Allogeneic unrelated bone marrow transplantation from older donors results in worse prognosis in recipients with aplastic anemia

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Supplemental Methods

Statistical analyses

Differences in pre-transplant patient characteristics and the causes of mortality between the younger and the older donor group were analyzed using the χ^2-test or Student's *t*-test. OS was calculated with the Kaplan-Meier method and compared using log-rank tests for each covariant related to pre-transplant patient characteristics. Factors with significance or borderline significance ($p<0.1$) in the univariate analysis and previously reported confounding factors (HLA disparity and conditioning regimens) were subjected to a multivariate analysis using the Cox proportional hazards model. Cumulative incidence of engraftment and GVHD was calculated using Gray's method and compared with Fine-Gray proportional models considering death or salvage transplantation (for engraftment failure) as a competing risk; hazard ratios (HRs) and *p* values were adjusted with potential confounding factors, such as patient age, HLA disparity, ABO disparity, harvested nucleated cell count (NCC), conditionings, and GVHD prophylaxis. Statistical analyses were performed using Stata (version 13.1, Stata Corp LP, College Station, TX, USA). The alpha level of all tests and the *p* value were set at 0.05.

Supplemental Tables

Supplemental Table 1. List of conditioning regimens

MAC	Total	Younger donor	Older donor	*p*
CY/TBI	40	30	10	1.00
+ATG	26	19	7	0.79
Others	18	14	4	
total	84	63	21	

RIC	Total	Younger donor	Older donor	*p*
CY +/- TBI	68	41	27	0.53
+ATG	56	35	21	0.86
CY/Flu +/- TBI	37	24	13	0.86
+ATG	109	69	40	0.95
Flu/Mel/TBI	10	6	4	0.81
+ATG	5	5	0	0.09
Flu/Bu/TBI	6	4	2	0.87
CY/Flu/Ale/TBI	7	4	3	0.72
Others	45	30	15	
total	343	218	125	

Abbreviations; CY, cyclophosphamide; TBI, total-body irradiation; Flu, fludarabine; Mel, melphalan; Bu, busulfan; and Ale, Alemtuzumab. Other abbreviations are shown in Table 1.

Supplemental Table 2. Overall mortality according to each variable before BMT (treating donor age as a continuous variable)

Variables		Multivariate analysis		
		HR	95%CI	*p*
Donor age	per 1 year increase	1.03	1.01 – 1.05	< 0.01*
	per 10 years increase	1.36	1.08 – 1.70	
Patient age	- 29 y	1.00	reference	
	30 y -	1.94	1.32 – 2.85	< 0.01*
HLA disparity	Matched	1.00	reference	
	Mismatched	1.30	0.88 – 1.92	0.18
ABO disparity	Matched	1.00	reference	
	Minor mismatched	1.34	0.87 – 2.08	0.18
	Major mismatched	1.54	0.97 – 2.44	0.06
	Both	1.26	0.68 – 2.33	0.45
Conditioning	MAC	1.00	reference	
	RIC	0.83	0.53 – 1.29	0.41
GVHD prophylaxis	CyA-based	1.00	reference	
	Tac-based	0.73	0.49 – 1.07	0.11
Year of BMT	- 2005	1.00	reference	
	2006 -	0.60	0.40 – 0.90	0.01*

Abbreviations are shown in Table 1 - 2.

Supplemental Table 3. Comparisons of the causes of mortality in patients who died beyond 1 year after BMT

	Younger donor (N=281)		Older donor (N=146)		p
	N	%	N	%	
Infection	4	1.4	4	2.7	0.34
Bacteria	2		1		
Virus	0		2		
Fungus	2		1		
Organ failure	8	2.8	5	3.4	0.74
Lung	4		1		
CNS	1		0		
Liver	1		1		
Kidney	2		3		
GVHD	2	0.7	3	2.1	0.22
Hemorrhage	1	0.4	0	0.0	0.47
Secondary Malignancy	2	0.7	0	0.0	0.30
Others/unknown	4	1.4	2	1.4	
Total	21	7.5	14	9.6	

Abbreviations are shown in Table 1 - 3.

Figure Legend

Supplemental Figure 1. Relationship of patients' age and donors' age

Ages of the patient and the donor of each BMT are plotted. Each dot represents one BMT.
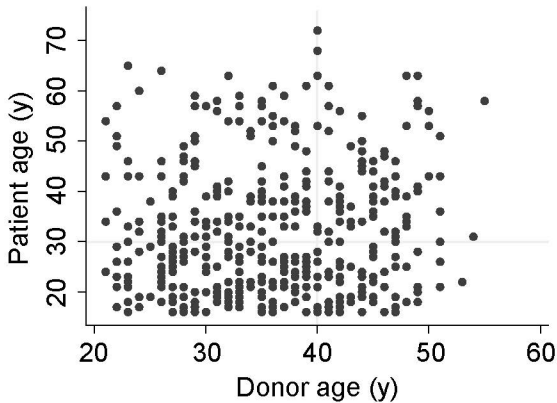
Supplemental Figure 2. Overall survival after BMT according to patients' age

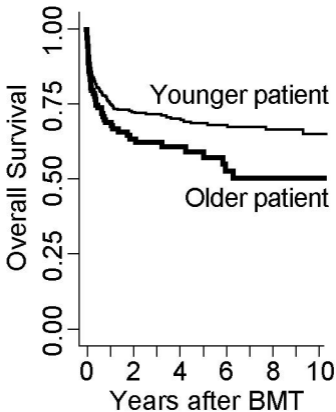OS is calculated with the Kaplan-Meier method according to patients' age ($\geq$30 years old vs. $\leq$29 years old).

Supplemental Figure 3. Overall survival after BMT in each subgroup

OS is calculated with the Kaplan-Meier method in each subgroup of (**A**) patient age, (**B**) HLA disparity, and (**C**) conditioning regimens, because patient age is a known prognostic factor and HLA and conditioning regimens were closely related to donor age (Table 1). Abbreviations; D, donor; and Pt, patient.

Supplemental Figure 1

Supplemental Figure 2

Supplemental Figure 3

A

Overall Survival vs Years after BMT

Younger D to Pt ≤29yo
Younger D to Pt ≥30yo
Older D to Pt ≥30yo
Older D to Pt ≤29yo

B

Overall Survival vs Years after BMT

Matched Younger donor
Mismatched Younger donor
Mismatched Older donor
Matched Older donor

C

Overall Survival vs Years after BMT

MAC Younger donor
RIC Younger donor
RIC Older donor
MAC Older donor