


Haploidentical Hematopoietic Stem Cell Transplantation Versus Umbilical Cord Blood Transplantation in Hematologic Malignancies: A Systematic Review and Meta-Analysis

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Abstract

Haploidentical hematopoietic stem cell transplantation (Haplo-SCT) and umbilical cord blood transplantation (UCBT) are two important alternatives when a matched sibling donor is unavailable. Several studies have reported inconsistent clinical outcomes comparing Haplo-SCT and UCBT. Therefore, it is necessary to synthesize the existing evidence regarding outcomes of stem cell transplantations comparing Haplo-SCT with UCBT. We searched article titles that compared transplantation with Haplo-SCT and UCBT in MEDLINE (PubMed), Cochrane library, and EMBASE database. To compare clinical outcomes between Haplo-SCT and UCBT, we performed a meta-analysis of 12 studies and reported the pooled odds ratios (ORs) of 6 end points including overall survival (OS), progression-free survival (PFS), nonrelapse mortality (NRM), relapse rate (RR), acute graft-versus-host disease (aGVHD), and chronic graft-versus-host disease (cGVHD). We found that Haplo-SCT was associated with a significantly superior OS (pooled OR of 0.74, 95% confidence interval [CI] 0.68 to 0.80) and PFS (0.77, 95% CI 0.72 to 0.83), as well as a lower NRM (0.72, 95% CI 0.64 to 0.80) and aGVHD (0.87, 95% CI 0.77 to 0.98) compared to the UCBT group. We also found a significantly increased risk of cGVHD in Haplo-SCT group (1.40, 95% CI 1.22 to 1.62). In terms of RR, Haplo-SCT was comparable to UCBT (0.91, 95% CI 0.79 to 1.05). Results of this meta-analysis demonstrate that Haplo-SCT results in better clinical outcomes compared to UCBT in terms of OS, PFS, TRM, and aGVHD, but is inferior to UCBT in terms of increased cGVHD risk. Further prospective comparisons between Haplo-SCT and UCBT are needed.

Keywords

haploidentical hematopoietic stem cell transplantation, umbilical cord blood transplantation, hematologic malignancies, meta-analysis

Introduction

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a well-established curative treatment for hematologic malignancies^{1,2}. Human leukocyte antigen (HLA)-matched sibling donor (MRD) is the first choice for allo-HSCT. Unfortunately, only about 30% of patients have an MRD available³. In the past, haploidentical hematopoietic stem cell transplantation (Haplo-SCT) was not routinely used for fear of significant GVHD or graft rejection⁴. The alternative strategy was pursuing an HLA-matched unrelated donor (MUD). Unfortunately, even with large donor banks worldwide, many patients are still unable to find a suitable MUD⁵. Through advances in basic and clinical research, alternative donor platforms using Haplo-SCT^{6,7} or umbilical cord blood

transplantation (UCBT)^{8,9} have been developed in the past few decades to solve the obstacle of donor unavailability for allo-HSCT.

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Up to now, two most popular T-cell-repleted Haplo-SCT protocols have been widely performed worldwide^{10–12}. The GIAC Haplo-SCT protocol developed by the Beijing group integrates granulocyte colony-stimulating factor primed grafts, intensive immunosuppression, anti-thymocyte globulin (ATG), and combined peripheral blood stem cell and bone marrow^{13–15}. Post-transplantation cyclophosphamide (PTCy) Haplo-SCT protocol was initiated by the Baltimore group^{7,16}. It has been documented that the GIAC Haplo-SCT protocol produced similar outcome to that of MRD for patients with acute leukemia^{14,17}. PTCy prevents GVHD by directly inhibiting alloreactive T cells, while preserving memory or regulatory T cells¹⁸. PTCy protocol was associated with high engraftment rates and low rates of infections, nonrelapse mortality (NRM), severe acute graft-versus-host disease (aGVHD), and chronic graft-versus-host disease (cGVHD)¹⁹. UCBT offers several benefits such as immediate graft availability, less strict HLA matching requirements, reduced incidence of cGVHD, and favorable graft-versus-leukemia (GVL) effects^{8,9,15}. Experienced UCBT centers reported comparable progression-free survival (PFS) and overall survival (OS) rates to MUD SCT²⁰. The main disadvantages for UCBT include higher graft failure rate, delayed engraftment and immune reconstitution, higher rates of opportunistic infections, relatively high rate of NRM, and lack of donor lymphocyte infusion in the event of relapse post transplantation²¹.

Currently, under condition of no MRD available, the best alternative graft source, MUD, umbilical cord blood, or Haplo donors, remains controversial. In order to optimize donor selection algorithm, it is imperative to compare the clinical outcome of various stem cell sources. Herein, we aim to synthesize the recent evidence regarding outcomes of Haplo-SCT, as compared with UCBT for patients with hematologic malignancies. Our primary endpoints are OS, PFS, NRM, RR, aGVHD, and cGVHD.

Materials and Methods

Search Strategy

We searched the MEDLINE (PubMed), Embase, and Cochrane Registry of Controlled Trials databases (updated November 2019), using the following terms: haploidentical transplant/transplantation, umbilical cord blood transplant/transplantation, alternative graft source. The PubMed and Embase searches were restricted to humans and English language articles. We limited the publication type to comparative clinical studies. The titles, abstracts, and reference lists were screened to identify eligible studies, and clearly nonrelevant articles were discarded. In addition, the reference lists of relevant studies and reviews were reviewed to identify other potentially eligible studies^{22,23}.

Study Selection and Data Extraction

We included all published clinical studies of regarding Haplo-SCT and UCBT with survival outcomes. Studies were included if they fulfilled the following criteria: patients with hematologic malignancies; prospective or retrospective studies reporting on more than 10 patients undergoing Haplo-SCT and UCBT in each group; comparison with transplants from Haplo-SCT and UCBT as graft type. Two authors independently extracted the data from the chosen studies. The following information was extracted from the included studies: the name of the first author, year of publication, study design, GVHD prophylaxis, type of disease, type of transplant, number of participants, type of conditioning regimen, length of follow-up, and so on. Main end points for data synthesis were OS, PFS, NRM, relapse rate (RR), grade II to IV aGVHD, and overall cGVHD.

Data Synthesis

The meta-analysis was performed using STATA (version 12.0) software. The threshold of significance was $P < 0.05$. Egger's test, Begg's test, and funnel plots were used to investigate publication bias. I^2 statistic was used to assess statistical heterogeneity, with $I^2 > 50\%$ set as the cutoff to indicate significant result heterogeneity. Hazard ratios (HRs) and 95% confidence intervals (CIs) were collected from each study. When HRs and CIs were not given in a paper, data were calculated by the method of Tierney²⁴. A forest plot with combined odds ratio (OR) (with 95% CIs) for OS, PFS, NRM, RR, aGVHD, and cGVHD benefits of Haplo-SCT versus UCBT was constructed using fixed-effects analysis^{22,23}.

Results

General Description of Included Studies

The initial search yielded 902 articles; 865 were excluded from the title and abstract review, which were not pertaining to our research. A total of 37 articles underwent full-length review; 23 of them were excluded because they only evaluated patients receiving either Haplo-SCT, UCBT, or combined Haplo-SCT and UCBT, nonhematologic cancers, and lack of direct comparison results; 2 articles were excluded due to insufficient data. The final analysis included 12 studies including 2 prospective clinical studies^{25,26} and 10 retrospective cohort studies^{27–36}. This included 2,793 patients who underwent Haplo-SCT (1,432 patients) or UCBT (1,361 patients). Table 1 describes the characteristics of the 12 included studies. The median sample size was 173 patients (range 45 to 526). Two hundred seventy-seven patients were pediatric patients. Diseases that underwent Haplo-SCT or UCBT were mainly acute leukemia, other hematologic malignancies including myelodysplastic syndrome, chronic myelogenous leukemia, and lymphoma.

Table 1. Clinical Characteristics of Patients.

Study (year)	n	Age, median (range), years	Male, %	Disease	Conditioning	Cord blood unit s/d, %	Graft source for Haplo	GVHD prophylaxis	F/U, median (range), months
Brunstein (2011)									
Haplo	50	48 (7-70)	NR	ALL, AML, HL, NHL	RIC 100%		BM 100%	PTCy+Tac+MMF	11.9 (3.4-14.7)
CBT	50	58 (16-69)	NR	ALL, AML, HL, NHL	RIC 100%	0/100		CSA+MMF	12 (1.8-13.7)
Sanz J (2019)									
Haplo	22	41 (18-55)	68	AML, ALL, MDS, CML	MAC 100%		BM 100%	PTCy+CSA+MMF	32 (13-46)
CBT	23	45 (24-54)	48	AML, ALL, MDS, CML	MAC 100%	100/0		CSA+Pred	32 (21-46)
El-Cheikh (2015)									
Haplo	69	44 (19-68)	57	various	NIMAC 100%		BM 72%, PB 28%	PTCy+CSA+MMF	24 (1-103)
CBT	81	47 (18-66)	57	various	NIMAC 100%	21/79		CSA+MMF	14 (1-52)
Mo XD (2016)									
Haplo	65	10 (3-14)	51	ALL	MAC 100%		BM+PB 100%	ATG+CSA+MTX+MMF	20.7 (1.3-58.3)
CBT	64	9 (2-14)	65	ALL	MAC 100%	100/0		CSA+MMF	14.5 (0.7-58.4)
Mo XD (2014)									
Haplo	111	15 (4-18)	70	Various	MAC 100%		BM+PB 100%	ATG+CSA+MTX+MMF	36 (1.2-134.4)
CBT	37	9 (2-18)	62	Various	MAC 100%	100/0		CSA+Methylpred	39.6 (1.2-141.6)
Raiola (2014)									
Haplo	92	45 (17-69)	NR	Various	MAC 77%, RIC 23%		BM 100%	PTCy+CSA+MMF	19.2 (0.37-52.6)
CBT	105	40 (18-64)	NR	Various	MAC 83%, RIC 17%	100/0		CSA+MMF	12.4 (0.07-89.1)
Robin (2019)									
Haplo	222	61 (51-66)	55	MDS	MAC 30%, RIC 70%		BM 45%, PB 55%	PTCy	24
CBT	168	57 (45-64)	58	MDS		NA		NA	37
Kanate (2019)									
Haplo	49	55 (20-74)	57	Various	MAC 35%, RIC/NMA 65%		BM 45% PB 55%	PTCy+CNI+MMF	31
CBT	37	44 (21-63)	51	Various	MAC 22%, RIC/NMA 78%	0/100		CNI+MMF	48
Versluis (2017)									
Haplo	193	51 (18-75)	57	AML	MAC 54% RIC 46%		BM 52% PB 48%	PTCy/ATG	22 (1-120)
CBT	333	48 (18-72)	44	AML	MAC 44% RIC 45%	s/d		CNI+MMF±ATG	24 (2-214)
Giannotti (2018)									
Haplo	186	44.3 (18.5-66.1)	45.7	AML	MAC 100%		BM 80% PB 20%	PTCy+CNI+MMF	22.07 (0-96.3)
CBT	147	42.6 (18-67.9)	44.2	AML	MAC 100%	100/0		CNI+MMF	24.42 (0-83.1)
Deix (2019)									
Haplo	127	55 (20-73)	56	AML	MAC 33% RIC 67%		BM 32% PB 68%	PTCy+CNI+MMF	18
CBT	153	49(15-73)	51	AML	MAC 45% RIC 55%	s/d		CNI+MMF	18
Ruggeri (2019)									
Haplo	246	60 (18-76)	69	sAML	MAC 41% RIC 59%		NA	PTCy	16.9 (3-101)
CBT	163	56 (19-73)	58	sAML	MAC 34% RIC 66%	s/d		CSA+MMF	24.3 (3-112)

ATG: anti-thymocyte globulin; BM: bone marrow; CNI: calcineurin inhibitor; CSA: cyclosporin; MAC: myelo-ablative-conditioning; Methylpred: methylprednisolone; MMF: mycophenolate mofetil; MTX: methotrexate; NMA: nonmyeloablative; PB: peripheral blood; pred: prednisone; PTCy: post-transplantation cyclophosphamide; RIC: reduced intensity conditioning; Tac: tacrolimus.

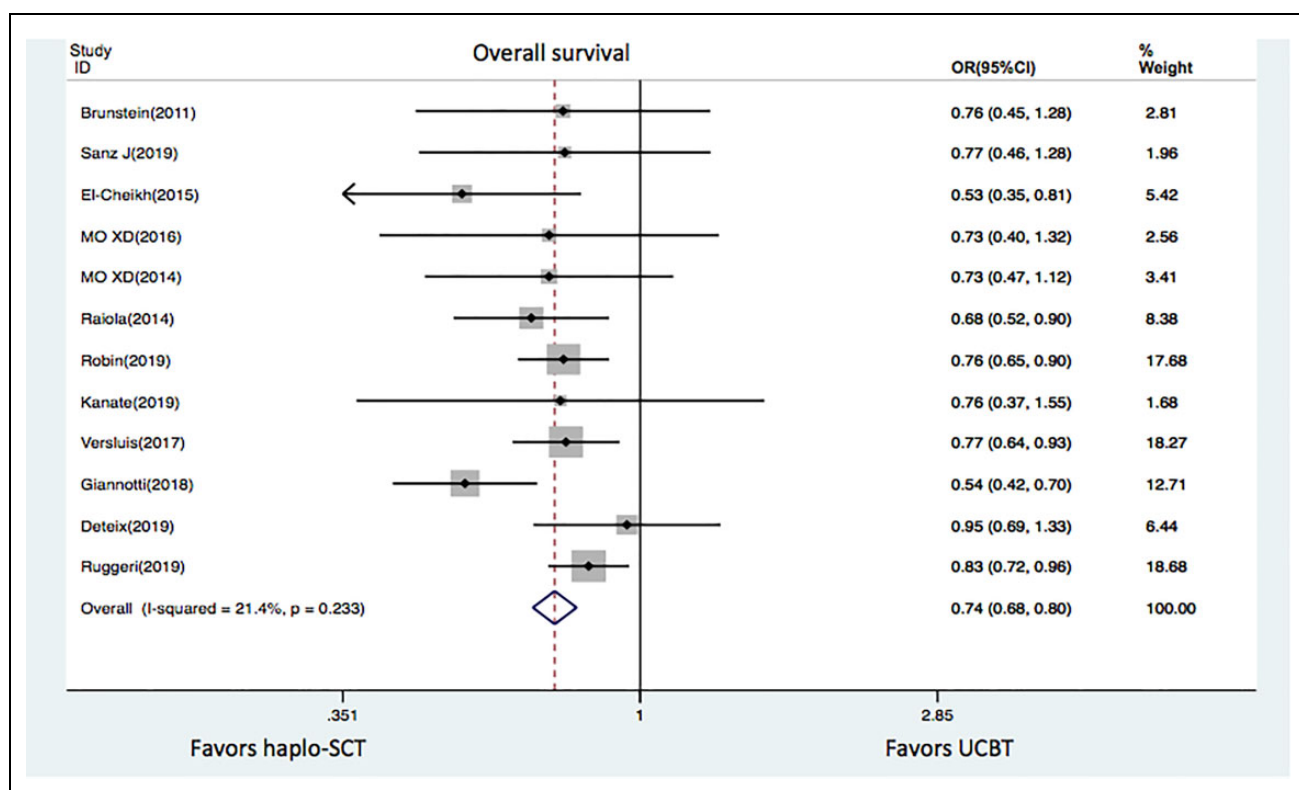


Figure 1. Meta-analysis result of overall survival.

CI: confidence interval; OR: odds ratio; haplo-SCT: haploidentical hematopoietic stem cell transplantation; UCBT: umbilical cord blood transplantation.

Majority of patients received myelo-ablative-conditioning (MAC) regimen. Patients in UCBT group received either single-unit cord blood or double-unit cord blood infusion. Graft source for Haplo-SCT includes bone marrow, mobilized peripheral blood, or both. Protocol for Haplo-SCT is T cell repletion (unmanipulated), which includes GIAC protocol or PTCy protocol. GVHD prophylaxis for Haplo-SCT includes ATG based or PTCy based combined with calcineurin inhibitor plus mycophenolate mofetil. GVHD prophylaxis for UCBT mainly combined calcineurin inhibitor with mycophenolate mofetil.

Meta-Analysis Results

Prior to meta-analysis, we checked for publication bias using Egger's test, Begg's test, and funnel plot method. The results showed that all studies investigating end points including OS, PFS, NRM, RR, aGVHD, and cGVHD were not statistically significant ($P = 0.1, 0.06, 0.48, 0.5, 0.37, \text{ and } 0.5$ for OS, PFS, NRM, RR, aGVHD, and cGVHD, respectively, by Egger's test). The funnel plot also suggested that there was no publication bias for these six end points.

OS data were evaluable for 12 studies, and the interstudy heterogeneity was nonsignificant ($P = 0.233$), with $I^2 = 21.4\%$. In a fixed-effects forest plot, the combined OR for

OS was pooled OR of 0.74, 95% CI 0.68-0.80, indicating that Haplo-SCT could increase OS of patients compared with UCBT (Fig. 1). PFS data were available for 11 studies, and the interstudy heterogeneity was nonsignificant ($P = 0.38$), with $I^2 = 5.8\%$. In a fixed-effects forest plot, the combined OR for PFS was pooled OR of 0.77, 95% CI 0.72 to 0.83, suggesting that Haplo-SCT could increase PFS of patients compared with UCBT (Fig. 2). NRM data were evaluable for 12 studies, and the interstudy heterogeneity was significant ($P = 0.007$), with $I^2 = 57.2\%$. In a fixed-effects forest plot, the combined OR for NRM was pooled OR of 0.72, 95% CI 0.64 to 0.80, suggesting that Haplo-SCT could reduce NRM of patients compared with UCBT (Fig. 3). RR data were available for 12 studies, and the interstudy heterogeneity was nonsignificant ($P = 0.1$), with $I^2 = 37.2\%$. In a fixed-effects forest plot, the combined OR for RR was pooled OR of 0.91, 95% CI 0.79 to 1.05, indicating that Haplo-SCT was associated with similar RR outcome compared with UCBT (Fig. 4). aGVHD data were available for 11 studies, and the interstudy heterogeneity was significant ($P = 0.006$), with $I^2 = 59.3\%$. In a fixed-effects forest plot, the combined OR for aGVHD was pooled OR of 0.87, 95% CI 0.77 to 0.98, suggesting that Haplo-SCT could reduce aGVHD of patients compared with UCBT (Fig. 5). Chronic GVHD data were available for 11 studies, and the

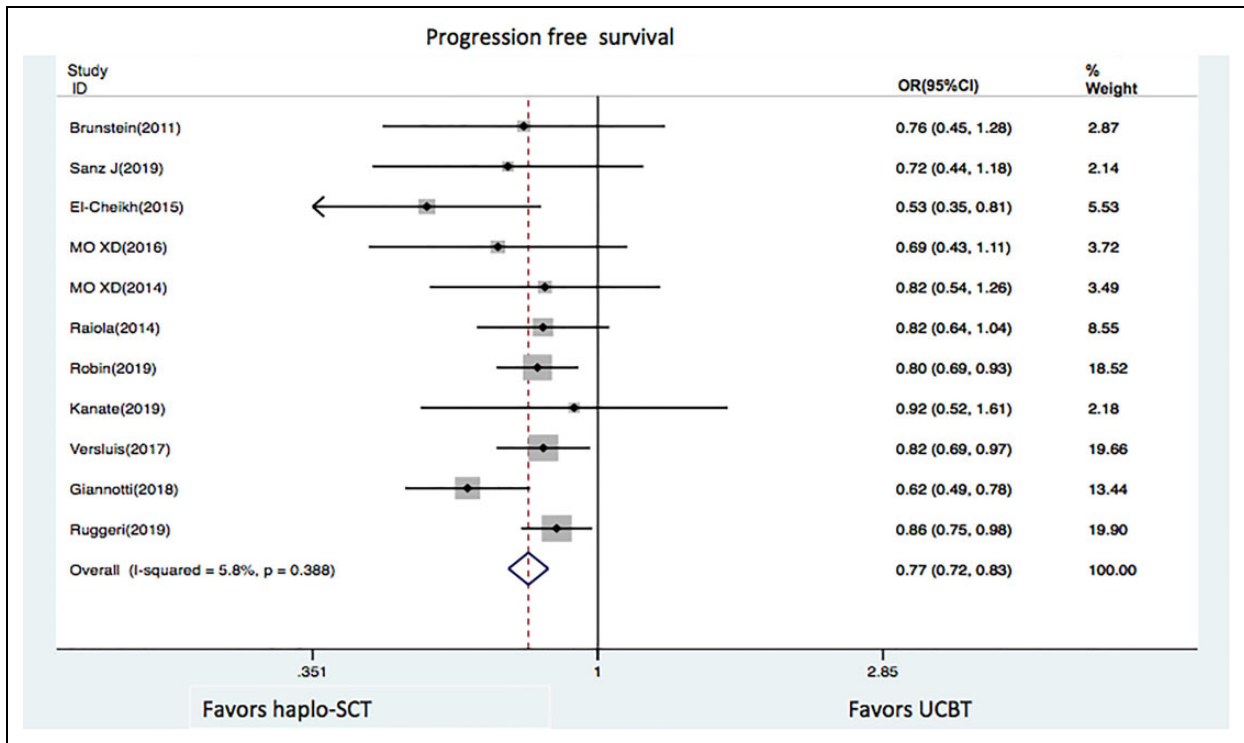


Figure 2. Meta-analysis result of disease-free survival. CI: confidence interval; OR: odds ratio; haplo-SCT: haploidentical hematopoietic stem cell transplantation; UCBT: umbilical cord blood transplantation.

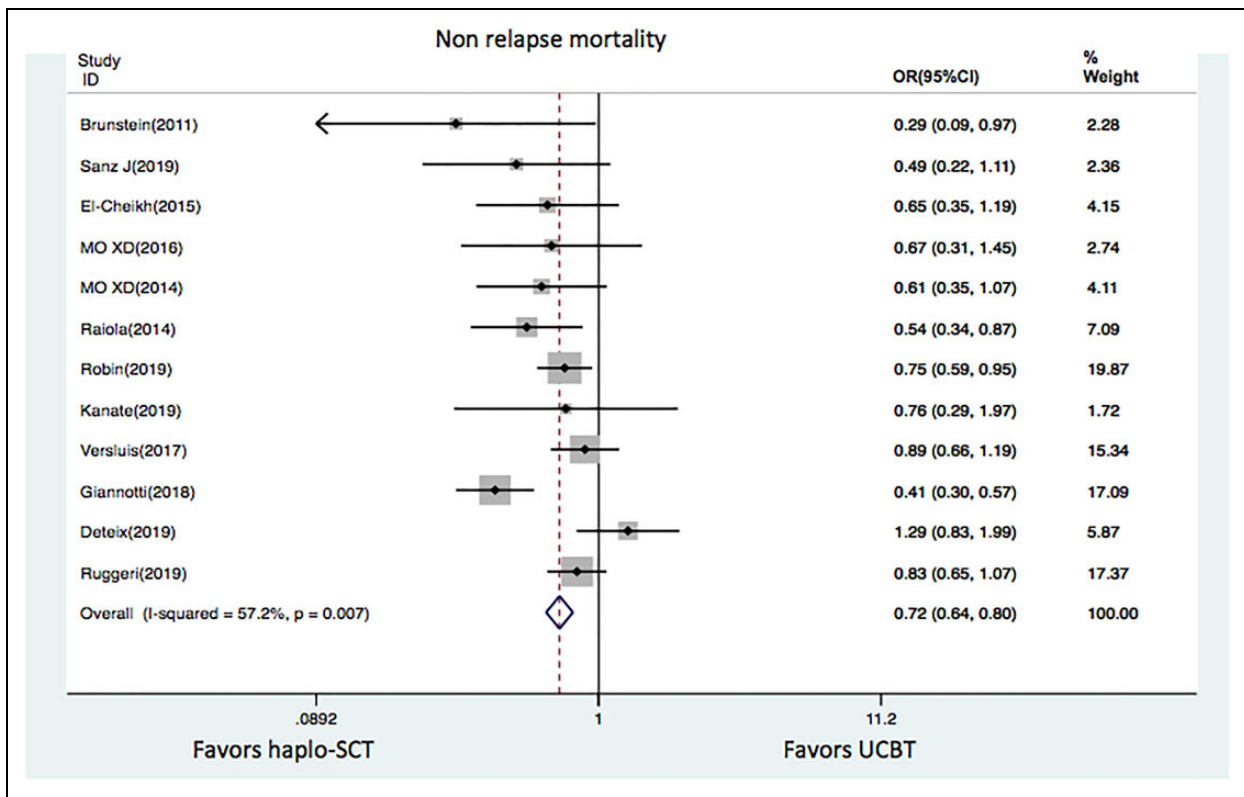


Figure 3. Meta-analysis result of nonrelapse mortality. CI: confidence interval; OR: odds ratio; haplo-SCT: haploidentical hematopoietic stem cell transplantation; UCBT: umbilical cord blood transplantation.

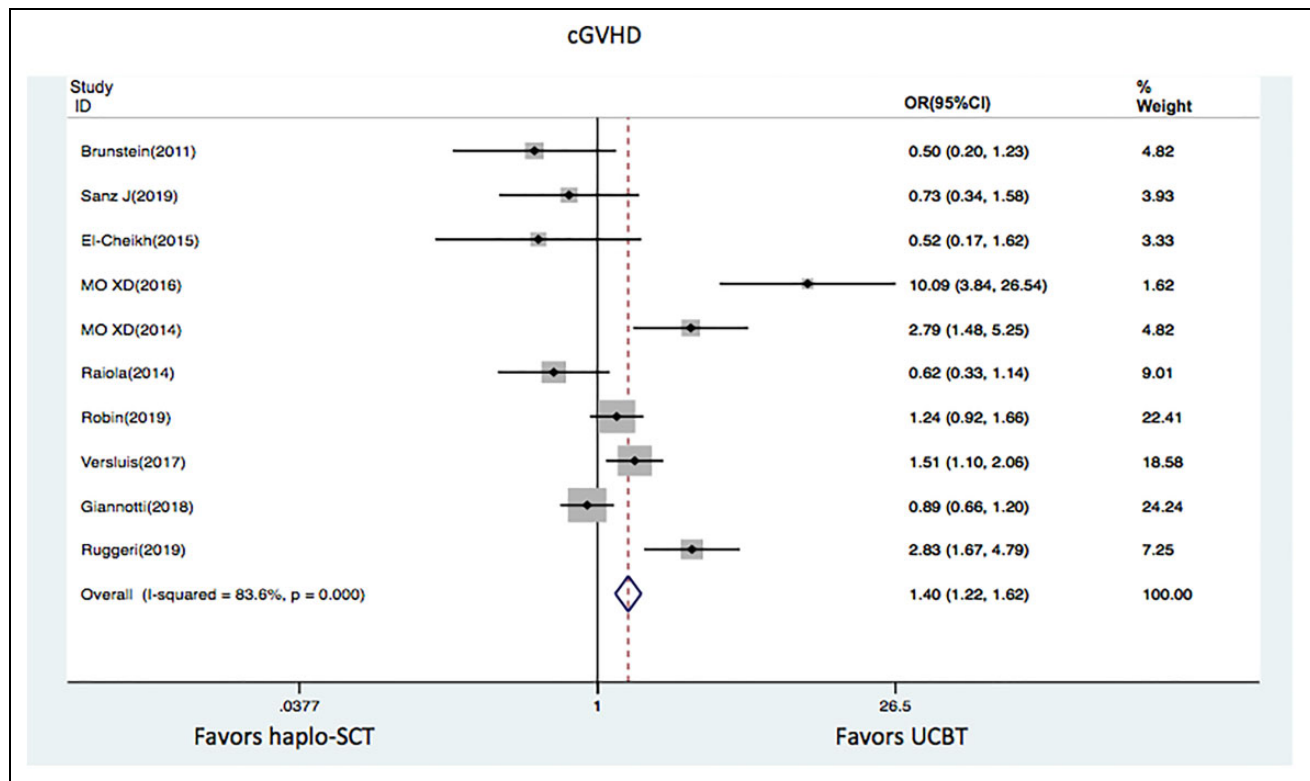


Figure 6. Meta-analysis result of chronic GVHD. cGVHD: chronic graft-versus-host disease; CI: confidence interval; OR: odds ratio; haplo-SCT: haploidentical hematopoietic stem cell transplantation; UCBT: umbilical cord blood transplantation.

interstudy heterogeneity was significant ($P = 0.001$), with $I^2 = 83.6\%$. In a fixed-effects forest plot, the combined OR for cGVHD was pooled OR of 1.40, 95% CI 1.22 to 1.62, indicating that Haplo-SCT could increase cGVHD of patients compared with UCBT (Fig. 6). There are 10 studies associated with PTCy-based Haplo-SCT, while the other 2 studies from China were ATG-based. We analyzed outcomes of Haplo-SCT compared with CBT according to PTCy- or ATG-based regimen in subgroup meta-analysis (Table 2 and Fig. 7), which demonstrated that Haplo-SCT resulted in better clinical outcomes compared to UCBT in terms of OS, PFS, and TRM, but was inferior to UCBT in terms of increased cGVHD risk both in PTCy-based and ATG-based protocols.

Discussion

For patients with hematologic malignancies requiring allo-HSCT but who lack an MRD, the best choice of alternative stem cell source remains unclear. The different types of alternative donors have disparate advantages and drawbacks in terms of rapidity of obtaining stem cells, efficacy, and tolerability, and the criteria or algorithm for selecting one type of alternative donor over another are not well established²⁷. In general, comparing Haplo-SCT and UCBT outcome in the absence of randomized prospective studies is

Table 2. Outcomes of Haplo-SCT Compared With CBT According to PTCy- or ATG-based Regimen.

End point	GVHD prophylaxis			
	PTCy based		ATG based	
	Pooled OR (95%CI)	I^2	Pooled OR (95%CI)	I^2
OS	0.741 (0.684-0.802)	35.5	0.725 (0.507-1.038)	0
PFS	0.776 (0.720-0.837)	22	0.756 (0.551-1.038)	0
NRM	0.721 (0.640-0.812)	64	0.635 (0.402-1.004)	0
RR	0.919 (0.792-1.066)	43	0.829 (0.472-1.456)	38
aGVHD	0.776 (0.677-0.890)	0	1.629 (1.200-2.210)	74
cGVHD	1.180 (1.015-1.372)	74	4.627 (2.769-7.734)	79

aGVHD: acute graft-versus-host disease; ATG: anti-thymocyte globulin; CBT: cord blood transplantation; cGVHD: chronic graft-versus-host disease; CI: confidence interval; haplo-SCT: haploidentical hematopoietic stem cell transplantation; NRM: nonrelapse mortality; OR: odds ratio; OS: overall survival; PFS: progression-free survival; PTCy: post-transplantation cyclophosphamide; RR: relapse rate.

difficult. There are so far only two prospective studies comparing Haplo-SCT and UCBT^{25,26}. One study from the blood and marrow transplantation clinical trials network conducted two parallel multicenter phase 2 trials for individuals with leukemia or lymphoma who do not have suitable related donor. Reduced-intensity conditioning was used with either unrelated double umbilical cord blood (dUCB) or HLA-

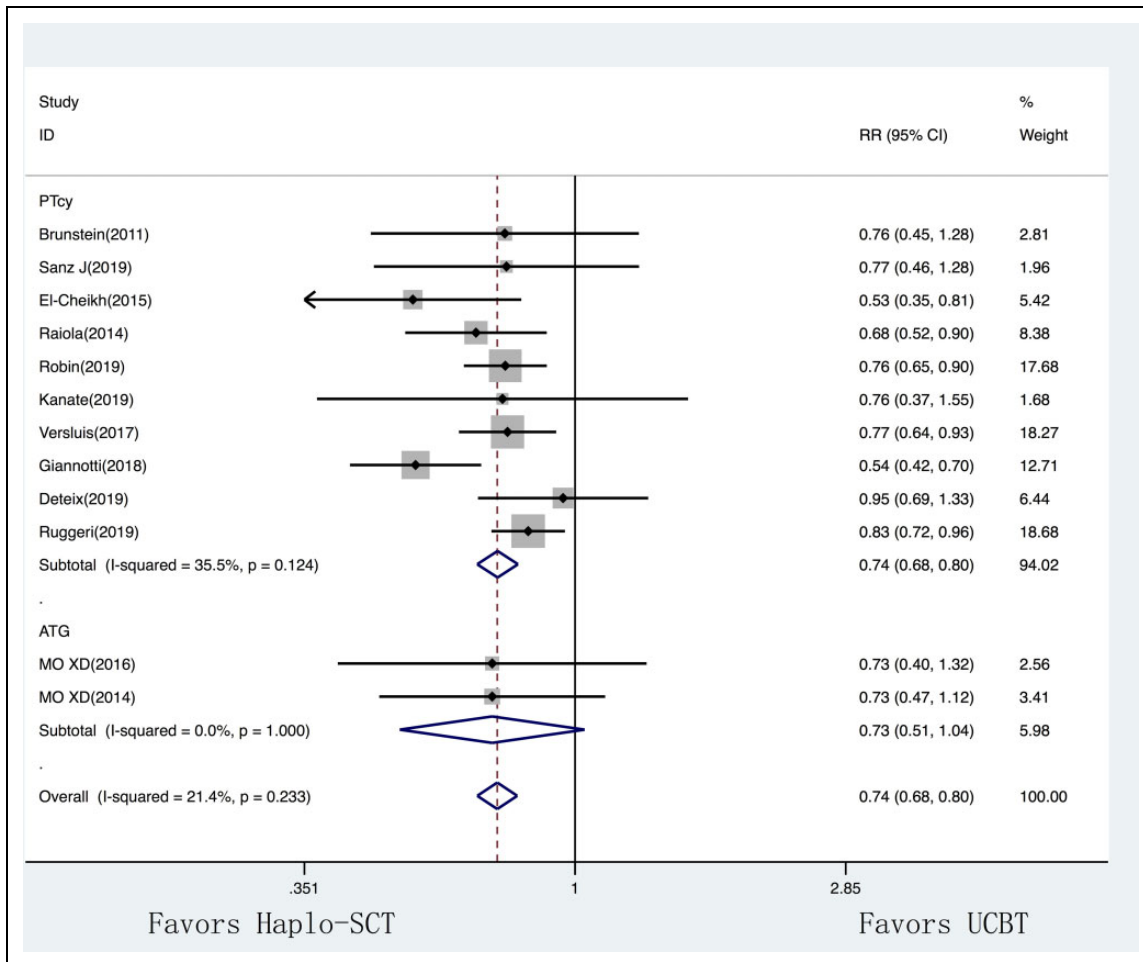


Figure 7. Subgroup meta-analysis result of overall survival of Haplo-SCT compared with CBT according to PTCy- or ATG-based regimen. ATG: anti-thymocyte globulin; CI: confidence interval; haplo-SCT: haploidentical hematopoietic stem cell transplantation; OR: odds ratio; PTCy: post-transplantation cyclophosphamide; RR: relapse rate; UCBT: umbilical cord blood transplantation.

haploidentical related donor bone marrow (Haplo-marrow) transplantation. The 1-year probabilities of OS and PFS were 54% and 46%, respectively, after dUCB transplantation and 62% and 48%, respectively, after Haplo-marrow transplantation. The 100-day cumulative incidence of grade II-IV aGVHD was 40% after dUCB and 32% after Haplo-marrow transplantation. The 1-year cumulative incidences of NRM and RR after dUCB transplantation were 24% and 31%, respectively, with corresponding results of 7% and 45%, respectively, after Haplo-marrow transplantation²⁵. Another study compared the outcomes of single-unit UCBT and unmanipulated Haplo-SCT with PTCy in adults with hematologic malignancies. All patients received an MAC regimen. Twenty-three underwent UCBT and 22 underwent Haplo-HSCT. Rates of aGVHD grade II-IV or grade III-IV, overall cGVHD, and extensive cGVHD in the UCBT and Haplo-SCT arms were 43% versus 36%, 9% versus 9%, 66% versus 43%, and 41% versus 23%, respectively. Two-year NRM and relapse in the two arms were 52% versus 23% and 17% versus 23%, respectively. Two-year DFS, OS, and

GVHD/RFS in the two arms were 30% versus 54%, 35% versus 59%, and 17% versus 40%, respectively, indicating that in the context of an MAC regimen, Haplo-SCT with PTCy provides improved outcomes compared with ATG-containing single-unit UCBT²⁶. A retrospective single-institutional study by Raiola et al³¹ revealed that despite having more patients older than 50 (40% versus 23%) and with advanced disease (58% versus 41%), Haplo SCT using PTCy and bone marrow had superior 3-year NRM (18% versus 35%) and 4-year OS (52% versus 34%) than single-unit UCBT. The Acute Leukemia Working Party of EBMT analyzed more than 1,000 patients undergoing UCBT or Haplo-SCT and found similar relapse, NRM, and leukemia-free survival rates between the two groups. But high heterogeneity between different groups exists in this study, as the UCBT group had a higher complete remission rate at the time of SCT and less patients with poor cytogenetic risk ALL^{15,37}.

Up to now, there is only one meta-analysis conducted by Poonsombudlert K et al²², which compared clinical

outcomes of patients who underwent Haplo-SCT or UCBT. The authors found a significantly decreased risk of aGVHD and relapse in the PTCy-haplo group compared to the UCBT group, and a significantly increased rate of cGVHD and OS. In contrast, in our current meta-analysis, we demonstrated that Haplo-SCT had better clinical outcomes compared to the UCBT in terms of OS, PFS, NRM, and aGVHD, but was inferior to UCBT in terms of increased cGVHD risk. Though these two meta-analysis results both demonstrated reduced aGVHD and increased cGVHD incidence in Haplo-SCT cohort, our meta-analysis result showed somewhat discrepancy with that of Poonsombudlert. We speculated that the underlying reason might be that (1) 12 studies were included in our analysis, but only 7 studies in their analysis; (2) only PTCy-based studies were included in their analysis, but both GIAC- and PTCy-based studies were included in our analysis; (3) 2 studies associated with pediatric patients were excluded in their analysis; (4) 2 studies with high intergroup heterogeneity or obvious publication bias was excluded from our analysis.

In our meta-analysis, we found reduced aGVHD incidence in Haplo-SCT cohort. It is believed that PTCy selectively depletes the alloreactive T cells while preserving the non-alloreactive T cells, thus preventing against aGVHD while preserving the GVT effect¹⁸. Recent findings suggest that PTCy may not fully eliminate alloreactive T cells. Rather, PTCy may induce functional impairment of CD4+ and CD8+ alloreactive T cells, thereby preventing new donor T cells from causing GVHD³⁸. NRM is one of the main complications influencing the outcomes of allo-HSCT, and in our meta-analysis, we found that NRM rate was lower in Haplo-SCT cohort, which was concurrent with other researches^{39,40}, while NRM of UCBT was relatively high due to delayed engraftment, slow immune reconstitution, and high rates of opportunistic infections²¹. This low rate of NRM in Haplo-SCT was associated with superior OS and PFS in our meta-analysis result. As for relapse, our result showed no significant difference between Haplo-SCT and UCBT. It was documented that PTCy Haplo-SCT has relatively higher RR when using non-myeloablative conditioning regimen, while comparable RR was found with MAC regimen^{7,41}. In addition, UCBT can reduce RR in those high-risk acute leukemia patients⁹. In our results, we did not find increased relapse rate in Haplo-SCT cohort or decreased relapse rate in UCBT cohort, and we did not perform subgroups analysis such as MAC versus non-myeloablative, complete remission versus non complete remission at transplant, which was a limitation of our work. In regard to cGVHD, many previous studies have shown that the rate of cGVHD is significantly lower in UCBT versus other types of graft source⁴², which perhaps that naive fetal stem cells from umbilical cord are naturally less exposed to foreign antigen, thus resulting in less alloreactivity⁴³. Finally, we performed subgroup meta-analysis (Table 2 and Fig. 7) comparing Haplo-SCT with CBT according to PTCy- or ATG-based regimen, which further demonstrated that Haplo-SCT

resulted in better clinical outcomes compared to UCBT in terms of OS, PFS, and TRM, but was inferior to UCBT in terms of increased cGVHD risk both in PTCy-based and ATG-based protocols.

Our study has several limitations: (1) most of the studies included were retrospective clinical trials, and lacking randomized controlled prospective clinical trials could possibly influence the objectivity and accuracy of meta-analysis; (2) our meta-analysis is limited by the heterogeneity between different studies, which originates from various indications for transplant, adult patients and pediatric patients, pretransplant comorbidities, disease status at transplant, conditioning regimen, and GVHD prophylaxis strategy. Subgroup analysis for factors such as prospective studies and retrospective studies, different diseases, adult and pediatric patients, disease status at transplant, and conditioning regimen should be performed. We found only two prospective studies, and two pediatric patient-associated studies were included in our meta-analysis. Furthermore, some studies were lacking in detailed information or outcomes regarding different disease types, disease status at transplant, and conditioning regimen, making it difficult to do subgroup analysis. (3) Different follow-up duration in different studies might influence the meta-analysis result, which is a common concern in all meta-analyses.

Conclusion

Results of this meta-analysis demonstrates that Haplo-SCT gives better clinical outcomes compared to the UCBT in terms of NRM and aGVHD, and while inferior to UCBT in terms of increased cGVHD risk, the OS and PFS are still superior over UCBT. Further large-scale, multicenter, prospective, controlled trials are needed to investigate the long-term outcomes of Haplo-SCT versus UCBT, which will provide unequivocal evidence for doctors to select the best alternative graft source.

Ethical Approval

Ethical approval is not applicable to this study.

Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

Not applicable because this study did not directly involve human subjects.

Declaration of Conflicting Interests

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