Analysis of the survival of patients undergoing Allogeneic Hematopoietic Progenitor Cell Transplantation before and during the COVID-19 Pandemic in a Hospital in Rio de Janeiro

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Análise da Sobrevida de Pacientes Submetidos a Transplante Alogênico de Células Progenitoras Hematopoiéticas na Pré e na Pandemia de Covid-19 em um Hospital do Rio de Janeiro

Análisis de la Supervivencia de Pacientes Sometidos a Trasplante Alogénico de Células Progenitoras Hematopoyéticas antes y durante la Pandemia de COVID-19 en un Hospital de Río de Janeiro

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ABSTRACT

Introduction: The COVID-19 pandemic has changed the dynamics of graft conservation and performance of allogeneic hematopoietic progenitor cell transplantation (HPCT), which may have affected patient survival. **Objective:** To analyze the survival of patients after immediate post-HPCT (100 days after HPCT) according to exposure to different types of transplants and graft sources, before and during the COVID-19 pandemic. **Method:** Hospital-based retrospective cohort study with 246 patients who underwent HPCT at a referral hospital in the city of Rio de Janeiro between January 2016 and December 2021. The log-rank and Kaplan-Meier methods were used to estimate the survival functions of immediate post-HPCT. **Results:** The mortality rate was slightly higher during the pandemic when compared to pre-pandemic (10.1% *vs.* 8.8%). The graft most utilized throughout the period investigated was bone marrow (BM, 85%). However, during the pandemic, 50.5% of allogeneic collections were performed using mobilized peripheral blood (MPB). Eight percent of cryopreserved grafts were not infused. No differences in survival were observed among patients who used MPB as a graft source compared to BM. **Conclusion:** Graft types and transplant sources did not influence patient survival in either period. Cryopreservation proved to be an important tool to overcome the logistical challenges associated with the COVID-19 pandemic, however, a relevant percentage of cryopreserved grafts were not used. Therefore, transplantation centers should resume HPCT with fresh products, reducing the percentage of grafts unused.

Key words: COVID-19; Bone Marrow Transplant; Cryopreservation; Survival.

RESUMO

Introdução: A pandemia de covid-19 alterou a dinâmica de conservação dos enxertos e de realização dos transplantes de células progenitoras hematopoiéticas (TCPH) alogênicos, o que pode ter afetado a sobrevida dos pacientes. **Objetivo:** Analisar a sobrevida dos pacientes pós-TCPH imediato (100 dias pós-TCPH) segundo a exposição aos diferentes tipos de transplantes e fontes de enxerto, na pré-pandemia e na pandemia de covid-19. **Método:** Estudo de coorte retrospectivo de base hospitalar com 246 pacientes que realizaram TCPH em hospital de referência no município do Rio de Janeiro entre janeiro/2016 e dezembro/2021. Os métodos de *log-rank* e Kaplan-Meier foram utilizados para estimar as funções de sobrevida de pós-TCPH imediato. **Resultados:** A taxa de mortalidade foi ligeiramente superior na pandemia quando comparada à pré-pandemia (10,1% *vs.* 8,8%). O enxerto mais utilizado em todo o período estudado foi medula óssea (MO) com 85%. Porém, na pandemia, 50,5% das coletas alogênicas foram realizadas utilizando o sangue periférico mobilizado (SPM). Oito por cento dos enxertos criopreservados não foram infundidos. Não foram observadas diferenças na sobrevida entre pacientes que utilizaram SPM como fonte de enxerto em relação à MO. **Conclusão:** Os tipos de enxerto e as fontes de transplantes não influenciaram a sobrevida dos pacientes em ambos os períodos. A criopreservação se apresentou como uma ferramenta importante para superar os desafios logísticos ligados à pandemia de covid-19, porém, um percentual relevante de enxertos criopreservados não foi utilizado. Assim, é necessário que os centros transplantadores voltem a realizar TCPH com produtos frescos, reduzindo o percentual de inutilização dos enxertos.

Palavras-chave: COVID-19; Transplante de Medula Óssea; Criopreservação; Sobrevida.

RESUMEN

Introducción: La pandemia de COVID-19 cambió la dinámica de conservación del injerto y la realización de trasplantes alogénicos de células progenitoras hematopoyéticas (TCPH), lo que puede haber afectado la supervivencia de los pacientes. **Objetivo:** Analizar la supervivencia de los pacientes inmediatamente después del TCPH (100 días después del TCMH) según la exposición a diferentes tipos de trasplantes y fuentes de injerto, antes de la pandemia y durante la pandemia de COVID-19. **Método:** Estudio de cohorte retrospectivo hospitalario con 246 pacientes sometidos a TCPH en un hospital de referencia de la ciudad de Río de Janeiro entre enero/2016 y diciembre/2021. Se utilizaron los métodos log-rank y Kaplan-Meier para estimar las funciones de supervivencia inmediatas post-TCPH. **Resultados:** La tasa de mortalidad fue ligeramente mayor durante la pandemia en comparación con la prepandemia (10,1% vs. 8,8%). El injerto más utilizado durante todo el periodo estudiado fue el de médula ósea (MO, 85%). Sin embargo, durante la pandemia, el 50,5% de las recolecciones alogénicas se realizaron utilizando la sangre periférica movilizada (SPM). El ocho por ciento de los injertos criopreservados no fueron infundidos. No se observaron diferencias en la sobrevida entre los pacientes que utilizaron SPM como fuente de injerto en relación con la MO. **Conclusión:** Los tipos de injerto y fuentes de trasplantes no influyeron en la supervivencia de los pacientes en ambos períodos. La criopreservación se presentó como una herramienta importante para superar los desafíos logísticos relacionados con la pandemia de COVID-19, sin embargo, un porcentaje relevante de injertos criopreservados no fue utilizado. Por lo tanto, es necesario que los centros de trasplantes vuelvan a realizar TCPH con productos frescos, reduciendo el porcentaje de injertos que quedan inutilizables.

Palabras clave: COVID-19; Trasplante de Médula Ósea; Criopreservación; Supervivencia.

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INTRODUCTION

COVID-19, initially identified in China in December 2019[1], is a highly transmissible infectious disease that quickly spread throughout the world. On February 3, 2020, Brazil's Ministry of Health declared a Public Health Emergency of National Concern due to the human infection by the SARS-CoV-2 virus[2].

Brazil was the first country in South America to register a case of the disease on February 26, 2020[3]. On March 11, 2020, the World Health Organization (WHO) characterized COVID-19 as a pandemic due to the breakout in every continent[4].

Since then, 38 million cases have been notified and over 700 thousand deaths up until May 10, 2024, placing Brazil as the second country with the greater number of cases and deaths in the world[5] emerging as a new epicenter of the COVID-19 pandemic. This context demanded that health professionals dedicated to cancer treatment redesigned the oncological care to mitigate the potential effects of COVID-19 infection in patients undergoing treatment.

When performing an unrelated allogeneic hematopoietic progenitor cell transplantation (HPCT) there must be a close communication between the collector center and the transplantation center, since this kind of transplantation becomes more complex due to the transportation logistics of collected hematopoietic progenitor cells (HPC) sent to the transplantation center[7].

In normal conditions, most allogeneic HPC grafts collected from related or unrelated donors are infused fresh, while cryopreservation is restricted to exceptional conditions related to donor unavailability[8]. In order to perform risk-free HPCT during the pandemic, the Ministry of Health guided Brazilian transplantation centers to initiate the conditioning regimen in recipients only after the products from related or unrelated donors had been delivered and cryopreserved[9]. This allowed for additional monitoring of the donor in case they were exposed to COVID-19 before the graft infusion[10].

In this scenario, an increase in the cryopreservation of HPC is expected, once this measure minimizes the risk of collecting a cellular product from a donor that tested positive for SARS-CoV-2, as well as the logistic challenges (border closures) imposed by the pandemic, with the aim of ensuring that patients have a graft available at the transplantation day, which can directly impact the survival of transplanted patients.

Thus, the present study aims to analyze the survival of patients after immediate post-HPCT (100 days after HPCT) according to exposure to different types of transplants and graft sources, before and during the COVID-19 pandemic.

METHOD

Hospital-based retrospective cohort study with patients who underwent allogeneic transplants at a HPCT treatment referral hospital in the city of Rio de Janeiro between January 2016 and December 2021. The institution was chosen due to allogeneic HPCT being a high complexity procedure performed by few hospitals in the State of Rio de Janeiro. The hospital cares for adults and children from Rio de Janeiro and other Brazilian regions through the National Health System (SUS).

During the studied period, 287 grafts were collected. Of those, 31 were excluded for not presenting complete information for calculating survival and ten for not being effectively infused. A total of 246 grafts were included in the present study.

Patients were divided in two groups, according to the period in which the transplantation was performed: pre-pandemic group (n=147), from January 2016 to February 2020, in which the HPCT and post-transplantation phase occurred in the pre-pandemic period; and pandemic group (n=99), from March 2020, when the COVID-19 pandemic state was declared in Brazil[11], to December 2021.

The utilized data were extracted from the National Center for Bone Marrow Transplantation (Cemo) of the National Cancer Institute (INCA) through the *Sistema de Gestão do Cemo (SGC)* software, a computerized database management tool developed by the hospital.

The following variables were analyzed according to recipient, donor and graft utilized in the HPCT. The recipient is the patient who needs HPCT; donor is the person whose body is the source of HPC; and graft is the product to be infused in the patient.

The donor variables included the type of donation (related or unrelated to the patient). As to the recipient, the following were analyzed: age group (under 20 years old, 20 to 59, and 60 or over), main diagnosis that led to the transplantation, date of HPCT, time (days) between HPCT and death or end of follow-up (date of censorship), sex (male/female), type of HPC donor (related/unrelated), death (yes/no). The graft variables were original country of the graft, HPC source (bone marrow – BM/mobilized peripheral blood – MPB), cryopreservation (yes/no), graft condition at the moment of infusion (fresh/cryopreserved).

In the method used by the studied hospital unit, cryopreservation is prepared by adding dimethyl sulfoxide (DMSO – 99.9%), hydroxyethyl starch (16.6%) and albumin (20%) in the HPC product, with final concentrations of 5%, 6%, and 2%, respectively. Then, the product is transferred to a cryopreservation pouch (100 mL) and cooled in a freezer to -80°C.

The number of processed allogeneic cell therapy products was estimated according to the evaluated period (2016-2020). Graft frequencies were calculated according to source, processing type and original country according to the pre-pandemic and pandemic periods. Absolute and relative frequencies were also estimated to describe sociodemographic characteristics, main diagnosis and type of HPC donor of the transplanted patients according to the pre-pandemic and pandemic periods. Death distribution was estimated following sex, main diagnosis, type of HPC donor and graft source. Differences in distribution of the analyzed variables were assessed using Pearson's chi-squared (X^2) test. Survival was estimated from the HPC allogeneic transplantation date up to death due to any cause. Survivor patients were censored in the date of their last follow-up, within each group, and up to 100 days after transplantation.

To compare survival in the pre-pandemic *vs.* the pandemic periods, fresh infusion *vs.* cryopreserved infusion, and use of bone marrow *vs.* mobilized peripheral blood, the log-rank statistical method was used. Next, the Kaplan-Meier method was used to estimate the survival probabilities 100 days after transplantation.

All the analyses were performed using software Stata12 (version 17.0). A p-value inferior to 0.05 will be considered significant.

The study has been approved by the Research Ethics Committee of the *Instituto de Estudos e Saúde Coletiva da Universidade Federal do Rio de Janeiro (Iesc/UFRJ)*, approval report number 6609979 (CAAE (submission for ethical review): 54261921.0.0000.5286), and INCA approval report number 5367767 (CAAE (submission for ethical review): 54261921.0.3001.5274), in compliance with Resolution 466/12[13] of the National Health Council.

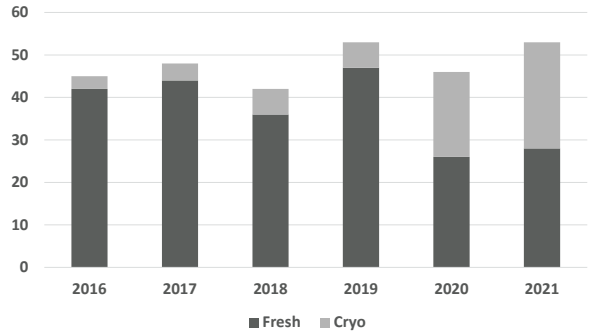
RESULTS

The number of allogeneic cell therapy products processed in the last years of the pre-pandemic period is smaller than the number found in the pandemic period (Graph 1).

Regarding the origin of the unrelated collection of HPC product received for patients undergoing treatment, it was observed that 64.7% of the collections in the pre-pandemic period were carried out in Brazil. As to the pandemic period, the percentage increased to 69.2%.

In the pre-pandemic period, only autologous products were routinely cryopreserved and most allogeneic products were infused fresh (92.5%), which decreased to 54.5% in the pandemic period (Table 1).

Since Brazil was in the COVID-19 pandemic epicenter during the studied period, there was a need to perform



Graph 1. Number of allogeneic cell products processed a year, from 2016 to 2021, in a referral hospital in allogeneic hematopoietic progenitor cell transplantation in the city of Rio de Janeiro (n=287)

Note: Pre-pandemic: Jan/2016 through Feb/2020; pandemic: Mar/2020 through Dec/2021.

alterations to the processing and cryopreservation routines to protect the health and safety of our donors, recipients, and team. As a consequence, in the pandemic period, allogeneic products (related and unrelated) began to be cryopreserved (Table 1).

The type of HPC most used in transplantation throughout the analyzed period was BM (72.8%). However, in the pandemic period, 50.5% of allogeneic collection were performed through MPB, in comparison to 11.6% before the pandemic. There was also a proportional increase in the number of cryopreservation procedures of this type of product. From Mar/2020 to Dec/2021, 45 of the 99 HPC products collected, BM or MPB, (45.5%) were cryopreserved. In the pre-pandemic period, only 7.5% of grafts were cryopreserved (Table 1).

Of the 246 patients submitted to allogeneic hematopoietic progenitor cell transplantation in the studied period, 58.5% were male, 37.4% were aged up to 19 years old, with that being the most frequent in all the periods. As to clinical characteristics, 35.0% presented acute lymphoblastic leukemia (ALL) as the main diagnosis, being the most frequent before and during the pandemic. The most performed HPCT type in both periods were from a related donor (64.6%) (Table 2).

In the pre-pandemic period, 13 patients died. Of those, 76.9% were male, 38.5% were aged 40 to 59 years-old, 69.2% had an ALL diagnosis, 69.2% used BM as HPC source, 76.9% received the product fresh and 61.5% received the product from an unrelated donor. In the pandemic period, ten patients died, which happened mostly to male patients (70%), in the 20 to 39 years-old age group (50%), who had an ALL diagnosis (50%), used MPB as HPC source (60%), received the product fresh (70%) from related donors (80%) (Table 3).

Graph 2 presents the transplanted patients' survival curves. When determining the survival curve by graft condition in the infusion, it was possible to observe that

Table 1. Number (n) and relative frequency (%) according to processing and cryopreservation (cryo) of grafts during the pre-pandemic period (2016-2020)* and pandemic period (2020-2021)** in a HPCT referral hospital in the city of Rio de Janeiro (n=246)

	Pre-pandemic*		Pandemic**		*p****
	n	%	N	%	
Mobilized peripheral blood	**17**	**11.6**	**50**	**50.5**	**<0.0001**
Fresh	12	8.2	21	21.2	
Cryo	5	3.4	29	29.3	
Bone marrow	**130**	**88.4**	**49**	**49.5**	**<0.0001**
Fresh	124	84.3	33	33.3	
Cryo	6	4.1	16	16.2	
Total fresh	136	92.5	54	54.5	<0.0001
Total cryo	11	7.5	45	45.5	
Total	**147**	**100.0**	**99**	**100.0**	

(*) pre-pandemic: Jan/2016 through Feb/2020.
(**) pandemic: Mar/2020 through Dec/2021.
(***) chi-squared test.

Table 2. Sociodemographic characteristics and main diagnosis of patients submitted to transplantation and number of deaths of allogeneic HPC in a HPCT referral hospital in the city of Rio de Janeiro according to the pre-pandemic (2016-2020)* and pandemic (2020-2021)** periods (n = 246)

Variables	Pre-pandemic*		Pandemic**		*P****
	n = 147	%	n = 99	%	
Sex					0.002
Male	90	61.2	54	54.5	
Female	57	38.8	45	45.5	
Age group					0.229
Up to 19 years-old	60	41.0	32	32.1	
20-39 years-old	42	28.7	30	30.1	
40-59 years-old	38	26.1	28	28.2	
60 years-old and over	6	4.2	9	9.1	
Main diagnosis					0.004
Acute lymphoblastic leukemia	52	35.1	34	34.3	
Acute myeloid leukemia	28	19.1	21	21.2	
Chronic myeloid leukemia	10	6.9	8	8.1	
Non-Hodgkin lymphoma	4	2.7	1	1.0	
Hodgkin disease	9	6.4	14	14.1	
Myelodysplastic syndrome	5	3.7	3	3.0	
Others	38	26.1	18	18.2	
HPCT donor					0.404
Related	84	56.9	75	75.8	
Unrelated	63	43.1	24	24.2	
Deaths	13	8.8	10	10.1	

(*) pre-pandemic: Jan/2016 through Feb/2020.
(**) pandemic: Mar/2020 through Dec/2021.
(***) chi-squared test.
HPCT = hematopoietic progenitor cell transplant.

Table 3. Characterization of deaths of patients undergoing allogeneic HPCT in a referral hospital for HPCT in the city of Rio de Janeiro according to the pre-pandemic period (2016-2020)* and the pandemic period (2020-2021)** (n=23)

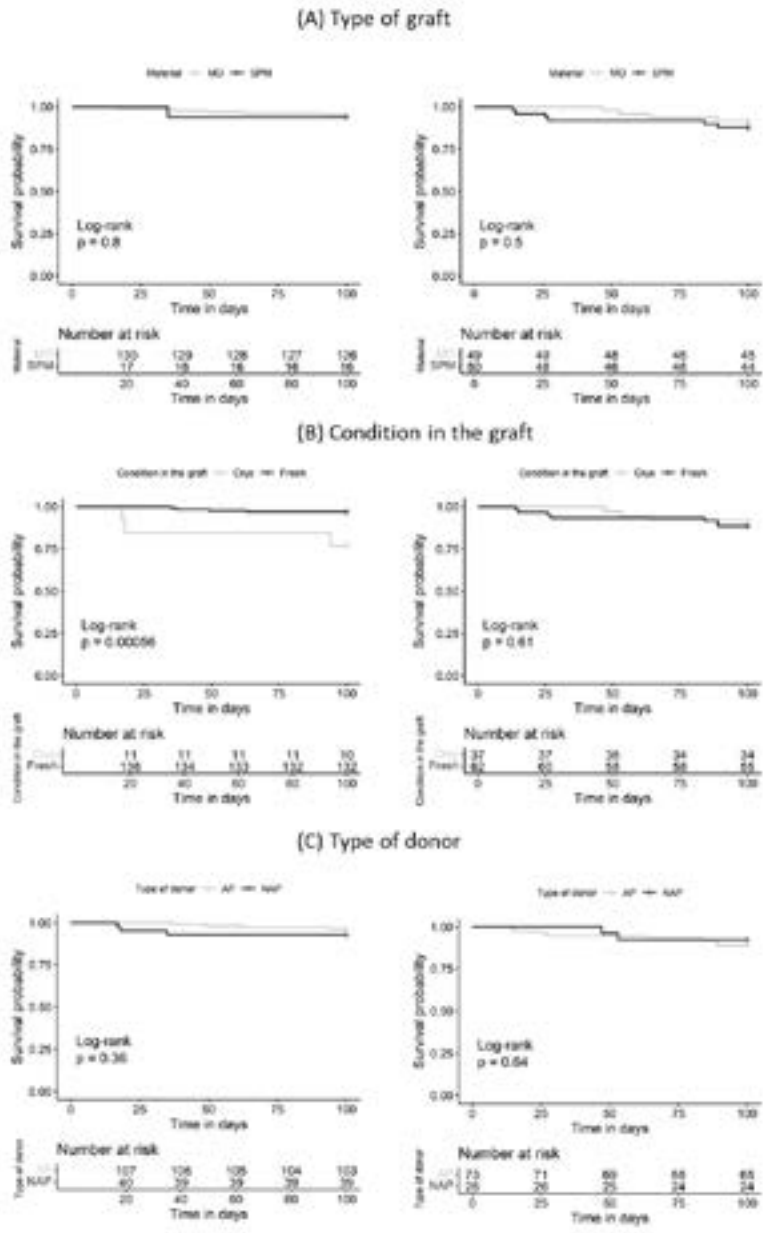
Variables	Pre-pandemic*		Pandemic**		*p****
	n = 13	%	n = 10	%	
Sex					
Male	10	76.9	7	70.0	0.5839
Female	3	23.1	3	30.0	
Age group					
Up to 19 years-old	2	15.4	2	20.0	0.4045
20-39 years-old	4	30.8	5	50.0	
40-59 years-old	5	38.5	1	10.0	
60 years-old and over	2	15.4	2	20.0	
Main diagnosis					
Acute lymphoblastic leukemia	9	69.2	5	50.0	0.2733
Acute myeloid leukemia	1	7.7	4	40.0	
Chronic myeloid leukemia	2	15.4	0	0.0	
Non-Hodgkin lymphoma	0	0.0	0	0.0	
Hodgkin disease	1	7.7	0	0.0	
Myelodysplastic syndrome	0	0.0	0	0.0	
Others	0	0.0	1	10.0	
Graft type					0.3744
Bone marrow	9	69.2	4	40.0	
Mobilized peripheral blood	4	30.8	6	60.0	
Graft condition upon infusion			0.5839		0,5839
Fresh	10	76.9	7	70.0	
Cryopreserved	3	23.1	3	30.0	
HPCT donor			0.0003		0,0003
Related	8	61.5	8	80.0	
Unrelated	5	38.5	2	20.0	

(*) pre-pandemic: Jan/2016 through Feb/2020.
(**) pandemic: Mar/2020 through Dec/2021.
(***) chi-squared test.
HPCT = hematopoietic progenitor cell transplant.

the curve related to the cryopreserved graft was lower than that of the fresh graft in the pre-pandemic period. No difference was observed in the survival curve when comparing the type of donor and the type of graft during the first 100 days post-transplant.

DISCUSSION

In the present study, immediate post-HPCT mortality rates were slightly higher in the pandemic period (10.1%) when compared to the pre-pandemic period (8.8%), with a value above those observed in the literature. Kong et al.[14] indicates that the cumulative incidence rate of 100-day HPCT-related mortality was 8.3%. The survival of patients submitted to HPCT has increased mainly due to improvements in the support offered, in the selection of patients and donors, in the addition to the transplantation techniques used[15,16]. The 100 days after transplantation is a critical period for recovery in which patients face more vulnerability to infections and other acute complications due to progressive leukopenia, making the patient more exposed to bacterial, fungal, viral and parasitic infections[17].



Graph 2. Survival curves 100 days after HPCT in a HPCT referral hospital in the city of Rio de Janeiro in the COVID-19 pre-pandemic* (n=147) and pandemic** (n=99) periods, according to the graft type (A), condition of the graft upon infusion (B) and donor type (C)

(*) pre-pandemic: Jan/2016 through Feb/2020.
(**) pandemic: Mar/2020 through Dec/2021.
MO = bone marrow; SPM = mobilized peripheral blood; AP = related; NAP = unrelated.

The graft types did not influence patient survival when comparing the pre-pandemic and pandemic periods. In contrast, a study by Hsu, et al.[18], who examined 7,379 patients submitted to transplantation from 2013-2018, demonstrated that cryopreserved unrelated MPB grafts showed delayed hematopoietic recovery, increase in recurrence and decrease in survival. Additionally, cryopreserved MPB grafts from related donors showed delayed platelet recovery, inferior overall survival (OS) and higher rates of acute graft-versus-host-disease (GVHD)[18].

When determining survival by graft condition during infusion, it was not possible to observe significant differences in the survival curve for cryopreservation and the fresh curve, in the pre-pandemic and pandemic periods. Studies comparing cryopreserved HPC of MPB *vs.* fresh HPC of allogeneic donor showed similar clinical results in terms of OS, mortality with no recurrence, acute and chronic GVHD and hematopoietic recovery[19,20]. However, Lioznov, et al.[21] showed increased rates of graft failure in the infusions performed with cryopreserved

MPB. In a recent study, Bankova, et al.[22] observed that cryopreserved allogeneic grafts were associated to delayed graft, higher rates of primary graft failure, worse OS and recurrence-free survival.

The COVID-19 pandemic changed the conduction of cell therapy in the country, including the collection and processing of HPC, with the aim of minimizing the risk to donors and recipients. As a result of the guidance provided by the Ministry of Health[9], given the potential risk of COVID-19 exposure and restriction to travels in the period, the choice for fresh BM infusion reduced from 84.3% in the pre-pandemic period to 33.3% during the pandemic; on the other hand, the option for cryopreserved MPB increased from 3.4% to 29.3%. According to the USA National Marrow Donor Program (NMDP), the option for fresh BM reduced 69.9% and, inversely, the choice for cryopreserved MPB showed an expressive increase that corresponded to 811.0%[23].

A change in the graft source preference was observed. Before the pandemic, BM represented 88.4% of processed grafts, while, in the pandemic period, this percentage represented 49.5%. That was observed in other studies that attributed this reduction to logistic challenges during the pandemic[23-25]. This fact may also be related to the need to subject the donor to an invasive procedure under the effect of anesthetics in a surgical center. This modality has been replaced by MPB, since the collection is carried out by a minimally invasive procedure, with the use of a peripheral catheter[26].

In the pandemic, 99 products were processed and 91 infused up to 12/31/2021. As observed, a total of eight cryopreserved grafts were not infused, which means that 8% of donations remained in storage. That result is similar to the one obtained by Allan[27] in Canada, in which approximately 7% of cryopreserved grafts were never infused. A study conducted by the German donor registry center concluded that 5-10% of cryopreserved grafts will not eventually be transfused[28]. This generates ethical concerns for donors, who may have suffered not only inconveniences due to the HPC collection, but also potential exposure to SARS-CoV-2 while being attended at collection centers in areas with high prevalence of the disease[29]. It is worth stressing that fresh cell infusion may reduce the costs associated to processing, cryopreservation, and storage[8].

The number of processed allogeneic cell therapy products has remained relatively constant, a similar result to the one found by Valentini et al.[24] and Tanhehco & Schwartz[30].

The study also characterized the patients regarding sex and age, and found percentages near the three groups, with most of them being male and 33 years-old on average, similar to the results of studies conducted in Minas Gerais and Rio Grande do Norte[31,32]. A study conducted in centers in the USA and Canada, between 2006 and 2012, also showed a greater number of men (63%)[33]. Thus, considering the analyzed studies, a predominance in adult male patients that have been submitted to allogeneic HPCT was observed, converging with the results of this study.

Regarding the diagnosis that most led to allogeneic transplantation, ALL prevailed in both periods (35.1% and 34.34%, respectively), which establishes a direct relationship with the age group of the analyzed patients, since the age group with the greater percentage was that of up to 19 years-old in the analyzed periods (41.0% and 32.1%, respectively). This type of leukemia is the most prevalent in children, with a greater incidence between 2 to 5 years-old, being responsible for 80% of cases in children and 20% in adults[34] and is four times more frequent than acute myeloid leukemia (AML)[35], the second most frequent disease in this study. ALL was also the disease that most claimed lives (69.2% and 50.0%, respectively).

For many authors, HPC cryopreservation can be considered an option in the COVID-19 pandemic, balancing the risks and benefits of the procedure[36,37]. The disadvantages of this procedure are related to the potential toxicity connected to the DMSO cyopreservant, the loss of cell viability and additional costs[38].

A limitation to this study is that, in addition to the cohort heterogeneity, that received a variety of conditioning regimens and GVHD prophylaxis, there was no differentiation among the transplants regarding compatibility to the human leukocyte antigen (HLA). However, this article offers a perspective on how a HPCT referral hospital in Brazil was affected and continued to function efficiently during the COVID-19 pandemic.

CONCLUSION

The study shows scientific evidence relevant to the epidemiological, clinical profile and survival of patients submitted to allogeneic HPCT, considering a context of global crisis such as the COVID-19 pandemic was. The cryopreservation of allogeneic HPC is an important tool in a moment when there was a lot of uncertainties in terms of graft availability and transportation, since it ensured that conditioned patients performed HPCT safely. However, the significant number of non-transfused HPC products is an issue that requires individual attention regarding the best approach for each patient.

Nevertheless, this study indicates that cryopreserved products should be carefully used for allogeneic

transplant, though there was no significant difference in the survival of patients who used fresh products in comparison to those who used cryopreserved products. A longer follow-up and a deeper investigation of those findings are needed to fully explore how cryopreservation and the age of allogeneic grafts can impact the safety and efficacy of the transplant.

Moreover, a detailed investigation that considers the diverse factors that may have contributed to the increase in deaths during the pandemic is needed. The analysis should include aspects such as the impact of COVID-19 in the health conditions of patients, access to medical care, and possible complications deriving from the virus as well as from social isolation measures.

It is important that transplantation centers and unrelated donor registries encourage the practice of fresh HPCT, with the aim of protecting the interests of donors, patients, and minimizing the costs for the institutions.

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CONTRIBUTIONS

Pedro Felipe Couto Vieira contributed to the study design and planning, analysis and interpretation of the data and wording. Jackeline Christiane Pinto Lobato Vasconcelos and Amanda de Moura Souza have contributed to the study design, analysis and interpretation of the data, wording, and critical review. Carla Cristina Pedrosa de Lira contributed to the study design and planning, wording and critical review. Rômulo Gonçalves Galvani and Marina Vieira Agostinho Pereira have contributed to the analysis and interpretation of the data, wording, and critical review. All the authors approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

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