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Haploidentical

Haploidentical Transplantation with Post-Transplant Cyclophosphamide versus Unrelated Donor Hematopoietic Stem Cell Transplantation: A Systematic Review and Meta-Analysis

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A B S T R A C T

Hematopoietic stem cell transplantation (HSCT) is the standard treatment for patients with high-risk hematologic malignancies. Only approximately 25% of siblings are HLA-matched, and thus alternative donors—unrelated or haploidentical—are usually the only options available. This meta-analysis aimed to compare haploidentical HSCT with post-transplantation cyclophosphamide and unrelated donor (URD) HSCT. We searched the PubMed and Cochrane databases for pertinent studies indexed between 2008 and 2018. Twenty observational studies (with a total of 1783 haploidentical HSCT recipients and 6077 URD HSCT recipients) were included. Results for overall survival, graft-versus-host disease (GVHD), nonrelapse mortality (NRM), and relapse incidence were pooled. Measures of association used were hazard ratios and risk differences. The median age was 51 years for haploidentical transplant recipients and 52 years for URD transplant recipients. Peripheral blood stem cell (PBSC) grafts were more frequent in the URD transplant recipients (85%) than in the haploidentical transplant recipients (31%). Overall survival was not different between the 2 groups. NRM was lower for haploidentical transplantation. All forms of GVHD (acute grades II-IV and III-IV and moderate, severe, and extensive chronic) were lower with haploidentical donor HSCT. The risk of chronic GVHD was fairly proportional to the differential use of PBSC grafts across studies, however. All included studies were retrospective, representing the major limitation of this meta-analysis. In conclusion, haploidentical HSCT for hematologic malignancies achieved the same overall survival as URD HSCT, with a lower incidence of GVHD and NRM. The increased frequency of PBSC use in the unrelated donor group could partially explain the higher cGVHD rate. Haploidentical transplantation with post-transplantation cyclophosphamide should strongly be considered as the first option for adult patients with hematologic malignancies who do not have matched sibling donors in experienced centers. This systematic review has been registered at PROSPERO (65790).

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is the standard of care treatment for many high-risk hematologic malignancies. A matched sibling donor (MSD) is the gold standard, but only a few patients—approximately 25%—will have an MSD donor. Thus, HSCT from an alternative donor (unrelated, cord blood, or haploidentical) will be the sole available option for most patients. Volunteer donor registries, despite their increasing success around the world, might not be able to find a suitable unrelated donor (URD) for some individuals, particularly for those from ethnic minority groups [1]. A related haploidentical donor (at least 50% HLA-identical) is usually available.

Both URDs and haploidentical donors are well-established options for patients who require HSCT. Refinement in HLA typing and advances in post-transplantation supportive care over the last several decades have improved URD HSCT outcomes, while the post-transplantation cyclophosphamide (PTCy) approach pioneered by Luznik et al [2] has nearly revolutionized haploidentical HSCT.

Some recent studies have focused on comparing different types of donors for HSCT. The objective of the present study was to systematically review and compare the results of haploidentical HSCT and URD HSCT.

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Questions Being Addressed

Is overall survival (OS) inferior for patients with hematologic malignancies who underwent PTCy-based HSCT from a haploidentical donor compared with those who underwent HSCT from a URD?

Are the incidence rates of nonrelapse mortality (NRM) and graft-versus-host disease (GVHD) lower for patients with hematologic malignancies who undergo PTCy-based HSCT from a haploidentical donor compared with those who undergo HSCT from a URD?

Is relapse incidence higher for patients with hematologic malignancies who undergo PTCy-based HSCT from a haploidentical donor compared with those who undergo HSCT from a URD?

METHODS

We followed the PRISMA statement for conducting and reporting systematic reviews and meta-analysis [3,4]. We searched PubMed and the Cochrane Library for articles comparing PTCy-based haploidentical HSCT and URD HSCT indexed between 2008 and 2018. References from relevant reviews in the field and textbooks were also screened for articles missed in our primary search. A detailed description of the search strategy is provided in the Supplementary Material. We performed the search on July 21, 2018, and updated it on January 1, 2019. The inclusion criterion was studies comparing haploidentical transplantation with PTCy to URD transplantation for hematologic malignancy. Exclusion criteria were cord blood transplantation, redundant publications, and studies combining MSDs with URDs in all analyses. Gray literature was not searched.

Two reviewers independently screened abstracts and selected full-text articles eligible for review. Disagreements between the 2 reviewers were resolved by discussion or by a third reviewer. The 2 reviewers performed data extraction independently.

We extracted the following outcomes: OS, relapse incidence, NRM, acute GVHD (aGVHD), and chronic GVHD (cGVHD). The measures of association extracted were risk differences (RDs), in percentage points (pp) of Kaplan-Meier or cumulative incidence estimates, at reported time points, and hazard ratios (HRs) from Cox or Fine and Gray models. Outcomes from studies with stratified analyzes were extracted as if they were 2 unique studies; for example, if a study reported outcomes separately for low-risk and high-risk disease, each result was extracted separately.

Risk differences between haploidentical and URD transplants for OS or cumulative incidence of events, and their standard deviations (SDs), were calculated as shown in the Supplementary Materials.

HRs and their SDs were log-converted, and the reference category was URD. In the quantitative meta-analysis, we included only studies reporting sufficient data for both point estimates and SD extraction for any outcome.

We also extracted the nature of the study (single-center, multicenter, or registry-based), where it was conducted, time period, number of patients, underlying diseases, median age, sex, proportion of mismatched URDs, proportions of peripheral blood stem cell (PBSC) and bone marrow (BM) grafts, proportion of myeloablative conditioning regimens (as defined by each author), pattern of GVHD prophylaxis in haploidentical donor and URD groups, and proportion of active/high-risk disease. The proportion of active disease was collected directly when available, but in many cases, only the proportion of high-risk disease was reported; when the Disease Risk Index [5,6] was reported, we grouped high risk and very high risk into a single one category of high-risk disease for our analysis.

We used random-effects models [7] to obtain summary estimates for HR and RD and 95% confidence intervals (CIs) for each outcome. We chose random-effects models because they are more conservative than fixed-effects models. Stratified meta-analyses or meta-regressions were carried out when heterogeneity was high (I^2 >40%).

Bias was assessed at the study level with the Newcastle-Ottawa Quality Assessment Scale [8]. Publication bias [9] was assessed by funnel plot visual inspection and by a rank correlation asymmetry test. Outcomes without extractable SDs were excluded from the quantitative analysis; however, because we believed SDs would be more likely to be unextractable in studies with negative results, we performed a secondary analysis in which missing SDs were imputed. Imputation was carried out by regressing same-treatment SD by a function of the number of patients [10]. The linearity between SDs and the function of the number of patients was verified. Because some patients may have been reported more than once, sensitivity analyses were performed excluding registry studies (eg, Center for International Blood and Marrow Transplant Research [CIBMTR] or European Society for Blood and Marrow Transplantation [EBMT] registry studies), and arms of individual studies with patients included more than once (eg, when the same group of haploidentical transplants was compared with 2 or more different groups of URD transplants). Another sensitivity analysis was performed by excluding 1 study at a time (ie, leave-one-out method).

This systematic review was registered at PROSPERO (65790). This systematic review did not received any third-party funding. All analyses were carried out in R version 3.4.0, with the "meta" and "metafor" packages.

RESULTS

A total of 113 abstracts were screened, and 46 full-text articles [11-56] were reviewed for eligibility (Figure 1). Twenty-six studies were excluded because they lacked patients who received PTCy (n = 16), did not compare haploidentical donors and URDs (n = 2), included non-PTCy haploidentical donor HSCT in all analyses (n = 2), were redundant publications (n = 1), did not included haploidentical donor HSCT (n = 1), analyzed URDs and MSDs as a single group (n = 1), focused on comparing different GVHD prophylactic strategies (n = 1), was a cost-effectiveness analysis (n = 1), or was a review (n = 1).

Twenty observational studies were then included in the qualitative analysis [13,17,18,22,23,26,34,35,37,46-56]. These 20 studies included a total of 1783 haploidentical donor HSCT recipients and 6077 URD HSCT recipients. Only 1 study [53] did not report any extractable SDs and thus was not included in the quantitative analysis. Two studies stratified patients based on remission status [51] or conditioning regimen intensity [23]. Four studies compared a unique group of haploidentical donor HSCT recipients with 2 different groups of URD HSCT recipients, based on antithymocyte globulin (ATG) use in URD transplants [34] or the degree of URD HLA matching [47,48,52]. One study combined matched URDs and MSDs in a single group in a multivariable analysis [51]; another reported HRs, including all patients, but also reported outcomes from Kaplan-Meier and cumulative incidence curves excluding non-PTCy-based haploidentical strategies [47]. Table 1 summarizes study characteristics. In brief, PBSC grafts were more frequent in URD transplants than in haploidentical donor transplants (85% versus 31%); active/high-risk disease accounted for 39% and 51% of haploidentical donor and URD transplants, respectively. The weighted median age of recipients was 51 years for haploidentical donor HSCT and 52 years for URD HSCT; and conditioning regimen was myeloablative in 25% of haploidentical donor HSCTs and in 44% of haploidentical donor HSCTs. Table 2 summarizes the pooled results.

OS

OS was not different between haploidentical donor HSCT and URD HSCT (Figure 2). The random-effects pooled HR for haploidentical donor HSCT was 0.98 (95% CI, .88 to 1.08). The risk difference for death was −4 pp (95% CI, −8 to +1 pp). Sensitivity analysis omitting registry studies and study arms comparing the same haploidentical group with different groups of URD HSCT recipients led to the same results (Supplementary Materials).

Relapse

The relapse risk difference was 2 pp higher in haploidentical donor HSCT (95% CI, −2 to +6 pp), and the HR was 1.06 (95% CI, .95 to 1.19). The results for risk difference and HR were not different when we stratified our analysis by the proportion of active or high-risk disease (Supplementary Materials).

NRM

NRM was lower for haploidentical donor transplant recipients in studies in which all haploidentical donor HSCTs used a PTCy approach: 6 pp lower (95% CI, 10 to −3 pp) and an HR of .85 (95% CI, .72 to 1.00) (Figure 4).

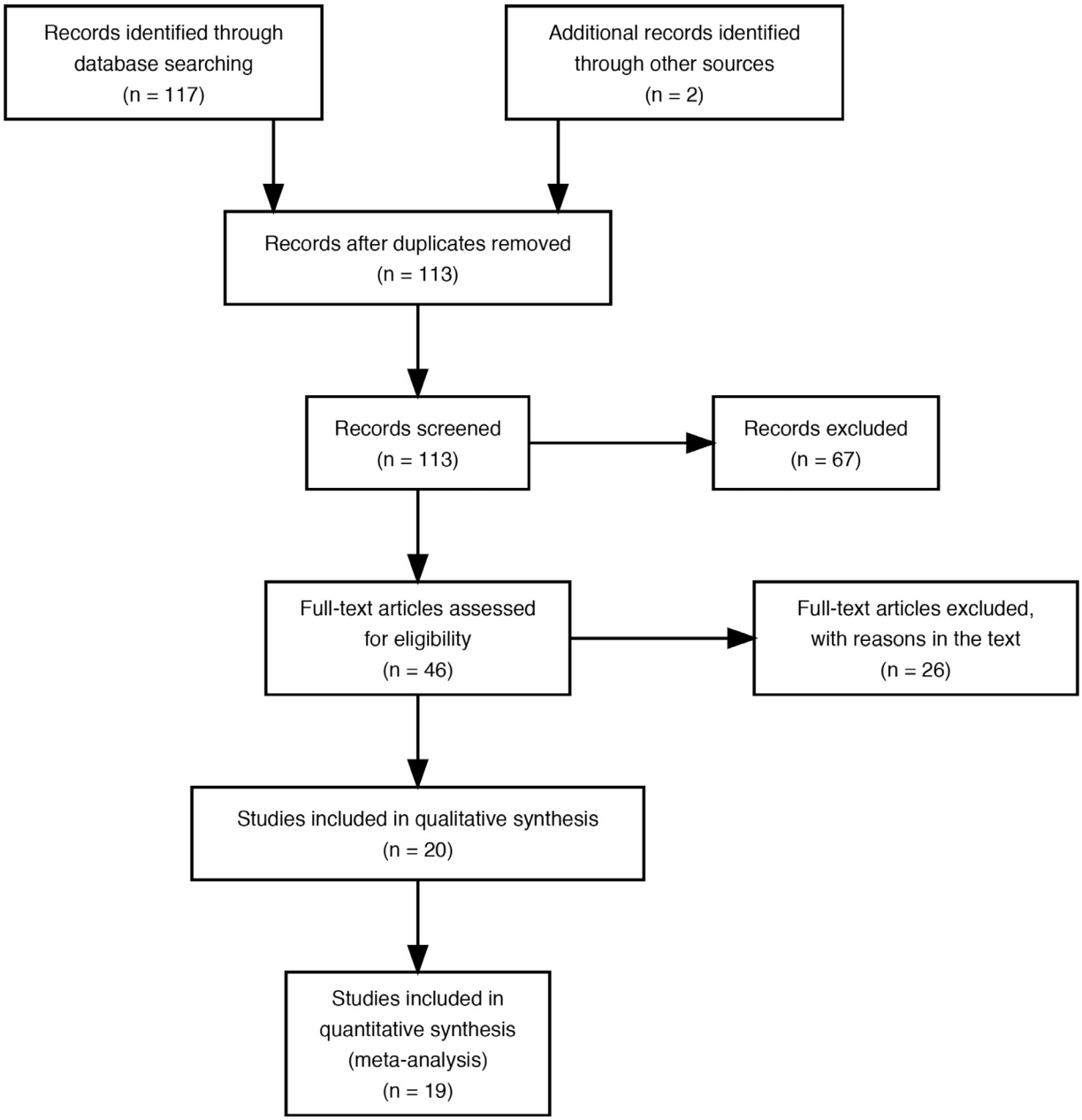

Figure 1. PRISMA flow diagram.

GVHD

The risk difference of cGVHD was 12 pp lower in the haploidentical donor HSCT group (95% CI, −20 to −4 pp). Heterogeneity was extremely high (I^2 = 86%). Because of the differential use of PBSCs—and its classical association with cGVHD—we ordered the studies by the PBSC proportion difference, and an ordered forest plot shows that cGVHD was fairly closely related to the PBSC proportion difference between haploidentical donor and URD HSCTs (Figure 5). A meta-regression confirmed this finding; cGVHD was 3.7 pp lower in the haploidentical donor HSCT group for each 10-pp PBSC proportion difference (P< .001; R^2 = 70%), which means that the PBSC proportion difference explains 70 pp of the heterogeneity (Figure 6). In the meta-regression, the type of donor was not significantly associated with cGVHD (P= .73). Three studies did not report CIs, but their risk difference point estimates did not depart from the estimated regression line in the meta-regression (Figure 6), which suggests a low likelihood of bias. HLA-matching in the URD group did not influence GVHD risk. cGVHD risk seemed higher when <40% of the URD transplant recipients received ATG, PTCy or alemtuzumab; however, differential use of PBSCs was also higher in this group of studies (Supplementary Materials). The HR for cGVHD for haploidentical donor HSCT was .25 (95% CI, .17 to .38), but only 3 studies reported HR.

Extensive, moderate, or severe cGVHD was 5 pp lower (95%CI −14 to +4 zero pp; 4 studies) for haploidentical transplants (Supplementary Materials). The corresponding HR was .55 (95% CI, .31 to .99), favoring the haploidentical group. aGVHD grade II-IV (RD, −12 pp; 95% CI, −17 to −7 pp; HR, .52; 95 %CI, .47 to .82; Supplementary Materials) and grade III-IV (RD, −9 pp; 95% CI, −13 to −5 pp; HR, .66; 95% CI, .48 to .92; Supplementary Materials) were also lower for haploidentical donor HSCT.

Table 1
Study Characteristics

Study	Multicenter	Disease	Number			% PBSC		% MAC		GVHD Prophylaxis, %		Age, yr		Active or High-Risk Disease, %	
										Haplo	URD				
			Haplo	URD	% MMURD	Haplo	URD	Haplo	URD	PTCy	PTCy or in vivo TCD	Haplo	URD	Haplo	URD
Burroughs et al, 2008 [50]	Yes	Hodgkin lymphoma	28	24	25	0	100	0	0	100	0	32	28	43	38
Di Stasi et al, 2014 [51]	No	AML/MDS	19	26	0	5	62	0	0	100	100	55	62	0	0
Di Stasi et al, 2014 [51]	No	AML/MDS	13	82	0	0	51	0	0	100	100	52	62	100	100
Raiola et al, 2014 [52]	No	Malignant	92	43	0	0	40	77	72	100	100	45	42	58	42
Raiola et al, 2014 [52]	No	Malignant	92	43	100	0	35	77	72	100	100	45	47	58	56
Ciurea et al, 2015 [23]	Yes	AML	88	737	0	13	89	0	0	100	39	78% >50	95% >50	16	22
Ciurea et al, 2015 [23]	Yes	AML	104	1245	0	18	81	100	100	100	23	42% >50	43% >50	34	25
Garciaz et al, 2015 [53]	Yes	NHL	26	28	12	50	100	0	0	100	100	53	61	43	29
Baker et al, 2016 [13]	No	Malignant	54	59	39	56	68	0		100	91	50,5	57	44	51
Bashey et al, 2016 [18]	No	Malignant	116	178	0	45	82	40	51	100	28	51	53	40	31
Blaise et al, 2016 [22]	No	Malignant	31	63	0	87	95	0	0	100	100	62	64	39	30
Gaballa et al, 2016 [35]	No	Malignant and nonmalignant	60	46	100	3	17	0	0	100	100	45	51	38	40
Kanate et al, 2016 [34]	Yes	Lymphoma	185	241	0	13	91	0	0	100	100	55	55	6	18
Kanate et al, 2016 [34]	Yes	Lymphoma	185	491	0	13	94	0	0	100	0	55	55	6	11
Rashidi et al, 2016 [54]	No	AML	52	88	0	100	100	44	44	100	0	54	63	42	41
How et al, 2017 [46]	No	Refractory AML	24	43	19	100	98	67	79	100	24	54	55	100	100
Martinez et al, 2017 [55]	Yes	Hodgkin lymphoma	98	273	0	39	88	10	31	100	74	31	32	15	16
McCurdy et al, 2017 [56]	No	Malignant	372	120	0	0	0	0	100	100	100	55	50	19	29
Bashey et al, 2018 [17]	No	Malignant	33	57	4	48	79	6	30	100	4	66	65	17	24
Brissot et al, 2018 [48]	Yes	AML, relapsed/ refractory	199	1111	0	53	94	54	42	100	78	52	52	100	100
Brissot et al, 2018 [48]	Yes	AML, relapsed/ refractory	199	383	100	53	92	54	38	100	88	52	52	100	100
Devillier et al, 2018 [26]	No	AML	33	30	10	94	97	0	17	100	97	64% > 65	50% > 65	24	7
Dulery et al, 2018 [37]	Yes	Refractory malignant	27	29	24	78	100	78	79	100	100	42	63	100	100
Lorentino et al, 2018 [47]	Yes	AML, adverse karyotype	48	433	0	62	81	53	49	100	76	49	53	100	100
Lorentino et al, 2018 [47]	Yes	AML, adverse karyotype	48	123	100	62	83	53	54	100	86	49	51	100	100
Pagliardini et al, 2018 [49]	No	Malignant	81	81	0	73	96	17	28	100	100	50	50	32	25

MMURD indicates mismatched unrelated donor; TCD, T cell depletion; AML, acute myelogenous leukemia; MDS, myelodysplastic syndrome; NHL, non-Hodgkin lymphoma.

Table 2
Summary of Results

Outcome	RD (95% CI)*	Number of Studies†	HR (95% CI)	Number of Studies†
OS	−4 (−8 to +1)	11 (15)	0.98 (0.88- 1.08)	11 (15)
Relapse	+2 (−2 to +6)	12 (16)	1.06 (0.95-1.19)	10 (13)
NRM	**−6 (−10 to −3)**	10 (14)	**0.85 (0.72-1.00)**	10 (13)
aGVHD grade II-IV‡	**−12 (−17 to −7)**	10 (14)	**0.52 (0.47-0.82)**	7 (9)
aGVHD grade III-IV‡	**−9 (−13 to −5)**	10 (13)	**0.48 (0.32-0.72)**	6 (8)
cGVHD, all‡	**−12 (−20 to −4)**	12 (16)	**0.25 (0.17-0.38)**	3 (4)
cGVHD, moderate‡	−5 (−14 to +4)	4 (5)	**0.55 (0.31-0.99)**	5 (5)

Statistically significant results are in bold type.
* For RD, negative values favor haploidentical donor HSCT and positive values favor URD HSCT.
† Number of published studies (number of actual comparisons in parentheses).
‡ High heterogeneity.

Bias Assessment and Sensitivity Analyses

Funnel plots are presented in the Supplementary Materials. Asymmetry tests suggest publication bias only for the OS outcome. We used the trim and fill method, which did not substantially change that result. We also used the trim and fill method for relapse because we could not rule out publication bias on visual inspection of the funnel plot; the results were no different.

The leave-one-out method (ie, omitting 1 study at a time) indicated no evidence that a single study could have driven any result. Repeating the analyses including studies with imputed missing SDs or excluding arms of studies with patients included twice and stratifying by type of study—registry study (eg, CIBMTR or EBMT study) and nonregistry study—have not changed any result substantially. These analyses are presented in the Supplementary Materials.

DISCUSSION

Our data show that HSCT from a haploidentical donor with PTCy-based GVHD prophylaxis achieves the same survival rate as URD HSCT. Moreover, the incidence of all forms of GVHD was lower with haploidentical donor HSCT compared with URD HSCT, and NRM was also lower for haploidentical donor HSCT with PTCy-based GVHD prophylaxis.

GVHD is the most common complication following HSCT, and its incidence was lower with haploidentical donors. One one hand, this suggests that PT-Cy based GVHD prophylaxis for haploidentical donor HSCT is more effective than conventional or ATG-based GVHD prophylaxis for URD HSCT. On the other hand, patterns of PBSC use differed greatly within and across studies. Based on the meta-regression of our cGVHD analysis, we were not able to rule out the possibility that a significant fraction of the lower risk of cGVHD in haploidentical donor HSCT could be related to the higher frequency of PBSC use in URD HSCT. To our knowledge, that finding has not been reported previously. However, we were not able to analyze its impact on quality of life and immunosuppressive burden in our meta-analysis, because these data were not available in the included studies.

Our meta-regression included 1032 haploidentical donor HSCTs and 5388 URD HSCTs across 12 studies. The incidences of grade II-IV and grade III-IV aGVHD were lower with

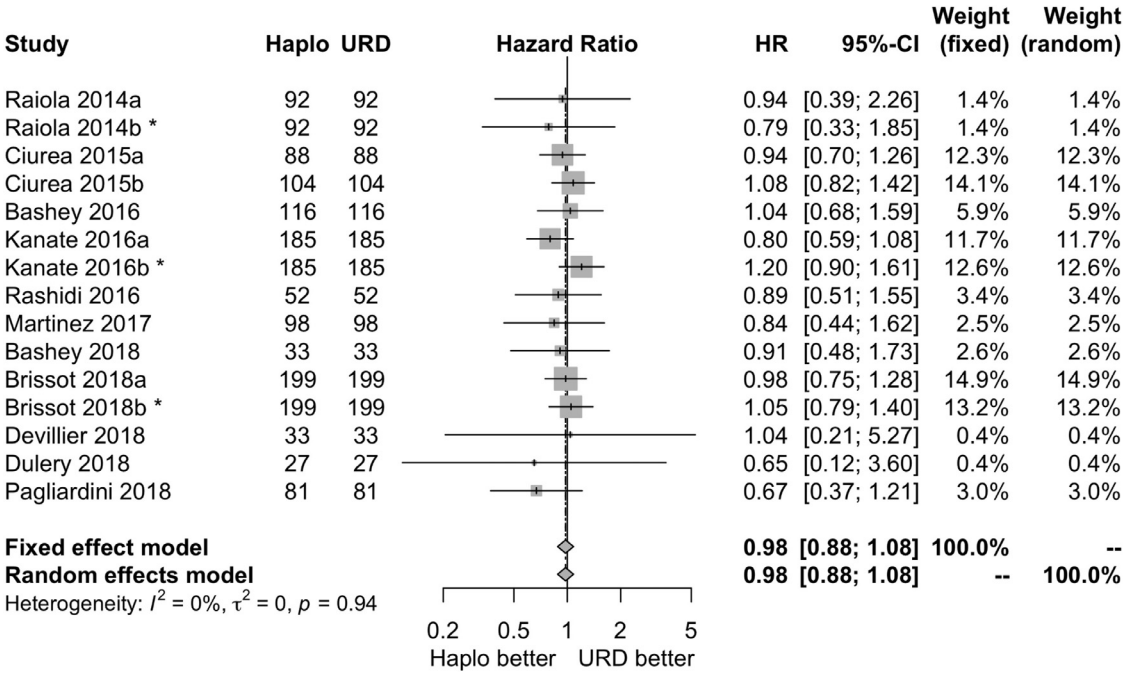

Figure 2. OS with HR. Asterisks indicate studies comparing the same group of haploidentical donor HSCT recipients with different groups of URD HSCT recipients.

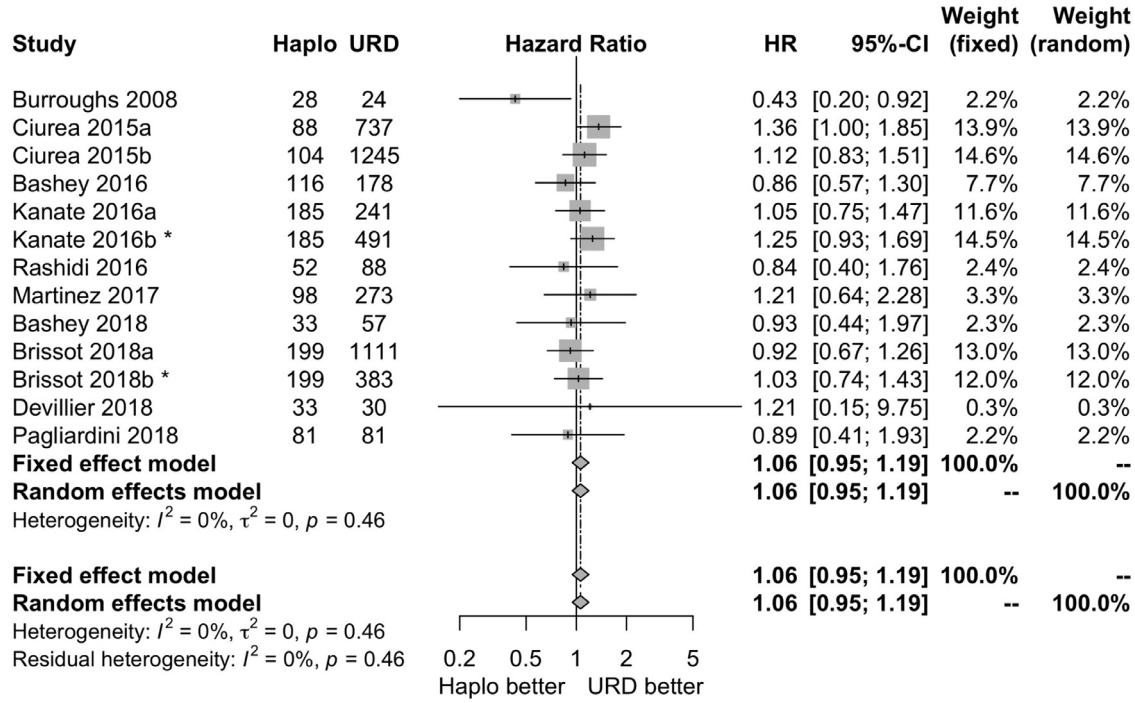

Figure 3. Relapse incidence with HR. Asterisks indicate studies comparing the same group of haploidentical donor HSCT recipients with different groups of URD HSCT recipients.

haploidentical donors compared with URDs regardless of stem cell source. The CIBMTR [57] and EBMT [58] have reported a higher incidence of aGVHD with PBSC grafts in PTCy-based haploidentical donor HSCT, but had conflicting results regarding the risk of cGVHD. Indirectly supporting our results, a meta-analysis of randomized controlled trials [59] that included mainly matched or single-locus mismatched related or unrelated donors confirmed that cGVHD, but not aGVHD, is more frequent with PBSC grafts in both related donor and URD HSCT. However, from the donors' standpoint, PBSC collection has better toxicity and recovery profiles than bone marrow (BM) harvest [60], and thus related donors may be more willing than URDs to undergo BM harvest. PTCy-based GVHD prophylaxis has recently been incorporated in URD HSCT with promising results [36,61]. Kanakry et al [62], in a noncomparative study of PTCy in HLA-matched related donor and URD transplants found a similar global immunosuppressive burden as that reported in ATG studies, but whether PTCy will prove

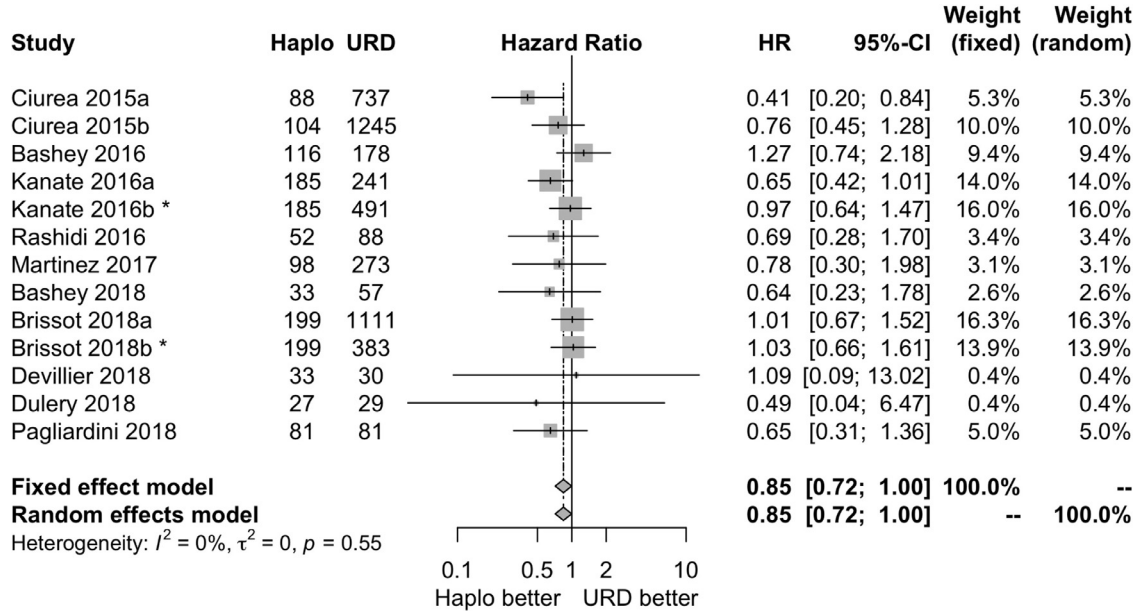

Figure 4. NRM with HR. Asterisks indicate studies comparing the same group of haploidentical donor HSCT recipients with different groups of URD HSCT recipients.

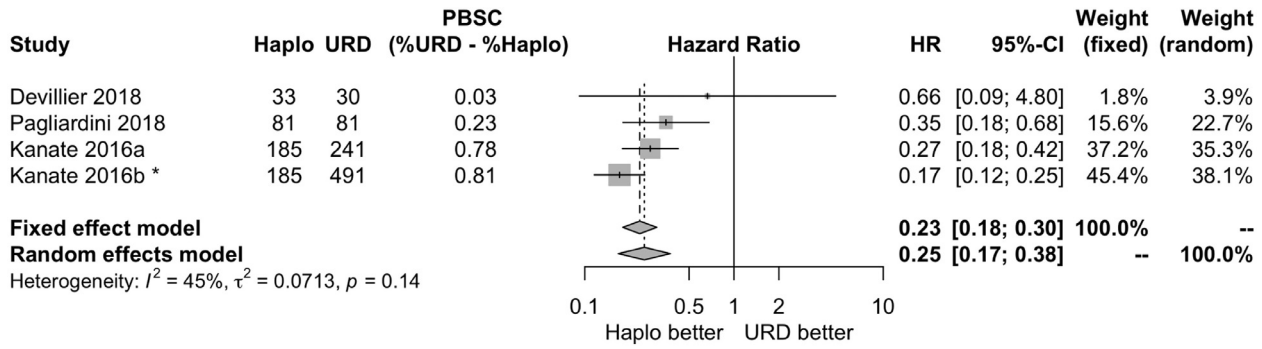

Figure 5. cGVHD incidence with HR. PBSC (%URD − %Haplo) indicates the differential use of PBSC source in URD and haploidentical donor HSCT. Asterisks indicate studies comparing the same group of haploidentical donor HSCT recipients with different groups of URD HSCT recipients.

more effective than conventional ATG-based GVHD prophylaxis in the URD setting, especially with PBSC as the graft source, remains an open question.

We found no evidence of a higher relapse rate with haploidentical donors, even in patients with active or high-risk disease. Although it is a commonly held belief, no solid evidence showing higher relapse rates in PTCy-based haploidentical donor transplantation has been published. Actually, reports of a high relapse rate are almost limited to the original haploidentical donor PTCy study [2], which included patients with poor-risk disease profile who received nonmyeloablative conditioning and had a relatively high rate of graft failure. Moreover, NRM was low in that study, and interpreting cumulative incidence curves for competing risks is not always straightforward; a low NRM usually leaves more patients susceptible to relapse. We found no evidence of higher relapse risk even when only studies with high-risk diseases were analyzed. This finding is important because, from a practical standpoint, waiting for an URD for a patient with very high-risk or refractory disease is often a risky, or even unreasonable, option. Identifying a suitable URD usually takes longer than 2 months, even in high-income countries [63], which delays the transplantation procedure [64] and impairs the optimal timing for these urgent transplantations, whereas a haploidentical donor can be cleared for donation in just 2 weeks.

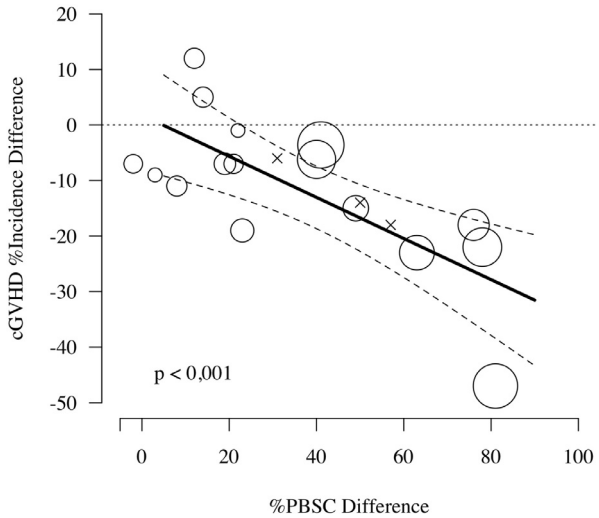

Figure 6. GVHD and PBSC use. Circled areas are proportional to fixed-effects weights. "x" represents point estimates of studies without 95% CIs.

URD HSCT is an established option for patients without an MSD, with almost 40 years of experience [65], whereas haploidentical donor HSCT with PTCy is a relatively new approach. Nevertheless, data on haploidentical donor HSCT have been increasingly published. In a quick PubMed search for "haploidentical transplantation," we found that almost one-half of all articles on haploidentical donor HSCT have been published in the last 5 years. Indeed, all but 1 of the studies included in our analysis were published in that time period. However, the choice of type of donor has relied mainly on personal beliefs and experience [66-68].

Based on our analyses, a conservative recommendation would be that as a general rule in experienced centers, haploidentical donor HSCT with PTCy may be preferred over a URD HSCT for an adult patient with hematologic malignancy in remission, especially for a patient who cannot wait 2 to 3 months to find a suitable URD. OS for haploidentical donor HSCT is not inferior to that for URD HSCT, and NRM and incidence rates of all forms of GVHD are lower compared with those in URD HSCT. Extrapolating this recommendation to children can be troublesome, given that most of the patients included in the studies in our analysis were adults. Needless to say, caution is advisable, especially in centers that have little experience in haploidentical donor HSCT but that have already performed a large number of URD HSCTs. In addition, patients with high levels of anti-HLA antibodies may not find a suitable haploidentical donor [69], and the role of PTCy-based haploidentical donor HSCT has not yet been established for benign diseases [70].

Our study has some limitations. During our data extraction process, there was some information that we simply could not gather. Stem cell transplantation outcomes were sometimes reported as cumulative incidence without CIs, as HRs derived from Cox models with an inadequate reference category, or not reported at all. Randomized controlled trials are seldom available in the field of HSCT. Indeed, we found no intervention trials in our search, and all of the included studies were observational. It is unlikely that results of randomized controlled trials comparing URDs and haploidentical donors will be available in the coming years. Although there are several comprehensive reviews on statistical methods for data analysis in HSCT [71-73], to our surprise we found no definitive guideline or recommendation on how to report HSCT outcomes in observational studies. We believe that there is an urgent need for standardization. To overcome this limitation, all analyzed outcomes included 2 association measures, and our main results included most haploidentical donor transplant recipients, so it is unlikely that this could have impacted our results. At least for cGVHD, graphic visualization of the meta-regression shows

that the exclusion of the 3 studies that did not report CIs did not biased our results. We did not included gray literature because in preliminary searches, we found a considerable number of studies that were presented in more than 1 publication with slightly different titles, author order, and results or that were updated and published later. We also performed extensive sensibility analyses imputing missing SDs and excluding studies or arms of studies that potentially could have biased some results. However, no outcome was substantially different. Even though myeloablative conditioning, which has been historically associated with lower relapse rates [74,75], was more frequent in the URD group than in the haploidentical donor group (44% versus 28%), relapse rates were not different.

In conclusion, we have shown that adult patients with hematologic malignancies achieve similar survival with haploidentical donor HSCT and URD HSCT. We have also demonstrated that haploidentical donors may be preferred over URDs in certain clinical situations, but the alleged lower risk of cGVHD may be due to the greater use of BM grafts. Experience with PTCy-based haploidentical donor HSCT has grown, and it is now established as a valid option for patients without a matched donor. Despite advances in HSCT procedures and support, donor selection remains one of the keys to success, and we hope that this study will help centers optimize donor selection.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.bbmt.2019.07.028.

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