O Impacto da COVID-19 nas Anemias

Luiz Guilherme Darrigo Junior, MD PhD
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Biol Blood Marrow Transplant 26 (2020) 1247–1256

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Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

ASTCT American Society for Transplantation and Cellular Therapy

Guideline

Indications for Hematopoietic Cell Transplantation and Immune Effector Cell Therapy: Guidelines from the American Society for Transplantation and Cellular Therapy

Table 4
Indications for HCT in Pediatric Patients (Generally Age < 18 Years)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Acute myeloid leukemia		
CR1, low risk	N	N
CR1, intermediate risk	C	N
CR1, high risk	S	N
CR2+	S	N
Not in remission	S	N
Acute promyelocytic leukemia, relapse	R	R
ALL		
CR1, standard risk	N	N
CR1, high risk	S	N
CR2	S	N
CR3+	C	N
Not in remission	C*	N
Chronic myeloid leukemia		
Chronic phase	C	N
Accelerated phase	C	N
Blast phase	C	N
Myelodysplastic syndromes		
Low risk	C	N
High risk	S	N
Juvenile myelomonocytic leukemia	S	N
Therapy related	S	N
T cell non-Hodgkin lymphoma		
CR1, standard risk	N	R
CR1, high risk	R	R
CR2	S	C
CR3+	C	C
Not in remission	C	N
Burkitt lymphoma		
First remission	N	N
First or greater relapse, sensitive	C	C
First or greater relapse, resistant	C	N
Hodgkin lymphoma		
CR1	N	N
Primary refractory, sensitive	N	C
Primary refractory, resistant	C	N
First relapse, sensitive	N	S
First relapse, resistant	C	N
Second or greater relapse	C	C
Solid tumors		
Germ cell tumor, relapse	D	C
Germ cell tumor, refractory	D	C
Ewing sarcoma, high risk or relapse	D	S
Soft tissue sarcoma, high risk or relapse	D	D
Neuroblastoma, high risk or relapse	D	S†
Wilms tumor, relapse	N	C
Osteosarcoma, high risk	N	C
Medulloblastoma, high risk	N	C
Other malignant brain tumors	N	C
Nonmalignant diseases		

Table 4 (*Continued*)

Indication and Disease Status	Allogeneic HCT	Autologous HCT
Severe aplastic anemia, new diagnosis	S	N
Severe aplastic anemia, relapse/refractory	S	N
Fanconi anemia	R	N
Other bone marrow failure syndrome‡	R	N
Sickle cell disease	C	N
Thalassemia	S	N
Congenital amegakaryocytic thrombocytopenia	R	N
SCID	R	N
T cell immunodeficiency, SCID variants	R	N
Wiskott-Aldrich syndrome	R	N
Hemophagocytic disorders	S	N
Severe congenital neutropenia	R	N
Chronic granulomatous disease	R	N
Other phagocytic cell disorders	R	N
IPEX syndrome	R	N
Juvenile rheumatoid arthritis	D	R
Systemic sclerosis	D	R
Other autoimmune and immune dysregulation disorders	R	N
Mucopolysaccharidosis I (severe; Hurler syndrome)	R	N
Other mucopolysaccharidoses (II, IV, VI)	D	N
Other lysosomal metabolic diseases	D	N
Osteopetrosis (severe, recessive)	R	N
Osteopetrosis (intermediate)	D	N
Globoid cell leukodystrophy	R	N
Metachromatic leukodystrophy	R	N
Cerebral X-linked adrenoleukodystrophy	R	N

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Germ cell tumor, refractory	D	C
Ewing sarcoma, high risk or relapse	D	S
Soft tissue sarcoma, high risk or relapse	D	D
Neuroblastoma, high risk or relapse	D	S†
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Bone Marrow Transplantation
https://doi.org/10.1038/s41409-020-0919-0

PERSPECTIVE

The challenge of COVID-19 and hematopoietic cell transplantation; EBMT recommendations for management of hematopoietic cell transplant recipients, their donors, and patients undergoing CAR T-cell therapy

Recomendações Gerais

- Cuidados com equipe de saúde
- Postergar tratamento sempre que possível (não malignas?) *Br J Haematol. 2020 May;189(4):635-639.*
- Testar paciente e doadores para SARS-CoV-2 antes do transplante
- Recomenda-se o congelamento do produto antes do início do condicionamento, em situações em que isso não seja possível, ter um doador alternativo-*backup*

Ljungman P et al, BMT, Maio - 2020

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Ljungman P et al, BMT, Maio - 2020

Hematopoietic Cell Transplantation with Cryopreserved Grafts for Severe Aplastic Anemia

Mary Eapen[1,2,*], Mei-Jie Zhang[1,3], Xiao-Ying Tang[1], Stephanie J. Lee[4], Ming-Wei Fei[1], Hai-lin Wang[1], Kyle M. Hebert[1], Mukta Arora[5], Saurabh Chhabra[1,2], Steven M. Devine[6], Mehdi Hamadani[1,2], Anita D'Souza[1,2], Marcelo C. Pasquini[1,2], Rachel Phelan[1,7], J. Douglas Rizzo[1,2], Wael Saber[1,2], Bronwen E. Shaw[1,2], Daniel J Weisdorf[5], Mary M. Horowitz[1,2]

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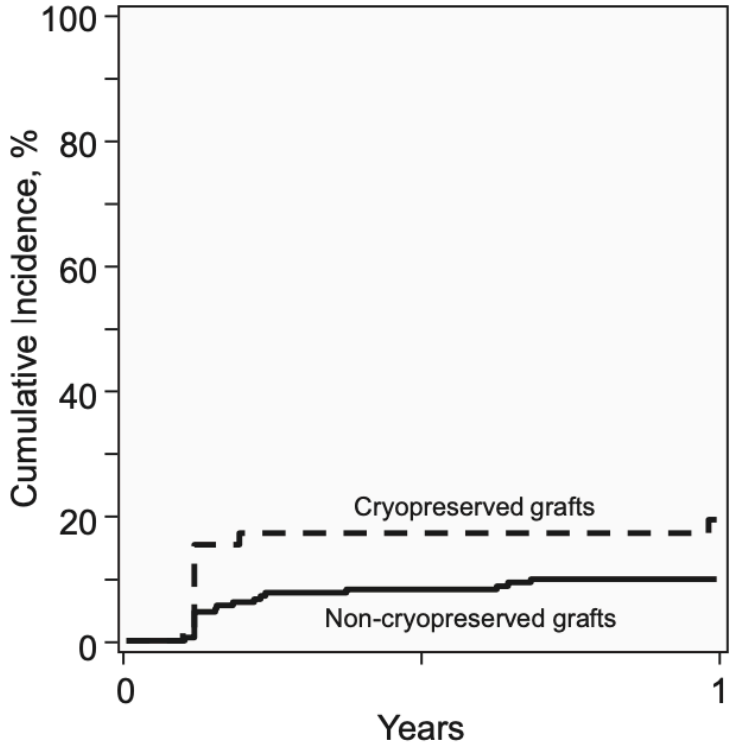
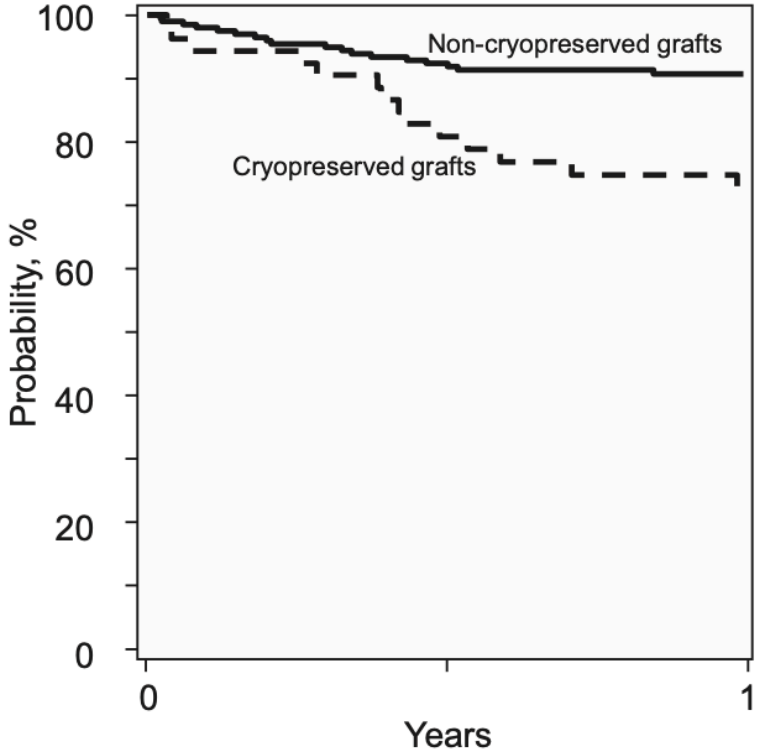


Graft Failure



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Eapen M et al, BBMT, Maio - 2020

Bone Marrow Transplantation
https://doi.org/10.1038/s41409-020-0919-0

PERSPECTIVE

The challenge of COVID-19 and hematopoietic cell transplantation; EBMT recommendations for management of hematopoietic cell transplant recipients, their donors, and patients undergoing CAR T-cell therapy

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- Regime de condicionamento, profilaxia para GVHD e IST pós transplante não devem ser alterados
- Disponibilidade do doador (CTH) pode ser restrito devido à infecção do doador, razões logísticas dos centros de coleta e restrições de viagens (fronteiras internacionais)
- O sangue periférico deve ser usado preferencialmente

Ljungman P et al, BMT, Maio - 2020

Bone Marrow Transplantation
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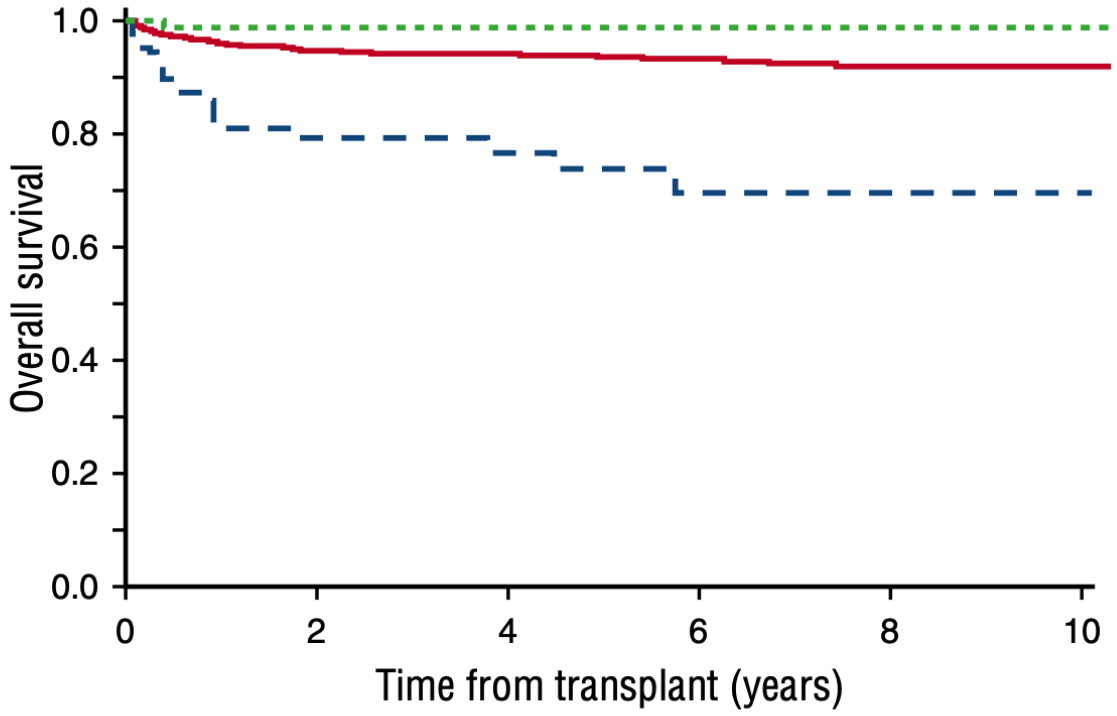
Ljungman P et al, BMT, Maio - 2020

Sickle cell disease: an international survey of results of HLA-identical sibling hematopoietic stem cell transplantation

Eliane Gluckman,[1,2] Barbara Cappelli,[2] Francoise Bernaudin,[3] Myriam Labopin,[4] Fernanda Volt,[1,2] Jeanette Carreras,[5] Belinda Pinto Simões,[6] Alina Ferster,[7] Sophie Dupont,[8] Josu de la Fuente,[9] Jean-Hugues Dalle,[10] Marco Zecca,[11]

American Society of Hematology
Helping hematologists conquer blood diseases worldwide



number of at-risk patients

BM	839	673	546	446	383	322	262	215	177	152	120
PB	73	49	41	33	28	24	14	10	9	7	5
CB	88	81	70	60	47	37	29	27	24	17	13

Gluckman et al. Blood, 2017

Bone marrow *versus* peripheral blood as the stem cell source for sibling transplants in acquired aplastic anemia: survival advantage for bone marrow in all age groups

Andrea Bacigalupo,[1] Gérard Socié,[2] Hubert Schrezenmeier,[3] Andre Tichelli,[4] Anna Locasciulli,[5] Monika Fuehrer,[6] Antonio M. Risitano,[7] Carlo Dufour,[8] Jakob R. Passweg,[4] Rosi Oneto,[1] Mahmoud Aljurf,[9] Catherine Flynn,[10] Valerie

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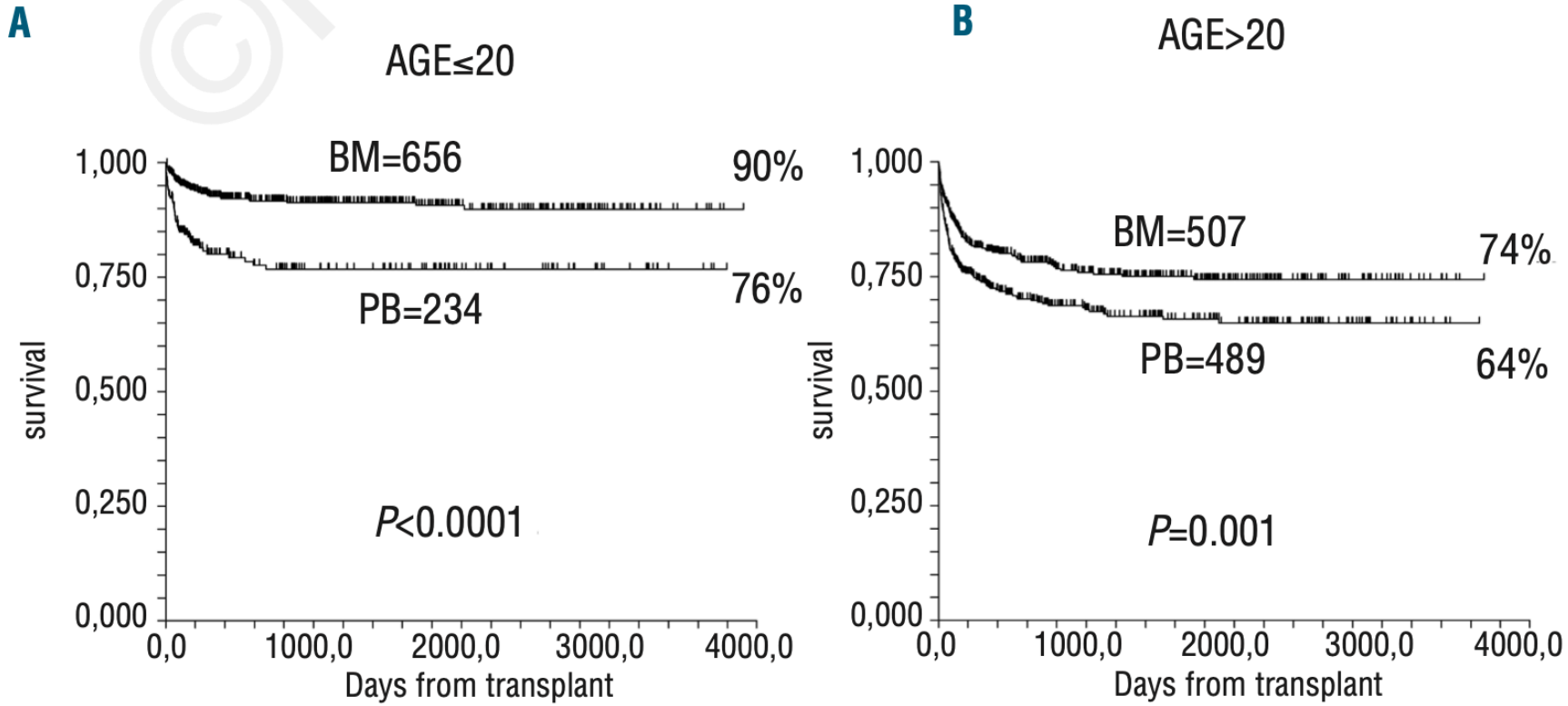

Bacigalupo A et al. Hematologica, 2012

Outcomes after related and unrelated umbilical cord blood transplantation for hereditary bone marrow failure syndromes other than Fanconi anemia

Renata Bizzetto,[1,2] Carmen Bonfim,[3] Vanderson Rocha,[1,4] Gérard Socié,[4] Franco Locatelli,[5] KaWah Chan,[6] Oscar Ramirez,[7] Joel Stein,[8] Samir Nabhan,[3] Eliana Miranda,[2] Jakob Passweg,[9] Carmino Antonio de Souza CA,[2] Eliane Gluckman[1] on behalf of Eurocord and SAA-WP from EBMT*

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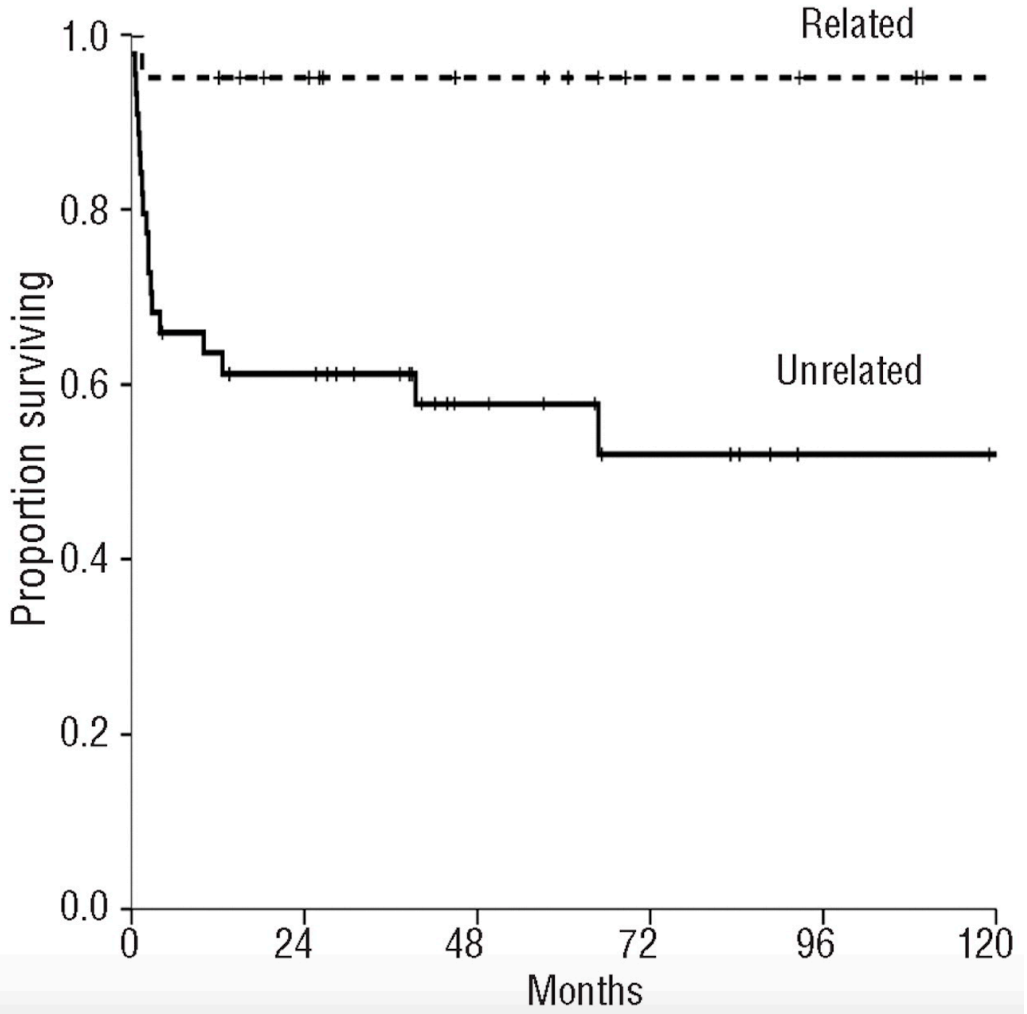

Bizzetto R et al. Hematologica, 2011

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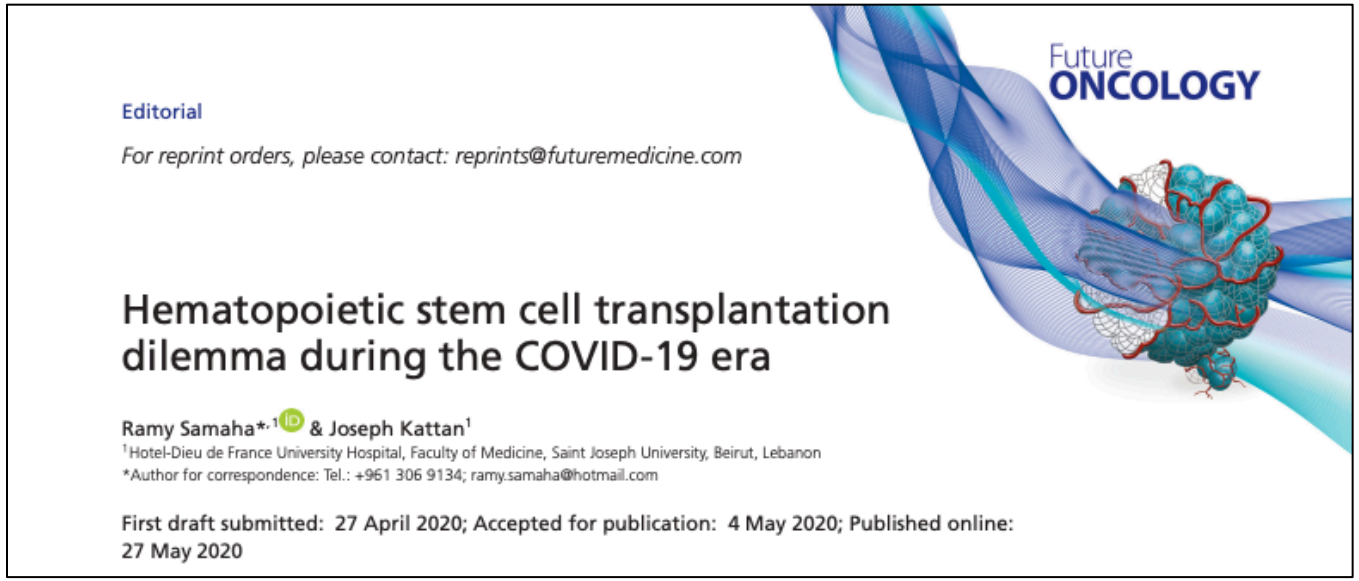
Recomendações Gerais

- Desenvolver no **pós transplante** medidas para diminuir exposição ao SARS-CoV-2
  - Telemedicina
  - *Homecare*
  - Evitar visitas
  - Repetir exames dos cuidadores?
  - Equipe restrita a área *COVID-19 free*

Ljungman P et al, BMT, Maio - 2020



Editorial

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Future ONCOLOGY

Hematopoietic stem cell transplantation dilemma during the COVID-19 era

Ramy Samaha*,[1] & Joseph Kattan[1]
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*Author for correspondence: Tel.: +961 306 9134; ramy.samaha@hotmail.com

First draft submitted: 27 April 2020; Accepted for publication: 4 May 2020; Published online: 27 May 2020

- Recommendation for COVID-19 and hematopoietic stem cell transplantation
  - **ASTCT**
  - **EBMT**

Recommendation for COVID-19 and hematopoietic stem cell transplantation (ASTCT and EBMT).

	ASTCT	EBMT
HSCT recipient		
SARS-Cov2-positive	HSCT deferred until patient is asymptomatic and two negative PCR tests are obtained at least 1 week apartConsider minimum intensity conditioning regimen	Low risk of disease: deferred for 3 months
		High-risk of disease: deferred until patient is asymptomatic and two negative PCR at least 24 h apart
Close contact with SARS-Cov2-positive person or travel to high-risk area according to CDC or close contact with a person who has traveled to high-risk area	Deferred for 14–21 days of last contact, or two negative PCR tests are obtained at least 1 week apartClose monitoring for symptoms	Low risk of disease: deferred for 14–21 days of last contact
		High-risk of disease: deferred for 14–21 days of last contact according to clinical judgment
		A negative PCR must be confirmed before proceeding
High prevalence of COVID-19 in community	SARS-Cov2 PCR at initial evaluation and 2 days before conditioning	
	Consider interim treatment or longer deferral when possible	

Doador

Donor		
SARS-Cov2-positive	Donor is ineligibleWill be eligible again if asymptomatic after 28 days and a negative PCR	Donor is excluded and duration is unclear
Close contact with SARS-Cov2-positive person or travel to high-risk area according to CDC or close contact with a person who has traveled to high-risk area	Excluded for 28 days	
	In high-risk situation donor may be considered eligible if asymptomatic with a negative PCR. Close follow-up	Excluded for 28 daysException is made if bone marrow transplant is urgent and donor asymptomatic with a negative PCR and no other eligible donors: earlier collection is possible

Survey of HSCT protocols in Brazilian units in the face of the SARS-CoV-2 pandemic

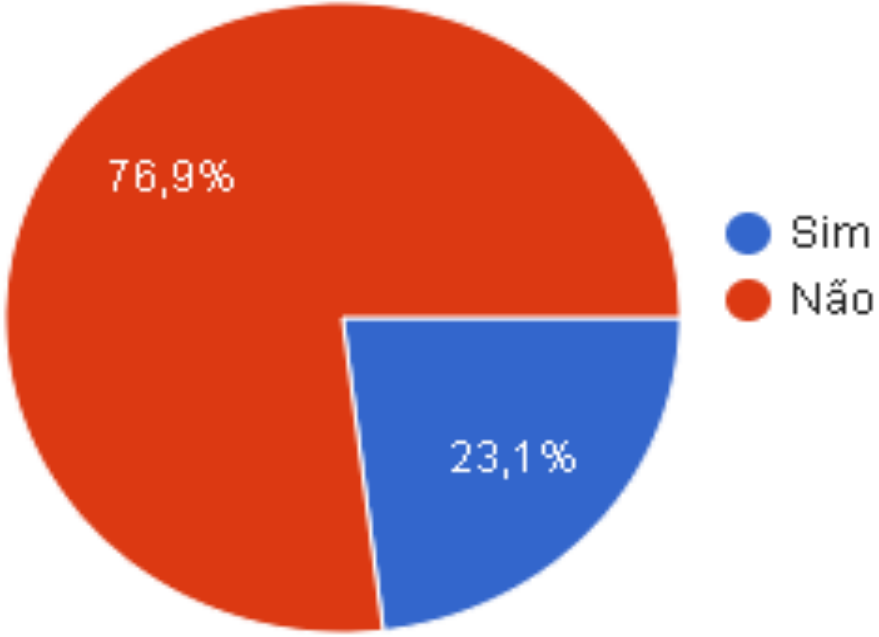
- ✓ Observational and cross-sectional study, managed in May and **June 2020**, using a questionnaire sent to transplant centers:

- ✓ 52 centers answered (total of 86) in June 2020 = aprox. 60%

Submitted, May/2020

Did you have patients who developed COVID-19 during intra-transplantation?

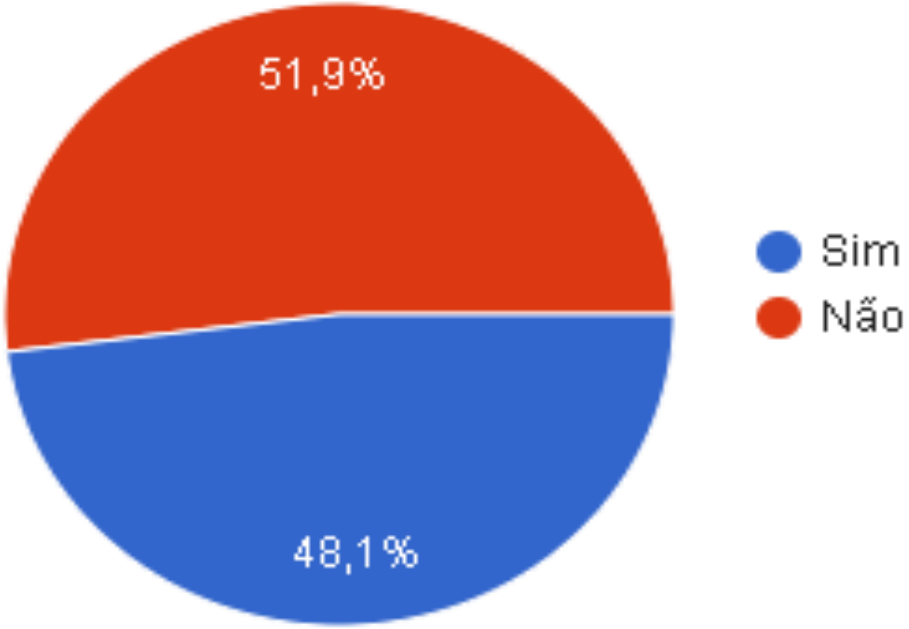
June 2020



Submitted, May/2020

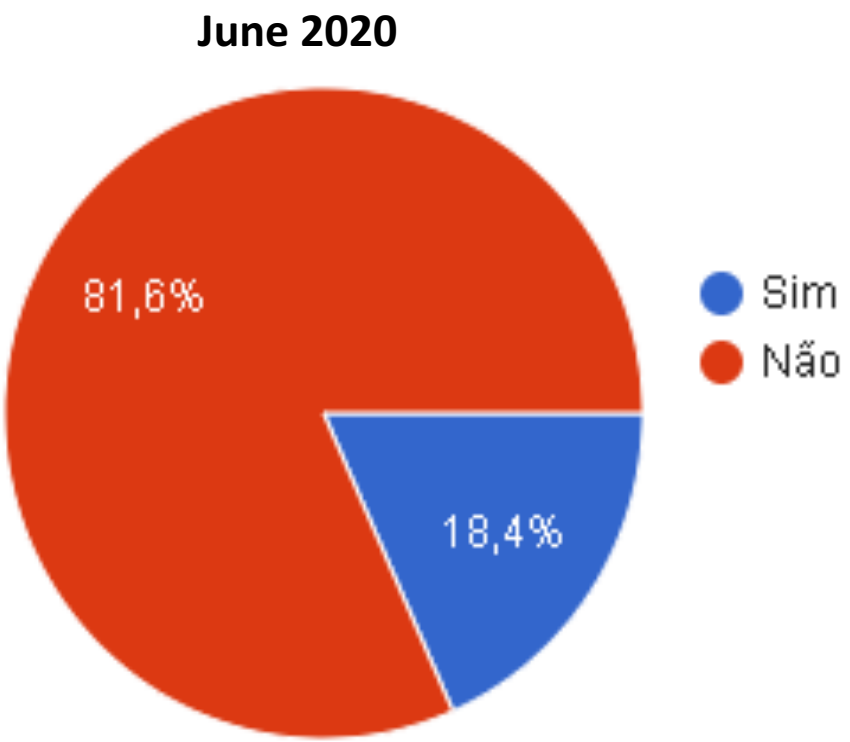
Did you have patients who developed COVID-19 in the post HSCT?

June 2020



Submitted, May/2020

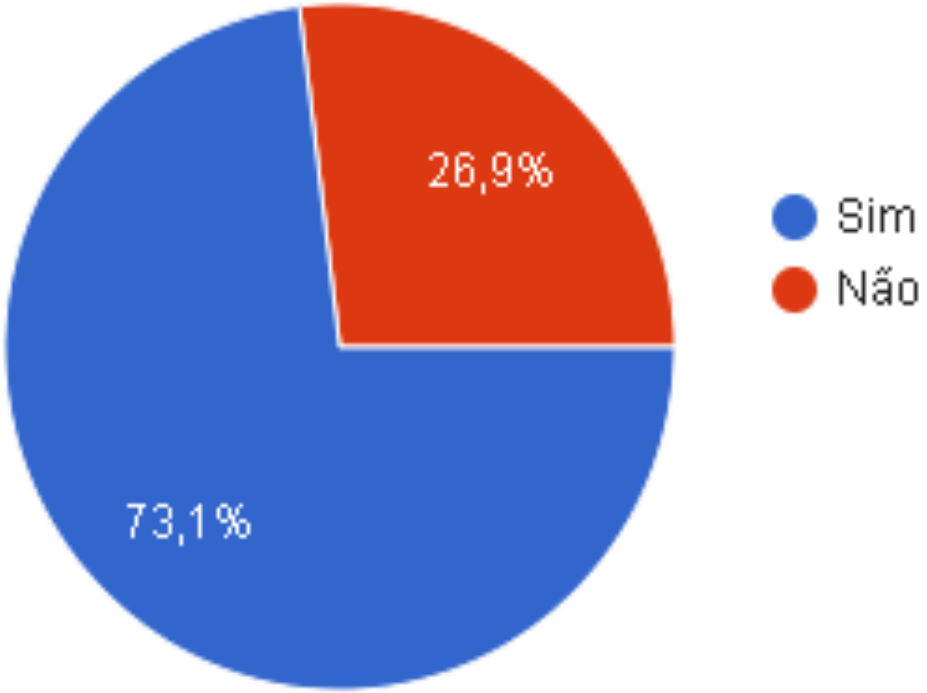
There was death due to COVID-19 in the intra or post HSCT?



Submitted, May/2020

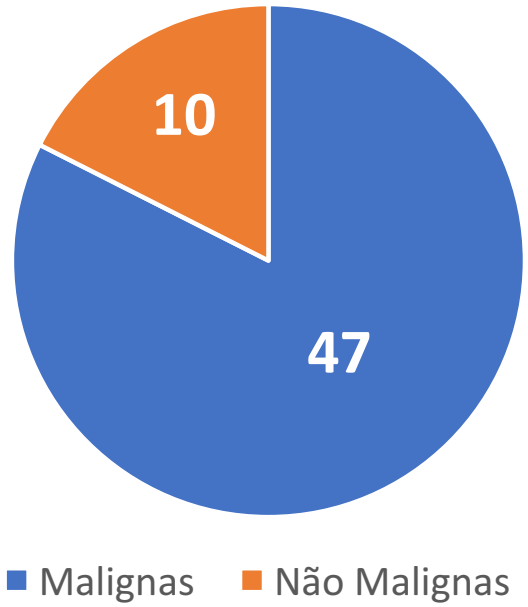
There were health professionals who contaminat with COVID-19?

June 2020



Submitted, May/2020

Estudo Colaborativo de COVID-19 em TCTH no Brasil



- Anemia Aplásica Adquirida: 2
- Anemia aplásica constitucional: 1
- Talassemia: 1
- Anemia falciforme: 1
- Imunodeficiência primária: 5

Contatos:

mmichalowski@hcpa.edu.br

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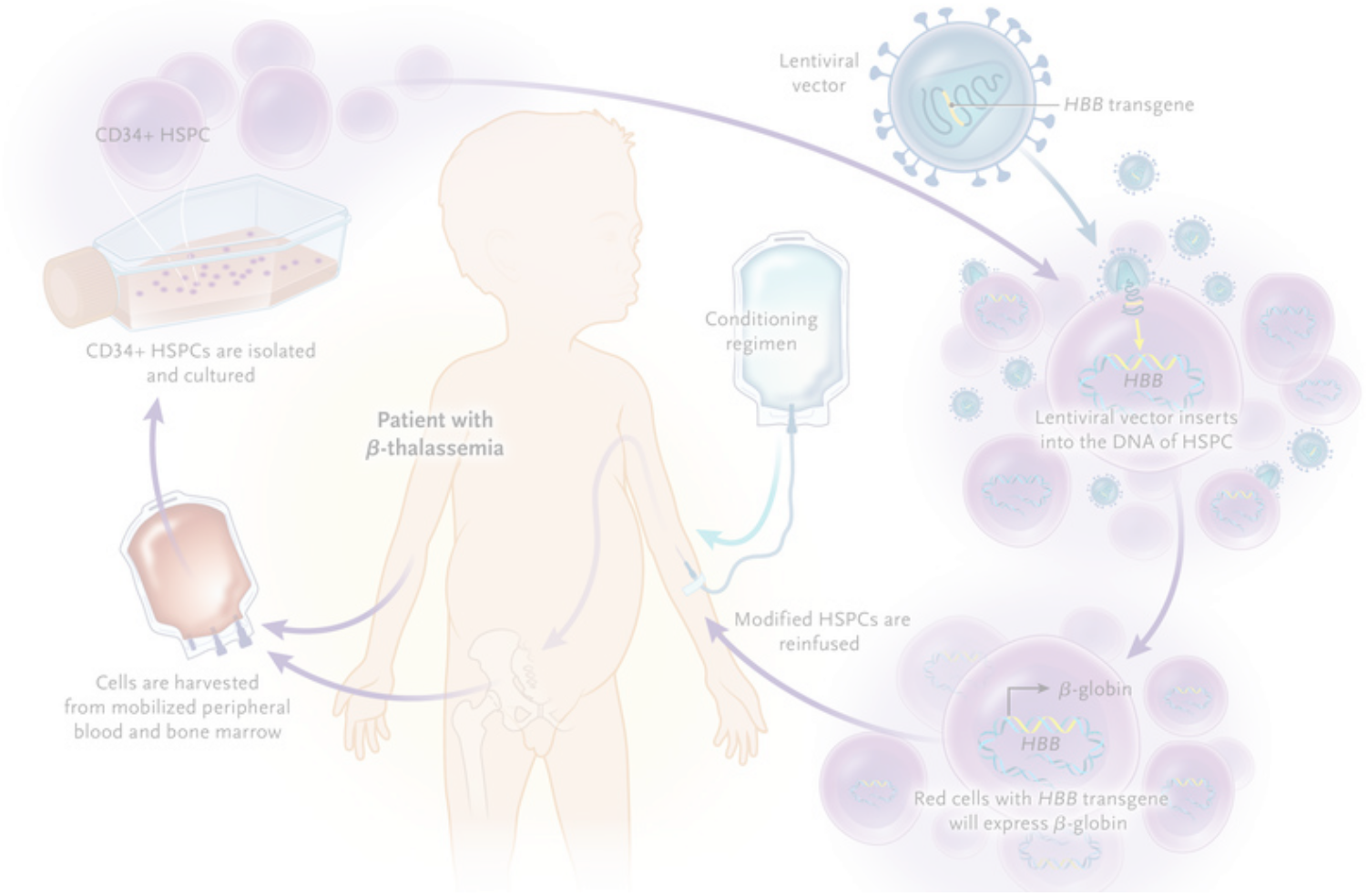
RECOMENDAÇÕES PARA MANEJO DA COVID-19 PARA SBTMO

(ATUALIZADO EM 07 DE JULHO DE 2020 – POR DRA. CLARISSE MACHADO)

Gene Terapia



Conclusão

- Estamos vivenciando uma nova realidade.

- Necessidade de mudanças

- Provavelmente até que apareça uma vacina ou tratamento eficaz para a COVID-19 nos precisaremos nos reinventar como profissionais da saúde para melhor atender nossos pacientes

Agradecimento

ABHH

SBTMO

Profa Liane Daudt

Profa Mariana Michalowski

Prof Fernando Barroso

Contato: darrigo.jr@gmail.com

Classification of Indication	Definition
Standard of care (S)	This category includes indications that are well defined and are generally supported by evidence in the form of high-quality clinical trials and/or observational studies (eg, through CIBMTR or European Society for Blood and Marrow Transplantation).
Standard of care, clinical evidence available (C)	This category includes indications for which large clinical trials and observational studies are not available. However, HCT/IECT has been shown to be an effective therapy with acceptable risk of morbidity and mortality in sufficiently large single-center or multicenter cohort studies. HCT/IECT can be considered as a treatment option for individual patients after careful evaluation of risks and benefits. As more evidence becomes available, some indications may be reclassified as "Standard of care."
Standard of care, rare indication (R)	Indications included in this category are rare diseases for which clinical trials and observational studies with sufficient number of patients are not currently feasible because of their very low incidence. However, single-center or multicenter or registry studies in relatively small cohorts of patients have shown HCT/IECT to be effective treatment with acceptable risks of morbidity and mortality. For patients with diseases in this category, HCT/IECT can be considered as a treatment option for individual patients after careful evaluation of risks and benefits.
Developmental (D)	Developmental indications include diseases where preclinical and/or early-phase clinical studies show HCT/IECT to be a promising treatment option. HCT/IECT is best pursued for these indications as part of a clinical trial. As more evidence becomes available, some indications may be reclassified as "Standard of care, clinical evidence available" or "Standard of care."
Not generally recommended (N)	HCT/IECT is currently not recommended for these indications where evidence do not support the routine use. However, this recommendation does not preclude investigation of HCT/IECT as a potential treatment and may be pursued for these indications within the context of a clinical trial.