ORIGINAL ARTICLE

The effect of donor type on outcomes in adults with acute myeloid leukemia after reduced-intensity hematopoietic peripheral blood cell transplant – a retrospective study

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SUMMARY

We retrospectively analyzed outcomes in patients with acute myeloid leukemia (AML) receiving reduced-intensity conditioning (RIC) hematopoietic stem cell transplants (HCT) from a peripheral blood (PB) source. We identified 46 haploidentical HCT (haplo), 59 matched unrelated donor HCT (MUD), and 40 matched related donor HCT (SIB) patients at a single institution. Haplo had improved overall survival (OS) when compared to MUD, HR 2.03 ($P = 0.01$) but not SIB, HR 1.17 ($P = 0.61$). There were no differences in relapse rates or treatment-related mortality (TRM). Haplo had higher rates of acute graft-versus-host disease (GVHD) grade II–IV at day 180 than MUD (44% vs. 25%, $P = 0.03$) and SIB (44% vs. 13% $P < 0.01$). Rates of acute GVHD III–IV and chronic GVHD were similar among the groups. Haplo had slower engraftment rates compared to MUD with neutrophil engraftment at 87% vs. 93%, ($P < 0.01$) and platelet engraftment at 59% vs. 86%, ($P < 0.01$) at 28 days. Although patients receiving haplo had higher acute GVHD II–IV and slower engraftment, they did not have increased TRM. These data may suggest that patients receiving haplo have improved OS compared to MUD for AML patients receiving RIC transplants. This should be confirmed using a larger cohort.

Transplant International 2020; 33: 1089–1098

Key words
bone marrow transplantation, haploidentical, mobilized peripheral blood, reduced intensity conditioning

Received: 20 March 2020; Revision requested: 15 April 2020; Accepted: 19 May 2020; Published online: 19 June 2020

Introduction

Hematopoietic stem transplantation (HCT) offers a potential cure for patients with acute myeloid leukemia (AML). RIC regimens have allowed older adults or patients with comorbidities to better tolerate HCT. The Blood and Marrow Transplant Clinical Trials Network (BMT CTN) recently performed a phase III clinical trial demonstrating significantly lower treatment-related mortality (TRM) with RIC versus myeloablative regimens [1]. This study, with other studies, also showed that RIC was associated with higher rates of relapse with a trend toward lower overall survival (OS) despite lower TRM [2]. Consequently, while RIC regimens are

doi:10.1111/tri.13659

attractive on several levels, improved survival is contingent on reducing the risk of relapse following transplantation.

The rise of haploidentical (haplo) donor HCT may represent an opportunity. Haplo transplants are now widely utilized option because nearly every patient will have at least one haploidentical family member. Recent retrospective studies using data from Center for International Blood Marrow Transplant Research (CIBMTR) have demonstrated that overall survival for haplo HCT in some settings is comparable in patients receiving HCT from matched unrelated donors (MUD) and matched related donors (SIB) [3,4]. Further, some evidence suggests that haplo HCT is associated with a greater graft-versus-leukemia (GvL) effect than MUD or SIBs given the higher degree of HLA mismatch. In particular, previous studies have shown superior GvL responses for patients receiving haplo HCT for high-risk acute leukemia [5,6].

In the drive to decrease relapse following HCT, the graft source may also represent another important variable. A recent study by Bashey et al compared haplo HCT from bone marrow (BM) with haplo HCT from mobilized peripheral blood (PB) and found no differences in overall mortality. However, recipients of PB HCT were found to have lower relapse rates but higher rates of acute graft-versus-host disease (aGVHD) II–IV when compared to patients receiving BM transplants [7]. Notably, the vast majority of patients receiving haplo transplants in the previous studies received BM transplants. PB stem cells are not only easier to collect, but also yield a significantly higher number of T cells and CD34+ stem cells [8]. The use of PB grafts from haploidentical donors in the setting of RIC regimens has not been extensively studied. Consequently, we hypothesized that the combination of haplo donors with a PB source in AML patients may work synergistically to lower relapse rates traditionally seen with RIC and may produce improved outcomes relative to traditional HLA-matched donors.

Methods

Patients

This study received IRB approval through Washington University. It included patients 18 years or older with AML who received a HCT from 2010 to 2017 at Washington University in St. Louis, MO. We excluded all patients who received myeloablative regimens or transplants from a bone marrow source. All patients with prior allogeneic transplants were also excluded. Patients with *t*(15;17)(q24;q21) were excluded. Data were collected from our medical records and institutional HCT database. Other examined variables that were evaluated were age, sex, HCT-specific comorbidity index (HCT-CI), cytomegalovirus (CMV) status, type of AML including de novo disease, therapy-related disease, or secondary AML occurring after a prior myelodysplastic syndrome (MDS) or myeloproliferative neoplasm (MPN), disease status at transplant, cytogenetic risk, disease risk index (DRI), presence or absence of FLT3-ITD and NPM1 mutations, ABO mismatch, and donor age.

Definitions

Overall survival was defined as the time from day 0 of HCT to death from any cause, and those patients alive were censored at the time of last follow-up. Relapse-free survival was defined as the time from day 0 of HCT to relapse or death from a cause other than relapse of disease. Treatment-related mortality was defined as death prior to day 28 after transplant or due to any cause other than relapsed disease thereafter. Neutrophil engraftment (NE) was defined by absolute neutrophil count >500/μl for three consecutive days. Platelet engraftment (PE) was defined by platelet >20,000/μl for seven consecutive days without transfusion support. Acute GVHD (aGVHD) was determined using the Keystone criteria [9], and chronic GVHD (cGVHD) was determined using National Institute of Health criteria [10]. Disease status at transplant was separated into complete remission 1 (CR1), >CR1 (complete remission 2, primary induction failure, first relapse), or active disease (≥5% blasts in bone marrow). Cytogenetic risk was determined based on CIBMTR criteria [11] with inversion 16 as favorable, ≥4 abnormalities as adverse, and all other abnormalities as intermediate. DRI was determined using validated criteria to stratify patients based on cytogenetic risk and stage risk as previously described [12]. HCT-CI is a validated risk assessment tool that places patients in high, intermediate, and low risk depending on their comorbidities [13].

End point

Our primary end points were cumulative incidence of relapse and OS. Secondary end points were relapse-free survival, treatment-related mortality, neutrophil engraftment, platelet engraftment, aGVHD, and cGVHD.

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Table 1. Baseline characteristics.

	Donor type			
	Haplo *N* = 46	MUD *N* = 59	SIB *N* = 40	*P* value*
Age at transplant				
<65	29 (63%)	26 (44%)	19 (48%)	0.144
≥65	17 (37%)	33 (56%)	21 (52%)	
Sex				
M	22 (48%)	26 (44%)	15 (38%)	0.624
F	24 (52%)	33 (56%)	25 (62%)	
HCT-CI				
High	37 (80%)	44 (75%)	27 (67%)	0.39
Moderate/low	9 (20%)	15 (25%)	13 (33%)	
CMV status				
D+/R+	19 (41%)	12 (20%)	13(33%)	0.143
D+/R−	6 (13%)	5 (8%)	4 (10%)	
D−/R+	9 (20%)	25 (42%)	9 (23%)	
D−/R−	12 (26%)	17 (29%)	11 (27%)	
Unavailable	–	–	3(7%)	
AML type				
De novo	29 (63%)	40 (68%)	28 (70%)	0.969
Secondary (MDS or MPN)	11 (24%)	12 (20%)	8 (20%)	
Therapy related	6 (13%)	7 (12%)	4 (10%)	
Months from diagnosis to transplant				
Median	6	6	6	0.098
Range	2–68	2–58	2–16	
Disease status at transplant				
CR1	15 (33%)	32 (54%)	22 (55%)	**0.014**
>CR1	23 (50%)	19 (32%)	7 (18%)	
Active	8 (17%)	8 (14%)	11 (27%)	
Cytogenetic risk				
Adverse	10 (22%)	14 (24%)	10 (25%)	0.937
Favorable/intermediate	36 (78%)	45 (76%)	30 (75%)	
DRI				
High/very high	19 (41%)	24 (41%)	24 (60%)	0.121
Moderate/low	27 (59%)	35 (59%)	16 (40%)	
FLT3-ITD mutation				
Yes	5 (11%)	5 (8%)	8 (20%)	0.211
No	33 (72%)	36 (61%)	22 (55%)	
Unavailable	8 (17%)	18 (31%)	10 (25%)	
NPM1 mutation				
Yes	2 (4%)	9 (15%)	9 (23%)	**0.017**
No	31 (68%)	27 (46%)	16 (40%)	
Unavailable	13 (28%)	23 (39%)	15 (37%)	
Donor sex				
F	17 (37%)	15 (25%)	21 (52%)	**0.023**
M	29 (63%)	44 (75%)	19 (48%)	
Sex mismatch				
R = M/D = F†	7 (15%)	6 (10%)	15 (38%)	**0.002**
Others	39 (85%)	53 (90%)	25 (62%)	
ABO mismatch				
Matched	31 (67%)	30 (51%)	29 (73%)	0.074
Minor	8 (17%)	14 (24%)	2 (5%)	
Major	7 (15%)	15 (25%)	8 (20%)	
Unavailable	–	–	1(2%)	
Donor age				
Median	43	26	61	**<0.001**
Range	18–71	18–52	21–76	

Table 1. Continued.

	Donor type			
	Haplo *N* = 46	MUD *N* = 59	SIB *N* = 40	*P* value*
Conditioning regimen				
Flu + Cy + TBI	39 (85%)	4 (7%)	5 (13%)	N/A[§]
Flu + Bu + ATG	0 (0%)	31 (53%)	6 (15%)	
Flu + Bu2	1 (2%)	22 (37%)	28 (70%)	
Flu + Mel	6 (13%)	2 (3%)	1(2%)	
GVHD prophylaxis				
Tacro + MMF + PTCy	46 (100%)	3 (5%)	1 (2%)	N/A[§]
Tacro + MMF	0	6 (10%)	6 (15%)	
Tacro + MTX	0	27 (46%)	23 (58%)	
Tacro + MMF + MTX	0	19 (32%)	6 (15%)	
Other[‡]	0	4 (7%)	4 (10%)	

ATG, anti-thymocyte globulin; Bu, busulfan; Cy, cyclophosphamide; Flu, fludarabine; MMF, mycophenolate mofetil; MTX, methotrexate; PTCy, post-transplant cyclophosphamide; TBI, total body irradiation.

* The parametric *P*-value is calculated by ANOVA for numerical covariatesand chi-square test for categorical covariates.

[†] R = M (male recipient); D = F (female donor).

[‡] Others include tacrolimus alone, methotrexate alone, MMF + PTCy, and Taco + MTX + PTCy.

[§] N/A = not applicable. *P* values were not calculated as conditioning regimens and GVHD prophylaxis typically vary based on donor source.

The bold values are to identify which of the *P* values are significant (defined as <0.05).

Statistical analysis

Patient demographics and clinical characteristics were summarized using descriptive statistics for categorical variables or means and standard deviations for continuous variables. The distributions of these baseline factors across different types of transplants (Haplo, SIB, and MUD) were compared using the analysis of variance (ANOVA), chi-square test, or Kruskal–Wallis rank-sum test as appropriate.

The differences in the OS and RFS across different types of transplants were described using Kaplan–Meier product limit methods and compared by log-rank test. Cumulative incidences of relapse, TRM, aGVHD, cGVHD, neutrophil engraftment, and platelet engraftment were estimated using Gray's subdistribution regression to account for competing risks. TRM was considered a competing risk for relapse. Relapse was considered a competing risk for TRM. Death without count recovery was considered a competing risk for

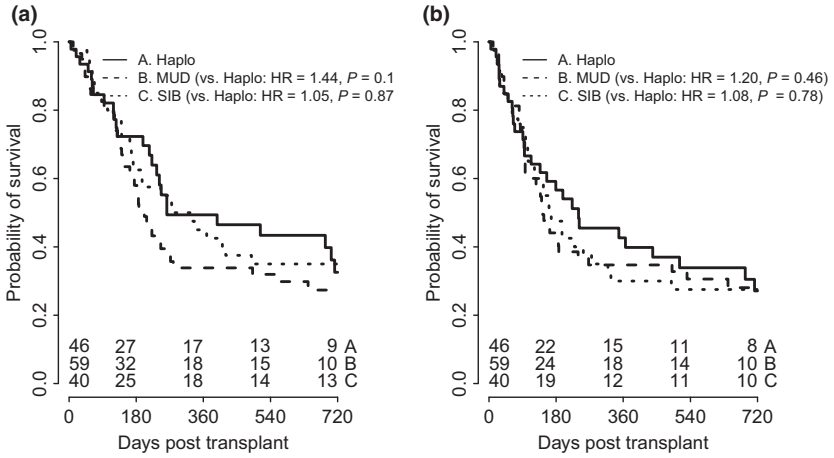

Figure 1 Overall survival and relapse-free survival. (a) The probability of overall survival by donor type prior to adjustment for variables affecting overall survival. (b) The probability of relapse-free survival by donor type prior to adjustment.

count recovery. Graft failure, relapse, or death without GVHD was considered competing risks for GVHD. Multivariate Cox proportional hazard models were also used to assess the association between the types of transplants and OS or RFS, after adjusting the potential confounding effects of baseline characteristics that had a *P*-value below 0.2 in the univariate analyses. The assumptions of proportional hazards were assessed graphically using the scaled *Schoenfeld* residuals. All tests were two-sided, and significance was set at a *P*-value of 0.05. Statistical analyses were performed using library cmprsk (http://biowww.dfci.harvard.edu/~gray) in statistical package R for competing risk analysis and SAS 9.4 (SAS Institutes, Cary, NC, USA) for all other analyses.

Results

Baseline characteristics

Table 1 shows the baseline characteristics. There were 46 patients receiving haplo, 59 patients receiving MUD,

Table 2. Analysis of overall survival.

	Univariate analysis				Multivariate analysis	
		N	Hazard ratio (95% CI)	*P* value	Hazard ratio (95% CI)	*P* value
Donor type	MUD	59	1.44 (0.88–2.35)	0.151	2.03 (1.19–3.28)	**0.01**
	SIB	40	1.05 (0.61–1.81)	0.87	1.17 (0.65–2.09)	0.606
	Haplo	46	–		–	
Age	<65	74	1.06 (0.71–1.59)	0.779		
	≥65	71				
Sex	M	82	0.87 (0.58–1.30)	0.492		
	F	63	–			
HCT-CI	Low/moderate	37	0.5 (0.2–0.45)	**0.007**	0.72 (0.42–1.23)	0.229
	High	108	–		–	
CMV status	D+/R–	15	0.81 (0.35–1.87)	0.62		
	D–/R+	43	1.09 (0.66–1.81)	0.735		
	D–/R–	40	1 (0.59–1.70)	0.999		
	D+/R+	44	–			
AML type	Secondary	31	1.56 (0.97–2.49)	0.068	1.42 (0.86–2.33)	0.17
	Therapy	17	1.76 (0.94–3.28)	0.077	1.67 (0.88–3.17)	0.116
	De novo	97	–		–	
Time to transplant		145	0.98 (0.95–1.01)	0.161		
Disease status at transplant	>CR1	49	1.87 (1.17–2.98)	**0.009**	1.76 (1.05–2.96)	0.079
	Active	27	2.79 (1.67–4.67)	**<0.001**	1.76 (0.93–3.33)	
	CR1	69	–		–	
Cytogenetic risk	Favorable/intermediate	111	0.41 (0.26–0.63)	**<0.001**	0.74 (0.42–1.3)	0.299
	Adverse	34	–		–	
DRI	Low/moderate	78	0.28 (0.18–0.43)	**<0.001**	0.39 (0.21–0.74)	**0.004**
	High/very high	67	–		–	
FLT3-ITD	Yes	18	1.13 (0.61–2.11)	0.699		
	No	91	–			
NPM1	Yes	20	0.81 (0.42–1.57)	0.529		
	No	74	–			
Donor sex	M	92	0.85 (0.58–1.30)	0.421		
	F	53	–			
Sex mismatch	R = M/D = F	28	0.92 (0.55–1.52)	0.737		
	Others	117	–			
ABO mismatch	Minor	24	0.91 (0.53–1.58)	0.743		
	Major	30	0.59 (0.34–1.03)	0.063		
	Matched	90	–			
Donor age		145	1 (0.99–1.01)	0.912		

Number of observations in original data set = 145.

Number of observations used = 145.

The bold values are to identify which of the *P* values are significant (defined as <0.05).

and 40 patients receiving SIB. All of the patients received reduced-intensity conditioning prior to transplant, and all of the transplants were from a PB source. There was no significant difference in age, sex, HCT-CI, CMV status, type of AML, time from diagnosis to transplant, cytogenetic risk, DRI, presence of FLT-ITD mutation, or ABO mismatch. There were differences in disease status at transplant, presence of NPM1 mutation, donor sex, sex mismatch, and donor age. There were also differences among the conditioning regimens and GVHD prophylaxis as they are generally decided based on donor type. For recipients of haplo HCT, the majority of patients (80%) received fludarabine (150 mg/m^2, 4 days) and cyclophosphamide (140 mg/kg, 2 days) with low-dose total body irradiation (200 cGy). Ninety percent of MUD and 85% of SIB received fludarabine (150 mg/m^2, 4 days) and busulfan (8–10 mg/kg, 2 days). The majority of MUD who received fludarabine and busulfan also received ATG (2 mg/kg for 4 days). Other conditioning regimens used were melphalan (140 mg/m^2, 2 days) with fludarabine (150 mg/m^2, 4 days). For GVHD prophylaxis, nearly all of the patients received tacrolimus with methotrexate and/or mycophenolate. All of the patients undergoing haplo HCT received post-transplant cyclophosphamide (50 mg/kg/day on day +3, +4).

Overall survival

There were 96 patients who died and 62 patients who relapsed. The median follow-up time was 7 months (range 0.1–87.1 months). The one-year OS for haplo, MUD, and SIB were 49%, 34%, and 45% respectively (Fig. 1a). The multivariate analysis of OS demonstrated worse survival in MUD compared to haplo (HR: 2.03, $P = 0.01$). There was no difference in OS in haplo compared to SIB in the univariate (HR: 1.05, $P = 0.87$) or multivariate analysis (HR: 1.17, $P = 0.61$; Table 2). In addition to donor type, DRI also had a significant impact on OS in the multivariate analysis with low/moderate DRI having improved survival compared to high/very high DRI. The most common cause of death in all three cohorts was relapse with 14 in haplo, 22 in MUD and 16 in SIB. Other common causes of death included infection with 9 in haplo, 6 in MUD, 3 in SIB and aGVHD with 1 in haplo, 5 in MUD, and 5 in SIB. All causes of death are summarized in Appendix S1.

Relapse and relapse-free survival

There was no significant difference in RFS among the three groups (Fig. 1b) or in relapse rates (Fig. 2a). The one-year cumulative incidence relapse rate in haplo, MUD, and SIB was 39% (CI 24–54%), 35% (CI 23–48%), and 48% (CI 31–62%), respectively (Fig. 2a). The multivariate analysis did show a trend toward higher relapse in MUD compared to haplo (HR 1.6) but this was not significant with a P value of 0.069 (Table S1). It also showed that both DRI and disease status at transplant were independent risk factors for relapse with high/very high DRI and >CR1/active disease with poorer outcomes (Table S1).

Treatment-related mortality

The rates of TRM were similar among the three cohorts. The cumulative incidence of TRM at one year for haplo, MUD, and SIB was 19% (CI 8–32%), 30% (CI 19–42%), and 23% (11–37%), respectively (Fig. 2b).

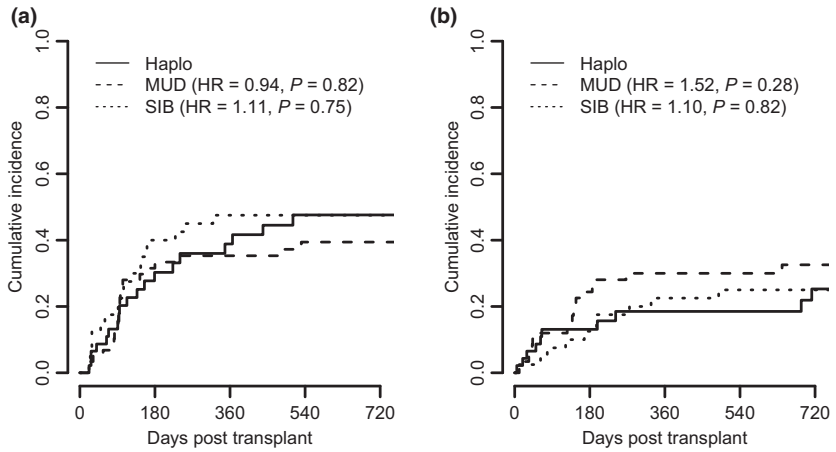

Figure 2 Relapse and treatment-related mortality (TRM) (a) cumulative incidence of relapse. (b). Cumulative incidence of TRM.

Neutrophil and platelet engraftment

Recipients of haplo HCT had slower neutrophil and platelet engraftment when compared to recipients of MUD HCT but not recipients of SIB HCT. The 28-day incidence of NE after haplo compared to MUD was 87% (CI 72–98%) and 93% (CI 71–95%). respectively, $P < 0.01$. The corresponding rates of PE were 59% (CI 43–72%) and 86% (CI 74–93%), $P < 0.01$. The rates for NE and PE for patients after SIB HCT were similar to haplo at 28 days ($P > 0.05$; Table 3). We wanted to test if lack of full donor chimerism could be driving slow engraftment rates. Among the three cohorts, there was no difference in donor chimerism at day 30 with rates of full donor chimerism being 76%, 62%, and 67% for haplo, MUD, and SIB, respectively, $P = 0.31$.

Acute and chronic graft-versus-host disease

The cumulative incidence of aGVHD II–IV at day 100 for haplo, MUD, and SIB was 41% (CI 26–56%), 22% (CI 12–35%), and 10% (CI 3–22%), respectively (Table 4). The haplo group had significantly higher rates of aGVHD II–IV when compared to SIB ($P < 0.01$) and MUD ($P = 0.03$). There was no significant difference in rates of aGVHD III–IV with haplo vs MUD ($P = 0.58$) or SIB ($P = 0.19$; Table 4). The 1-year cumulative incidence rates of cGVHD were also similar among the three groups (Table 4). There were fewer patients with moderate and severe cGVHD in the haplo group when compared to MUD and SIB (2% vs. 5% vs. 21%, respectively, $P = 0.01$; Table S2). Interestingly, patients receiving MUD with aGVHD had significantly higher rates of relapse ($P = 0.01$) while the development of aGVHD did not affect relapse rates in haplo or MUD (Fig. S1).

Discussion

Many studies have shown increased incidence of relapse after undergoing RIC prior to transplant. We were interested to see if donor type could have an impact on relapse rates in AML patients receiving RIC. Our hypothesis was that recipients of haplo HCT would have lower relapse rates due to a superior graft-versus-leukemia effect.

This study did not demonstrate a significant difference in the cumulative incidence of relapse or relapse-free survival in AML patients undergoing haplo HCT when compared to MUD and SIB in patients receiving RIC transplant from a peripheral blood source.

Table 3. Neutrophil engraftment (NE) and platelet engraftment (PE).

	Haplo	MUD	SIB	*P* value (haplo vs. MUD)	*P* value (haplo vs. SIB)
Median days to NE (range)	17 (5–222)	13.5 (0–47)	15 (0–90)		
NE at day 28 (95% CI)	87% (72–94%)	93% (82–98%)	88% (71–95%)	**<0.01**	0.12
Median days to PE (range)	23.5 (5–222)	13.5 (0–87)	13.5 (0–366)		
PE at day 28 (95% CI)	59% (43–71%)	86% (74–93%)	80% (63–90%)	**<0.01**	0.4
PE at day 100 (95% CI)	93% (79–98%)	98% (81–100%)	90% (74–96%)		

The bold values are to identify which of the *P* values are significant (defined as <0.05).

Table 4. Cumulative Incidence of GVHD.

	Haplo (95% CI)	MUD (95% CI)	SIB (95% CI)	*P* value (haplo vs. MUD)	*P* value (haplo vs. SIB)
aGVHD II–IV	44 (28–58%)	25 (14–37%)	13 (5–26%)	**0.03**	**0.01**
aGVHD III–IV	19 (8–34%)	16 (7–27%)	8 (2–20%)	0.58	0.19
cGVHD I–IV	29 (15–44%)	20 (10–31%)	38 (22–53%)	0.23	0.32
Severe cGVHD	3 (0–12%)	7 (2–17%)	23 (10–40%)	0.54	**0.04**

aGVHD was measured at 180 days.

cGVHD was measured at 360 days.

The bold values are to identify which of the *P* values are significant (defined as <0.05).

However, it did show that haplo was associated with a significantly improved OS when compared to MUD, but not SIB. The etiology of this phenomenon is unclear. While the three groups were well matched in regard to cytogenetic risk, DRI, HCT-CI, the haplo cohort did have significantly more patients with more advanced disease at transplant with 67% who were >CR1 or had active disease at transplant compared to 46% in MUD ($P = 0.014$). One possible hypothesis is patients with advanced disease have improved outcomes after receiving haplo HCT. Patients who are >CR1 or have active disease at transplant are typically considered higher risk. Given that haplo HCT could be beneficial in this cohort, this should be further explored with a larger cohort or a prospective study.

We did see significant differences in rates of aGVHD II–IV among the three cohorts. The cumulative incidence of aGVHD seen in haplo and MUD HCT recipients was similar to those seen in other studies [14,15]. Although there were significantly more patients in the SIB group with male recipients with female donors, we did not see increased GVHD rates in this group. There was no significant difference in aGVHD III–IV. A previous study that compared haplo HCT from a bone marrow source versus a peripheral blood source also showed higher rates of aGVHD, but lower rates of relapse [8]. It is well established that donor alloreactive T cells are responsible for both GVHD and GvL and sparing the desired GvL effect from GVHD has been challenging [16]. We wanted to see if there was any correlation to GvL and GVHD among the three cohorts. There was no correlation between aGVHD and RFS in haplo and SIB. Interestingly, patients receiving MUD with aGVHD had significantly higher rates of relapse ($P = 0.01$; Fig. S2). Another unexpected finding in the MUD cohort was that although the patients had lower rates of aGVHD compared to haplo, patients in the MUD had more deaths resulting from aGVHD with five deaths in the MUD group and one death in the haplo group.

Overall rates of cGVHD were not different among the three groups. Patients who underwent haplo HCT did have lower rates of moderate and severe cGVHD compared to MUD and SIB. This has been described in previous studies and is thought to be partially secondary to the use of post-transplant cyclophosphamide [17]. Another explanation could be that only 53% MUD and 15% of SIB were given ATG with their conditioning regimens (Table 1). Recent studies have shown that using ATG in MUD leads to lower rates of cGVHD [18].

There were significant differences in neutrophil and platelet engraftment in the haplo group compared to MUD but not SIB. This finding has been observed in similar reports comparing outcomes of haplo HCT versus MUD [19,20]. This is likely due to the use of post-transplant cyclophosphamide in haplo recipients [15].

While it is biologically plausible that the haplo HCT recipients have a stronger GvL response, we did not observe this finding. We did see a trend toward less relapse in haplo compared to MUD; however, this was not significant ($P = 0.069$). An important limitation of this study is the minimal residual disease (MRD) status was not routinely assessed prior to transplantation. In the setting of RIC, we would expect MRD status to have a powerful impact on post-transplant relapse, and unfortunately, this variable was not available for our cohort. In addition, the relatively small sample size limited the power of the study, and findings of modest effect size may not be detected. In conclusion, our study shows improved OS in patients receiving RIC haplo HCT compared to MUD HCT but not SIB HCT. Given the small sample size, we were not able to fully explore the etiology of our results. We did see increased aGVHD rates and slower engraftment in haplo compared to MUD, but this was not associated with increased TRM. Therefore, these data suggest that for patients who are undergoing HCT using a PB source after a RIC, haplo could possibly be a better option compared to MUD. Further studies using a larger

Transplant International 2020; 33: 1089–1098

database should be performed to verify these results and more accurately assess if haplo can be associated with improved relapse.

Funding

The authors have declared no funding.

Conflicts of interest

The authors have declared no conflicts of interest.

Acknowledgments

Data from this manuscript have been previously presented as a poster at the American Society of Clinical Oncology Annual Meeting in June 2018. This publication was supported by the National Cancer Institute (NCI) and the National Institute of Health (NIH), grants 5R35CA210084-02 and 5R01CA194552-03 and the National Center for Advancing Translational Sciences of the NIH under Award Number TL1TR002344. The material presented in this manuscript does not represent the official view of the NIH and NCI.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Cumulative incidence of GVHD.
Figure S2. Acute GVHD and relapse free survival.
Table S1. Analysis of relapse.
Table S2. Chronic GVHD grade by donor type.
Appendix S1. Cause of death.

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