorly known how CMV causes oral lesions post-transplant.

CASE: 2 year-old-girl, with juvenile myelomonocytic leukemia, CMV-positive, who underwent HSCT with a match unrelated donor 10/10, DPB1 permissive. CMV positive donor, with major ABO incompatibility. Conditioning regimen included Busulfan (AUC 3600 um/min), Fludarabine 120 mg/m2 and Melphalan 140 mg/m2. Graft-versus-host-disease (GVHD) prophylaxis consisted of methotrexate 10 mg/m2 and cyclosporin (CSA). Graft source was fresh bone marrow, with TNC/kg 14,3x10*8/kg. Neutrophil engraftment was achieved on day +23 and she was discharged on day 28. CSA was suspended at day +50 after chimerism dropped to 98%, and was reintroduced at day +79 due to grade III acute skin GVHD, resolved at day +105. During this period, she also received IV steroid which was able to be successfully reduced after two weeks. Weekly viral vigilance, done through polymerase chain reaction (PCR), detected CMV at day +65 and at day +72 it was no longer detectable. Six months post-transplant she presented a severe case of chronic GVHD, affecting skin, mouth and liver. The disease is currently controlled by the use of Tacrolimus, steroids and phototherapy. Seven months post-transplant, PCR detected CMV reactivation, treated with Ganciclovir for a month, until PCR was negative, and then switched to Valganciclovir. Eight months post-transplant two lesions appeared at the basis of her tongue. The lesions were contiguous, nodular, with defined limits and firm consistency, measuring 2x2 centimeters each. The patient had no pain, bleeding or difficulty breathing and eating. The lesions were submitted to an incisional biopsy with immunophenotyping analysis showing no signs of leukemia, and pathology revealing neutrophilic exudate in the surfice, viral research was positive for CMV, with 487500 copies/mL (IU/mL). Complete surgical resection was done, as well as continuous treatment with Valganciclovir, and evolved well 11 months post-transplant.

CONCLUSION: The clinical presentation discussed is uncommon, which reinforces the need for a multidisciplinary monitoring and viral vigilance even after 100 days post transplant in patients with risk factors, such as unrelated donors, chronic GVHD, history of infection by CMV, steroid use and anti T-cell therapies. Factors involved in the late manifestation of CMV and therapeutic response in patients post HSCT are yet unclear, with more studies being necessary to elucidate these questions.

Keywords: Cytomegalovirus infection. Stem cell transplant. Oral lesion.

FIGURE 1. **Lesions at the basis of tongue,viral research positive for CMV.**

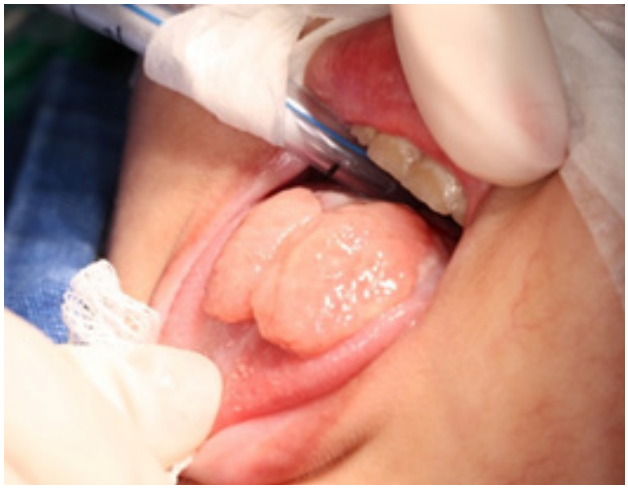


FIGURE 2. **Complete surgical resection of the lesions.**

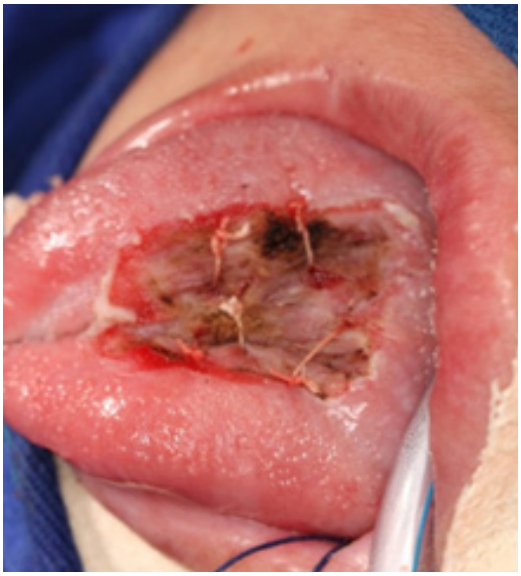
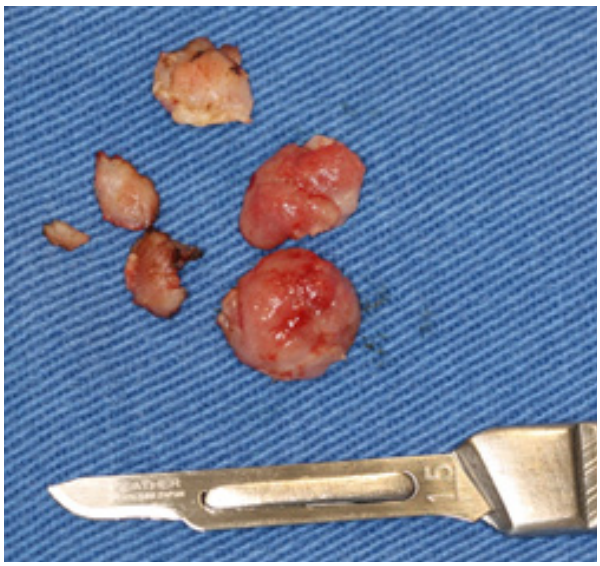


FIGURE 3. **Surgical resection of the lesions.**



UPDATE OF THE VIRAL INFECTION PROFILE IN PATIENTS SUBMITTED TO HEMATOPOETIC STEM CELL TRANSPLANTATION IN A REFERENCE HOSPITAL IN THE STATE OF CEARÁ

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INTRODUCTION: Hematopoietic Stem Cell Transplantation (HSCT) remains established as the main therapeutic option for numerous hematological disorders. However, it is associated with a series of complications. In the case of Allogeneic Transplantation, viral reactivation stands out, impacting the morbidity and mortality of these patients. The most epidemiologically relevant viruses in this context are CMV, EBV, BKV and HV6, and their post-transplant screening is essential.

OBJECTIVES: To evaluate the profile of viral infection in patients undergoing Allogeneic Hematopoietic Stem Cell Transplantation in the last 5 years at the Bone Marrow Transplant Service in a reference hospital in Ceará.

METHODS: This is a retrospective, descriptive, analytical and quantitative study with analysis of exam results and medical records. Allogeneic transplants performed in the last 5 years, in patients aged 16 years or older, were analyzed.

RESULTS: Between 01/01/2017 and 12/31/2021, 341 transplants were performed, of which 215 were autologous and 126 were allogeneic. Nine patients (5 related and 4 unrelated) were excluded from the series due to the absence of viral screening records in the files, leaving 117 patients in the study (68 related, 15 unrelated and 20 haploidentical). Of these, 50.43% were women and 49.57% were men, with a median age of 37.9 years (ranging from 16 to 70 years). Regarding the diagnosis, most patients had AML (30%), followed by ALL (27%), aplastic anemia (14%), CML (9%) and MDS (9%), followed by other less frequent diseases. The investigation of viral reactivation was performed by PCR and cutoff points of 1000 copies were used for CMV and EBV and detectable or undetectable for BKV and HV6. 81.75% of the patients had some virus detected (in any titer) during the post-BMT period. There was a prevalence of viral reactivation in haploidenticals, with 90.91% of detection. CMV reactivation was the most frequent. Among the 117 patients, 70.94% had detectable values for CMV, 17.95% <1,000 copies and 52.99% >1,000 copies; 29.06% remained undetectable. Next are the EBV numbers: among the tested patients, 40.28% had >1000 copies and 26.39% <1000 copies, while 33.33% remained undetectable. Among all detectable patients, 53.26% had more than one virus and 6.52% had detection of all 4.

CONCLUSION: Viral reactivation is frequent in allogeneic HSCT, especially with the use of alternative donors, with emphasis on CMV reactivation. Knowledge of the viral reactivation profile of each service is essential to guide screening strategies and preemptive treatment.

Keywords. Hematopoietic Stem Cell Transplantation. Allogeneic Transplantation. Viral Reactivation.

NON-INFECTIOUS COMPLICATIONS

BULLOUS CUTANEOUS CHRONIC GRAFT-VERSUS-HOST DISEASE (GVHD) – RARE CLINICAL PRESENTATION ON POST ALLOGENIC BONE MARROW TRANSPLANT: A CASE REPORT

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INTRODUCTION: Chronic graft-versus-host disease (GVHD) is the main cause of long-term morbimortality following allogenic stew cell transplantation[1]. Regarding Chronic GVHD, the skin is the most frequently affected organ[2] and cutaneous manifestations include sclerotic lesions, poikiloderma and/or lichen-planus like eruption[3]. Bullous lesions, on the other hand, are rarely documented on the literature[4, 5], being a differential diagnosis from other diseases. We report a case of bullous chronic GVHD.

OBJECTIVE: Describe the rare clinical presentation that is the chronic cutaneous bullous GVHD.

CASE REPORT: A 54-year-old male patient, diagnosed with Philadelphia+ acute lymphoblastic leukemia. After induction and consolidation chemotherapy with HyperCVAD protocol, he underwent bone marrow transplantation – fullmatch unrelated donor and the neutrophil engraftment occurred on D+13. Post-transplant evaluation demonstrated morphologic remission and negative measurable residual disease on flow cytometry. After months of follow-up, the patient showed skin, mouth, and gastrointestinal GVHD. Skin involvement was less than 18%, presenting with keratosis pilaris, lichen-planus-like lesions and nail pterygium. Immunosuppressive therapy with prednisone and cyclosporine was introduced, associated with topical treatment. After 7 months of good clinical response, the patient reduced dose of immunosuppression and, after that, it was observed skin, nail and month lesions progression (40% of body surface). Narrow band UVB phototherapy was associated and immunosuppression returned to its previously dosage. Five months later, phototherapy location was changed (switched from closed cabin to single-board phototherapy). The patient developed flaccidly ruptured on the back, associated with multiple chest and gluteal ulcers. Biopsy confirmed the hypothesis of chronic GVHD, excluding differential diagnoses such as bullous pemphigoid, pharmacodermia and burn lesions secondary to phototherapy. Closed cabin phototherapy was restarted, in order to increase effectiveness and immunosuppressive therapy was maintained at the same dosage. There was an improvement in body lesions and reasonable disease control.

DISCUSSION: Chronic cutaneous GVHD is presented in many different ways and blisters are a rare but possible form of presentation[3]. Having a high clinical suspicion over these atypical manifestations is paramount to achieving a sooner diagnosis and treatment of this condition. This report revealed that medication nonadherence was the main factor leading to clinical deterioration and GVHD decompensation.

CONCLUSIONS: The bullous presentation of cutaneous GVHD is a warning sign not only of possible differential diagnosis but also of a disease impairment, which must be identified, diagnosed, and properly treated. Patients suffering from chronic disorders should be guided to follow the treatment in order to reduce nonadherence and increase therapeutic effectivity.

Keywords: Graft-versus-host-disease. Cutaneous. Bullous. Skin lesions.

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EXCLUSIVELY CUTANEOUS SCURVY IN A PATIENT WHO UNDERWENT AUTOLOGOUS STEM CELL TRANSPLANT DUE TO POEMS SYNDROME: A CASE REPORT

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INTRODUCTION: Nutritional and dermatological support are connected to the precautions involved in hematopoietic stem-cell transplantations (HSCT). Vitamin C deficiency is mainly observed after the acute stage of HSCT[1], and scurvy is the clinical condition associated to that. We report the case of a patient with a rare skin manifestation compatible with scurvy following an autologous HSCT due to POEMS syndrome.

CASE REPORT: LTBA, male, 67, hospitalized in 2021 with chronical demyelinating sensorimotor polyneuropathy associated with gammopathy and high Lambda light chain; showing sclerotic spots on the bones, enlargement of the organs and polycythemia, thus confirming the POEMS syndrome diagnosis. Treated with Bortezomib, cyclophosphamide and dexamethasone, and further autologous HSCT. On D+5, the patient developed isolated purpuric erythematous micropapulae, some with central micropustules on the back of his hands, temples, torso and all limbs. No mucous bleeding. Biopsy of the lesion on this thigh revealed purpuric perifolliculitis, indicative of vitamin C deficiency. Low serum levels of vitamin C confirmed the scurvy diagnosis. Intravenous vitamin C treatment initiated, causing fast healing of the lesions. Currently, the patient is stable and doing regular dermatology and hematology follow-ups.

DISCUSSION: We report a rarely documented case of exclusively cutaneous scurvy following an autologous HSCT. Literature shows that serum levels of vitamin C are deficient in the acute stage of post HSCT, even among patients who keep an appropriate daily supplementation[2]. The deficiency is strongly associated with systemic inflammation, whereas adequate amounts of vitamin C are associated with the better development of NK cells and immune reconstitution[3]. Mucocutaneous symptoms are the most common ones related to scurvy, with manifestations characterized by follicular hyperkeratotic papulae, perifollicular hemorrhage, purpura, gingival bleeding and ecchymosis. Skin biopsy may contribute to differentiate it from cutaneous vasculitis. The treatment consists of administering vitamin C and reversing the conditions that led to the deficiency. In most cases, the symptoms remit in 24-72 hours after supplementation begins[4,5].

CONCLUSION: Although the skin manifestation with the highest morbimortality during post-HSCT is graft-versus-host disease, we should be aware of the observable skin signs that lead to the diagnosis of other clinical entities which, albeit rare, may be present in a patient of such complexity. The correct dermatological diagnosis promotes the correct treatment and improves the quality of life of the ill.

Keywords: Autologous stem cell transplant; Scurvy; vitamin C; POEMS syndrome

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NEUROTOXICITY INDUCED BY IMMUNOSUPPRESSIVE THERAPY WITH SIROLIMUS: A CASE REPORT

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INTRODUCTION: Allogeneic hematopoietic stem cell transplantation (HSCT) consists of replacing a diseased or deficient bone marrow with hematopoietic cells from a healthy donor. Graft-versus-host disease (GVHD) is an immunological phenomenon in which the donor's healthy lymphocytes recognize them as foreign and attack the recipient's tissues. Despite the use of immunosuppressants, approximately 50% of HSCT recipients develop GVHD in the first year after transplantation. Sirolimus is an immunosuppressive inhibitor of mTOR and its main adverse effects are related to peripheral edema, metabolic changes, abdominal pain and renal dysfunction. Central nervous system (CNS) effects are uncommon, serious complications such as PRES Syndrome (Posterior Reversible Encephalopathy Syndrome) are rare.

OBJECTIVE: case report of a patient undergoing HSCT, who used sirolimus for the treatment of GVHD and presented a condition compatible with PRES.

METHODS: case report of a patient treated at the Bone Marrow Transplantation Unit of a hospital in southern Brazil. The patient provided consent for publication.

RESULTS: Male patient, 27 years old, diagnosed with idiopathic medullary aplasia, submitted to Allogeneic HSCT, HLA identical donor, conditioning with Cyclophosphamide and immunosuppression with Thymoglobulin, Cyclosporine and Methotrexate. Infusion of 1.4x10^6 of CD34 cells/kg of the recipient, neutrophilic pick up on D+18 and platelet D+30. Diagnosis of acute GVHD of upper gastrointestinal tract and skin on D+28, Grade III. Refractory skin GVHD, multiple immunosuppressive therapies, with complete response after D+50 using high-dose corticosteroid therapy, mycophenolate mofetil, ruloxotinib and replacement of cyclosporine with sirolimus. Twelve days after starting sirolimus, he presented with sensorium lentification, focal seizures and after generalized tonic-clonic seizures, with transfer to the intensive care unit. Prophylactic antiviral and antifungal therapy was started, with Foscarnet and Amphotericin, in addition to a broad antimicrobial regimen. The diagnostic arsenal included multiple magnetic resonance imaging (MRI) of the skull and sequential lumbar punctures that ruled out microorganism-induced encephalitis, raising the hypothesis of drug toxicity. Radiological signs of PRES were never found. With the suspension of sirolimus, there was a progressive improvement of the sensorium, without recurrence of seizures and with an excellent evolution, antimicrobial medications were suspended.

CONCLUSION: Neurotoxicity related to PRES is described as a possible side effect of Sirolimus, but its occurrence is so rare that cannot be estimated from the available data. Drug neurotoxicity should be suspected in cases of behavioral changes and/or seizures in patients using immunosuppressants, even with normal MRI, as long as diagnoses of infectious diseases are excluded.

Keywords: Bone Marrow Transplantation. Immunosuppressive Agents. Graft vs Host Disease.

MULTIDISCIPLINARY

ASSESSMENT OF THE FUNCTIONAL CAPACITY OF PATIENTS INTERNED IN THE BONE MARROW TRANSPLANTATION SECTOR OF A HOSPITAL IN THE CITY OF SÃO PAULO.

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INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is performed for the treatment of hematologic malignancies such as multiple myeloma, Hodgkin's and non-Hodgkin's lymphoma, and acute and chronic myeloid leukemia. Patients undergoing HSCT have altered functional capacity during the period of hospitalization, caused by isolation and the combination of toxicity of chemotherapeutic agents, resulting in cardiovascular and musculoskeletal changes.

OBJECTIVE: The objective of the study was to analyze the functional capacity of hospitalized patients during the month of July 2021 to May 2022, through the 1-minute sit-and-stand test (TSL) and the Timed Up and Go (TUG).

METHODS: A retrospective case study by reviewing the medical records of patients hospitalized in the bone marrow transplant sector from July 2021 to May 2022. The patients in the sample were evaluated by the physical therapy team on the 1st day of hospitalization and on the last day of hospitalization after HSCT. In the evaluation, the patients were submitted to the TUG, a test that assesses the degree of mobility and functional balance, which consists of getting up from a chair and walking in a straight line 3 meters away, turning, walking back and sitting down again. The shorter the time used, the better the test performance; and the 1-minute TSL, which assesses the functional physical capacity and peripheral resistance of the lower limbs, in which the patient is asked to sit and stand up from a chair, without any support, in which the lower limbs must be flexed. at 90 degrees and feet should be flat on the floor, and the number of repetitions of the movement is counted. Patients underwent physical therapy twice a day, in the morning and afternoon.

RESULTS: An analysis of 41 medical records was performed from July 2021 to May 2022. Of the 41, 9 were excluded due to the absence of post-HSCT evaluation (failure, refusal or death). From the sample of 32 patients, the mean age was 58.3, 65% male and 35% female. With respect to the 1-minute TSL, the average score at baseline was 18.7 repetitions and the average at discharge was 15.4 repetitions. Of the sample, 28% evolved with improvement, 12% with maintenance and 59% with worse performance when compared to the initial evaluation. Regarding the TUG, 12 patients were removed from the analysis due to the absence of post HSCT evaluation, of the 20 patients in the sample, an average time of 15 seconds was found to perform the test in the initial evaluation and an average of 16 seconds to perform the post HSCT test , with 45% progressing with improvement, 10% with maintenance and 45% with worsening performance.

CONCLUSION: The results of this study showed that patients undergoing HSCT evolve with a decline in functional capacity and the importance of evaluating the functional capacity of patients for better referral after hospital discharge.

Keywords: Bone Marrow Transplantation. Physical Therapy. Physical Functional Performance.

BARRIERS TO ACCESSIBILITY OF HEMATOPOIETIC STEM CELL TRANSPLANTATION: AN INTERNATIONAL PERSPECTIVE REVIEW

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INTRODUCTION: Bone marrow transplantation is a treatment that even rich countries with universal health systems do not have uniformity in accessibility. Each nation has its own dilemmas facing the access barriers, which can be subdivided into four categories: geographic, socioeconomic, organizational and of information.

OBJECTIVE: To review the barriers to accessibility to bone marrow transplantation from an international perspective.

METHODS: Integrative review based in search strategies to answer the question: "What does the scientific literature present about access barriers to bone marrow transplantation?". Descriptors according to the DeCS and MeSH were used for the search in BVS portal, Pubmed and Scopus. Only scientific articles in Portuguese, English and Spanish published from 2012 to February 2022 were included. Other categories of documents were excluded. The search resulted in 8147 documents, and after removing the duplicates, applying the inclusion and exclusion criteria, reading the titles and abstracts, 22 were selected for this review.

RESULTS: Most studies were carried out in the United States (15). The participants analyzed corresponded to populations of patients with acute leukemia, multiple myeloma and sickle cell disease, candidates for transplantation or already transplanted. Two studies of sickle cell disease also analyzed the perspective of caregivers and family members. Some nationwide studies involved the population with a transplant indication when the issues discussed involved financing modalities or geographic distance. Studies with health professionals asked about geographic difficulties, regulation and changes in management during COVID-19 pandemic. It was demonstrated that access was hampered by the distance from the residence to the transplant center, with greater population (high demand for services) and transport difficulties. There was better access in countries with higher GDP per capita, a greater number of centers and for populations with higher incomes. The issue of ethnic differences was evident, with whites having better access than blacks and hispanics in the United States, in general. Coverage by insurance companies, support by public policies, better allocation of financial resources, attendance at academic centers, organization of regulation and prioritization of urgent indications in the pandemic facilitated access. The understanding of the diseases, adherence to proposed therapy, the perception of better survival by patients and the good technical updating of professionals improved access.

CONCLUSIONS: All categories of access barriers were addressed and the causes are multiple and interrelated. The socially vulnerable population is the most affected. The identification of the determinants is important for the discussion and formulation of public policies and there is a need for more studies in underdeveloped countries with the objective of improving equity in access to health services.

Keywords: Barriers to access of Health Services. Health Services Accessibility. Hematopoietic Stem Cell Transplantation.

DEATH EDUCATION IN CHILDHOOD: TALKING TO THE 5-YEAR-OLD SON OF A PATIENT ADMITTED FOR BONE MARROW TRANSPLANT

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Although death is an expected event in the course of development, the contact with the issues of finitude can mobilize intense and contradictory emotional experiences. The proximity to these issues can generate in children many concerns and doubts, since the acquisition of the concept of death is gradual, dependent on the development, the sociocultural environment in which they are inserted and their life experiences involving ruptures and permanences. This study aims to understand the concept of death of a child whose father, diagnosed with a life-threatening disease, was hospitalized for a Bone Marrow Transplant. This is a qualitative, descriptive-exploratory study, with a methodological design of a single case study. The participant, herein renamed Lucas, was 5 years old. As an instrument of data collection, a ludodiagnostic session was applied, a type of psychological care structured with games and toys, having as a trigger and mediator of the dialogue the children's book "The little Poli bee". This book is the result of a previous study that used a multidimensional approach to the concept of death to mediate the child's contact with the theme and allow him/her to express the feelings and questions that were aroused. The children's verbalizations were transcribed literally and submitted to the Thematic Reflexive Analysis. Five categories were elaborated: a) Irreversibility: Lucas presents the notion that one does not come back to life after death, although, in some moments, he presents arguments that the dead bee may be somewhere; b) Causality: the child admits that death is expected for the adult, but not for the child: we only die when we grow up; c) Functionality: Lucas associates dying with sleeping, showing that he has not yet acquired the full notion of non-functionality; d) Purpose: it is evident that he has not yet reached the cognitive stage that allows him to formulate hypotheses to justify death; e) New elements: Luke comments on the death of a man, although there is no human character in the story. The child is found to have the notions expected for his chronological age, presenting only the dimension of the irreversibility of death in process of consolidation. The fact that it includes the death of a man is probably related to the father's serious illness and confirms the results of other studies, which point to the influence of the social environment on the child's understanding of death and dying. It is expected that this study brings subsidies for the understanding of such a delicate theme that is the understanding of death in children, as well as some dimensions that may influence the process of gradual acquisition of this concept, pointing to the need to offer interventions in the field of education for death.

Keywords: Death; Child; Terminality; Bone marrow transplant.

DEMOGRAPHIC PROFILE AND INCIDENCE OF ORAL CGVHD IN PATIENTS AFTER ALLOGENEIC HSCT IN LATE FOLLOW-UP AT A REFERRAL CENTER.

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INTRODUCTION: Allogeneic hematopoietic stem cell transplantation (HSCT) is a highly complex procedure and the main treatment option for several onco-hematological pathologies, some solid tumors, primary immune deficiencies and autoimmune diseases. It is well established that HSCT is an excellent alternative for the treatment of diseases, as well as the increase in survival of patients undergoing the procedure. There is, however, a need for long-term follow-up due to the various complications that may arise. Chronic Graft Versus Host Disease (cGVHD) is the main immunological complication resulting from allogeneic HSCT and all the factors that may be related to its development are still widely discussed. Objective: To describe the profile of patients in late follow-up after HSCT at a referral hospital in southern Brazil.

METHOD: Descriptive study, with a quantitative approach, developed over a period of 65 months (2017 to 2022) involving patients who attended routine consultations at a referral hospital. The variables gender, age, type of donor, underlying pathology, development of cGVHD and mortality were collected through a search in the medical records. The presence of cGVHD in sites other than the mouth was collected together with the medical team during the consultation. Examination of the oral cavity was performed during medical consultation, as part of the clinical examination, using a flashlight, gauze and wooden spatula. The present work is part of project 17-0181, approved by the Research Ethics Committee of Hospital de Clínicas de Porto Alegre.

RESULTS: 232 patients were evaluated, 137 men (59.1%) and 95 women (40.9%). Of the total HSCT performed, 65.9% were related donors (father, mother or brother) and 34.1% were unrelated, with a mean post-HSCT follow-up time of 10.6 years (minimum 1 and maximum 26 years). Leukemias, AML (Acute Myeloid Leukemia) and ALL (Acute Lymphoblastic Leukemia) together accounted for 39% of HSCTs, followed by bone marrow aplasia with 22%. Of the total number of patients evaluated, 85.5% developed some type of cGVHD (cutaneous, hepatic, pulmonary, ocular, oral) in the late follow-up period. Oral cGVHD present in 54% of patients, being concomitant with another site in 62%. In only 5% of patients, the oral cavity was the exclusive site of the disease. 12 patients died during the late follow-up period.

CONCLUSION: This study made it possible to know the demographic profile of patients in late follow-up after allogeneic HSCT and the incidence of cGVHD. Data found are in agreement with the current literature. More studies are needed to better understand the possible correlation of data with the development of cGVHD in order to optimize the treatment of these patients with the aim of improving quality of life and consequent improvement in survival.

DEVELOPMENT OF A TOOL FOR PHARMACOTHERAPEUTIC MONITORING OF HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) PATIENTS

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INTRODUCTION: The pharmaceutical care of patients undergoing Hematopoietic Stem Cell Transplantation (HSCT) is of paramount importance for the optimization of the pharmacotherapy used, monitoring of adverse effects and outpatient compliance. The development of tools for monitoring and tracking pharmacotherapy and subsequent analysis of the data obtained is essential to map the profile of patients and align strategies to improve care.

OBJECTIVE: To describe the development of a tool for pharmacotherapeutic monitoring of patients seen at the bone marrow transplant (BMT) service of a teaching hospital.

METHODS: The electronic database in the RedCap® platform was structured based on data from the pharmacotherapy review of patients undergoing BMT in a teaching hospital in Fortaleza/CE.

RESULTS AND DISCUSSION: The database, in the RedCap® system, was divided into three tabs: 1) pre-transplantation - includes recipient demographic data, donor-recipient compatibility and past pharmacotherapy, comorbidities, and history of adverse reactions and allergies 2) conditioning and infusion regimen - information referring to actual pharmacotherapy, adverse drug reactions (ADR) and infusion (IR), and medication-related problems (DRP) was entered; 3) post-transplant - data referring to immunosuppressive therapy, GVHD prophylaxis, antibiotic therapy, and outpatient therapeutic adherence were entered.

CONCLUSION: The development of tools for the optimization of pharmaceutical care facilitates the identification of the profile of patients followed, improvement of the service provided, promote the rational use, observe the effectiveness, toxicity, substitutions and adequacy of therapies when necessary.

Keywords: Pharmacotherapy. Hematopoietic Stem Cell Transplantation. Monitoring tools.

EFFECT OF FUNCTIONAL REHABILITATION AFTER CHEMOTHERAPY PROTOCOL FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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INTRODUCTION: Leukemia is a cancer that causes exacerbated leukocyte cells in the bone marrow. The main treatment for acute lymphoblastic leukemia (ALL) in adults is the use of chemotherapy drugs. Among the side effects of the treatment we can mention gastrointestinal problems, fatigue, dyspnea, infections, pancytopenia and polyneuropathy. Due to the complexity of the effects caused by the therapy used, the follow-up of a multidisciplinary team throughout the treatment is necessary. Physiotherapy plays an important role in the care of patients with ALL, preventing and treating such side effects, but the risk of adverse events such as bleeding, tachycardia and fainting/syncope must be taken into account.

OBJECTIVES: To describe the performance of physical therapy in patients with functional loss after treatment for ALL and need for ICU admission. To verify the feasibility of exercises in a pancytopenic patient and the occurrence of adverse events.

METHODOLOGY: Case report.

RESULTS: Male patient, 45 years old, previously healthy, regular physical exercice practitioner (300 minutes per week), recent diagnosis of ALL, admitted to the Hematological Therapy Center of a private hospital in the south of the country for induction therapy with GRAAL 2005 protocol. In the initial evaluation, he had a score on the Barthel Scale: 100, KPS: 100. He started the protocol and after 20 days he presented neutropenia with septic shock due to gran-negative bacteria (GNB) requiring care in an intensive care unit (ICU), with Barthel scores: 76, KPS: 70. He remained in the ICU for 22 days, where he underwent continuous hemodialysis, evolving with ventilatory failure requiring orotracheal intubation and mechanical ventilation (MV) for 13 days. Upon returning to the inpatient unit, he had peripheral polyneuropathy, significant functional loss, Barthel: 15 and KPS: 30. As for physical therapy, it was performed twice a day, 7 days a week, for 20 to 30 minutes and included breathing exercises, assisted kinesiotherapy progressing to active and after resistance, proprioceptive neuromuscular facilitation, trunk control training, orthostasis and progression to gait training and/or cycle ergometer. Periodic reassessments were performed and the exercises progressed according to clinical and laboratory conditions. Data were recorded in medical records and the treatment realigned. She was discharged after 90 days of hospitalization, with no need for supplemental oxygen, with Barthel: 62 and KPS: 70.

CONCLUSION: We verified that the physiotherapeutic care during the period of pancytopenia was feasible and beneficial for the evaluated patient. According to the collected data, no adverse event/intercurrence was observed during the exercises. Monitoring the exams minimizes failures in the process and periodic reassessments are necessary for adjustments when necessary.

Keywords: Oncohematology. Rehabilitation. Physical therapy.

EMOTIONAL AND SUFFERING HEALTH IN PATIENTS WITH GRAFT-VERSUS-HOST DISEASE UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION: According to the literature, Graft versus Host Disease (GVHD) can trigger anxiety, stress and hopelessness, besides causing a depreciation in the domains of quality of life in patients undergoing Hematopoietic Stem Cell Transplantation (HSCT).

OBJECTIVE: This study aimed to analyze the emotional health and distress related to GVHD in patients undergoing HSCT.

METHODS: This is an integrative literature review. The following databases were consulted: LILACS, SciELO and MedLine, using the descriptors: Graft-Host Disease and Bone Marrow Transplantation, and their correspondents in English, retrieving publications from 2017 to 2022.

RESULTS: A total of 171 records were identified, of which 32 were selected from reading the titles and abstracts. After the refinement of the sample, through reading in full, it was verified that 14 articles met the inclusion criteria and composed the corpus of analysis. Results were organized in three thematic categories: (1) Persistent fear of developing GVHD: even patients who did not have the disease reported insecurity and fear, enhanced by the fact of having contact with patients who developed the disease; (2) Worsening of quality of life with GVHD: the variable GVHD is predictive of substantial worsening in quality of life, since affected patients had lower indices in most domains of this construct; (3) Insecurity about the future after GVHD: patients being treated for GVHD were fearful of the evolution of the disease and had the feeling of having exchanged one disease for another, and those who already had control of the disease feared the recurrence of the underlying disease. CONCLUSION: The results point to the emotional impact of GVHD on patients' quality of life, with increased insecurity and fear of dying. An unexpected finding is that the disease also impacts the mental health of transplant recipients who did not develop this complication, but are vulnerable to anticipatory anxiety and fear that they may develop it at some point; patients with controlled GVHD, who have recovered their previous quality of life, but still feel insecure about the future, are also affected. It is critical that the healthcare team consider these data when planning supportive interventions in the context of HSCT recovery.

Keywords: Quality of life, Graft versus Host Disease; Hematopoietic Stem Cell Transplantation.

ENDODONTIC INFECTION AND PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION: The oral cavity is a frequent site of hematopoietic stem cells transplantation (HSCT) complications, most often resulting from immunosuppression. Acute oral complications of HSCT regimens include pain, mucositis, oral ulcerations, oral bleeding, virus infections, pericoronitis, and exacerbation of periodontal and endodontic infections. Chronic apical periodontitis is arguably one of the most common forms of endodontic biofilm-induced diseases that affect humans and develops after dental pulp necrosis and infection as a result of caries and trauma. Considering that dental infections may increase the susceptibility to infections before and after transplantation, apical periodontitis (AP) must be actively sought and treated accordingly in transplant candidates. Association between endodontic diseases and systemic health is well described in the literature, although the risk of endodontic disease in patients undergoing HSCT is not established.

OBJECTIVE: The aim of this study was to investigate the prevalence of AP and endodontic treatment in patients with indication of HSCT.

METHODS: One hundred patients with indication for HSCT were selected and the presence of endodontic disease was evaluated prior to transplantation. Intraoral periapical radiographs were obtained and analyzed (by the PAI index), and specific endodontic treatment was planned and performed. The following demographic and clinical data were collected from the patients' medical records: age, gender, transplantation stage, primary disease, transplant type, medication used, complete blood count at the time of visit, and need for endodontic treatment.

RESULTS: The mean age of the participants was 51 years with a predominance of males (54%). Lymphoma represented 35% of the hematological diseases, followed by multiple myeloma and leukemia (29% each) and other diagnoses (7%), all with indication for allogeneic and autologous transplantation (1:1). Fifty-eight percent of patients had at least one previous endodontic treatment. Thirty-seven percent were diagnosed with endodontic disease, requiring endodontic treatment before transplantation. Radiographic signs of AP in one or more teeth were found in 27 of patients and 20% presented lesions larger than 5mm in diameter. All patients (100%) had no complications before and after transplant. Acute apical abscess was observed in only two patients prior to endodontic treatment and HSCT during an immunosuppression period.

CONCLUSION: The dental evaluation prior to HSCT and monitoring patients with endodontic disease is imperative, due to the risk of exacerbation during and after transplanta tion. Endodontic therapy was effective and safe and is the primary treatment for teeth with AP.

EXPERIENCE REPORT OF A BONE MARROW TRANSPLANTATION CENTER THAT IS RESUMING ITS ACTIVITIES IN THE CARE ASPECTS AND INCLUDING THE RESEARCH CONTEXT ITS DAILY PRACTICES

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INTRODUCTION: Bone marrow transplantation is a therapy that has been growing in terms of indications and complexity in recent decades.

OBJECTIVE: To report the experience of the team of a hematopoietic cell transplantation center that is resuming its activities in the care and research aspects.

METHODS: This summary is an experience report of the multidisciplinary team of a Bone Marrow Transplant Center. The service is located in a city in the interior of the southern region of Brazil, has six active beds and performs Autologous, Allogeneic Relatives Transplants, including Haploidentical Transplants.

EXPERIENCE REPORT: The Bone Marrow Transplant Center has been operating since 1997, performed 338 transplants from 1997 to December 2020, had its peak of assistance activities in the first decade of the 2000s, gradually decreasing the annual frequency of transplants, starting the unit to receive clinical hematological patients at risk. In the second half of 2021, transplant activities resumed with the arrival of a new transplant doctor, where 18 transplants have been performed so far, of which two allogeneic related, 14 autologous and two haploidentical, a modality that had not yet been performed on this service. In the last quarter, the center has managed to maintain an average of three transplants per month, a routine that is sometimes altered by the natural conditions of the southern region of Brazil where, due to the low temperatures, patients end up manifesting Influenza Syndrome, which delays hospitalizations for transplants and also the COVID-19 that affected some patients who were waiting to perform the procedure that had to be suspended for them. The Center's multiprofessional team is also seeking to implement the research. For this, the enrollment in the Brazilian Society of Bone Marrow Transplantation took place, inclusion for participation in Multicentrica research, already approved by the ethics committee together with other bone marrow transplant centers in Brazil, under the leadership of the Research Center of Hospital Israelita Albert Einstein with the title "Multicentric Registry of Autologous and Allogeneic Hematopoietic Stem Cell Transplants for Malignant and Non-Malignant Diseases performed in Brazil and reported at the Center for International Blood and Marrow Transplant Research (CIBMTR)".

CONCLUSION: The search continues for consolidation of Bone Marrow Transplantation services meets the health needs where there are more and more therapeutic indications with this treatment modality and the further away from the big centers the services, the more people will have access to treatment with Bone marrow transplant.

Keywords: Health management. Bone marrow transplant. Multi-professional team.

HUMANIZATION OF MULTIPROFESSIONAL CARE IN A HEMATOPOIETIC STEM CELL TRANSPLANTATION WARD IN A REFERENCE ONCOLOGIC HOSPITAL OF SÃO PAULO COUNTRYSIDE

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INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is a highly complex therapeutic modality characterized by prolonged hospitalizations and frequent and specific multi-professional care. During this period, the patient goes through critical stages, which may result in loss of physical conditioning, along with psychological and social changes. Fear, longing and isolation are frequent problems, and it is necessary to develop coping and humanization strategies to make this process as less stressful as possible and prevent psychosocial problems.

OBJECTIVE: Describe coping and humanization strategies implemented in an adult HSCT inpatient unit.

METHODS: Descriptive study.

RESULTS: Strategies are implemented on a daily basis in order to alleviate the emotional and psychological challenges during HSCT hospitalization. These practices are performed by different team members, and at different times. In pre-HSCT, the multidisciplinary team starts building the bond and provides initial care guidelines. At this point, the patients' needs are identified. During hospitalization, distraction resources such as movies, series, games, video games and the origami's confection to "decorate" the room are made available. The patient has access to the internet using the hospital network. During this period, patients are encouraged to write daily messages on the room board about what they consider important during that day. It's a way to reduce anticipatory thoughts and fear of the future. The construction of positive thoughts is also stimulated with symbolism techniques such as the "tree of life" drawing technique. These are 3 trees composed only of the trunk, roots and branches and that symbolize the three stages of HSCT: pre-HSCT; post-infusion of CTH; grafting and hospital discharge. The objective is the patient to express himself through the free construction of the other tree's components. Another humanization resource are the customized and personalized HSC bags, with patients and family members' photos. The goal is to make the HSC infusion a unique moment for each patient. After grafting, and as soon as possible, patients take supervised outings that symbolize the proximity of hospital discharge. Catholic patients, or those who use faith as a coping tool, walk the path between the inpatient unit and the hospital chapel, and can visit the chapel at certain times. As a form of final celebration, there is the grafting cake, which is prepared with the patient chosen flavor, being cheered with the "happy birthday" choir upon receiving it, which marks their "rebirth".

CONCLUSIONS: Humanization practices have helped patients to cope with the HSCT stages, as they reduce the psychological impact and prevent future psychosocial problems.

Keywords: HSCT ward. Multidisciplinary team. Humanization.

IMPLEMENTATION OF A PREVENTION BUNDLE OF PRIMARY BLOOD CURRENT INFECTION IN A PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT

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INTRODUCTION: Patients undergoing hematopoietic stem cell transplantation (HSCT) are more vulnerable to the development of healthcare-associated infections (HAIs), due to the immunosuppression to which they are submitted, long hospital stays and the use of invasive devices such as central venous catheters. (CVC) for its therapy. Bloodstream infections are the main infections that affect this population, occurring more frequently in early post-HSCT and when associated with a central venous catheter, they are called primary bloodstream infections (PBI). A bundle is a package of preventive measures applied systematically by the team, with the aim of reducing infections.

OBJECTIVE: to analyze the impact of implementing the PBI prevention bundle focusing on central venous catheter maintenance in a pediatric HSCT unit on the unit's laboratory-confirmed PBI incidence densities.

METHOD: A descriptive retrospective study analyzing data from the Epidemiology and Hospital Infection Control Service (HICS) on laboratory-confirmed PBI density (according to ANVISA criteria) and compliance with the PBI prevention bundle of the HSCT Unit. The bundle was implemented at the HSCT Unit in August 2021, with audits carried out by the HICS and later by the nursing team. The bundle analyzes PBI prevention measures with a focus on CVC maintenance, including: hand hygiene before medication preparation and central venous catheter manipulation, integrity and validity of the CVC dressing, CVC protection during bathing, disinfection of connections and knowledge/guidance on patient/family catheter care. Audit feedback is performed in real time and allows the team to act on points that present opportunities for improvement.

RESULTS: The PBI prevention bundle was implemented in the unit in August 2021 and presented a compliance of 93% in the first month, with an average of 96% during the 9 months of implementation. During this period, 46 transplants were performed in the unit. The mean incidence density of laboratory confirmed PBI from July 2020 to July 2021 was 4.6 PBI/1000 patients/CVC/day. The mean PBI density at 9 months after bundle implementation was 2 PBI/1000 patients/CVC/day, representing a 43.5% reduction in laboratory-confirmed PBI incidence density after bundle implementation.

CONCLUSION: The implementation of the laboratory PBI prevention bundle resulted in a significant decrease in the incidence density of this topography. The adoption of systematic measures for the prevention of infections by the nursing team allows the diagnosis of weaknesses and adequacy of care practices in real time, in addition to appropriating the care team in the prevention and control of infection.

Keywords: HAI. Laboratory IPCS. HSCT. IPCS prevention bundle.

INTERVENTION OF RESPIRATORY PHYSICAL THERAPY IN A PATIENT WITH CHRONIC GRAFT VERSUS HOST DISEASE: A CASE STUDY

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INTRODUCTION: Graft versus Host Disease (GVHD) is a consequence of an immunological reaction and is one of the complications that result from bone marrow transplantation. GVHD can develop from a chronic form, with systemic repercussions. Patients undergoing bone marrow transplantation are submitted to the use of corticosteroids as a form of treatment and this contributes to the development of atrophies and myopathies. This condition can affect the muscles and respiratory mechanics which when associated with disuse can worsen the condition. In order to reduce these impairments, physical therapy can develop strategies to prevent complications and also increase the cardiorespiratory capacity of these patients.

OBJECTIVE: To analyze the respiratory capacity of a patient with chronic GVHD in a teaching clinic in Fortaleza, Ceara.

METHODOLOGY: This is a case report study of a 26-year-old female patient who underwent bone marrow transplantation five years ago due to Acute Lymphoblastic Leukemia. Maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP), hand grip strength were evaluated using a dynamometer, submaximal aerobic capacity through the 6-minute walk test (6MWT) and the 1 Maximum Resistance (1RM) were performed to establish the protocol.

RESULTS: During the first evaluation, on 09/22/2021, the manovacuometry test resulted in a maximum inspiratory pressure (MIP) = - 45cmH2O and maximum expiratory pressure (MEP) = + 38 cmH2O. The hand grip strength of the right limb was 19.6 Kg/lb and the left limb recorded 23.9 Kg/lb. Furthermore, in the 6MWT, a speed of 4.14 km/h was obtained. The physical therapy treatment protocol was based on a mixed of aerobic and resistance training. Aerobic exercise was performed using a treadmill, with an initial load of 75% of the average 6MWT speed and with 5-10% increases in speed each week, and from mild to moderate intensity, using the modified Borg scale. Resistance training started with a load of 50% of the RM, in peripheral muscles. In addition, a linear pressure load device was used aiming to strengthen the inspiratory muscles with a load of 30% of the MIP, progressing to a load of 50% of the MIP. After 10 visits, the patient was reevaluated on 11/01/2021. An MIP of -90 cmH2O and a MEP of 40 cmH2O were identified. The hand grip strength of the right limb was 23.4 kg/lb and that of the left limb was 24 kg/lb. When checking the results of the 6MWT, the average speed was 4.23 km/h.

CONCLUSION: From the parameters collected, the physical therapy performance showed favorable results in chronic GVHD, indicating a better cardiorespiratory performance in the MIP, MEP, palm grip and 6MWT tests.

Keyword: Graft versus Host Disease. Physiotherapy. Cardiorespiratory.

LETERMOVIR PROPHYLAXIS FOR CYTOMEGALOVIRUS IN HEMATOPOIETIC-CELL TRANSPLANTATION: CASE REPORT

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INTRODUCTION: Cytomegalovirus (CMV) remains a clinically important complication after hematopoietic stem cell transplantation (HSCT). Advances in CMV diagnosis and management, such as CMV viral load measure by quantitative PCR and the use of preemptive antiviral therapy, have reduced the risk of developing CMV infection, particularly in the first few months post-HCT. Even with the advances mentioned, CMV-seropositive HSCT recipients have shorter overall survival, as well as CMV-seronegative recipients with positive donors have less favorable clinical outcomes, demonstrating the impact of CMV in HSCT outcomes. The strategy of using preemptive therapy for CMV has become standard and has been successful in reducing the incidence of the disease. Some drugs used, such as Ganciclovir, are limited by clinically unacceptable myelosuppression post HSCT. Thus, the development of new safe and effective antiviral agents for CMV prophylaxis remains an important goal in HSCT. Letermovir is an antiviral agent indicated for the prophylaxis of infection and disease caused by CMV in allogeneic, CMV-seropositive HSCT recipients. Letermovir inhibits the CMV DNA terminase complex, which is required for cleavage and assembly of new viral DNA, affecting the formation of specific genome units and interfering with virus maturation.

OBJECTIVE: To describe the first use of letermovir in our center.

METHOD: Case report.

RESULTS: Male patient, 34 years old, with Hodgkin Lymphoma and Haploidentical HSCT, conditioning regimen with FluCy+TBI and GVHD prophylaxis with Tacrolimus, Mycophenolate and Cyclophosphamide. Patient started CMV prophylaxis on D+6 with letermovir 480 mg. On D+22 patient with neutrophilic engraftment, hemoglobin of 5.4 and 15000 platelets, even with BID platelets transfusion, in addition to suspension of tacrolimus and undetectable CMV. In literature review we found a description of severe thrombocytopenia and anemia related to Letermovir, and have decided to suspend Letermovir. A diagnosis of HSCT-related thrombotic microangiopathy (TA-TMA) was later confirmed and counts improved. We plan to reintroduce the drug soon.

DISCUSSION: Letermovir is well tolerated, with most common adverse effects such as gastrointestinal toxicity and effects such as fatigue, headache, rash and peripheral edema. Letermovir can have hematopoietic effects such as grade IV thrombocytopenia in 27% and grade IV anemia in 2%. As the experience with the use of letermovir increases and more randomized clinical trials are conducted, we will be able to understand the real impact of letermovir toxicity post HSCT, where we have a huge range of clinical situations and several differential diagnoses occurring at the same time in this high complexity patient.

LEVETIRACETAM AS AN ALTERNATIVE DRUG TO PREVENT BUSULFAN-RELATED SEIZURES IN HEMATOPOIETIC STEM CELL TRANSPLANTATION: CASE REPORT

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INTRODUCTION: Busulfan is one of the most frequently used drugs in conditioning regimens for patients undergoing hematopoietic stem cell transplantation (HSCT). It is a bifunctional alkylating agent and can cause neurotoxicity associated with seizures. This happens because busulfan freely crosses the blood-brain barrier, reaching significant concentrations in the central nervous system. These concentrations are similar to plasma ones, which explains the mechanism of neurotoxicity observed with the drug use at high doses. Routinely, anticonvulsant drugs such as phenytoin are used for prophylaxis of busulfan-induced seizures. However, several issues are associated with the use of this drug. Phenytoin has a prolonged half-life and may require a loading dose to achieve adequate concentrations. In addition, it induces cytochrome P450, which can affect the pharmacokinetics of busulfan and interact with several other drugs. Alternatively, levetiracetam has a linear pharmacokinetic profile and little intra- and inter-individual variability. Its bioavailability is close to 100%, and equilibrium state concentrations are reached within 48 hours. Because of its uniform absorption, plasma levels can be predicted after oral administration, eliminating the need of monitoring. Levetiracetam is well tolerated and drowsiness and irritability may be the main adverse effects. In addition, it does not affect cytochrome P450 and probably does not affect the pharmacokinetics of busulfan or other drugs used concomitantly. Literature data demonstrates that levetiracetam has comparable efficacy and safety to phenytoin in terms of preventing busulfan-induced seizures.

OBJECTIVE: To describe the use of levetiracetam at our center as an alternative to busulfan-associated anticonvulsant prophylaxis. Method: case series of 11 patients who underwent HSCT in our unit and used busulfan in conditioning and levetiracetam as anticonvulsant prophylaxis. Results: Levetiracetam was used in 11 patients since January 2020. Of these patients, 7 were male and 4 were female. Six patients were submitted to allogeneic HSCT with matched-related donors, 2 patients using matched-unrelated donors and 3 patients underwent autologous HSCT. Standard prophylaxis with phenytoin was replaced by levetiracetam 1000 mg 12/12h, starting 48h before the first dose of busulfan, continuing until 48h after the last dose. No patients had seizures and 2 had adverse effects possibly related to the use of levetiracetam. No drug interactions were observed.

CONCLUSION: Levetiracetam can be used to effectively prevent busulfan-induced seizures. In addition, it is convenient due to the low risk of significant adverse effects during concomitant administration of antineoplastic drugs and no interactions with other medications used in the HSCT process.

MANIFESTATION OF MANTLE CELL LYMPHOMA IN ATYPICAL LOCATION IN HARD PALATE - CASE REPORT

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Mantle cell lymphoma is a rare subtype of neoplasm contained in the group of non-Hodgkin's lymphoma (NHL) that occurs in B cells, arises from cells originating in the mantle zone, and may present with agressives or indolent characteristics. The aim of this study is to report a case of a refractory manifestation of mantle cell lymphoma in an unusual location, in the hard palate region. A previously healthy 80-year-old male patient noticed the onset of night sweats associated with the appearance of a painless nodulation in the cervical region. The complementary exams performed revealed the diagnosis of mantle cell lymphoma (MCL), starting R CHOP and lonquex for treatment, and performing rituximab for maintenance in the 02 consecutive years. In 2020, the patient presented recurrence of new sites in the intestine and lung, compatible with MCL, starting a new line of treatment with acalabrutinib. In July 2021, he presented bulging in the hard palate with progressive growth, which after biopsy showed a manifestation of MCL in the hard palate, opting for treatment with local radiotherapy with 40Gy, associated with IBTK (Inhibitor Of Bruton Tyrosine Kinase). The patient was submitted to dental evaluation prior to radiotherapy, opting in the planning to make a mouth opener. Radiotherapy sessions were performed in 20 fractions of 200cGy. Due to the area where the irradiated field is located, daily follow-up was proposed through preventive laser therapy for radio-induced mucositis. At the end of the radiotherapy treatment, the bulging of the hard palate region was in total clinical remission and without areas of hyperuptake on PET. Despite the location of the uncommon manifestation, it is extremely important for the dental surgeon to know the therapeutic approaches of chemotherapy or immunotherapy associated or not with radiotherapy, for the treatment and multidisciplinary follow-up of these pathologies, as well as the follow-up of the case.

NURSE NAVIGATOR PROGRAM IN BONE MARROW TRANSPLANTATION: AN EXPERIENCE REPORT

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INTRODUCTION: The National Cancer Institute (INCA) estimates that for each year of the triennium 2020-2022, there will be about 625 thousand new cases of cancer, of which there are estimated around 24 thousand cases between Leukemia and Lymphomas.(1) A modality The therapy used for these pathologies is Bone Marrow Transplantation (BMT). Considering this scenario, the implementation of a Nurse Navigator Program in BMT benefits the patient, as it aims to increase treatment adherence, reduce bureaucratic barriers, direct and accompany patients and families throughout their journey, guiding and educating throughout the transplant. Navigation is performed by a specialized person, the "navigator", who guides people with a diagnosis or suspicion, helping them to "navigate" through the health system and services.(2)

OBJECTIVE: to describe the Nurse Navigator Program implemented for bone marrow transplant patients in a hospital in southern Brazil.

METHODS: experience report on the navigation of bone marrow transplant patients.

RESULTS: The Hematological Therapy Center of Hospital Moinhos de Vento (CTHMV) was created in 2015, since then 184 transplants have been performed. The process begins with the physician with the diagnosis and definition of the need for BMT, which in turn includes the patient in a list with their data and the therapeutic planning, forwards the documentation for authorization of the procedure and communicates to the navigator nurse. The nurses navigate this patient and help with bureaucratic procedures such as authorization of the agreement, date of hospitalization, request for release of a companion, telephone contact prior to hospitalization, among others. In cases of unrelated allogeneic transplants (NAP), the patient is entered in the Bone Marrow Recipients Registry (REREME), they collect the material for confirmation of HLA typing and accompany the medical team and the blood bank throughout the process until receiving at the transplant center. In bedside care, they perform the systematization of nursing care, elaborating the therapeutic planning according to daily assessment, based on the best clinical practices. They are also an important presence in the multidisciplinary rounds and family meetings that take place along this journey. At discharge, they provide guidance on general care and follow-up on an outpatient basis.

CONCLUSION: Patient navigation, performed by nurses, is an intervention that helps to reduce delays in accessing health services and provides personalized care throughout the course of treatment with a direct impact on quality of care and customer satisfaction. The TMO navigation program is fundamental because it is a patient-centered model, promoting the timely movement and effective direction of a patient through a continuum of healthcare in a complex area, favoring the humanization of this route.

Keywords: Patient Navigation. Bone Marrow Transplantation. Hematology.

NURSING INTERVENTIONS BEFORE SKIN TOXICITY AFTER BONE MARROW TRANSPLANTATION: A CASE REPORT

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INTRODUCTION: Bone marrow transplantation (BMT) is a complex and aggressive treatment where the patient is submitted to high doses of chemotherapy, inducing bone marrow aplasia. In this process, there are wide side effects/toxicity, including skin toxicity. With the use of Busulfan medication, it is possible to observe this toxicity, where 57% of the manifestations are skin rashes, 28% itching, in addition to erythema, desquamative dermatitis, skin discoloration, among others.1

OBJECTIVE: To describe nursing care for skin prevention and treatment in patients with post-BMT skin toxicity.

METHODS: This is an experience report experienced by nurses at an oncohematology inpatient unit in a private hospital in Brazil.

RESULTS: It was found that patients who used the drug Busulfan and presented skin toxicity, manifested extreme skin fragility, hyperpigmentation and desquamation. Some skin changes worsened when subjected to pressure, friction, moisture and contact with medical adhesives, causing pressure injuries and MARSI injuries, even in the presence of prevention protocols installed according to the Braden scale.2 To prevent pressure injuries, we used a pneumatic mattress, body hydration with moisturizer based on allantoin and vegetable oils, cream based on vitamin B5 in scaly areas and/or barrier cream when associated with intestinal changes (diarrhea). The patient was instructed to perform self-care: warm bath, use of neutral and liquid soap, alcohol-free and perfume-free products, soft bath towel avoiding friction on the skin. In cases of category II pressure injuries, a dressing with a silicone plate and essential fatty acids was used, fixed with a transparent film and removed with adhesive remover spray in order to prevent injury from a medical device. In wet pressure injuries with exudate, non-adhesive polyurethane foam was chosen with a minimum of fixative film, lasting for 7 days. For the prevention of MARSI lesions we use the adhesive remover, skin hydration with allantoin and barrier spray.

CONCLUSION: Assistance to maintain skin integrity in patients with cutaneous toxicity is challenging. It is extremely important that the patient and the multidisciplinary team are engaged in offering care following preventive guidelines. Knowledge of skin toxicity is necessary to design an individualized care plan, which must be adjusted according to the nurse's daily assessment and clinical reasoning, based on best care practices. This contributes to maintaining skin integrity, reducing complications, preventing infectious processes, preventing trauma and minimizing impacts that occur when the skin barrier is breached.

Keywords: Bone Marrow Transplantation. Injuries. Toxicity.

NUTRITIONAL STATUS OF VITAMIN A IN THE PRE - ALLOGENIC TRANSPLANTATION PERIOD IN ADULT PATIENTS IN A BONE MARROW TRANSPLANTATION CENTER

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INTRODUCTION: Allogeneic Hematopoietic Stem Cell Transplantation (ASCT) comprises a treatment modality widely used in individuals with diseases that affect blood cell lines. Vitamin A or retinol is an essential micronutrient and its role in human health is highlighted by its functionality: (i) during pregnancy, (ii) in maintaining adequate vision function, (iii) belonging to the antioxidant complex, in addition to other known physiological functions. There are few studies that propose to evaluate serum levels of micronutrients in patients who are candidates for ASCT. However, the role of this micronutrient in clinical outcomes in these patients is not yet well established. OBJECTIVE: To evaluate serum levels of Vitamin A in the pre-transplant period between days D-8 to D0 in patients who underwent ASCT.

METHODS: Cross-sectional study, in which the population of this study included a cohort of 47 patients undergoing ASCT from February 2017 to July 2020. Blood samples of 5 ml were evaluated for the quantification of serum retinol, using High Performance Liquid Chromatography (HPLC-UV). For the classification of Vitamin A adequacy, adequate values of serum retinol ≥ 1.05 µmol/L were considered, with the cut-off point < 1.05 µmol/L used to diagnose Vitamin A Deficiency (VAD). Data were analyzed in SPSS 20.0 where simple descriptive analyzes of frequency, means and standard deviation were performed. RESULTS: The mean serum level of Vitamin A in the population studied in the pre-transplant period was 0.89 ± 0.31 µmol/L. There was a prevalence of VAD in 44.7% (n=21) of the population. As for the degrees of VAD, (34.0% (n=16)) presented mild VAD (8.5% (n=4)) presented moderate VAD.

CONCLUSION: There was a relevant prevalence of patients with reduced levels of Vitamin A in the pre-transplant period, indicating a population at risk of acute and late complications associated with VAD in the post-transplant period. Other studies are essential to assess the impact of VAD in patients undergoing ASCT.

Keywords: Vitamin A. Hematopoietic Stem Cell Transplantation. Vitamin A Deficiency

PALLIATIVE CARE AND BONE MARROW TRANSPLANTATION: AN INTEGRATIVE LITERATURE REVIEW

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INTRODUCTION: Bone Marrow Transplantation (BMT) is a treatment with important curative potential, which raises great hope in patients experiencing diseases that pose a serious threat to the continuity of life. The treatment is permeated by high risks, in addition to the possibility of relapse of the disease after it, it is important, therefore, to consider care approaches that cover this unpredictability, such as Palliative Care.

OBJECTIVE: The objective of this review was to describe the contributions of the palliative care approach in the care of patients undergoing BMT.

METHODS: This is an Integrative Literature Review carried out in the Scopus, PubMed, PsychINFO and LILACS databases, covering studies from 2011 to 2021. The studies were categorized based on content analysis. After applying the inclusion criteria (articles submitted to peer review; written in Portuguese, English or Spanish; published between January 2011 and October 2021; that presented the theme of palliative care associated with bone marrow transplantation; that presented results empirical studies that made the abstract available in the databases) there were six studies that made up the corpus of this work.

RESULTS: The results showed that the most frequent themes brought up by patients in consultation with the palliative care team were the management of physical and emotional symptoms, coping with treatment and establishing rapport (bonding). There was an important impact on the management of physical symptoms in these patients, who were more likely to use different forms of analgesia and other drugs to control pain, in addition to improving emotional symptoms, especially depression and post-traumatic stress. The importance of the advance care planning approach was also verified, in which most patients reported feeling comfortable with the topics discussed in consultations with the palliative care team and identified gains in knowledge about shared decision-making, development goals and advanced care planning.

CONCLUSION: There are numerous challenges involved in integrating the palliative care approach within BMT clinics, such as the unavailability of professionals in this area in different centers, the difficulty of conceptualizing palliative care, still present in many professionals, which is often linked to the end-of-life care, as well as the difficulty in assessing the prognosis of patients with hematological diseases, in view of the advance in curative treatments. It is also noted the scarcity of studies involving the two themes and the need for new studies that can promote this practice within BMT clinics.

Keywords: Bone marrow transplant. Palliative Care. Psychology

PHYSICAL THERAPY INTERVENTION IN THE FUNCTIONALITY OF A PATIENT WITH CHRONIC GRAFT VERSUS HOST DISEASE: CASE REPORT

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INTRODUCTION: Graft versus Host Disease (GVHD) consists of a complication resulting from bone marrow transplantation. One of the chronic repercussions is scleroderma, which is characterized by tissue fibrosis, and directly impacts the performance of activities of daily living and social participation. In order to reduce the limitations generated by chronic GVHD, a physical therapy treatment protocol is elaborated based on a kinetic-functional diagnosis aiming to return the patient to his functional abilities.

OBJECTIVE: To analyze the functional abilities of a patient with scleroderma in a teaching clinic in Fortaleza, Ceara.

METHODOLOGY: This is a case report study of a female patient, 26 years old, transplanted for five years, due to Acute Lymphoblastic Leukemia. She looked for Physical therapy treatment with complaints of pain in the left knee and difficulty in standing for a long period of time, which was limiting the performance of her activities of daily living. During the evaluation, three functional scales were used: the Barthel scale, the Timed Up and Go test (TUG) and the 5 times Sitting-rising test (SRT). In addition, the six-minute walk test (6MWT) and the 1 Maximum Resistance Test (1RM) were performed to establish the protocol.

RESULTS: In the first evaluation, on 09/22/2021, she was scored with 80 points on the Barthel Scale, reporting not being able to dress herself independently, and also reporting difficulties with her urinary tract and to climb stairs. The average time in TUG was 9.05 seconds and in SRT 11.74 seconds. The physical therapy protocol was based on flexibility exercises at the beginning, and mixed training of aerobic and resistance exercises. Aerobic exercise was performed using a treadmill with an initial load of 75% of the mean 6MWT speed and with 5-10% increases in speed each week, and from mild to moderate intensity, using the modified Borg scale. Resistance training started with a load of 50% of the 1RM. After 10 visits, the patient was reassessed on 01/11/2021. An increase of 10 points on the Barthel Scale was identified, which showed independence when dressing and an increase of 1.21 seconds in the TUG and 1.61 seconds in the TSL5.

CONCLUSION: It can be inferred from the kinetic-functional parameters, that the physical therapy treatment brought favorable results in GVHD, indicating a better musculoskeletal performance obtained in the tests and, consequently, a better functional capacity.

Keywords: Physiotherapy. Functionality. Graft Versus Host Disease.

PHYSIOTHERAPY EVALUATION IN CHILDREN WITH LEUKEMIA SUBMITTED TO BONE MARROW TRANSPLANTATION

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INTRODUCTION: Leukemia is a disease manifested by changes in the leukocyte cells of the hematopoietic tissue. The main treatment is chemotherapy, and when indicated, hematopoietic stem cell transplantation (HSCT).

JUSTIFICATION: The physiotherapeutic evaluation before HSCT can identify comorbidities caused by cancer treatment such as immobility, muscle weakness and decrease quality of life.

OBJECTIVE: To evaluate the functionality, physical conditioning and quality of life of patients diagnosed with ALL hospitalized for HSCT.

METHOD: Case series of patients with ALL, admitted at the hospital undergoing HSCT. Age, weight, hand grip strength through dynamometry, three-minute step test (TD3), quality of life through PesQL-tm 4.0 and fatigue through the application of the PedsQL fatigue scale were collected between May and August 2021.

RESULTS: three patients were evaluated, two male, aged between 12 and 14 years old, with adequate height for their age and 02 with thinness status. All of them had palm grip, respiratory muscle strength and TD3 values below the normal range for pediatrics. All patients had a better perception of quality of life compared to their parents, and in the evaluation of fatigue, the parents' perception was better than the children's perception.

CONCLUSION: Adverse effects from cancer treatment are present and interfere with the functional capacity and quality of life of patients with ALL. Physiotherapeutic assessment can identify functional and social impairments and guide conducts in pre-HSCT treatment, due to the risk of compromising functionality and repercussions on the patient's survival and autonomy during hospitalization.

Keywords: Bone Marrow Transplantation. Child. Functional status.

PROTOCOL OF PSYCHOLOGICAL ASSESSMENT AND INTERVENTION IN BONE MARROW TRANSPLANT UNITS: AN ACCUMULATED EXPERIENCE IN 22 YEARS

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INTRODUCTION: The potentially fatal illness, combined with the imminent need to undergo a highly complex procedure such as bone marrow transplantation (BMT), triggers emotional reactions in patients and their families. This suffering needs to be welcomed and understood by the multiprofessional team, especially by the psychologists.

OBJECTIVE: The objective of this study is to present a proposal for a protocol of psychological assessment and intervention developed in an MWT Unit, based on the experience of 22 years of clinical practice.

METHODS AND RESULTS: The protocol was systematized according to steps that accompany the medical procedure and involved patients and family members. After testing the model and submitting it to the necessary adjustments, the protocol that proved to be most appropriate was: 1) Pre-BMT: Mental health assessment through clinical interviews, instruments to measure stress (ISSL inventory), anxiety and depression (HAD scale) and health-related quality of life (SF-36 questionnaire), applied to patients and family members (with special attention to potential companions and donors); Interventions: Individual appointments, family meetings and waiting line groups (supportive and informative), guidance and emotional support to the healthy sibling; 2) BMT itself: Assessment: Reapplication of the scales and clinical interview; Interventions: Individual bedside care for the patient, support in coping with terminality and grief, storytelling and dodo project (in partnership with ABRALE) for children, musicalization for adolescents and adults, and companion groups for family members; 3) Post-BMT: Assessment: Reapplication of the scales and clinical interview (repeated every six months); Interventions: individual care, psychological support groups, activity workshops (aimed at recovering functionality), evaluations and specific interventions in the case of Graft versus Host Disease (GVHD).

CONCLUSION: The services can be provided in person or online, and at the moment the post-BMT support group takes place remotely. Some experienced difficulties: the time required to apply the instruments and activities (which impact the ambulatory's routine) and the availability of an adequate space to hold the group (especially for companions, since they have difficulties in distancing themselves from the patient's bed). A fundamental prerequisite for the viability of the protocol implementation is the support and recognition, by the multidisciplinary team, of the need to follow the evolution of the psychological dimensions. The results systematized so far point to the adequacy of the instruments chosen to measure the emotional changes of patients and relatives in the different stages of BMT. The results contribute to guide both the modalities of intervention (such as, for example, the need for referral for further evaluation by other mental health professionals), and the definition of the frequency of psychological interventions, which can be offered once a week or even more than once a day. This study contributes to estimate the effectiveness of the protocol proposal.

Keywords: Protocol. Psychology. Bone marrow transplantation. Health professionals.

PSEUDOTUMOR CEREBRI ASSOCIATED WITH CYCLOSPORIN USE FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION. Pseudotumor cerebri (PC) is a syndrome characterized by the presence of intracranial hypertension (ICH) and no alteration in the ventricular system. It manifests mainly with headache, nauseas and vomiting, a reduction in visual acuity, and diplopia. Among the associated etiologies, there are drug causes.

OBJECTIVE. To describe the association between the use of Cyclosporine after Hematopoietic Stem Cell Transplantation (HSCT) and the occurrence of Pseudotumor Cerebral.

CASUISTRY. S.R.S.M., 26 years old, female, allogeneic unrelated HSCT on 03/15/2022 for relapsed B-ALL.

RESULTS. The patient complained of intense, progressive, holocranial, pulsatile headache, and around D+36 she started nausea and vomiting, associated with blurred vision. In an ophthalmological evaluation, bilateral papilledema was observed, which led to hospitalization for etiological investigation. Cranial CT showed partially empty sella turcica and tortuosity of optic nerves, suggestive of Pseudotumor cerebri. In the contrasted exam, there were no findings consistent with thromboembolic events. CSF puncture was performed with an opening pressure of 33cmH2O, without other abnormalities or infectious findings. The use of cyclosporine can lead to the onset of intracranial hypertension associated with the development of a pseudotumor cerebri. This reaction may be partially associated with the mechanism of renal vasoconstriction and sodium retention that culminate in an increase in blood pressure, thus contributing to the onset of characteristic symptoms of PTC, such as severe headache, visual abnormalities and seizures. The neurological alterations caused by this immunosuppressant are usually reversible after dose reduction or therapy suspension and, in some cases, the association of antihypertensive drugs is necessary. In this case report, the therapeutic procedures consisted of replacing cyclosporine with mycophenolate mofetil (MMF) and the use of acetazolamide, a diuretic drug that acts by reversibly inhibiting the enzyme carbonic anhydrase, resulting in reduced secretion of hydrogen ions in the renal tubule and increasing renal excretion of sodium, potassium, bicarbonate and water, leading to decreased production of aqueous humor. Its action at the central nervous system stems from the inhibition of carbonic anhydrase in the choroid plexus, resulting in reduced production and flow of cerebrospinal fluid, leading to the delay of abnormal and excessive discharge of CNS neurons. After the measurements, the patient evolved with remission of symptoms. CONCLUSION. Cyclosporin (CsA) is a rare cause of PC, scarcely reported in the literature, and should be considered in the differential diagnosis of ICH and papilledema in those patients.

Keywords. Pseudotumor Cerebri. Cyclosporin. Hematopoietic Stem Cell Transplantation.

PSYCHOLOGICAL AND PSYCHIATRIC EVALUATION AND FOLLOW-UP IN HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION: The context of Hematopoietic Stem Cell Transplantation (HSCT) involves long hospitalization, maximum care due to immunosuppression that results in greater isolation, low quality of life and emotional suffering. High rates of anxiety and/or depression are found in this period, conditions that can persist even one year after HCST. In the onco-hematology unit routine, pre-transplant evaluation is performed with all patients by the multidisciplinary team, including psychology and psychiatry.

OBJECTIVE: The objective of this study is to describe the psychological and psychiatric evaluation protocol performed with patients who are candidates for HSCT in the routine of our transplant unit.

METHODS: The present work consists of an experience report.

RESULTS: The pre-transplant mental health assessment seeks to identify potential and possible psychological and psychiatric risks, contributing to the planning of multidisciplinary interventions that can help the patient`s confrontation e and contribute to HSCT success. The evaluation protocol is performed individually by a psychologist and psychiatrist at different moments, based on an interview with the patient and caregiver, followed by a discussion with the multidisciplinary team. In the psychological assessment, a semi-structured interview script, based on the literature, is used in order to assess the patient's understanding of the diagnosis; understanding related to the HSCT process; history of adherence to previous treatments; network support; mental health history and presence of psychopathologies and history of use/abuse of psychoactive substances. The psychiatric evaluation, in turn, consists of an initial open interview, addressing the history of hematological and other physical diseases, the patient's expectation regarding the HSCT, psychiatric history and dysfunctional emotional conflicts and their treatments, and socio-social and professional issues. In a second step, a semi-structured psychiatric interview based on the DSM-V (Diagnostic and Statistical Manual of Mental Disorders) criteria is applied with the objective of screening psychotic and non-psychotic psychiatric disorders. Mental health monitoring is offered to the patient, donor and caregiver, following a frequency plan established in the evaluation. Both the psychological and psychiatric assessed risk, as well as the attendance plan, are subject to changes during follow-up period. The psychological assistance provided during follow-up aims to address HSCT-related demands, such as adaptation and adjustment to prolonged hospitalization; development of adapting coping strategies; management of techniques for anxiety and other emotional symptoms; empowerment of the treatment and health care plan; resignification of changes generated by the HSCT; developing communication strategies with the care team and patient-family-care team relationship. When a mental disorder that requires the prescription of psychotropic drugs is detected in the initial psychiatric interview, the psychiatrist starts the treatment, considering the underlying hematological disease profile, the patient's medical history and possible drug interactions between all the medications used in the pre and post-transplant phases. Psychiatric follow-up visits are planned according to the patient's severity and evolution.

CONCLUSION: Mental health management throughout the HSCT process is challenging, as it involves organic and neuropsychiatric aspects. The assistance provided by the psychology and psychiatry team in line with the multidisciplinary unit is essential for the optimization of clinical and socio-emotional results.

Keywords: Psychiatric evaluation. Psychological care. Mental health.

QUALIFICATION OF MULTIDISCIPLINARY WORK FROM THE ANALYSIS OF SOCIODEMOGRAPHIC, EMOTIONAL AND EDUCATIONAL DATA OF CHILDREN AND YOUNG PEOPLE SUBMITTED TO HEMATOPOIETIC STEM CELL TRANSPLANTATION

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INTRODUCTION: We present the project Multidisciplinary work, sociodemographic, emotional profile and school performance: quali-quantitative evaluation in an oncology-hematology service. This is unprecedented research in Latin America, highlights the relevance of multidisciplinary teams in complex treatments.

OBJECTIVE: To qualify multidisciplinary work by correlating health, sociodemographic, emotional and educational data, verifying how these variables interfere in the treatment and continuity of studies, with a view to creating strategies to overcome the problems identified.

CASUISTRY: Patients with hematologic and hematopoietic stem cell transplantation (TCTH) of the Pediatric Hospital.

SAMPLE: 48 student-patients. Median age: 7 years. Main diagnoses: oncologic diseases and rare diseases. Method: Descriptive-explanatory qualitative-quantitative approach, with design of intervention-research of the participant type.

RESULTS: Indicate the importance of reflecting on protocols to create multidisciplinary support networks. Retrospective data (2018-2021) were mapped characterizing the public and their needs during and after TCTH: 35 families from outside Curitiba, 13 of this municipality. Accommodation in Curitiba: 22 support houses, 03 house of relatives, 06 metropolitan region, 17 own house. 14 received social benefits, 34 received no benefits. 23 families with income equal to/less than R$2,000.00, 08 income equal to/ greater than R$5,000.00, 17 average incomes of R$3,000.00. Education: 14 completed higher education (one/both parents), 21 completed high school, 13 elementary school (attending or completing). Housing: 15 adaptations, 33 houses able. Psychological care: 48 patients, 04 psychiatric referrals. 48 attended by teachers. Continuity of schooling: 38. Being 28 of school return without support; 10 returns with support. 10s in school bond who requested classes during TCTH and were from Early Childhood Education. The survey provided an opportunity to review and improve interview forms, cross-referencing data, identifying interfering variables in treatment and schooling, and encouraged the creation of strategies to support families. Interfering factors: family ties with multidisciplinary teams, intra/extra-family support networks, prognosis, complications during/after treatment, family dynamics, socioeconomic profile, student's level of learning, link to learning/school, socio-emotional abilities.

CONCLUSIONS: Highlight the importance of multidisciplinary work to verify unique needs and improve protocols of action, in a co-responsible way. Social, psychological and educational support are considered essential support to work at TCTH, it is understood that this increases quality of life during and after treatment. It is argued by the essentiality of the articulation for humanization of the services provided, guaranteeing basic rights when exercising equitable social justice.

Keywords: Multidisciplinary Work. Intervention Research. Humanization of Services.

QUANTITATIVE ANALYSIS OF ORAL MUCOSITIS PRESENCE IN PATIENTS UNDERGOING HEMATOPOIETIC CELL TRANSPLANTATION

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INTRODUCTION: Oral mucositis (OM) is an important toxicity in patients undergoing hematopoietic cell transplantation (HCT), influencing in patients quality of life. Conditioning protocols can lead to neutropenia, thrombocytopenia, diarrhea, vomiting and mucositis. The Dental Surgeon (DS) on the HCT team prevents and treats changes in the oral cavity on this group of patients.

OBJECTIVE: The aim of this study was to describe the most frequent conditions that have an impact in the oral cavity, such as OM, in patients undergoing HCT.

PATIENTS AND METHODS: Patients undergoing HCT (n=133) were retrospectively analyzed from January 2020 to May 2022, taking into account OM grading and conditioning regimen.

RESULTS: All patients underwent a photobiomodulation (PBM) protocol using 660nm, 100mW, 1J, 10J/cm2 and cryotherapy (concurrent with Melphalan infusion). PBM was performed daily, starting on the second day of conditioning until stem cell engraftment day. OM occurred in 91 patients, 32 of whom underwent autologous HCT and 59 allogeneic, being grade 0 in 30.83%, I in 14.29, II in 33.83, III in 14.29 and IV in 6.77; 45 of 133 underwent cryotherapy, 45 total body irradiation (TBI) and 42 patients received busulfan (Bu). The most frequent diagnosis found was Acute Myeloid Leukemia (AML) and the conditioning regimen were BuFlu (Bu and Fludarabine) and FluCy (Flu and Cyclophosphamide), TBI corresponding to 15.03% in each conditioning; The conditioning regimen that presented the highest OM incidence was BuFlu, corresponding to 18.68% of the patients who presented any degree of MO.

CONCLUSION: The presence of CD, laser therapy and cryotherapy associated with the daily follow-up of the patient undergoing HSCT minimized the expected risk of severe OM (grade IV).

Keywords: Hematopoietic Cell Transplantation. Oral Mucositis. Photobiomodulation.

SOCIAL ASSESSMENT AS A STRATEGY FOR IDENTIFICATION AND EARLY INTERVENTION IN VULNERABILITY FACTORS IN HEMATOPOETIC STEM CELL TRANSPLANT

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INTRODUCTION: Hematopoietic Stem Cell Transplantation (HSCT) is a highly complex procedure that causes great physical, social and emotional impact on patients, requiring follow-up by a multidisciplinary team. In the pre-transplantation phase information is received by the patient about the treatment and procedures to be used, which may have a curative purpose or to control the disease. This stage is permeated by expectations, insecurities, stress and anxiety in the face of the unknown. Regarding social services team, the social assessment in the pre-transplantation phase consists of an interview with the patient and family/caregiver in order to identify aspects that may compromise adherence to care in the trans and post HSCT period, considering the family, economic context , housing, educational, cultural and social assistance.

OBJECTIVE: To reflect on the importance of early social assessment in the process of organizing HSCT hospitalization in order to identify demands that require previous interventions, minimizing risks to the procedures.

METHOD: This is an experience report carried out by the social service team included in the Assistance Program for Hematopoietic Stem Cell Transplantation (PATCH), composed of a multidisciplinary team, which provides assistance to patients and family members eligible for HSCT.

RESULTS: The social assessment carried out prior to the period of hospitalization makes it possible to identify potentialities and vulnerabilities in the social context of patients and families with the aim of planning early and focused actions and interventions. With the implementation of reception prior to hospitalization it is possible to intervene in risk and vulnerability indicators such as: absence of family support network, family conflicts, suspicion of violence or negligence in care, use of psychoactive substances by the patient and caregiver, economic vulnerability, housing risk, difficulties in accessing the Transplant Center. Throughout the pre-HSCT assessment, patients and caregivers receive guidance about aspects of family organization necessary to make the procedure possible, access to social rights and benefits, referrals to socio-assistance network, as well as legal and health networks. CONCLUSIONS: The demands identified by the professionals of the multidisciplinary team during the pre-HSCT assessments are discussed in weekly meetings with the aim of defining an integrated intervention plan and making sure the care areas responsible are able to meet the needs. Social assessment contributes to the identification of risk and vulnerability factors that impact treatment adherence, since HSCT imposes new coping strategies on the patient , their families and caregivers in the face of the changes involved with the procedure that directly affect social relations.

Keywords: Hematopoietic Stem Cell Transplantation. Social Service. Social Assessment.

SOCIODEMOGRAPHIC PROFILE AND CLINICAL OF ADULT PATIENTS SUBMITTED TO TRANSPLANT OF HEMATOPOIETIC STEM CELLS IN A PRIVATE HOSPITAL FROM SOUTHERN BRAZIL

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INTRODUCTION: Hematopoietic Stem Cell Transplantation (HSCT) is a therapeutic modality consisting of the infusion of hematopoietic progenitor cells for the treatment of malignant and non-malignant diseases that affect the bone marrow[1]. In view of the expressive growth of this procedure in Brazil in patients of various ages, it needs to recognize the sociodemographic and clinical profile of these patients in preparation of an integral care plan.

OBJECTIVE: describing the sociodemographic and clinical profile of cancer patients submitted to HSCT from a private hospital in a Capital State of Southern Brazil.

METHODS: a quantitative, observational, analytical cross-sectional study with 21 patients submitted to HSCT in a private hospital in Southern Brazil, from August 2021 to January 2022. Inclusion criteria were age ≥ 18, diagnosis of cancer, HSCT and hospitalization ≥3 days. Patients unable to respond to the instrument were excluded due to changes in mental or cognitive status. Data were collected with the aid of a sociodemographic and clinical instrument and analyzed by simple and relative frequency. The study was approved by the Research Ethics Committee under Opinion N 4,854,043.

RESULT: the average age was 50, with a higher concentration between 51 and 70 (N=12; 58%). There was a predominance of males (N=13; 43%), married or in stable union (N=16; 13%), in an average family composition of two children. Regarding the place of residence, 11 (52%) lived in the capital, seven (33%) in another State, two (10%) in the countryside of the State and one (5%) in the Metropolitan Region. Regarding education, 14 (67%) had higher education, five (24%) had high school and two (10%) had elementary school. Regarding occupation, 13 (62%) declared themselves economically active and eight (38%) were retired, the predominant monthly family income range was US$ 766,56 to US$ 1916,4 (N=11; 53%). Regarding clinical variables, the type of cancer prevalent was hematological (N=20; 95%), with a predominance of multiple myeloma (eight; 38%), followed by leukemias and lymphomas, (five; 24%, for both), myelodysplasias (two; 2%) and testicle tumor (one; 1%), with a prevalent diagnosis time of one to three years (nine; 43%). As for comorbidities and previous hospitalizations for cancer treatment, (N=14; 67%) had no associated diseases and 10 (48%) reported more than four hospitalizations.

CONCLUSION: recognizing the profile of hospitalized patients submitted to HSCT is important for the multidisciplinary team, especially for nurses, a fact that can provide subsidies for the planning of nursing care according to their needs and characteristics.

Keywords: Hematopoietic Stem Cell Transplantation. Nursing. Hospitalization. Patients. Oncology.

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THE INTEGRATION BETWEEN THE SUPPORT HOUSE AND THE TRANSPLANT CENTER'S ASSISTANCE TEAM IN THE PROMOTION OF CARE AFTER HEMATOPOETIC STEM CELL TRANSPLANTATION

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INTRODUCTION: Hematopoietic Stem Cell Transplantation (HSCT) is a therapy used in several onco-hematological, hereditary, and immunological diseases. It is a complex procedure that requires intensive and multidisciplinary care before, during and after the procedure. Regarding the post-HSCT period it is known that especially in the first months systematic follow-up are required directly at the Transplant Center through examinations, procedures, and frequent clinical appointments. Intercurrences must be evaluated and treated immediately by a specialized team, avoiding more serious outcomes. In this context a hosting space adapted to the health needs of patients undergoing transplantation, located close to the Transplant Center and integrated with the care processes carried out at the Hospital, play a key role in safeguarding basic social rights and access to health.

OBJECTIVE: The aim is to reflect on the care processes articulated between the Hospital care team and the team responsible for care at the Support House in the immediate post HSCT period.

METHOD: This is an experience report based on the work carried out by the Social Services team of a Transplant Center and the Support House managed and maintained by this Center during the period of accommodation for children and adolescents (0 to 18 years) and their companions.

RESULTS: The Support House is perceived by patients and teams as a place of support and temporary shelter for families in situations of psychosocial vulnerability. The structure of the Support House integrated into the Hospital enables the development of action and support strategies attending to the patient's care needs, allowing the recording of interventions and impressions in a single medical record accessed by the entire team. Multiprofessional meetings and individual interviews with caregivers and/or meetings with the family group held together (assistant team and Support House) favor approaches aimed at the strengths and weaknesses identified in each patient care context, addressing aspects such as family relationships, hygiene and food care, access and use of medicines, mental health issues and interruption/prevention of situations of violence and neglect. Recreational, socio-educational actions and group approaches strengthen social and community bonds.

CONCLUSIONS: The Support House integrated into the structure of the Transplant Center enables social rights by providing, at no cost, a welcoming environment similar to the home environment but adapted to the health needs of users undergoing transplantation following all hospital hygiene and safety protocols. In addition, it favors health education processes by offering a space where families perform care autonomously, receiving support from the care team.

Keywords: Hematopoietic Stem Cell Transplantation. Sheltering. Right to Health.

THE USE OF COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) IN HEMATOPOIETIC STEM CELL TRANSPLANT (HSTC) CANDIDATES: A DESCRIPTIVE STUDY IN ALLOGENEIC AND AUTOLOGOUS HSTC

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INTRODUCTION: Hematopoietic Stem Cell Transplantation (HSCT) is the therapeutic modality used in the treatment of many hematological diseases, benign or malignant, hereditary or acquired throughout life. Hematologic diseases affecting the myeloid lineage are predominant in the population over 60 years of age. The greater mastery and improvement of the HSCT technique, the creation of new drugs and less aggressive immunosuppressive regimens, along with advances in the treatment of post-transplant complications, and the increase in life expectancy have allowed the indications for allogeneic HSCT to be extended to people over 60 years of age. A detailed analysis of the patient's health condition can be translated into instruments such as the Comprehensive Geriatric Assessment (CGA), which is a determining factor for the patient to be considered suitable for bone marrow transplant, reducing the risk of post-TCTH complications. Considered a multidimensional diagnostic tool, it promotes an overview of the elderly's health by means of programmed screening of the most common syndromes and alterations in this age group.

OBJECTIVE: To identify results of applying CGA in patients over 60 years of age who will undergo allogeneic or autologous HSCT.

METHODS: This is a descriptive study on the applicability of CGA in candidates for autologous and allogeneic HSCT who were seen in a cancer hospital in the interior of the state of São Paulo from November 2021 to May 2022. The CGA identified six domains of individual health, namely: evaluation of functionality, balance and mobility, cognitive function, emotional state, family support, and nutritional state. All participants underwent the free and informed consent form after approval by the Research Ethics Committee, approval number 5.084.927. The data obtained were computed in spreadsheets and analyzed by R software, v4.1.0.

RESULTS: The population data are described in Table 1, with 57.5% representing the rate of autologous HSCT and 42.5% allogeneic HSCT, and the diagnosis of Multiple Myeloma prevails among the pathologies (42.5%). The analysis of the results (table 2) demonstrated the data obtained by applying the CGA and suggest the importance of developing strategies to incorporate the CGA in the care of elderly people with cancer, in order to ensure a comprehensive approach to all influential factors in the therapeutic proposal and care for this vulnerable population.

CONCLUSION: It was concluded that the application of CGA requires a trained professional, appropriate place, and time availability. The data revealed that depression can be an impact factor for the indication of the procedure, but further studies are necessary. Specific instruments, such as the AGA, may be decisive in indicating the procedure, because their particularities help in the identification of multidimensional factors and implications in the risks for the procedure.

Keywords: Hematopoietic stem cell transplantation. Geriatrics. Broad geriatric assessment.

TABLE 1. **Population Characteristics**

Total	***N (%)***
Gender	
Female	16 (40)
Male	24 (60)
Age	
mean(SD)	65.1 (3.6)
BMT	
No	14 (35)
Yes	26 (65)
Education	
Elementary school incomplete	19 (47.5)
Elementary school complete	7 (17.5)
High School incomplete	1 (2.5)
High School Complete	7 (17.5)
Higher Education Complete	6 (15)
Marital.status	
Married	26 (65)
Divorced	1 (2.5)
Single	6 (15)
Widower	7 (17.5)
Disability	
No	33 (82.5)
Yes	7 (17.5)
B	
Amyloidose	1 (2.5)
Hodgkin's lymphoma	1 (2.5)
Acute Lymphoid Leukemia	2 (5)
Acute Myeloid Leukemia	7 (17.5)
Non-Hodgkin Lymphoma	4 (10)
Multiple Myeloma	17 (42.5)
Acute myelofibrosis	1 (2.5)
Myelodysplastic Syndrome	7 (17.5)
BMT.Modality	
Allogeneic	17 (42.5)
Autologous	23 (57.5)

TABLE 2. **Descriptive analysis of CGA by type of HSCT**

	Allogeneic	***Autologous***	***P value***
Total	**17**	**23**	
Katz.Scale.Rating			0.970
independent for all activities	8 (47.1)	11 (47.8)	
depends for one activity	3 (17.6)	5 (21.7)	
dependent for two activities	2 (11.8)	3 (13)	
dependent for three activities	2 (11.8)	2 (8.7)	
dependent for four activities	2 (11.8)	1 (4.3)	
dependent for five activities	0 (0)	1 (4.3)	
L.B.Scale.Rating			0.489
independent	8 (47.1)	6 (26.1)	
light dependency	5 (29.4)	6 (26.1)	
moderate dependency	3 (17.6)	8 (34.8)	
severe dependency	1 (5.9)	3 (13)	
Tinetti.Scale.Rating			0.916
low fall risk	5 (29.4)	7 (30.4)	
moderate fall risk	8 (47.1)	12 (52.2)	
high fall risk	4 (23.5)	4 (17.4)	
MINI.MENTAL.Rating			0.867
effectively normal	7 (41.2)	11 (47.8)	
mild cognitive impairment	6 (35.3)	8 (34.8)	
moderate cognitive loss	3 (17.6)	4 (17.4)	
severe cognitive loss	1 (5.9)	0 (0)	
Depression.Scale.Rating			0.341
unlikely depression	11 (64.7)	17 (73.9)	
possible depression	4 (23.5)	6 (26.1)	
depression probable present	2 (11.8)	0 (0)	
Apgar.Family.Rating			1.000
good family functionality	10 (58.8)	13 (56.5)	
moderate family dysfunction	5 (29.4)	8 (34.8)	
high family dysfunction	2 (11.8)	2 (8.7)	
Mini.Nutritional.Assessment.Rating			0.312
adequate nutritional status	3 (17.6)	9 (39.1)	
risk of malnutrition	12 (70.6)	11 (47.8)	
malnutrition	2 (11.8)	3 (13)	

TABLE 3. **Descriptive Analysis Comprehensive Geriatric Assessment - Patient Gender**

	F	*M*	*P value*
Total	**16**	**24**	
Katz.Scale.Rating			0.579
independent for all activities	6 (37.5)	13 (54.2)	
depends for one activity	5 (31.2)	3 (12.5)	
dependent for two activities	2 (12.5)	3 (12.5)	
dependent for three activities	1 (6.2)	3 (12.5)	
dependent for four activities	1 (6.2)	2 (8.3)	
dependent for five activities	1 (6.2)	0 (0)	
L.B.Scale.Rating			0.663
independent	7 (43.8)	7 (29.2)	
light dependency	5 (31.2)	6 (25)	
moderate dependency	3 (18.8)	8 (33.3)	
severe dependency	1 (6.2)	3 (12.5)	
Tinetti.Scale.Rating			0.157
low fall risk	2 (12.5)	10 (41.7)	
moderate fall risk	10 (62.5)	10 (41.7)	
high fall risk	4 (25)	4 (16.7)	
MINI.MENTAL.Rating			0.818
effectively normal	7 (43.8)	11 (45.8)	
mild cognitive impairment	5 (31.2)	9 (37.5)	
moderate cognitive loss	4 (25)	3 (12.5)	
severe cognitive loss	0 (0)	1 (4.2)	
Depression.Scale.Rating			0.007
unlikely depression	8 (50)	20 (83.3)	
possible depression	8 (50)	2 (8.3)	
depression probable present	0 (0)	2 (8.3)	
Apgar.Family.Rating			0.135
good family functionality	7 (43.8)	16 (66.7)	
moderate family dysfunction	8 (50)	5 (20.8)	
high family dysfunction	1 (6.2)	3 (12.5)	
Mini.Nutritional.Assessment.Rating			0.376
adequate nutritional status	3 (18.8)	9 (37.5)	
risk of malnutrition	10 (62.5)	13 (54.2)	
malnutrition	3 (18.8)	2 (8.3)	

UFPR ON BONE MARROW DONATION AWARENESS: REALITY DURING COVID-19 PANDEMIC

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INTRODUCTION: The hematopoietic stem cell transplantation (HSCT) is a therapeutic option for many hematologic and autoimmune diseases. The efforts to increase the number of transplants are directed mainly for encouraging voluntary donations, since only 30% of patients are compatible with a related donor. Therefore, most of them depend on unrelated donors enrolled on bone marrow donors registries. However, politics of donation awareness were negatively affected by the Covid-19 pandemic. According to the World Marrow Donor Association (WMDA) report, there was a 3.5% drop in voluntary donations between 2019 and 2020, possibly as a consequence of the pandemic. The data draws attention, since there had been an average annual growth rate of 3.9% from 2015 to 2019. In face of this scenario, the need to readapt awareness strategies arose, considering the need for social isolation. In this terms, the extension project "Federal University of Paraná on Bone Marrow Donors Awareness", wich objective is aware the comunity about the importance of being a voluntary bone marrow donor, adapted its intervention strategy along the pandemic. The project's participants – undergraduates of health care on Federal University of Paraná – started to make interventions using instagram, through the profile "@doe.medula.ossea", sharing informations about HSCT and hematopoietic stem cells donation.

OBJECTIVE: Analise the impact of social media as intruments of voluntary hematopoetic stem cells donation awareness in the extesion project "Federal University of Paraná on Bone Marrow Donors Awareness", in the context of the Covid-19 pandemic.

METHODS: A bibliographic review was carried out on the subject, based on articles selected through Pubmed and SciELO databases.

RESULTS: Since the creation of the profile "@doe.medula.ossea", the project combined more than 2400 followers and 66 publications about HSCT (updated on July 2022). Thus, social media made it possible to bring information to a greater number of people compared to what happened in the project's interventions prior to the pandemic. In the same way, other HSCT profiles had a relevant reach during this period, such as "@CaçadoresdeMedula" and "@Valorizarvida", wich have 18.4 and 5.3 thousand followers, respectively. Moreover, it was possible to diversify the topics covered in the actions.

CONCLUSIONS: Social media can be an important tool to increase the scope of interventions and the awareness among new donors outside the project execution site.

Funders: FUNPAR-LIGH Agreement.

Keywords: Bone marrow transplant. Bone marrow donation. Social media. Covid-19.

USE OF BETHANECHOL AS AN ALTERNATIVE THERAPY IN THE MANAGEMENT OF XEROSTOMIA SECONDARY TO GRAFT VERSUS HOST DISEASE IN A POST-ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENT

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INTRODUCTION: Xerostomia is a condition characterized by the subjective sensation of dry mouth and is commonly associated with decreased salivary production (hyposalivation). Graft-versus-host disease (GVHD) is one of the causes of this issue, causing discomfort in speech and swallowing, altered taste, burning mouth, increased incidence of tooth decay and opportunistic fungal diseases. The management of xerostomia is a challenge for the dentist as available treatments are limited. Bethanechol is a cholinergic agonist drug that stimulates salivary gland function by acting on muscarinic receptors. Studies have shown its applicability in improving xerostomia and hyposalivation with minimal side effects, proving to be a viable therapeutic alternative in the management of patients affected by these conditions.

OBJECTIVE: to report a clinical case of xerostomia and hyposalivation secondary to GVHD in an allogeneic hematopoietic stem cell transplantation (HSCT) patient, treated with bethanechol, after unsuccessful use of other treatments.

METHOD: this is a case description from a patient attended in the Bone Marrow Transplantation Unit. The patient gave written consent for publication.

RESULT: A 58-year-old male patient, 1 year and 5 months after allogeneic HSCT, complained of xerostomia, oral functional difficulties, burning mouth and recurrent candidiasis. Clinically, it was observed the presence of whitish lesions, with a lichenoid aspect, suggestive of oral GVHD in the entire mucosa, hyposalivation, oral dryness and bilateral negative milking of the parotid glands, bilaterally. The use of bethanechol 25 mg orally every 12 hours was prescribed for the first 3 months, with a gradual dose reduction in the subsequent 3 months. He had previously used topical and oral pilocarpine 20mg/day, artificial saliva, sugar-free chewing gum and infrared laser therapy, without proper improvement. In addition, he was using systemic corticosteroids to control cutaneous GVHD. After 2 months of bethanechol use, the patient demonstrated an improvement in oral moisture and subjective dryness, with a positive impact on oral functionality, without new episodes of opportunistic fungal infection.

CONCLUSION: The use of bethanechol in this case proved to be a therapeutic alternative for a patient where all other resources for the management of xerostomia had failed. Saliva, in adequate volume, plays a fundamental role for a good quality of life, since, associated with good oral health, it protects the individual from mucosal infections, tooth decay and other dental issues. Thus, dental follow-up after allogeneic HSCT is essential, both for diagnosis and treatment of xerostomia and hyposalivation, as well as managing oral GVHD.

Keywords: Xerostomia. Hyposalivation. Saliva. Graft versus host disease. HSCT. Odontology

INTERCURRENCY PRESENTED BY USERS OF HEMATOPOIETIC STEM CELL TRANSPLANTATION AFTER HOSPITAL DISCHARGE

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INTRODUCTION: This work is one of the results of a doctoral thesis that sought to study and qualify nursing ecosystem care for bone marrow transplant users.

OBJECTIVE: To identify the complications presented by users of hematopoietic stem cell transplantation after hospital discharge.

CASUISTRY: The participants were forty users, selected at the outpatient clinic of the Bone Marrow Transplantation service of three university hospitals that perform this type of transplant: 1st- Rio Grande do Sul, Brazil; 2nd- Paraná, Brazil; 3rd- Murcia, Spain. The latter was the researcher's sandwich doctorate site. The selection criteria were: being at least 18 years old; being a bone marrow transplant user; attend the transplant clinic for medical and nursing consultations; be at home for a minimum of thirty days and a maximum of two years. As exclusion criteria, it was considered: having performed more than one bone marrow transplant.

METHOD: The research was descriptive and exploratory, with a qualitative and quantitative approach. Qualitative data analysis was performed using Bardin's Content Analysis method. For quantitative data, the Statistical Package for the Social Sciences program was used, based on the interview instrument. Descriptive statistical analysis was used and the frequency of clinical data was performed. Data were recorded by semi-structured interview, with open and closed questions, by the researcher and a duly qualified auxiliary member, being transcribed by the researcher. The research was approved by the Ethics Committee of the Health Area.

RESULTS: The questions were: "Did you have any complications in your current home? Which?". The most reported complications were those that compromised the gastrointestinal tract with 45% (n=18) of the interviewed users who were distributed among mucositis, nausea and vomiting and diarrhea. Symptoms of infection 23% (n=9). Symptoms of respiratory complications 15% (n=6). Symptoms of skin complications 5% (n=2). Pain symptoms 12.50% (n=5). Intercurrences with the use of Ciclosporin 15% (n=6). Occurrence of Graft Versus Host Disease, 7.50% (n=3). Occurrence of Bleeding 5% (n=2). 32.50% (n=13) had no complications.

CONCLUSIONS: Of the users who reported not having had post-transplant complications, 41.5% (n=5) had undergone Autologous Hematopoietic Stem Cell Transplantation, which has a faster recovery from myelosuppression, is not at risk of developing heart disease. Graft Against Host, which occurs only in Allogeneic transplants, thus providing a better recovery condition for this user. This study reinforces the need for early detection of signs and symptoms of some complications, as a way of contributing to the reduction of the occurrence of complications or, at least, minimizing their occurrence. The importance of follow-up in post-transplant outpatient consultations is highlighted.

Funding: Doctoral Sandwich Scholarship for the researcher, by the program of the Coordination for the Improvement of Higher Education Personnel (CAPES), in a reference Hematopoietic Stem Cell Transplantation service in Spain.

Keywords: Nursing Care. Health management. Bone marrow transplant.

USE OF LOW-INTENSITY LASER THERAPY IN ORAL MUCOSITIS IN HEMATOPOIETIC STEM CELL TRANSPLANTATION: LITERATURE REVIEW

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INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) aims, in general, to replace the diseased hematopoiesis with a new one, without the presence of the clone that originated the underlying disease. Oral mucositis (OM) affects about 60 to 80% of patients undergoing HSCT, and is considered one of the most uncomfortable and painful experiences during treatment. The World Health Organization classifies OM into four different grades, with its incidence and severity being associated with treatment-related factors such as myeloablative conditioning regimens, particularly those containing Total Body Irradiation, high doses of melphalan and busulfan, and use of methotrexate for graft-versus-host disease (GVHD) prophylaxis. OM requires specialized care, emphasizing low-level laser therapy (LLLT).

OBJECTIVE: to carry out a literature review regarding the importance of LTBI to patients with OM in HSCT.

METHODS: To search for articles, the descriptors "Hematopoietic stem cell transplantation", "Mucositis" and "Low-level laser therapy" were used, covering the period from 2012 to 2022, descriptors defined through a query to the Descriptors in Health Sciences (DeCS). Associating these descriptors, 21 articles were obtained as a result. Through the selection of titles, review articles were excluded, leaving 18 articles, which were read the abstracts and selected nine articles for reading in full and included in the literature review.

RESULTS: According to the selected articles, all studies highlight positive results and Effective improvement in the quality of life of patients with the use of LTBI; in 44.4% (four articles) pre-HSCT conditioning is a complicating factor that causes OM. Three articles (33.3%) demonstrate that LTBI delays and even prevents OM, as well as the others (67%) refer to LTBI as a safe form of treatment, acting as a comfort measure for the patient, bringing an analgesic and positively influencing nutritional status.

CONCLUSION: The LTBI proved to be an important ally in the prevention and treatment of the patient's OM in HSCT, it has been increasingly used in an attempt to reduce the incidence of OM, as well as the pain and discomfort brought by it, aiming at better quality of the patient's life.

Keywords: Hematopoietic stem cell transplantation. Mucositis. Low-level laser therapy.

VALIDATION OF THE PROCESSING OF HEMATOPOIETIC PROGENITOR CELLS (HPCS) IN A CLOSED SYSTEM: HOW TO ENSURE STERILITY WITHOUT A CLEAN ROOM?

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INTRODUCTION: The resolution RDC 508/2021 recommends processing and cryopreservation of HPCs products via closed system when it does not occur in a controlled atmosphere (clean room). Therefore, a closed system processing was developed and validated to replace the method currently used in the routine (open system).

OBJECTIVE: To validate HPCs processing with devices that allow manipulation in an uncontrolled environment.

MATERIAL: 20 HPCs collections were analyzed concurrently with the routine procedure.

METHODS: The connectors kept the processing and aliquoting of the product in a closed system (clave connector, spinning spiros, 3-way stopcock - ICU medical, USA). The process was done in laminar flow and involved the connection between the fluids used in the processing. At the beginning of the procedure, the connector (clave) was attached to the bag with HPCs and the other connector to the bag with cryoprotectant solution. Then, the 3-way stopcock was linked to the connector (clave) of the bag with HPCs. The device (Spinning Spiros) was attached to the syringe, enabling the aliquoting of the cryoprotectant solution for addition to the bag with HPCs through the 3-way stopcock and, later, the passage of the aliquoted product to the freezing bag, avoiding opening the system.

RESULTS: The system proved to be easy and practical in execution, offering no resistance during the passage of fluids. Safety has been proven, as all connections have not leaked, dripped or dropped during the process. Cell recovery, based on the initial (pre-processing) and final (post-processing and pre-cryopreservation) leukocytes/mm3 value, remained above 90%. There was a reduction in the average processing time, which contributed to the agility of the process, ensuring less interaction between DMSO with the product at room temperature. The comparison of the processing time of the products being validated and the technique used in the routine was statistically relevant ($p<0.001$), optimizing the cryopreservation routine (savings of 50 minutes). No sample had positive culture. The main advantages were: processing and cryopreservation in a closed system, greater precision of the volume to be aliquoted, less time and cost reduction.

CONCLUSION: Processing and cryopreservation, with the use of external connectors, proved to be accurate, safe, without difficulties or delay in the routine and, additionally, with a reduction in inputs (syringes, alcohol swab, needles). The National Health Surveillance Agency concluded that the external connectors are suitable for the transfer of fluids in a closed system. Thus, the system is in accordance with the recommended by RDC 508 with minimal handling, being a quick and reliable solution to ensure sterility in the absence of the clean room.

Keywords: Hematopoietic stem cells. Processing. Validation study.

QUALITY AND DATA MANAGEMENT

APPLICATION OF THE CADASTRAL UPDATE FORM IN THE PRE-TRANSPLANT PERIOD OF HEMATOPOIETIC STEM CELL TRANSPLANTATION: IMPACT ON POST-TCTH FOLLOW-UP

Aline Maglim Gonçalves de Oliveira Godoy[1], Anderson João Simione[1], Bruna Fernanda Sona Mathias[1], Jaine Cristina de Oliveira Silva[1], Ana Claudia Ferrari dos Santos[1], Iago Colturato[1], Fernanda Rodrigues Barbieri[1], Juliana Silva Santos[1], Erika Rodrigues Pontes Delattre[1], Anna Beatriz Coelho de Souza[1], Carolina Ferreira Mascarenhas[1], Leticia Galbier Ricetto Pegorari[1], Mair Pedro de Souza[1], Vergilio Antonio Rensi Colturato[1]

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INTRODUCTION: Hematopoietic Stem Cell Transplantation (HSCT) is one of the therapies available to treat, consolidate, or cure hematologic diseases. The post-HCT follow-up is essential for a better understanding of the monitoring of data that corroborate with research. Creating strategies for this follow-up is essential, but guided by the General Law of Data Protection (GLDP).

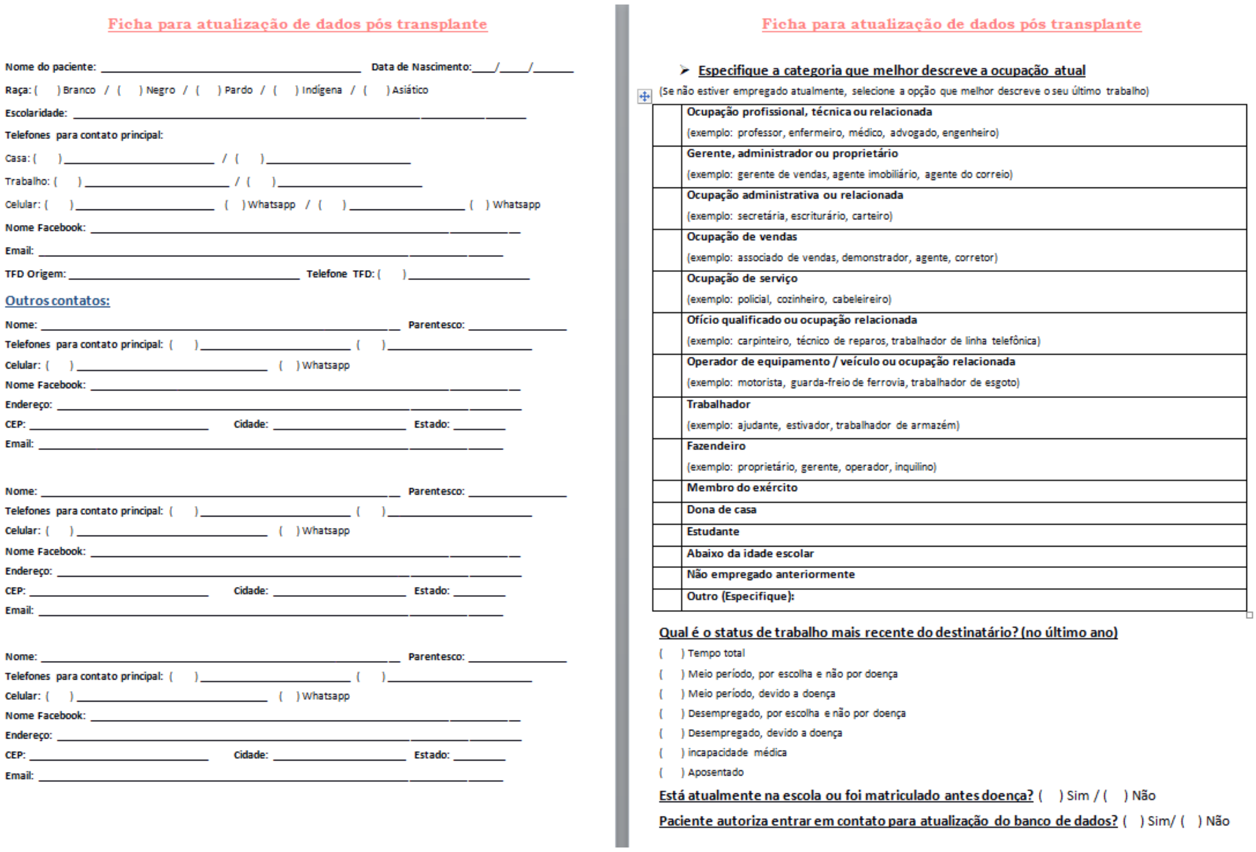
OBJECTIVES: To elucidate the application routine of one of the tools developed for systematized collection and analysis of pre-HSCT information in line with the GLDP.

METHODOLOGY: The transplant center reports HSCT production data regularly to the Center for International Bone Marrow Transplant Research (CIBMTR). The post- HSCT registry update and follow-up form (Figure 1) was created and developed as part of the post- HSCT follow-up flow in order to assist the submission process in a continuous and uninterrupted manner, ensuring the longevity of the information provided. Registration data is collected once a week by applying a printed form through an interview with the data management nurse as part of the routine developed for patients in the pre- HSCT period. When contacting each individual, the professional clarifies the purpose of the research and the way in which the information will be used, answering the questions of the recipients and emphasizing that the data will be treated securely and with tools that allow the anonymization of sensitive data. After signing the Free and Informed Consent Form, the data is stored for future contacts. The form will be scanned and filed in the patient's electronic medical record.

RESULTS: The application of the document began in January 2018 and since then 591 forms have been completed. Since the beginning of the interviews, the reach of patients served has gradually evolved over the years, and by May 2022, 94% of pre-transplant individuals have answered the questionnaire (Graph 1). This activity has contributed to adequate follow-up, noting that in the period from January 2018 to May 2022, the loss to follow-up post HSCT was 2 patients for the 938 transplants (0.21%).

CONCLUSION: The application of the cadastral update form corroborated the reliability and continuity of the data sent to the CIBMTR, keeping the established deadlines and ensuring a low rate of lost follow-ups.

FIGURE 1.



Ficha para atualização de dados pós transplante

Nome do paciente: ___ Data de Nascimento: ___/___/___

Raça: ( ) Branco / ( ) Negro / ( ) Pardo / ( ) Indígena / ( ) Asiático

Escolaridade: ___

Telefones para contato principal:

Casa: ( ) ___ / ( ) ___

Trabalho: ( ) ___ / ( ) ___

Celular: ( ) ___ ( ) Whatsapp / ( ) ___ ( ) Whatsapp

Nome Facebook: ___

Email: ___

TFD Origem: ___ Telefone TFD: ( ) ___

Outros contatos:

Nome: ___ Parentesco: ___

Telefones para contato principal: ( ) ___ ( ) ___

Celular: ( ) ___ ( ) Whatsapp

Nome Facebook: ___

Endereço: ___

CEP: ___ Cidade: ___ Estado: ___

Email: ___

Nome: ___ Parentesco: ___

Telefones para contato principal: ( ) ___ ( ) ___

Celular: ( ) ___ ( ) Whatsapp

Nome Facebook: ___

Endereço: ___

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Nome: ___ Parentesco: ___

Telefones para contato principal: ( ) ___ ( ) ___

Celular: ( ) ___ ( ) Whatsapp

Nome Facebook: ___

Endereço: ___

CEP: ___ Cidade: ___ Estado: ___

Email: ___

Ficha para atualização de dados pós transplante

➢ **Especifique a categoria que melhor descreve a ocupação atual**

(Se não estiver empregado atualmente, selecione a opção que melhor descreve o seu último trabalho)

	Ocupação profissional, técnica ou relacionada (exemplo: professor, enfermeiro, médico, advogado, engenheiro)
	Gerente, administrador ou proprietário (exemplo: gerente de vendas, agente imobiliário, agente do correio)
	Ocupação administrativa ou relacionada (exemplo: secretária, escriturário, carteiro)
	Ocupação de vendas (exemplo: associado de vendas, demonstrador, agente, corretor)
	Ocupação de serviço (exemplo: policial, cozinheiro, cabeleireiro)
	Ofício qualificado ou ocupação relacionada (exemplo: carpinteiro, técnico de reparos, trabalhador de linha telefônica)
	Operador de equipamento / veículo ou ocupação relacionada (exemplo: motorista, guarda-freio de ferrovia, trabalhador de esgoto)
	Trabalhador (exemplo: ajudante, estivador, trabalhador de armazém)
	Fazendeiro (exemplo: proprietário, gerente, operador, inquilino)
	Membro do exército
	Dona de casa
	Estudante
	Abaixo da idade escolar
	Não empregado anteriormente
	Outro (Especifique):

Qual é o status de trabalho mais recente do destinatário? (no último ano)

( ) Tempo total

( ) Meio período, por escolha e não por doença

( ) Meio período, devido a doença

( ) Desempregado, por escolha e não por doença

( ) Desempregado, devido a doença

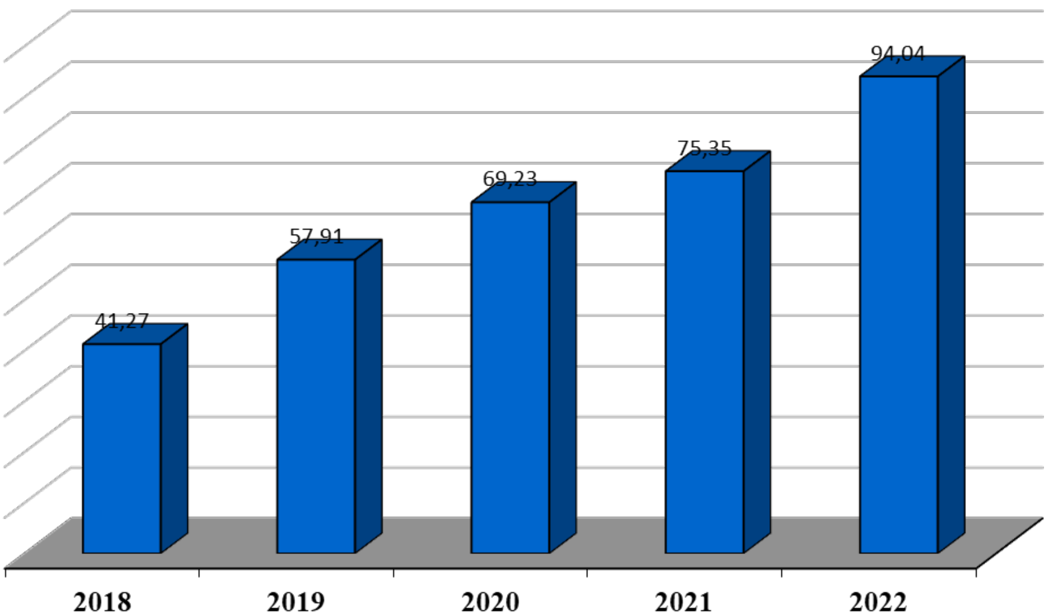
( ) incapacidade médica

( ) Aposentado

Está atualmente na escola ou foi matriculado antes doença? ( ) Sim / ( ) Não

Paciente autoriza entrar em contato para atualização do banco de dados? ( ) Sim/ ( ) Não

GRAPH 1. **Percentage of application of the registration form per year**



DEVELOPMENT AND IMPLEMENTATION OF AN ELECTRONIC TEMPLATE FOR GRAFT VERSUS HOST DISEASE

Heliz Regina Alves das Neves[1], Cristiano de Oliveira Ribeiro[2], Johny Bard de Carvalho[2], Vaneuza Araújo Moreira Funke[1], Ricardo Pasquini [1].

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2 Hospital Nossa Senhora das Graças, Curitiba-PR, Brazil

INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is a complex therapeutic modality with a high risk of complications, especially acute and/or chronic Graft Versus Host Disease (GVHD). The adequate description of this complication in the medical evolution and of the other professionals involved in patient care is essential to ensure its quality, as well as for the collection and recording of data. However, due to the complexity of the diagnosis and classification of GVHD, the information recorded during the assessment and care of these patients is often insufficient, compromising data collection and reporting.

OBJECTIVE: to describe the development and implementation of an electronic template for GVHD evolution in a private hospital located in a capital city in southern Brazil.

METHOD: this is a descriptive study, which aimed to report the experience on the development and implementation of an electronic model of evolution in template format for recording chronic GVHD (cGVHD) in the Tasy® Hospital Management System. The template was designed by a hematologist and developed with the support of the Information Technology (IT) sector, from September to December 2021. Initially, an electronic draft was prepared to define the content, adjustments and improvement. The definition of the fields and information that should be contained in the template was based on the questions about cGVHD provided in forms 2450 version R6 and 2100 version R7, from the Center for International Blood and Marrow Transplant Research (CIBMTR) and the classification of National Institute Health Consensus for Chronic GVHD (NIH).

RESULTS: the questions for the record covered information on the date of diagnosis, treatment, characteristics of the organs involved, functional impairment, score of each organ for cGVHD and the global grade. The template was validated by the medical specialist in the subject and by two data managers. After validation, the template was tested in three post-HSCT patients affected by cGVHD and proved to have easy applicability. This type of record proved to be agile and easy to perform and the information obtained through its use provided better details about the characteristics of the cGVHD for collecting and later reporting data on national and international platforms.

CONCLUSION: the development of the electronic instrument facilitated the proper recording of essential information for the diagnosis and follow-up of post-HSCT patients affected by cGVHD, providing subsidies for quality care, facilitating data collection and reporting. This type of instrument is in the process of continuous improvement and can be replicated and readapted in other transplant centers.

Keywords: Hematopoietic Stem Cell Transplantation. Data management. Oncology. Graft versus host disease.

DEVELOPMENT OF DISTANCE CONTINUING EDUCATION FOR DATA MANAGERS, USING THE DESIGN THINKING METHODOLOGY

Cinthya Muniz Corrêa Rocha da Silva[1], Flavia Ferreira da Costa[2], Heliz Regina Alves das Neves[3], Anderson João Simione[4], Paula Moreira da Silva Sabaini[5], Bruna Letícia Da Silva Santos Geraldo[6], Cristina Vogel[1], Tânia Michele Barreto Waisbeck[1], Lidiane Soares Sodre da Costa[1], Danielle Cristina Ovigli Silva Lopes[1], Elvira Deolinda Rodrigues Pereira Velloso[1], Carolina da Silva Costa[1], Larissa Lane Cardoso Teixeira[1], Morgani Rodrigues[1], Polianna Mara Rodrigues de Souza[1], Fabíola Germano de Castro[1], Fernanda de Paula Eduardo[1], Leonardo Javier Arcuri[1], Mariana Nassif Kerbauy[1], Adriana Mendes de Quadros Cavilha[3], Adriana Seber[6,7], Afonso Celso Vigorito[8], Eliana Cristina Martins Miranda[8], Alberto Cardoso Martins Lima[3], Vaneuza Araújo Moreira Funke[3], Ricardo Pasquini[3], Carmem Maria Sales Bonfim[9], Mair Pedro de Souza[4], Leonardo Jun Otuyama[10], Fernando Barroso Duarte[11], Karine Sampaio Nunes Barroso[11], Marcelo Pasquini[12], Monique Ammi[12], Sebastian Galeano[13], Andreia Ribeiro de Almeida[14], Andresa Melo[15], Nelson Hamerschlak[1]

1Hospital Israelita Albert Einstein; 2 Hospital Paulistano; 3 Universidade Federal do Paraná - Complexo Hospital de Clínicas; 4 Amaral Carvalho; 5 Barretos Cancer Hospital; 6 Associação da Medula Óssea; 7 Hospital Samaritano; 8 Universidade Estadual de Campinas; 9 Hospital Pequeno Príncipe; 10 Universidade de São Paulo; 11 Hospital Universitário Walter Cantídio; 12 Center for International Blood and Marrow Transplant Research; 13 Hospital Britânico; 14 Complexo Hospitalar de Niterói; 15 Hospital Brasília.

INTRODUCTION: Actions to consolidate the Brazilian registry of hematopoietic stem cell transplantation (BRHSCT), using the infrastructure of the Center for International Blood and Marrow Transplant Research (CIBMTR) were executed by the Brazilian Society of Cell Therapy and Bone Marrow Transplantation (SBTMO), CIBMTR and Data Managers Working Group (DMWG). From 2016 to 2021 there was a 127% increase (11to25) of active centers and 92% (595to1141) of registered transplants in the CIBMTR, reinforcing the need to train data managers (DM) to ensure accuracy of the data send to the CIBMTR. In 2017, the 1st national, free distance learning (DL) tutorial was developed. To maintain the continuing education of DM, in 12/2021, the 2nd version of the course started with the Design Thinking (DT) methodology (concept of Rolf Fast (Stanford teacher) and David Kelley, in the 70´s).

OBJECTIVE: To describe the development process of a distance learning course for DM, using the DT methodology.

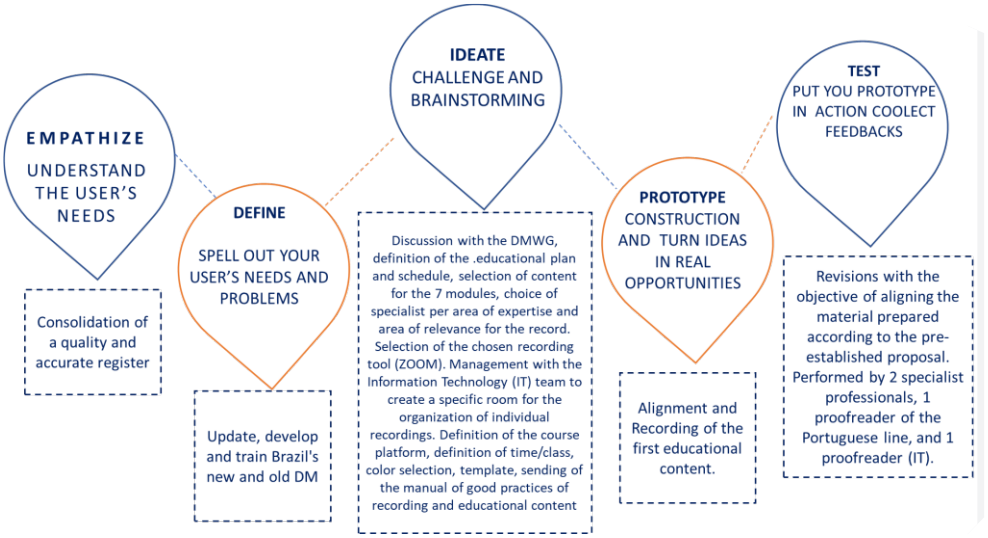
METHODOLOGY: The DT method promotes creative, empathetic, and collaborative solutions to solve problems through 5 steps (Figure 1), which were consolidation and creation of the course from 12/2021 to 04/2022. Steps: 1) Empathy: Consolidate the quality and accuracy of the reported data; 2) Definition: Update, develop and train DM; 3) Ideation: Definition of the educational schedule, the choice of the recording tool (ZOOM), definition of layout classes and selection of the digital platforms for transmission of the course; 4) Recording the first class; 5) Evaluation and revisions of the material according to the pre-established proposal.

RESULTS: There were 38 professionals mobilized to teach in the course voluntarily from 16 institutions (13 national and 3 international), with 41% (16) of them specialists (Graph 1) from several areas. The course was structured in 7 modules, containing 48 video classes, 13 support testimonials and 9 knowledge areas (Figure 2). When comparing the 1st and 2nd courses, there was an increase of 680% (5to39) in the number of instructors. Both were distance-learning, however, the first was a tutorial, containing 2 modules with a 0.75h duration, and the second was 48 classes, with 7 modules with a workload of 60h. There was an increase of 250% (2to7) of modules and 7,900% (0.75h to 60h) of workload. The courses were published on the digital platforms: CIBMTR and Hospital Israelita Albert Einstein, and the 2nd course in the Hematolog. In the 1st course 775 people completed the DL and, in the 2nd, so far, 65.

CONCLUSION: It was concluded that the DT was a facilitator for the elaboration of the educational content, because identified the main problems and adjustments to improve the education. It was observed that there was a national and international mobilization to maintain the continuing education of the DM and improve the accuracy of the data in the BRHSCT. Because it was publication in May 2022, the results of the training will still be published.

Keywords: Data manager. Hematopoietic Stem Cell Transplantation. Database.

FIGURE 1. **Design Thinking - the Process Has 5 Stages**



GRAPH 1. **Education Levels**

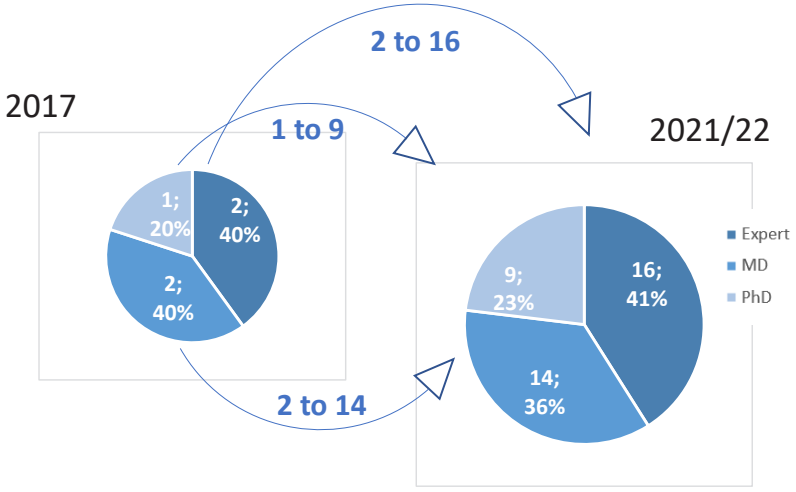
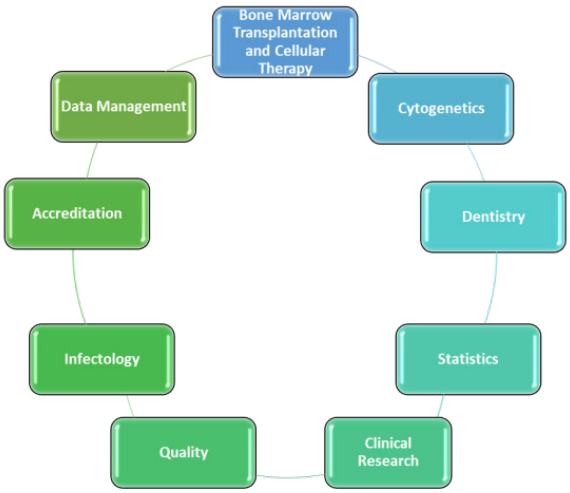


FIGURE 2. **Knowledge Area**



DEVELOPMENT OF REDCAP PROJECT FOR RECORDS OF PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A PUBLIC CENTER

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INTRODUCTION: The hematopoietic stem cell transplantation (HSCT) at University Hospital Walter Cantidio at Fortaleza, Ceará had an increasing number of HSCT procedures and complexities each year. Since the implementation of our transplant program, we have an Excel database to records our datas, but we need an official and safe mode to preserve these datas, optimizing the quality of information used in national and international registries and analysis our service to promote actions of improvement. In this scenario, two projects at REDCAP were created that contemplates the main variables that allow an analysis of the performed HSCTs. REDCAP (RESEARCH ELETRONIC DATA CAPTURE) is an international platform online, offered for the Federal University of Ceará (UFC), for collecting, managing and disseminating research data.

OBJECTIVE: This work aims to demonstrate the importance of developing a REDCAP database based on clinical records for the collection and subsequent analysis of data from patients undergoing hematopoietic stem cell transplantation.

METHODS: Data were collected prospectively from the medical records of all 167 patients who underwent autologous and allogeneic transplantation in 2020 until actual days at the Institution. The database was developed in REDCAP, contemplating innumerable variables involved in the process of transplantation of hematopoietic stem cells: sociodemographic, diagnosis, donor and recipient datas, complications, graft versus host disease, infections and others.

RESULTS: This tool is a platform to analysis our results and preserve confidential informations about the health and social datas from the patients. The database demonstrated the following profile of the transplanted patient: 108 patients made autologous HSCT to Multiple myeloma in 40,6% and Hodgkin lymphoma in 31,1% and 61 allogeneic (33 related donor, 11 non related donor, 17 haploidentical) to acute lymphoblastic leukemia in 31,1% and acute myeloid leukemia in 23%.

CONCLUSION: The collection and analysis of data from HSCT procedures can be used to constantly improve the service and made researches. The database developed in REDCAP proved to be an extremely important and security tool to record the data of patients undergoing HSCT as well as subsequent analysis and monitoring of indicators in the area.

Keywords: REDCAP. Hematopoietic Stem Cell Transplantation. Datas.

EVALUATION OF THE METHODOLOGY USED TO ACTIVELY SEARCH FOR LOST TO FOLLOW-UP PATIENTS

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1 Complexo do Hospital de Clínicas da UFPR, Curitiba-PR, Brazil;
2 Hospital Nossa Senhora das Graças, Curitiba-PR, Brazil.

INTRODUCTION: Data managers at hematopoietic stem cell transplant (HSCT) centers have an important task in updating transplant patient data. Data collection and information management related to HSCT are essential for centers, as they allow the assessment of short and long-term results and their implications for quality of life and survival after transplantation. The results of this modality of treatment also help researchers and healthcare professionals to decide on the best types of preventive care or treatment for current and future patients. In this context, loss to follow-up is a problem experienced by transplant centers and the experience of active search helping in patients' retrieval is of particular importance.

OBJECTIVE: to evaluate the methodology used to update records of lost to follow-up patients in two Hematopoietic Stem Cell Transplantation Centers, one in a public and another one in a private hospital, in southern Brazil.

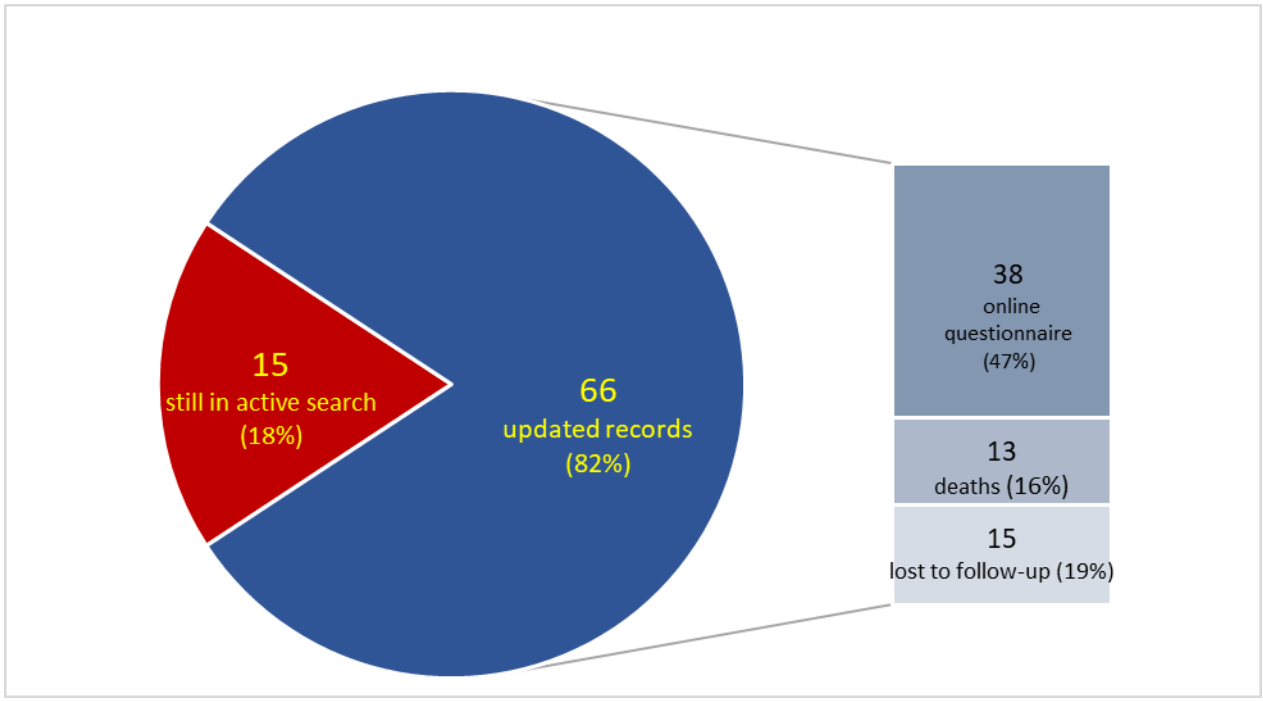
METHOD: an online questionnaire was developed using Microsoft Forms® to monitor lost to follow-up patients. Data for analysis and testing were extracted from the Database developed in Microsoft Access® and kept in an Excel spreadsheet format. For the initial evaluation of the questionnaire, were selected patients transplanted in a public hospital between 1992 and 2019, diagnosed with Severe Aplastic Anemia who underwent conditioning with busulfan and cyclophosphamide, totaling 168 patients. For 81, active search was necessary due to loss of follow-up and absence for appointments for more than two consecutive years.

RESULTS: the active search was carried out from December 2021 to June 2022 with the help of a social worker. Records of 66 (82%) patients were updated, of which 38 (47%) by completing the online questionnaire, 15 (19%) were considered lost to follow-up and 13 (16%) died (Figure 1). With the retrieval of information from this sample, it was possible to update 84 reports (49 lost to follow-up and 35 follow-up).

CONCLUSION: the geographic extension of the country and the economic difficulty to travel to the transplant center make it difficult to follow up patients in the long term. Even when patients are followed up in their origin city, data are not usually sent to the transplant center, since there is no unified system in Brazil. The difficulty of obtaining information on the outcome of patients' treatment, by the centers that perform HSCT, compromises the quality of the recorded information and the results of this treatment modality in the country. The methodology used for the active search proved to be efficient and can be used to update the records of other patients who have lost contact with transplant centers, even allowing the monitoring of their health conditions.

Keywords: Hematopoietic Stem Cell Transplantation. Data Management. Oncology. Lost to follow-up patients.

FIGURE 1: **Active search for patients lost to follow-up (N=81)**



HEMATOPOIETIC STEM CELL TRANSPLANTATION BRAZILIAN REGISTRY - DATA REQUEST FLOW TO THE BRAZILIAN SOCIETY OF CELL THERAPY AND BONE MARROW TRANSPLANTATION

Anderson João Simione[1], Heliz Regina A. Neves[2], Cinthya Corrêa Silva[3], Paula Moreira da Silva[4], Bruna Letícia da Silva Santos Geraldo[5], Mary E.D. Flowers[6], Afonso Celso Vigorito[7], Vergilio Antonio Rensi Colturato[1], Carmem Bonfim[2], Marcelo C. Pasquini[8], Monique S. Ammi[9], Adriana Seber[10], Ricardo Pasquini[2], Nelson Hamerschlak[3], Fernando Barroso Duarte[11]

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INTRODUCTION: Brazil has 125 Hematopoietic Stem Cell Transplantation (HSCT) centers recognized by the Ministry of Health. Until recently, outcomes of HSCT were not organized and publicly available. Since 2016, initiatives were developed to change this scenario by the Brazilian Society of Cell Therapy and Bone Marrow Transplantation (SBTMO), in partnership with the Center for International Bone Marrow Transplant Research (CIBMTR) and the Brazilian Data Managers Working Group (GTGD) partnership, resulting in the HSCT Brazilian Registry (HSCTBR) using the CIBMTR database. Through the increase in the CIBMTR-affiliated centers and the registered transplants number, it was possible to be aware of some of the Brazilian results and answer the research data request.

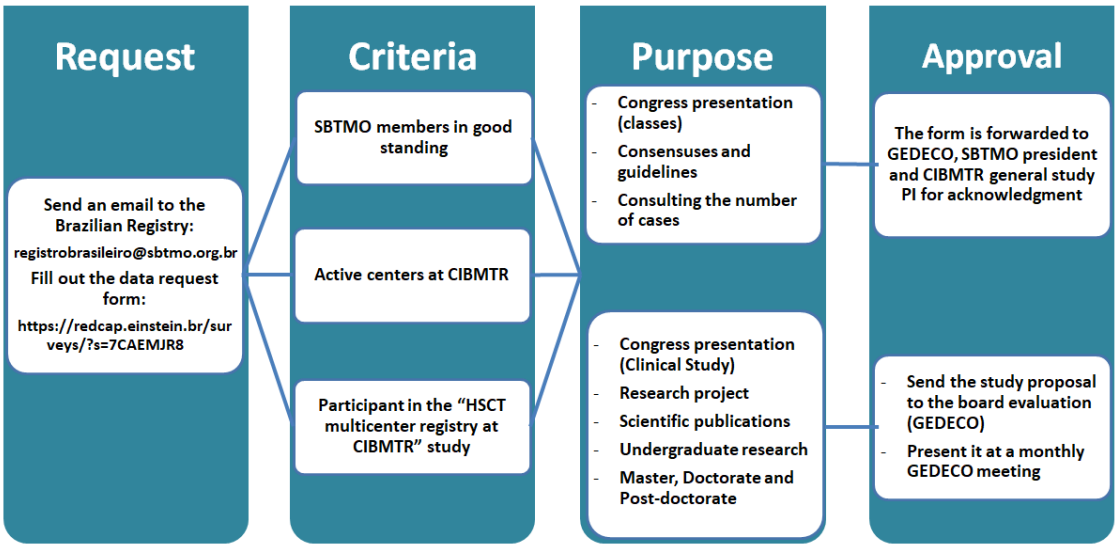
OBJECTIVE: To describe the methodology to access to HSCTBR data.

METHODS: Figure 1 shows the HSCTBR data requesting flow created to submit for approval by the SBTMO. Data from HSCTBR are available to SBTMO members in good standing from active centers or in the process of becoming affiliated with the CIBMTR, and who are participants "HSCT multicenter registry at CIBMTR" study. The application for the HSCTBR uses RedCap form, which includes applicant's identification and contact, eligibility criteria to the data request, the purpose of request data (Figure 2). The completed form is forwarded to GTGD for evaluation of the type of request such as presentation in congresses, use by the HSCT consensuses and guidelines, proposed studies, etc. GTGD consult the number of cases available and then forward the request to the SBTMO study committee "Graft-vs-Host Disease and Late Complications Study Group (GEDECO), to the SBTMO president and to the CIBMTR general study principal investigator for review and approval. If the data request is for purpose of a clinical study, research project, scientific publications, masters and doctorates, study proposal needs to be presented at the GEDECO using the SBTMO study form. Upon GEDECO approval, unidentifiable HSCTBR data is sent to the applicant by email as a Dashboard (Figure 3).

RESULTS: To date, 19 requests have been evaluated and approved, 16 from physicians and 3 from data managers. Requests have originated from 5 states (9 from São Paulo, 4 from Ceará, 3 from Paraná, 2 from Rio Grande do Sul and 1 from Minas Gerais). Most common purpose for the data request was for congresses presentation, 13 (68%).

CONCLUSION: The HSCTBR represents a milestone to better understand the HSCT in Brazil, to improve transplant results, to help development of public health policies and develop clinical trials to improve outcomes. As HSCTBR grows, establishing data requests flow allowed GTGD to organize and respond to requests in partnership with SBTMO scientific committee and important to meet the rigors of scientific community, clinical practice needs and governmental agencies.

FIGURE 1. Data requesting flow



Observational Studies Flowchart - GEDECO:

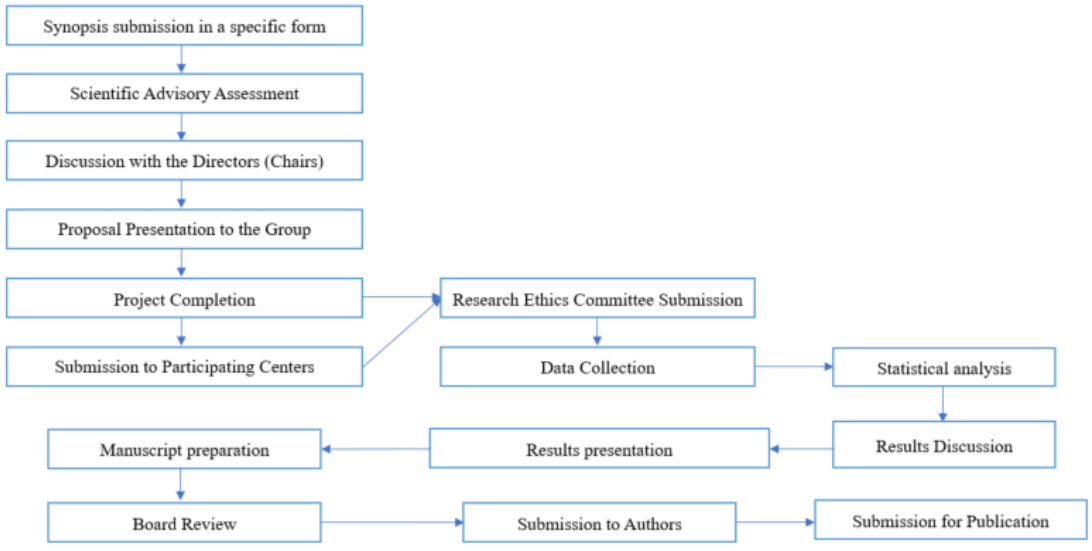
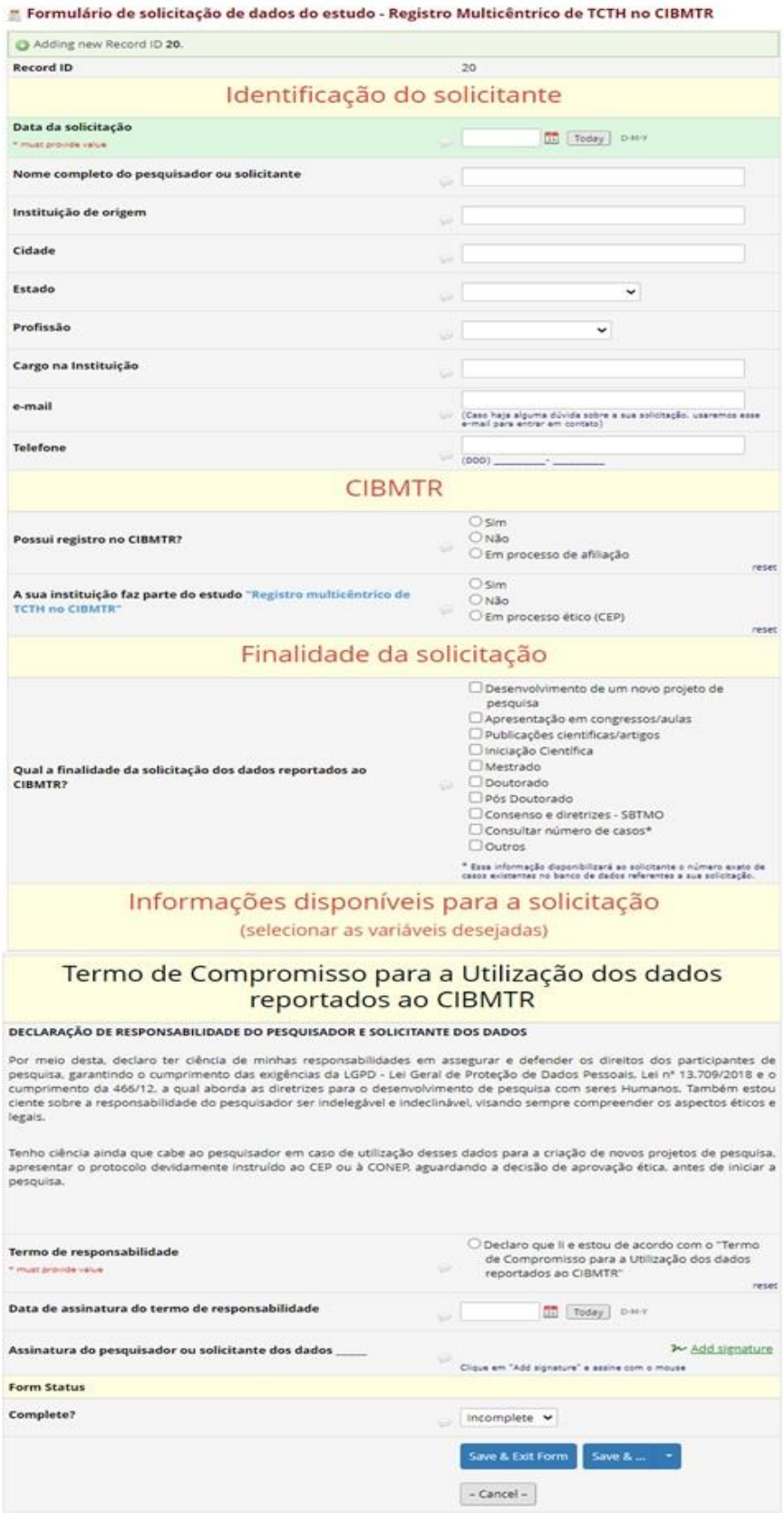


FIGURE 2. **Application for the HSCTBR data**



Formulário de solicitação de dados do estudo - Registro Multicêntrico de TCTH no CIBMTR

Adding new Record ID 20.

Record ID 20

Identificação do solicitante

Data da solicitação * must provide value — Today D-M-Y

Nome completo do pesquisador ou solicitante

Instituição de origem

Cidade

Estado

Profissão

Cargo na Instituição

e-mail (Caso haja alguma dúvida sobre a sua solicitação, usaremos esse e-mail para entrar em contato)

Telefone (DDD) _____-_____

CIBMTR

Possui registro no CIBMTR? Sim / Não / Em processo de afiliação — reset

A sua instituição faz parte do estudo "Registro multicêntrico de TCTH no CIBMTR" Sim / Não / Em processo ético (CEP) — reset

Finalidade da solicitação

Qual a finalidade da solicitação dos dados reportados ao CIBMTR?
- Desenvolvimento de um novo projeto de pesquisa
- Apresentação em congressos/aulas
- Publicações científicas/artigos
- Iniciação Científica
- Mestrado
- Doutorado
- Pós Doutorado
- Consenso e diretrizes - SBTMO
- Consultar número de casos*
- Outros

* Essa informação disponibilizará ao solicitante o número exato de casos existentes no banco de dados referentes a sua solicitação.

Informações disponíveis para a solicitação
(selecionar as variáveis desejadas)

Termo de Compromisso para a Utilização dos dados reportados ao CIBMTR

DECLARAÇÃO DE RESPONSABILIDADE DO PESQUISADOR E SOLICITANTE DOS DADOS

Por meio desta, declaro ter ciência de minhas responsabilidades em assegurar e defender os direitos dos participantes de pesquisa, garantindo o cumprimento das exigências da LGPD - Lei Geral de Proteção de Dados Pessoais, Lei nº 13.709/2018 e o cumprimento da 466/12, a qual aborda as diretrizes para o desenvolvimento de pesquisa com seres Humanos. Também estou ciente sobre a responsabilidade do pesquisador ser indelegável e indeclinável, visando sempre compreender os aspectos éticos e legais.

Tenho ciência ainda que cabe ao pesquisador em caso de utilização desses dados para a criação de novos projetos de pesquisa, apresentar o protocolo devidamente instruído ao CEP ou à CONEP, aguardando a decisão de aprovação ética, antes de iniciar a pesquisa.

Termo de responsabilidade * must provide value — Declaro que li e estou de acordo com o "Termo de Compromisso para a Utilização dos dados reportados ao CIBMTR" — reset

Data de assinatura do termo de responsabilidade — Today D-M-Y

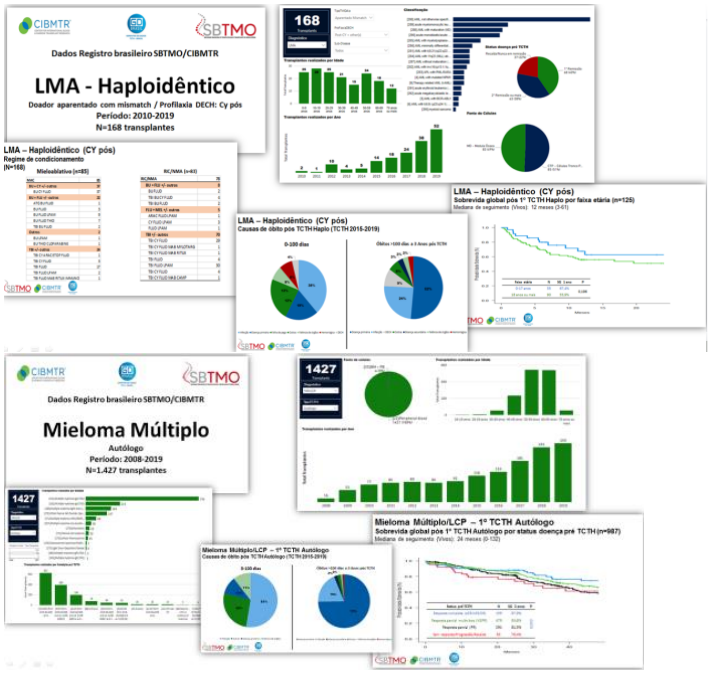
Assinatura do pesquisador ou solicitante dos dados _____ — Add signature — Clique em "Add signature" e assine com o mouse

Form Status

Complete? Incomplete

Save & Exit Form | Save & ... | - Cancel -

FIGURE 3. **Sent Dashboards**



HYBRID AUDITING OF DATA SENT TO THE CENTER FOR INTERNATIONAL BLOOD AND MARROW TRANSPLANT RESEARCH (CIBMTR) IN THE PANDEMIC SCENARIO

Cinthya Muniz Corrêa Rocha da Silva[1], Tânia Michele Barreto Waisbeck[1], Julia Lopes Garcia[1], Juliana Dall Agnol Da Rocha[1], Mariana Nassif Kerbauy[1], Lucila Nassif kerbauy[1], Juliana Folloni Fernandes[1], Leonardo Javier Arcuri[1], Cristina Vogel[1], Nelson Hamerschlak.[1]

1 Hospital Israelita Albert Einstein

INTRODUCTION: Data reporting to national and international centers enables transplant centers to analyze program performance when related to other services of similar complexity. The responsibility of data entry is a senior level professional with specific training in both the Cellular Therapy field and in database and statistics. International quality and safety standards recommend accuracy audits, as described by the Foundation for the accreditation of Cellular Therapy (FACT) and the Joint Commission International (JCI), through comparison of reported data and evidence recorded in medical records, by a professional trained in auditing. The COVID-19 Pandemic brought many challenges to the healthcare environment, among them the maintenance of administrative and management activities, making them adapted to the online environment.

OBJECTIVE: To describe the process of hybrid audit of data sent to the CIBMTR in the pandemic scenario.

METHOD: The audit was performed between 12/15/2021 and 01/28/20222, by 9 physicians and 1 biomedical. The 12 patients (6 adult and 6 pediatric) were randomly selected by type of HCT and age. The standard used to select the audited questions was the same used in CIBMTR, stratifying them into critical and non-critical fields, and target ≤ 3% non-compliance (NCs). As a form of pandemic compliance, 5 patients (2 adult and 3 pediatric) were audited online and 7 face-to-face. The physician accessed the electronic medical record and the data manager (DM) accessed Formsnet3 (CIBMTR data submission platform), comparing them to the evidence in the medical record. The DM recorded the results on the audit instrument and got the physicians' signatures to validate the documentation. All accesses occurred via individual and non-transferable username and passwords, with "audit access" signage, monitored by institutional information security.

RESULTS: Of the 12 selected patients, 58% (4 adult and 3 pediatric) were audited in person. In form complexity level, 92% (11) of the cases were basic. There were 1,167 questions audited on pre-HCT (788), post-HCT (294), HLA typing (61) and infusion data (24) forms. It was observed that 98.71% (1152) of the fields were compliant and 1.29% (15) NCs (Table 1), of which 60% (9) were found in the pre-HCT forms, with a loss in this rate when compared to the long historical process (Graphic1).

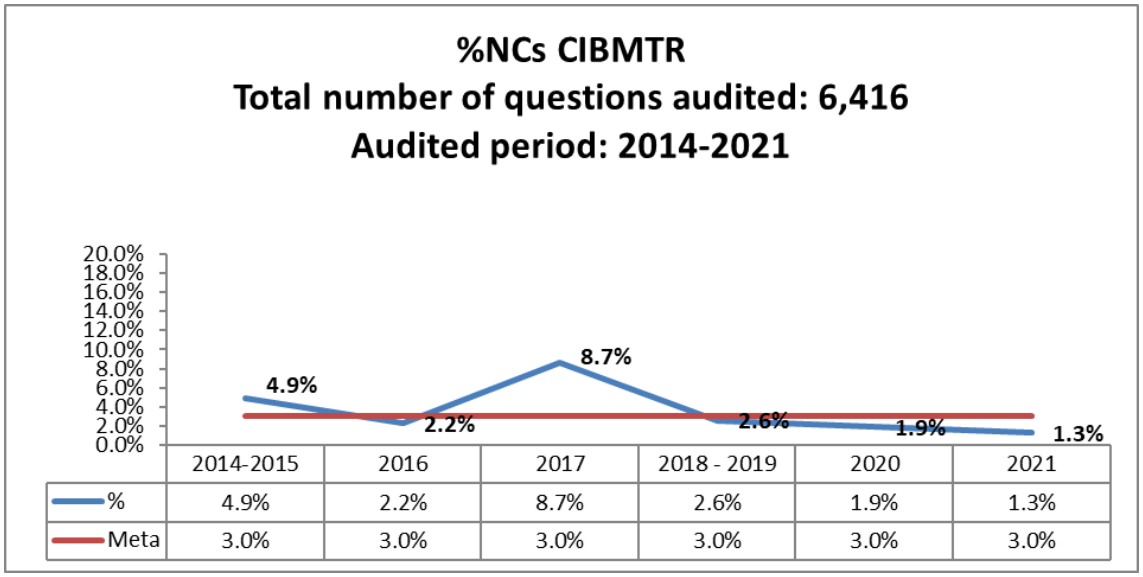
CONCLUSION: Auditing, as well as continuing education of the DM and the multiprofessional team, is fundamental to ensure the veracity of the data sent to HSCT registries. The adaptation of the process to hybrid was crucial and proved to be useful, as it facilitated the auditors' participation from a distance, avoiding it cut off in the pandemic scenario. Besides, the audit proved to be valid, as through data analysis, we observed significant advance with a drastic reduction in NCs (≤3%) over the years. As a future view, we believe that developing audit tools in an online system is as safe and effective as the direct evaluation.

Keywords: Data manager. Audit. Hematopoietic cell transplantation.

TABLE 1. **Results of audited items – Total data**

Total of patients (N=12)	**Total data**				
Audited forms	N Total Q.	Compliance	%	Non-compliance	%
Pre -TED 2400 and 2402/ Baseline 2000	788	778	98,73%	10	1,27%
Post -TED 2450 /Baseline 2100 / Specific disease follow up	294	289	98,30%	5	1,70%
HCT Infusion – 2006	24	24	100,00%	0	0,00%
HLA Typing	61	61	100,00%	0	0,00%
	1167	1152	98,71%	15	1,29%

GRAPHIC 1. **Total number of questions audited**



IMPLEMENTATION OF MANAGEABLE EVOLUTION OF HEMATOPOIETIC STEM CELL INFUSION: AN EXPERIENCE REPORT

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INTRODUCTION: The evolution of nursing care during the infusion of hematopoietic stem cells is fundamental for the quality of care. However, due to the absence of standardization, the registration of this activity has presented insufficient information, compromising adequate documentation and data reporting at the Center for International Blood and Marrow Transplant Research (CIBMTR).

OBJECTIVE: Describing the development and implementation of manageable evolution of hematopoietic stem cell infusion via the Tasy® Hospital Management System in a private hospital in southern Brazil.

METHOD: A descriptive study in the modality report of experience on the development and implementation of manageable evolution with information necessary for the recording of hematopoietic stem cell infusion. The creation and implementation occurred between January and February 2021, developed in four stages: adaptation of nursing evolution according to form 2006 - Hematopoietic Stem Cell Transplant Infusion - version 4 of CIBMTR; adjustments of the content with the nursing coordination of the unit; implementation of the standard electronic evolution with selection box and combination and descriptive fields for typing information in the Tasy Hospital Management System®, with the Information Technology sector; and validation of the tool by care nurses and training.

RESULT: Structuring the initial outline of the 170 items arranged in the 2006 form, questions 98 to 143 were used to make up the necessary information, among them: time of start and completion of infusion; infusion time; infusion route; presence of adverse event or incident during the procedure and need for interruption, with complementary intuitive fields according to positive response. After that, information related to the nursing and routine care of the unit was included, defined with the coordination, which is: type of transplantation; cell source; pre-infusion medication; ABO incompatibility; infusion protocol and the availability of a blank space for manual descriptive evolution in case of need for complement or registration of intercurrence.

CONCLUSION: The development of technological tools for the nursing evolution of hematopoietic stem cell infusion facilitates data collection and recording, optimizes the time of the activity avoiding the lack of relevant information, contributing to quality and safe care.

Keywords: Hematopoietic Stem Cell Transplantation. Data Management. Oncology. Nursing Records.

IMPLEMENTATION OF REMOTE DATA MANAGEMENT IN HEMATOPOIETIC STEM CELL TRANSPLANTATION: AN EXPERIENCE REPORT

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INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is a complex procedure that requires, in addition to a team prepared for assistance, monitoring, analysis and data management. During the triennium of 2020-2022, it was required to adapt models of works worldwide, due to the need for isolation and social distancing. For this, digital information and communication technologies (DICT) in telework are necessary for the continuity of some essential functions in the hospital routine. The use of DICT for telework should ensure access to hospital information, enabling the collection and recording of data in a safe and agile manner.

OBJECTIVE: Reporting the experience in implementing a remote data management model in a reference hospital in HSCT in Southern Brazil.

METHOD: A descriptive study of the type of experience report about the implementation of a work model for data collection and management in HSCT, via Remote Desktop and Virtual Private Network (VPN), which occurred between November and December 2021. The project was conceived by the Process and Quality Management service and developed in conjunction with the Information Technology sector of a Private Hospital in Southern Brazil. The activity was approved by the hospital's management and followed the General Data Protection Act 13,709/2018. RESULT: The notebook used for remote activity was evaluated by the Information Technology team in relation to device security, processing capacity and connection stability. This work model allowed access in a fast, practical and safe way to obtain essential information from transplanted patients, contained in electronic medical records, without connection instability, allowing data collection and management.

CONCLUSION: The implementation of the remote data management routine in HSCT allowed the continuity of data collection and registration in national and international platforms. This routine can serve as a support to analyze transplant outcomes and outcomes, qualify the care provided, assist in management and facilitate the conduct of future research in the area.

Keywords: Hematopoietic Stem Cell Transplantation. Data Management. Oncology. Teleworking.

PERFORMANCE IN MANAGING AND REPORTING DATA TO CIBMTR IN A HEMATOPOIETIC STEM CELL TRANSPLANTATION SERVICE

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INTRODUCTION: The first activities in the management and reporting of hematopoietic stem cell transplantation (HSCT) data date back to the 1970s through the pioneering initiatives of the North American (IBMTR) and European (EBMT) registries[1]. Later, in the 2000s, the foundation of the CIBMTR points to the consolidation of the North American registry[2]. The activities of these registries aim to improve access to information and research on HSCT, and the databases generated can be used locally by participating centers to contribute to decision-making in care processes to promote improvements in HSCT, as well as influence in national level the generation of public policies. In this sense, knowing the indicators that evaluate the performance of management and data reporting (MDR), as well as analyzing the performance of these indicators, is fundamental in the process of generating and using this information. This analysis is an important tool to understand the local reporting scenario, serving as a strategy for improving the quality of processes in generating this data.

OBJECTIVE: To evaluate the performance of MDR to CIBMTR in an HSCT service.

METHODS: This is a descriptive study in an HSCT center in the federal public network of Rio de Janeiro from Jan/2016 to Dec/2021. To evaluate the performance, the following indicators were used: 1) Rate of transplants submitted to CIBMTR; 2) Absolute number of forms submitted to CIBMTR; and 3) Absolute number of Forms DUE in FormsNet3. The Relative Change Percentage (RCP) was calculated for each indicator comparing the years 2016 vs. 2021, where RCP= (Final Value–Initial Value)/Initial Value x100. In addition, a trend line was added to each graph constructed to assess an increase or decrease in the forecast period. These data are available on the CIBMTR Portal and FormsNET3sm's Center Forms DUE.

RESULT AND DISCUSSION: There was an increasing trend and a RCP= 134.15% (from 41% to 96%) in the HSCT rate reported to CIBMTR. In addition, the reporting rate was above 95% after 2019 (Graph 1). For the Absolute Number of Forms Sent to CIBMTR there was also an increasing trend and an RCP= 1,865.5% (from 32 to 628) (Graph 2). Regarding the Absolute Number of Forms DUE there was a decreasing trend in the last six years and an RCP= -54.42% (from 294 to 134) (Graph 3). The indicators presented show a significant improvement in the performance of the report – mainly from 2019 onwards – and that may be mainly associated with the reorganization in the work processes, admission, qualification and profile of the new Data Managers (DM) of the service.

CONCLUSIONS: There was an improvement in MDR performance between the years 2016 to 2021 at CIBMTR, reflecting the new profile of the current DM's team. Although the results show an improvement in performance, these indicators are important tools in the reassessment and expansion of local goals, creating a process of continuous improvement that aims to maintain the quality of the MDR in HSCT.

Keywords: Data manager. performance. data reporting. TCTH

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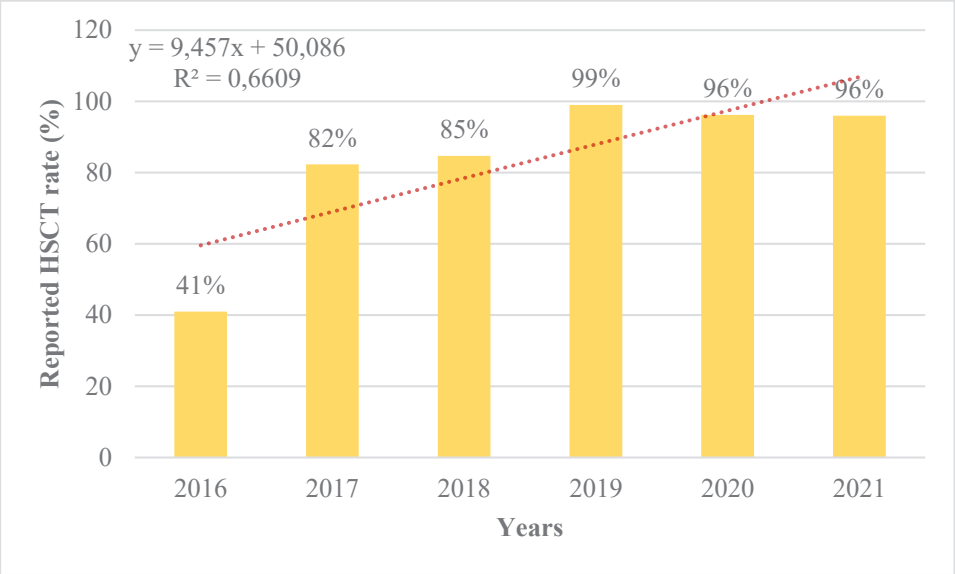
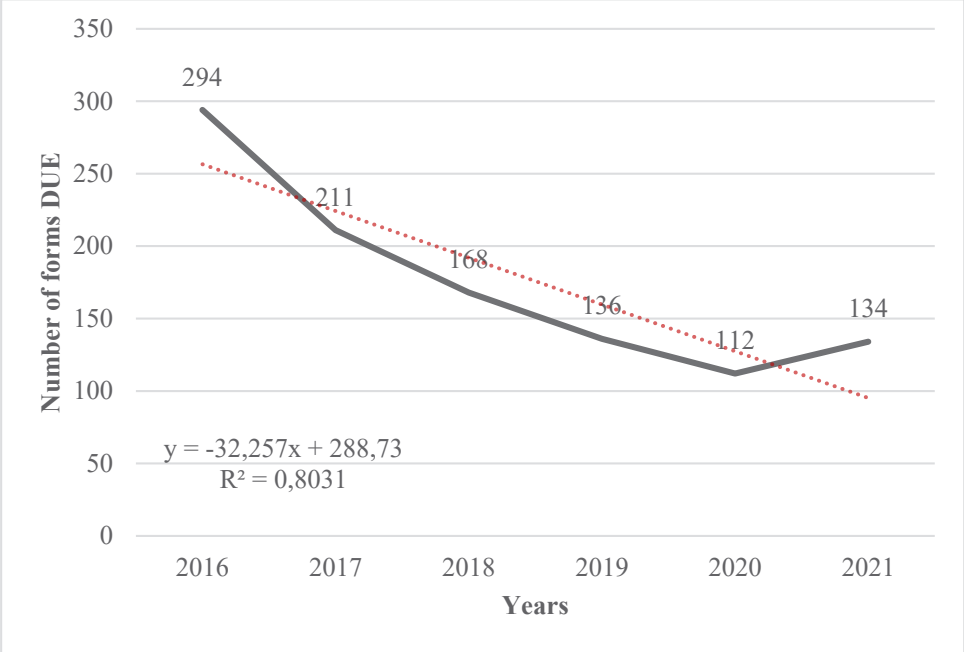
2. CIBMTR. Our history [Internet]. [update 1/21/2022; cited 2022 May 04]. Available from: https://www.cibmtr.org/About/WhoWeAre/History/Pages/index.aspx

GRAPH 1 **HSCT rate reported to CIBMTR (%) by year from 2016 to 2021**



GRAPH 2 **Absolute number of forms submitted to CIBMTR per year from 2016 to 2021**

GRAPH 3 **Absolute number of Forms with FomsNET3 per year from 2016 to 2021**



STRUCTURING AND IMPLEMENTING DATA MANAGEMENT IN A HEMATOPOIETIC STEM CELL TRANSPLANTATION UNIT OF AN ONCOLOGICAL HOSPITAL OF REFERENCE IN SÃO PAULO COUNTRYSIDE

Paula Moreira da Silva Sabaini[1], Ana Luiza Calmon Alves[1], Maria Fernanda Vasques Esteves[1], Gislaine Cristina Lopes de Melo[1], Tamires Fernanda Furlan Paschoa[1], Livia Cristina Ferreira de Oliveira[1], Regina Celia da Silva Dias[1], Neysimelia Costa Villela[1], Rafaela de Souza Ferreira[1], Angela Mandelli Venancio[1], Luiz Fernando Alves Lima Mantovani[1], Elisiane Tosta Paixão[1], Claudia Adriana Fernandes[1], Nayara da Silva Santos Cardozo[1], Vanessa Almeida Padua[1], Alessandra Degrande Petta[1], Lucas Alexandre Silva Vieira[1], Carlos Sitta Sabaini[1], Pablo Hernesto Tarram Via[1], George Mauricio Navarro Barros[1].

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INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is a complex treatment, rich in particularities. Managing HSCT data seek to organize the information, allowing the team to monitor its results and improve outcomes. The data manager (DM) is a person responsible for this task, creating processes to ensure that data collection is complete, accurate and reliable. The Barretos Cancer Hospital (BCH) HSCT Unit started its activities in September 2003.

OBJECTIVE: Describe the structuring and implementation of data management in adult and pediatric HSCT departments for data reporting to Brazilian and North American (Center for International Blood and Marrow Transplant Research - CIBMTR) registries.

METHODS: Experience report.

RESULTS: The partnership contract between BCH and the CIBMTR occurred in June 2019. In the following month, the 1st DM was hired, followed by the Research Ethics Committee approval and the institution was included in the Brazilian multicenter data reporting study to CIBMTR. Data reporting started in October 2019. From August 2019 to September 2020, the DM attended the 1st edition of the Data Managers Training in HSCT organized by the Bone Marrow Association (AMEO), which provided a database in Microsoft® Access format. By then, the BCH HSCT data was stored decentralized, and from that moment on, they were stored in a unified database. Concomitantly, 16 forms containing CIBMTR requested information were created and validated. Later, some of these forms were incorporated into medical records. In October 2020, a new electronic medical record was implemented in the institution, and the forms migrated to the digital model, making the data collection process faster and safer. It is known that the use of electronic medical records is not a fact in all Brazilian centers yet, which makes the DM work even more challenging. In April 2021, the service was certified by the Brazilian Society of Cell Therapy and Bone Marrow Transplantation and the National Transplant System, as recognition for the regular data reporting to CIBMTR. Due to the progressive increase of tasks, the need to hire a new DM was confirmed, which took place in June 2021. She is being trained and currently participates in the 2nd edition of AMEO Training Course. Until April 2022, 1,282 transplants were performed by the center, of which 321 were reported to the CIBMTR (197 adults and 124 pediatrics), and 230 are in follow-up.

CONCLUSION: Data management is a key activity that needs to be implemented in all HSCT units, as it allows services to know their results, develop processes to optimize outcomes, in addition to enabling participation in multicenter studies.

Keywords: HSCT. Data management. CIBMTR.

CELLULAR THERAPY

ADVERSE REACTIONS IN THE INFUSION OF ABO INCOMPATIBLE BONE MARROW GRAFTS

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The infusion of allogeneic bone marrow grafts with major ABO incompatibility may cause moderate to severe adverse reactions, but this may be the only donor choice. The risk of the transfusion can be minimized using plasmapheresis, according to the anti-donor isohemaglutinin titers, red blood cell depletion of the graft, adequate hydration and medications before the infusion and careful monitoring during the infusion.

OBJECTIVE: The aim of this study is to report the occurrence of adverse reactions in pediatric patients undergoing allogeneic bone marrow transplants with major ABO incompatibility.

PATIENTS AND METHODS: The infusion forms regularly completed by the nursing team of the Bone Marrow Transplantation Unit at the time of infusion were reviewed, as well as the patients' medical records of all allogeneic bone marrow transplants performed between January 2017 and May 2022 with major ABO incompatibility. The algoritm proposed by Rowley, 2001 was adopted to guide the pre-transplant procedures (Rowley SD. Hematopoietic stem cell transplantation between red cell incompatible donor-recipient pairs. Bone Marrow Transplant. 2001 Aug;28(4):315-21).

RESULTS: Thirty-four pediatric patients were included, 19 of them males. The median age was 8 years (0.10-16), median weight of 25.5 kg (9-68kg). The diagnoses were hematological malignancies (n=31) and bone marrow failures (n=4). Plasmapheresis was performed in 20 patients with isohemaglutinin titers > 1/16 (1/16 - 1/256). All 34 patients received diphenidramine prior to the infusion with mannitol and tylenol (26), tylenol (2), dipirone (5) or mannitol (1) per attending physician preference. A total of 80 bone marrow bags were infused, all of them after red blood cell depletion, with a median volume of 541 ml (222-1387) per patient. A total of 59 moderate adverse reactions were reported, as described in Table 1.

CONCLUSION: Severe transfusion reactions can be prevented in children undergoing ABO incompatible bone marrow transplants by decreasing hemagglutinin titers, removing the red blood cells from the graft, ensuring urinary flow, and assuring premedication before the infusion.

TABLE 1. Adverse reactions at the time of infusion of ABO incompatible grafts

Total reactions = 59	Number of adverse reactions	Percentage
Hypertension	17	30
Altered Heart Rate	13	22
Hypotension	5	8
Fever	4	7
Vomiting	3	6
Hypoxia	2	3
Nausea	2	3
Hemoglobinuria	2	3
Cough	2	3
Diarrhea	2	3
Headache	1	2
Other symtoms*	6	10

* abdominal pain, tremor, itching and eyelid edema.

ANALYSIS OF CRIOPRESERVATION AND INFUSION OF HAEMATOPOIETIC STEM CELL FROM MOBILIZED PERIPHERAL BLOOD BY A THERAPY CELL CENTER IN FORTALEZA DURING THE COVID-19 PANDEMIC

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INTRODUCTION: The Therapy Cell Center (TCC) of the Center for Hematology and Hemotherapy of the State of Ceará (HEMOCE) contributes to the growing number of autologous and allogeneic transplants performed in the public and private hospital of the state. The full functioning and experience during the pandemic period highlighted the importance of the TCC to enable bone marrow transplantation (BMT) in the five transplant centers attended.

OBJECTIVE: Analyze the number of patients treated at the HEMOCE Therapy Cell Center through cryopreservation and infusion of hematopoietic progenitor cells from mobilized peripheral blood for autologous bone marrow transplantation.

MATERIALS AND METHODS: A retrospective analysis of the patients treated by the TCC of Hemoce was carried out during the period of the COVID-19 pandemic in the years 2020 to 2021. The following parameters of the mobilized patients were evaluated: number of patients, age, sex, number of cryopreserved units, indication for BMT and number of transplants performed.

RESULTS: The total of 143 patients from five transplant centers in the state of Ceará were treated in the evaluated period, 63 patients in 2020 and 80 patients in 2021, totaling 415 cryopreserved Haematopoietic stem cell bags, 191 bags in 2020 and 224 in 2021. 142 autologous BMT were performed, 60 in 2020 and 82 in 2021. The mean age of patients was 49 years, with a minimum age of 16 years and a maximum of 70 years, 74 (51.74%) were female and 69 (48.26%) male. The main indications for autologous BMT were Multiple Myeloma (76 patients, 53.15%), Hodgkin's Lymphoma (29 patients, 20.28%), Non-Hodgkin's Lymphoma (29 patients, 20.28%), Leukemias (3 patients , 2.10%), others diseases (6 patients, 4.19%). There was a similarity in the number of patients seen by the TCC and transplanted during the study period and the increase in the number of patients seen (11.88%) in 2021 when compared to 2020.

CONCLUSION: The commitment of the Therapy Cell Center to develop the activities of processing, storage and distribution of HSC also during the period of the COVID-19 pandemic, had a participation in the increase in the realization of BMT that are widely carried out in the public and private health centers of the state of Ceara.

Keywords: Hematopoietic Stem Cell (HSC). Cryopreservation. Bone Marrow Transplantation (BMT).

CHARACTERISTICS OF THE GRAFT PROCESSING LABS THAT COMPOSE THE BRAZILIAN SOCIETY OF CELLULAR THERAPY AND BONE MARROW TRANSPLANTATION GRAFT PROCESSING GROUP.

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INTRODUCTION: The Brazilian Society of Cellular Therapy and Bone Marrow Transplantation (SBTMO) Graft Processing Labs (GPL) Group started its activities in August 2021. The coordinators developed a survey in which the first section had 10 general questions as well as laboratory infrastructure and techniques questions, for the registry of the Group.

OBJECTIVES: To describe the characteristics of the Brazilian GPL that composes the Group.

METHODS: The online questionnaire was prepared in Google Forms and was sent by e-mails and WhatsApp (groups or personal). The participant labs were selected by convenience. The analysis was performed with only one answer per institution. Descriptive statistical analysis was performed using Microsoft® Excel®. The survey stayed open for three months (from June to September 2021). Results were presented as the number and frequency (%).

RESULTS: Contact information was obtained from approximately 70 different labs, 13 of which are private Umbilical Cord Blood Banks (UCBB). Of the 57 remaining, 48 (84%) answered the survey, as well as 3 private UCBB, totaling 51 answers. Most labs were in the Southeast Region (31; 60.8%), followed by the South (7; 13.7%) and Midwest (7; 13.7%) Regions. Three labs in the Midwest Region were in implementation. In the Northeast Region, there were 4 (7.8%) implemented labs and in the North Region 2 (3.9%) labs, but only one in operation. Most of the labs (23; 45.1%) were private, 18 (35.3%) were public (including one military) and 10 (19.6%) philanthropic. Nevertheless, 35 (68.6%) labs had some type of reimbursement by the Brazilian public system, with 13 (25.5%) being exclusively reimbursed by it. Most of the labs were interested in voluntary laboratory accreditation (40, 78.4%). Most labs were providing services for one or two bone marrow transplantation units (BMT; 38, 74.5%) and were able to process three sources of cell therapy products (16, 31.4%; bone marrow [BM], peripheral blood stem cells [PBSC], and lymphocytes). Most of the labs (43; 84.3%) work with PBSC. Of these, 31 (72%) also process BM, 28 (65%) lymphocytes and 12 (27.9%) were also UCBB.

CONCLUSION: In Brazil, there is a great centralization of graft processing labs in the Southeast region. Most labs are interested in voluntary technical accreditation which exposes their commitment to graft quality and patient security; provides services for one or two bone marrow transplantation units that demonstrate that they are linked to specific BM transplantation units, and process three sources of cell therapy products which indirect tell us about the lab complexity and capacity to meet the demands of the transplantation units.

Keywords: Graft Processing Labs. Cryopreservation. Bone marrow transplantation.

CHARACTERIZATION OF CONTINUING EDUCATION ACTIVITIES PROMOTED BY THE BRAZILIAN SOCIETY OF CELLULAR THERAPY AND BONE MARROW TRANSPLANTATION GRAFT PROCESSING GROUP

Pedro Victorio de Almeida Marzano[1], Karen de Lima Prata[1,2], Andrea Tieme Kondo[3], André Rolim Belisário on behalf of Brazilian Society of Cellular Therapy and Bone Marrow Transplantation Graft Processing Group[1].

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INTRODUCTION: Continuing education activities are essential for professionals working in laboratories that process human cells for therapeutic use and clinical research (Cell Processing Centers - CPC). Accreditation agencies require professionals who work in CPC to participate in cell therapy continuing education activities. The Brazilian Society of Cellular Therapy and Bone Marrow Transplantation (SBTMO) Graft Processing Group (GPG) has been promoting virtual meetings in order to build upon the educational and experiential bases of the participating CPC.

AIM: to describe the continuing education activities of the GPL group and to characterize the attendance at the virtual meetings.

METHODS: The GPL group activities have been coordinated by a core of experts (KLP and ATK) on behalf of the Brazilian Society of Cellular Therapy and Bone Marrow Transplantation. An online self-administered mailed questionnaire was sent to the institutions in order to define priority topics to be discussed at the monthly virtual meetings. Attendance data were obtained from the analysis of the registered chat boxes of each meeting, in which the participants described their full name, representative institution, and e-mail. Data were recorded in an Excel spreadsheet and were analyzed to describe both individual and institution attendance.

RESULTS: From August 2021 to May 2022, the GPG promoted nine virtual meetings. The topic of each meeting was described as follows: 1) national survey on lab practices data; 2) quality indicators; 3) validation master plan; 4) cell viability assessment by trypan blue and flow cytometry; 5) contingency plan for critical materials; 6) red blood cell depletion without high-molecular-weight hydroxyethyl starch: automated systems; 7) red blood cell depletion without high-molecular-weight hydroxyethyl starch: manual techniques 8); stability plan for cell therapy products; and 9) supplier qualification program. There were 168 participants, representing 53 institutions. There were 3 individuals per institution on average. The average rate of individual attendance per meeting was 35%. Nineteen (11.2%) individuals attended 7 to 9 meetings, 53 individuals (31.2%) 4 to 6, 33 (19.6%) 2 to 3, and 63 (37%) individuals attended only one meeting. The meeting with the most and least individual attendance were topic 6 (45%) and topic 1 (30%) meetings, respectively. Out of 53 institutions, 15 (28.3%) attended 7 to 9 meetings, 24 (45.3%) 6 to 4, and 14 (26.4%) 1 to 3 meetings. The meetings had an average attendance of 58.5% of institutions, ranging from 43% to 68%. The meetings with the most and least institution attendance were topic 6 and topic 3 meetings, respectively.

CONCLUSION: In summary, the topics discussed at the meetings reflect the challenges of cell therapy processes, as well as the requirements of accreditation and regulatory agencies. There was a good individual and institutional attendance at the activities promoted by the GPG.

CHECKING DMSO INHIBITION POTENTIAL IN MICROBIOLOGICAL GROWTH

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INTRODUCTION: Dimethyl sulfoxide (DMSO), discovered in the 19th century, is used worldwide as a potent organic solvent. New anti-inflammatory and cryoprotective properties were discovered in 1980, since then it is widely used for cryopreservation in cellular processing centers. Even with the use of sterile techniques during the collection, processing and freezing of cell therapy products, bacterial contamination is an inherent risk associated with handling and/or patient/donor. In order to ensure the quality of the infused product, release tests are necessary, with microbiological culture being one of the most important quality parameters.

The microbiological studies are carried out in an automated system for continuous and simultaneous monitoring of blood samples for the detection of bacteria and fungus. The methodology is based on the detection of fluorescence emitted by a sensor, in the culture flasks. The system has ultra sensitivity and monitors samples in short time intervals and accelerates detection, providing visual and audible alarms in case of positivity. Due to the possible antibacterial capacity of DMSO, several regulatory entities and accreditation centers question its power to inhibit microbiological growth in hematopoietic progenitor cell cultures.

OBJECTIVE: The objective of this study is to evaluate the inhibitory capacity of DMSO on microbiological growth in blood samples, inoculated into blood culture flasks using the BD Bactec system. ®.

CASUISTIC: 20 samples were evaluated, 10 bottles containing blood and 10 containing blood + cryoprotectant solution. Half of the products were inoculated into aerobic flasks and the other half anaerobic+fungus.

METHOD: Whole blood samples from therapeutic bleeding and cryoprotective solution containing 50% DMSO and 50% Voluven were used.

Strains used for the assay: ATCC Candida albicans 14053, ATCC Escherichia coli 25922, ATCC Streptococcus agalactie 9e530 and ATCC Staphylococcus aureus 29213. The microorganisms were isolated on blood agar and the plates were incubated at 35ºC ± 1ºC for 24 hours in an incubator containing CO2. With the aid of a swab and a tube containing 3 mL of saline, a turbidity was performed in the 0.5 Mc Farland scale of each isolate (corresponding to 1.5x108 CFU/mL) using the Densicheck Plus turbidimeter. From this bacterial/fungal suspension, samples were inoculated into culture flasks and taken to the BD Bactec equipment®.

RESULTS: The results of aerobic, anaerobic and fungal cultures were evaluated after 120 hours of inoculation and all strains of the positive control had growth within 72 hours.

In 80% of the samples, there was delay in bacterial growth, 10% had equivalent growth and 10% were not affected by the cryoprotectant.

CONCLUSIONS: Culture flasks containing DMSO showed inhibition of microbiological growth, but within the standard growth time expected for the strain, up to 72 hours.

Keywords: DMSO. Cryopreservation. Cell Therapy. Microbiological Culture. Growth Inhibition. Blood Culture Bottles.

COMPARISON OF DIFFERENT CELL CONCENTRATIONS IN NOT PROGRAMMED FREEZING OF HPC

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INTRODUCTION: The quality of cryopreserved units directly impacts the outcome of bone marrow transplantation.The entire process, including product handling, cell concentration, cryoprotectant solution, freezing and storage method must be validated and opportunities for improvement must be evaluated. Higher cell concentration can reduce the number of bags and DMSO used, reducing the cost of the process and minimizing adverse reactions.

OBJECTIVE: To compare the hematological reconstitution of 30 patients submitted to an autologous HPC transplantation, with different freezing concentrations, considering the infused dose and cell viability.

CASUÍSTIC: Fifteen infusions performed between 03/2020 and 12/2020 were compared, with cryopreserved units with a concentration of 150 x 106/mL (A group) and 15 infusions performed between 07/2021 and 04/2022, with cryopreserved units with a concentration of 300 x 106/mL (B group).

METHOD: Retrospective analysis of infused dose, freezing cell concentration, cell viability and granulocytic recovery data from 30 transplant patients. The freezing of all units maintained the final concentration of 5% DMSO, being the units of A group, cryopreserved with 25% Voluven® and 20% albumin and the units of B group, with 6% Voluven®, 4% albumin and 35% Plasmalyte®. The thawing of the units took place at the bedside at the time of infusion, in a water bath at 37ºC (+/-1ºC) and only 1 pediatric patient, in group B, had a grade I adverse reaction.

RESULTS: The means of viability in total and CD34+ cells from A group were 85.2% and 95.9%, respectively, with an average storage time of 54 days. For B group, the means of viability in total and CD34+ cells were 81.9% and 91.5%, respectively, and mean storage of 21 days. The total number of nucleated cells, mean infused, for A and B Groups was 9.5 x 108/Kg (2.01 – 22.28) and 11.5 x 108/Kg (3.34 – 25.84), respectively. The infused dose of CD34+ cells was 5.4 x 106/kg in both groups, being A group (3.12 - 8.41) and B group (2.25 - 12.38) with volumes of 233 mL and 567 mL, for groups A and B. The average granulocytic recovery, in both groups, was maintained on D+11.

CONCLUSIONS: Aiming to optimize the cryopreservation process of the HPC units, it was possible to implement the cell freezing concentration, 300 x 106 / mL and associated cryoprotectant. Both proved to be safe, and have no alteration in the time of hematological reconstitution. There was a reduction in cryogenic bag use, DMSO volume and storage space.

Keywords: Not Programmed Freezing. Cell Concentration. Bone Marrow Transplantation. DMSO. Cell Viability. Grafting.

CRITICAL FAILURE OF A CELL THERAPY PRODUCTS STORAGE TANK: DESCRIPTION, INVESTIGATION AND IMPLEMENTED IMPROVEMENTS

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INTRODUCTION: Storage tank failure can lead to the loss of cryopreserved cell therapy (CT) products, which means the only possibility of treating serious illnesses.

AIM: to describe a serious vapor ST failure, as well as the improvements implemented in the storage procedure to increase the safety and quality of cryopreserved CT products.

METHOD: This is a case report of a vapor ST failure (CBS, isothermal V5000-AB series). The records were reviewed to obtain information regarding the frozen units.

RESULTS: On 07-dec-2021, the technical staff observed the accumulation of liquid nitrogen (LN2) at the bottom of the ST. The engineering team was contacted and adjusted the ST's maximum LN2 level. The problem recurred on 23-dec-2021. The engineering and maintenance company carried out a series of tests on the ST. On 06-Jan-2022, it was requested emptying and defrosting of the ST for 48 hours for corrective maintenance of the LN2 level sensor. Planning to transfer the inventory to another ST was started, including bags with serology/NAT reagent overwrapping. However, on 23-Jan-2022 (Sunday), the LN2 level sensor stuck at level zero leading the automated LN2 filling of the ST to start and not stop. There was an overflow of LN2 inside the vapor ST, and 3 of 4 rack positions were submerged in LN2. The engineering team performed the filling interruption manually, after being called by the concierge. There were 553 frozen bags from 307 patients/donors stored in the ST at the time of failure. Out of the 553 bags, 87 (15.7%) had positive serology or NAT tests. Of these, 11 (1.9%) were anti-HIV positive (NAT HIV negative) and two (0.3%) were HBsAg and NAT HBV reagents. Out of the 553 bags, 10 (1.8%) had a positive microbiological test, including four (0.7%) for multi-sensitive Salmonella sp. Excess of LN2 was manually removed from the ST and the actions to transfer the inventory to the backup ST were intensified, including changing the bags with positive tests (PT) to positions A or B of the racks, as well as finishing these bags overwrapping. The inventory was transferred and stored in the backup ST for approximately 72 hours. Surveillance actions were performed, including virtual meeting and discussion with the Brazilian National Health Surveillance Agency, visual examination to disclose leaking or breakage of seals, thawing of the unit with positive HBV NAT (authorized disposal) to confirm the absence of leaking or breakage of seals, and discussion of the possibility of cross-contamination with the bag supplier. Improvement actions in the storage procedure were implemented, including the modification of the storage location of the bags in quarantine and those with PT (positions A and B of the rack) and implementation of the routine use of overwrap in bags with PT.

CONCLUSION: Vapor ST may fail, leading to an unexpected accumulation of LN2. Improvements in the storage procedure can avoid the serious consequences of this failure, including cross-contamination.

Keywords: Cryopreservation. Quality assurance. Storage tank.

EVALUATION OF BLOOD CELL COUNT USING THE SYSMEX XN AUTOMATIC HEMATOLOGY ANALYZER TO OPTIMIZE COLLECTION OF PERIPHERAL BLOOD PROGENITOR CELLS BY LEUKAPHERESIS

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INTRODUCTION: Autologous stem cell transplantation (ASCT) is a treatment modality for several types of disease. Prediction of successful mobilization may be useful to optimize haematopoietic stem cell (HSC) collection. The Objective was to identify characteristics that can influence the effectiveness of mobilization and create a model to predict the success of mobilization in candidates for ASCT.

METHODS: This was a retrospective study, and data from patient candidates for ASCT between 09/2015 and 12/2021 were analyzed. Participants were assisted in five hospitals and laboratory procedures were performed at the Cell Processing Center (CPC) of Cetebio/Fundação Hemominas, Brazil. The medical records of the participants were reviewed to obtain the following information: gender, age, weight, diagnosis, mobilization, mobilization cycle, number of previous chemotherapy regimens and previous radiotherapy. The laboratory data analyzed were CD34+ cell enumeration and pre-collection peripheral blood (PB) blood count. Enumeration of CD34+ cell was performed using the ISHAGE protocol. The blood count was performed using an automated counter (SYSMEX XN-1000 AS-01). The studied outcome, good mobilization, was defined as a viable CD34+ cell count ≥ 20/uL in the PB. Model derivation was performed using logistic regression. The level of classification accuracy of model was tested in a subset of participants.

RESULTS: the study population consisted of 807 patients, 413 (51%) of whom were male. The median age was 54 (1-74) years. Multiple myeloma was the most common diagnosis (58,2%), followed by lymphoma. Of the 807 participants, 74 failed in previous mobilization attempts, totaling 881 cycles of mobilizations and collection attempts. Of the 623 participants, 353 were good mobilizers. Of the clinical and laboratory variables, the weight, the mean corpuscular volume (MCV), the nucleated red blood cell (nRBC), the peripheral blood mononuclear cells (PBMC) and the immature granulocyte count were significantly associated with good mobilization. In addition, participants diagnosed with multiple myeloma were two times more likely to be good mobilizers than patients with lymphoma (OR=1.92; 95%CI: 1.21 – 3.05; P=0.006). Participants who performed the collection in the first mobilization cycle were six times as likely (OR=6.87; 95%CI: 2.79-16.96; P<0.001) to be good mobilizers. The model was applied to the validation set to identify patients who underwent apheresis (CD34+ cells count ≥ 10 µL), resulting in a sensibility of 69%, a specificity of 95%, positive predictive value of 98%, a negative predictive value of 50%.

DISCUSSION: the results of our study are extremely relevant to institutions that do not have a flow cytometer and rely on other institutions to define HSC collection by apheresis. Cetebio serves nine transplant centers. The centers that perform the collection of HSC are located between 40 to 568 km away from Cetebio (place of quantification of CD34+ cells). Predicting the outcome of mobilization may allow the adoption of complementary measures, such as the use of plerixafor. Furthermore, it would better optimize the collection of CPH by apheresis. Thus, it would be possible to avoid additional collection days, reducing costs and risks related to administration of additional doses of G-CSF, catheter maintenance and prolonged hospital stay. CONCLUSION: Success in mobilization was greater in participants who underwent the first mobilization cycle and who had a diagnosis of multiple myeloma. Furthermore, higher weight and levels of nRBC, immature granulocytes, and PBMC, as well as lower levels of MCV, were associated with successful mobilization.

Keywords: CD34+ enumeration. Stem cell transplantation. Good mobilizers.

HEMATOPOIETIC STEM CELL TRANSPLANTATION: SETTING UP A MONITORING PLAN FOR THE CRITICAL EQUIPMENT USED IN CELL PROCESSING

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INTRODUCTION: The equipment used to prepare and cryopreserve cells for hematopoietic stem cell transplants (HCT) are considered critical and must be validated and monitored to ensure safety, traceability, compliance with good laboratory practices and the guidelines established by the regulatory bodies.

OBJECTIVE: The aim of this study is to report the methods used to continuously monitor the cold chain equipment used for HCT.

METHODS AND RESULTS: Monitoring of critical equipment and of the rooms is performed in person during office hours, twice a day, and the data is recorded in standard form. Off-hours, on weekends and holidays, monitoring is checked by the institution's electricians' team every 2 hours, and the data is also recorded in a standard document. An alarm system is used to continuously monitor temperature and electrical supply with a visual and audio alarm center installed at the electricians' room, that operates 24 hours and seven days a week. In case of mechanical failures or deficiency of electrical power of critical equipment, an alarm sounds and allows immediate action of electricians and laboratory staff. In addition to serving as a contingency plan, manual and automated registrations assist in the traceability of industry data. Under normal conditions, the parameters established and validated for the rooms are temperature 12°C-25°C and relative humidity of the air that can range from 40% to 80%. The thermohydrometers used fort his verification are calibrated annually. The ultrafreezers temperatures can range from -70° to -90°C, and preventive maintenance takes place annually and calibrations every six months. The parameters set for the refrigerator can vary from 2°C to 8°C and the periodicity of the preventive maintenance and calibration is annual. The temperature of the liquid nitrogen tank can range from -196°C to -136°C and nitrogen level from 20 to 30 inches. The temperature check of this equipment used a display, and the liquid level is checked with the aid of a standard ruler and is compared with the level that is also recorded by the display. Preventive maintenance and tank calibration takes place every six months. All reports of the services performed on the equipment are digitized and available in a software of the Clinical Engineering sector of the Institution.

CONCLUSION: All actions were developed to ensure the safety of the equipment, assist to identify instabilities or potential failures, prevent alterations in cell viability and the integrity of the bags of cell the hematopoietic stems stored.

SUCCESSFUL TREATMENT OF SARS-COV2 INFECTION IN A CAR-T CELLS THERAPY RECIPIENT

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INTRODUCTION: Hematologic malignancies patients are recognized to be highly immunocompromised due to the disease and the treatment, causing significant concern about a risk of mortality from SARS-CoV-2 infection (COVID-19).

CASE REPORT: A 62-year-old male patient with a diagnosis of Diffuse Large B-Cell Non-Hodgkin Lymphoma stage IVBX IPI 3 on February 23, 2020, refractory to 6 cycles of R-CHOP who was enrolled in the Phase III Belinda trial in October 2020 and was randomized to standard-care group treatment (salvage chemotherapy and autologous-HSCT). After three cycles of R-ICE, progressive disease was observed, and he crossed over to arm A (CAR-T cell treatment). As bridging chemotherapy, he was treated with two cycles of R-GemOx, and received lymphodepletion chemotherapy (Flu-Cy) followed by the CAR-T infusion - tisagenlecleucel (Kymriah) on February 23, 2021. Regarding CAR-T cell adverse effects, cytopenias (grade 2) were observed. In June 2021, four months after CAR-T infusion, he was admitted to the emergency department, referring cough and dyspnea in the past 72 hours. The patient had been diagnosed with (COVID-19) ten days before the hospitalization, with mild symptoms. Two days after the hospital admission, he was transferred to the intensive unit with persistent fever and a drop of oxygen saturation (SpO2) to 85%, despite nasal catheter supplemental oxygen therapy. On the day+18 of COVID-19 symptom, a progressive worsening of the respiratory pattern was observed. The patient received dexamethasone 6mg/day and high titer (97% inhibition -cPass Neutralization Antibody Detection Genscript) convalescent plasma infusion. Four days after the procedure, he improved respiratory parameters, and within ten days, he was discharged from the hospital without oxygen supplementation or glucocorticoid therapy. The patient was readmitted on July 17th with tachycardia, hypotension, and a new onset desaturation (SpO2 82%). Another SARS-CoV-2 PCR assay confirmed a positive result. Relevant laboratory findings were elevated d-dimer (>7500 ng/ml) and a reduced platelet count (21.000 uL). Afterward, an angiotomography was performed, and there was an acute segmentary pulmonary embolism (PE). Low molecular weight heparin 1 mg/kg once daily was started due to a reduced platelet count. Two days later, after achieving platelets count superior to 50000 uL, the dose was adjusted to 1 mg/kg twice daily. Ten days after hospital admission, on July 26th, the patient was asymptomatic; he was discharged with apixaban 5 mg twice daily. Nowadays, he is asymptomatic.

Conclusion: Hematologic malignancies patients with COVID-19 may be considered more vulnerable than the general population with high mortality. However, the exact outcome of SARS-CoV-2 infection in this setting of patients is still unclear, especially in South America. This is the first reported case of a patient treated with CAR-T cells, with COVID-19, PE, and was successfully treated in Latin America.

THE EXPERIENCE USING HYDROXYETHYLSTARCH 6% TO REMOVE ERYTHROCYTES FROM THE BONE MARROW GRAFTS IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTS (HCT) WITH MAJOR ABO INCOMPATIBILITY.

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In allogeneic bone marrow transplants, when there is a major ABO incompatibility, it is important to remove the erythrocytes to avoid severe hemolytic reactions at the time of transplant. An effective way is through centrifugation with the addition of 6%-Voluven® (hydroxyethylstarch - HAES). The aim of this study was to describe our experience using HAES 6%-Voluven® in a cellular processing center (CPC).

CASUISTIC AND METHODS: Retrospective evaluation of the laboratory documents and electronic medical records of 33 donor-recipient pairs undergoing HCT with major ABO incompatibility and bone marrow (BM) grafts from January 2017 to May 2022. The BM was collected in the operating room through multiple punctures in the posterior iliac crest and sent to the CPC in the same building. After collecting samples for quality control, the hematocrit (Ht) was adjusted to < 25% adding normal saline 0.9%. After adjustment, HAES6%- Voluven® was added in a 1:8 ratio. The bags were centrifuged in the inverted position at 1,700 rpm or 840 g, 5 minutes, room temperature, without brake. Red blood cells were slowly depleted. We subsequently removed aliquots to evaluate lymphomononuclear cell recovery.

RESULTS: Thirty-three procedures of erythrocyte removal were performed, 18 for unrelated and 15 for related HCT. There were 30 pediatric patients, median age of 8 years (0.1 - 16), median weight 27Kg (9 - 68), 17 males and 3 adults aged 19, 43 and 46 years, median weight 66.2Kg (50 - 94), all female. Most patients had hematological malignancies, but 3 with bone marrow failure. The result of erythrocyte removal is shown in Table 1. We could reduce the hematocrit from 30% to 10% and recover 93% of the mononuclear cells.

CONCLUSION: Red blood cell depletion performed with 6%-Voluven® HAES is a safe procedure that allowed the reduction of the hematocrit with excellent mononuclear cell recovery.

Keywords: Allogeneic transplantation. Lymphomononuclear cells. Erythrocyte depletion.

TABLE 1. Results of Erythrocyte removal.

	Median (variation)		
	Original Marrow Graft	**Post Erythrocyte Removal**	**Recovery**
Volume (ml)	848 (347 - 1925)	827 (222 - 1704)	
Hematocrit (%)	29,9 (19 - 41,4)	10 (7,9 - 24,5)	35% (23-77)*
Total nucleated cells (x109)	21,5 (6,6 - 47,9)	19,1 (6 - 41,9)	89% (71 - 100)
Total mononuclear cells (x109)	8,5 (1 - 16,3)	7,4 (1 - 13)	93% (73 - 100)
Total granulocytes (x109)	12,7 (2,6 - 33,8)	11,6 (1,9 - 30,4)	87% (64 - 100)

*Or 65% depletion

VALIDATION OF LONGER FRESH STORAGE TIME FOR PERIPHERAL BLOOD STEM CELLS INTENDED FOR CLINICAL USE

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INTRODUCTION: Peripheral blood stem cells (PBSC) storage conditions may influence cell quality and/or functionality, which may directly impact recipients' clinical outcomes. Thus, the Brazilian Health Regulatory Agency (ANVISA) demands validation of fresh storage times greater than 48 (forty-eight) hours, with technical-scientific evidence about the quality and safety of the product.

OBJECTIVE: The aim of this study was to verify the effects of longer fresh storage times in the viability and functionality of PBSC intended for Hematopoietic Progenitor Cells (HPC) transplantation.

METHODS: Ten aliquots of PBSC units were analyzed. The samples were storage fresh at 2ºC to 8ºC. Measurements were performed immediately and 72 h after PBSC collection, by flow cytometry analysis and clonogenic assays. CD45+ and CD34+ cells viability, white blood cells (WBC) counts and CD34+ cell concentrations and colony forming units (CFU) were evaluated. A descriptive analysis and T-dependent test were performed (SPSS 15 software). All clonogenic assays were performed in duplicate with 1x104 cells/mL. The results these assays were expressed as the arithmetical mean of the duplicates.

RESULT: The median time of fresh storage was 72 hours. Despite the significantly decreased CD45+ cells viability after storage, no significative changes were noted in CD34+ cell viability, as well as in WBC and CD34+ cell concentrations. (Table 1). Moreover, no significant decrease in colony-forming unit numbers was observed in units stored for 72 hours.

CONCLUSION: These results lead to the assumption that the fresh storage time of 72 hours had no significative impact in variables of concern (CD34+ cells and clonogenic assays) and thus does not impact the quality and safety of the product. Nonetheless, despite the strong recommendation of infusing fresh graft as soon as possible, our data suggest that, when necessary, it is safe to use PBSC until 72h after collection.

Keywords: Hematopoietic Progenitor Cells. Peripheral Blood Stem Cells. Bone Marrow Transplantation. Fresh Storage.

TABLE 1. Analysis results of variables immediately after collection and after fresh storage.

Variables	Immediately Collection median (min- max)	After Storage median (min- max)	P value
Storage time	-	72:00 (69:25 – 91:48)	-
% CD45+ viable cells	98,3 (94,5-99,3)	90,4 (78,5-97,1)	<0,0001
% CD34 viable cells	100 (98,8-100)	99,75 (97,1-100)	0,073
WBC/µl	248350 (76370-402880)	242705 (81900-398530)	0,737
CD34x106/kg	5,24 (1,67-10,51)	4,67 (1,38-9,18)	0,157
CFU (1x104/mL)	34,5 (9,5-114)	21,5 (4-102)	0,584

HISTOCOMPATIBILITY

ALLELECHECKER 2.0: AN IMPROVED TOOL TO CLASSIFY BONE MARROW DONORS ALLELES ACCORDING TO THE NEW CIWD 3.0 HLA LIST

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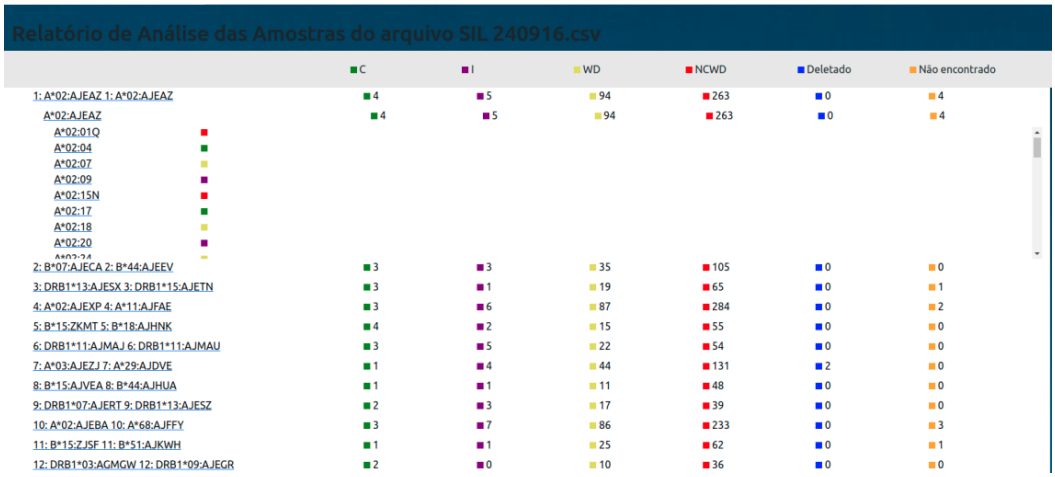
AIM: AlleleChecker was developed to avoid the upload of faulty information in genetic databases. To achieve that, it receives a CSV file containing HLA alleles for bone marrow donors for loci A, B, C, DRB1 and DBQ1 and generate a report for each sample (donor) classifying each allele as Common (C), Well-Documented (WD), Not Common nor Well-Documented (NCWD), Removed from CWD and NCWD list or not found. Therefore, for example, the user can verify if an allele not found or NCWD is really a rare allele or there was an error in the HLA typing or typo. This new AlleleChecker version was updated to use the brand new CIWD 3.0 list, instead of the old CWD. Thus, the Intermediate classification (I) was added to the tool. Moreover, on the original tool the analysis was based only on the two first fields of an allele. Now, for the high resolution samples, the complete allele is compared and classified.

METHODS: A program in Ruby language was developed to perform the allele classification. In the case of medium-resolution samples, that uses the NMDP code, the system checks all possible alleles related to that NMDP code, producing a list of C, I, WD and NCWD counters, and specifically classifying each possible allele according to one of these categories. To make AlleleCkecker user's work easier, a report in the form of a CSV file is also generated, so that the lab technician can double-check the analysis on donors that presented NCWD or not found alleles, for example. The system also allows administrator users to update CIWD and NCWD allele lists as well as the list of NMDP codes, to ensure that the data referring to these files is always as up-to-date as possible.

RESULTS: The figure below shows an example of an analysis report produced by AlleleChecker with the new Intermediate (I) field. The new system is being used by the HLA lab of Rio de Janeiro State University.

CONCLUSIONS: The allele classification allows technicians and researchers to identify possible errors in the analysis or typos more quickly and, therefore, help to improve the quality of data stored in the Brazilian National Registry of Bone Marrow Donors (REDOME).



Relatório de Análise das Amostras do arquivo SIL 240916.csv

	C	I	WD	NCWD	Deletado	Não encontrado
1: A*02:AJEAZ 1: A*02:AJEAZ	4	5	94	263	0	4
A*02:AJEAZ	4	5	94	263	0	4
A*02:01Q						
A*02:04						
A*02:07						
A*02:09						
A*02:15N						
A*02:17						
A*02:18						
A*02:20						
2: B*07:AJECA 2: B*44:AJEEV	3	3	35	105	0	0
3: DRB1*13:AJESX 3: DRB1*15:AJETN	3	1	19	65	0	1
4: A*02:AJEXP 4: A*11:AJFAE	3	6	87	284	0	2
5: B*15:ZKMT 5: B*18:AJHNK	4	2	15	55	0	0
6: DRB1*11:AJMAJ 6: DRB1*11:AJMAU	3	5	22	54	0	0
7: A*03:AJEZJ 7: A*29:AJDVE	1	4	44	131	2	0
8: B*15:AJVEA 8: B*44:AJHUA	1	1	11	48	0	0
9: DRB1*07:AJERT 9: DRB1*13:AJESZ	2	3	17	39	0	0
10: A*02:AJEBA 10: A*68:AJFFY	3	7	86	233	0	3
11: B*15:ZJSF 11: B*51:AJKWH	1	1	25	62	0	1
12: DRB1*03:AGMGW 12: DRB1*09:AJEGR	2	0	10	36	0	0

EVALUATION OF NANOTYPE - A NANOPORE-BASED NGS KIT FOR HLA HIGH-RESOLUTION TYPING

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INTRODUCTION: It is available a new nanopore-based DNA sequencing technology. Traditional methods are only able to sequence short lengths of DNA which must then be reassembled. It is therefore difficult to sequence repetitive regions for accurate genome assemblies without gaps, resolve large structural variations, or differentiate isoforms. Nanopore sequencing is limited only by the length of the DNA/RNA fragment presented to the pore and can resolve the above difficulties. Protein nanopores are tiny holes, that in nature form gateways across membranes. In the current approach, protein nanopores are embedded into a synthetic membrane bathed in an electrophysiological solution and an ionic current is passed through the nanopores. As molecules such as DNA moves through the nanopores, they cause disruption in the current. This signal can be analyzed in real-time to determine the sequence of bases in the strands of DNA passing through the pore. We have identified the potential of Oxford Nanopore technologiesTM (ONT) sequencing and developed a kit for the HLA genotyping applicable to clinical laboratories.

GOALS: The goal of this study was to evaluate the accuracy of genotyping using the ONT-based kit - NanoTYPETM - developed by OMIXON BIOCOMPUTING Ltd. (Budapest – Hungary).

METHOD: We have collected 96 samples with known reference HLA profiles of 11 loci previously tested by HolotypeTM HLA kit on a 4-field resolution. We used the NanoTYPE v1 kit to amplify the same 11 loci and prepared the library for sequencing on the MinION Mk1b (ONT) device using the Rapid Barcoding Kit 96 (ONT). We used the HLA TWIN software for analysis, which was specifically developed for long-read sequencing.

RESULTS: NanoTYPETM is being developed to provide 2 to 3-fields high-resolution HLA typing in a faster way. Among 96 samples we have identified a single failed-to-amplify case. We have typed 2112 alleles in total. The overall concordance reached 99.5% measured at the 2-field resolution. The concordance of individual loci was as following: 100 % HLA-A, 100 % HLA-B, 100 % HLA-C, 99.5 % HLA-DQA1, 97.4 % HLA-DQB1, 100 % HLA-DPA1, 99.0 % HLA-DPB1, 100 % HLA-DRB1, 99.5 % HLA-DRB3, 99.0 % HLA-DRB4, 100 % HLA-DRB5.

CONCLUSION: Based on the initial evaluation, NanoTYPETM kit is bringing a new powerful genotyping tool that is able to genotype HLA genes on 2 to 3-field resolution with superior accuracy and in a faster way. This evaluation study showed that one sample can be typed by NanoTYPETM in under 5 hours, and up to 24 samples can be batched and results obtained within 2 working days. The new NanoTYPETM v2, in its final stages of development, is expected to improve the results even more.

IMPLICATIONS IN THE USE OF BUCCAL MUCOSA CELLS AS A PRE-TRANPLANT SAMPLE IN THE ANALYSIS OF CHIMERISM

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Chimerism analyses with molecular techniques are strategies for monitoring donor and recipient cell levels after hematopoietic stem cell transplantation (HSCT). The basic principle for detecting chimerism lies in distinguishing differences between donors and recipients using genetic markers as short tandem repeats (STR). The profile of the STR markers of the post-HSCT sample is compared to the profile of the donor and recipient's pre-HSCT samples. In the absence of a pre-HSCT sample of peripheral blood (PB), cells from the buccal mucosa collected from the recipient after HSCT can be used as an alternative. This sample depicts the individual's constitutional pattern of STR markers and may eventually replace PB collection in the pre-HSCT period. This study aimed to describe the strategy used to assess the level of post-HSCT chimerism of a patient, using the information from the STR markers of the buccal swab (BS) sample contaminated with donor cells, as well as to emphasize the importance of establishing a collection protocol for PB samples from the patient before HSCT. In this case report, a 2-year-old female patient diagnosed with Krabbe disease underwent HSCT with the unrelated umbilical cord blood in 2021. Pre-transplant PB samples from the recipient and umbilical cord blood from the donor were unavailable for STR profiles. Thus, BS and PB were collected on D+30 post-HSCT to assess chimerism. During the analysis, contamination of donor cells in the BS sample was identified. This sample would be used as a pre-HSCT reference. A new BS sample was collected. However, contamination with donor cells persisted. Due to the BS sample containing STR alleles from the patient and donor, it was impossible to determine to whom the STR alleles detected in the post-transplant sample belonged. If we infer that certain alleles corresponded to the pre-HSCT sample and eliminate the others considered to be contaminants, comparing this profile with the post-HSCT sample would lead to the interpretation of the result of 100% donor cells. If other alleles are considered to belong to the pre-HSCT sample, the result would indicate an autologous recovery. The strategy to elucidate the case was requesting PB collection from the parents. The analysis of the profile of the parent's STR markers compared to the pre-HSCT sample of the recipient's mouth swab allowed us to identify which alleles were inherited by the patient. The chimerism analysis on D+30 allowed us to determine that the post-HSCT profile differed by 100% from the recipient's constitutional profile, indicating the establishment of the graft. This case demonstrates the importance of standardizing sample collection protocols for analyzing pre-HSCT chimerism of recipients and donors. Thus, making the analysis safer and more efficient to prevent recollections and retests that generate additional costs and delays in releasing the chimerism evaluation results.

Keywords: Buccal swab. Post-transplant chimerism. STR markers. Contamination of donor cells.

INTERLABORATORIAL COMPLEMENT-DEPENDENT CYTOTOXICITY CROSSMATCH AND FLOW CYTOMETRIC CROSSMATCH OF CADAVERIC DONORS IN RIO DE JANEIRO STATE

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Since the discovery that MHC polymorphisms can induce immune responses that have detrimental effects on graft outcomes, multiple advances have occurred in our knowledge of the HLA system and its role in allogeneic transplantation. First the complement-dependent cytotoxicity (CDC) test became standard protocol for determining eligibility for a specific renal allograft and HLA matching was shown to improve graft survival and to limit sensitization in patients. Also, the studies brought advances showing that cross reactivity among HLA antigens occurs to be due to epitopes that are shared between different HLA molecules. For this the flow-cytometric crossmatch (FCXM) shows greater sensitivity than the CDC crossmatch and identifies additional antibodies that are associated with reduced graft survival. We evaluate the importance of joint analysis of CDC and FCXM techniques including PRA analysis. For this interlaboratory study, 50 cases of cadaveric donors with recipients on the waiting list belonging to the Rio de Janeiro state transplant program (PET-RJ) were initially evaluated. Each donor had their blood collected in an ACD tube and the CDC and FCXM tests were performed according to the waiting list provided by the program. The serum collection of patients who were on the waiting list were collected up to 6 months, in addition we also correlated the results obtained in the PRA analysis for specific antibodies against the possible donor. Among the cases, we observed that there was a similarity in the HLA typing of class I in 63% of the cases and of class II in 74% of the cases. CDC tests were 81% of negative. The results obtained in the FCXM exam presented a percentage of 69% of negative results. The comparison of crossmatch tests by CDC and FCXM showed 75% of the results in agreement and 25% of the results obtained with negative CDC showed positive FCXM. Among the patients on the waiting list, 66% have negative PRA results for class I and for class II, but only 66% were negative for both class I and class II. Our results confirmed that the FCXM test is more sensitive than the CDC and, in both cases, a complementary analysis should be performed in search of specific antibodies against the donor. We hope to increase the number of tests evaluated and thus conduct a broader study of the importance of pre-transplant tests.