Different effects of HLA disparity on transplant outcomes after single-unit cord blood transplantation between pediatric and adult patients with leukemia

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Online Supplementary Table S1. Multivariate analyses of overall survival, relapse, and transplant-related mortality in HLA-A, HLA-B, and HLA-DR low-resolution-typed single-unit unrelated cord blood recipients.

		Overall mortality			Relapse			Transplant-related mortality		
Outcome	N	RR	95%CI	P value	RR	95%CI	P value	RR	95%CI	P value
Children 15 years or younger										
HLA disparity										
Matched (6/6)	135	1.00			1.00			1.00		
5/6	336	1.33	0.93 – 1.90	0.119	1.14	0.81 – 1.62	0.454	1.21	0.66 – 2.24	0.537
4/6	124	1.54	1.01 – 2.35	0.047	0.91	0.59 – 1.41	0.678	1.70	0.86 – 3.37	0.127
Adults 16 years or older										
HLA disparity										
Matched (6/6)	125	1.00			1.00			1.00		
5/6	535	1.14	0.88 – 1.47	0.329	0.75	0.56 – 1.01	0.06	1.50	1.00 – 2.25	0.048
4/6	1,607	0.99	0.78 – 1.26	0.941	0.79	0.60 – 1.04	0.097	1.20	0.82 – 1.77	0.347

For overall mortality, other predictive variables were advanced disease status at transplant in children, and age at transplant older than 50 years, male sex, advanced disease status at transplant, myelodysplastic syndrome or chronic myeloid leukemia (associated with a lower risk of mortality), and reduced-intensity conditioning in adults.
For relapse, other predictive variables were advanced disease status at transplant, and acute lymphoblastic leukemia or myelodysplastic syndrome (associated with a lower risk of relapse) in children, and advanced disease status at transplant and myelodysplastic syndrome (associated with a lower risk of relapse) in adults.
For transplant-related mortality, there was no other predictive variable in children. In adults, other predictive variable were age at transplant older than 50 years and female to male donor-recipient sex mismatch.

Online Supplementary Table S2. Multivariate analyses of overall survival, relapse, and transplant-related mortality in adult recipients with standard-risk disease status at transplant, advanced-risk disease status at transplant, with acute myeloid leukemia, with acute lymphoblastic leukemia, recipients of myeloablative conditioning, and recipients of reduced-intensity conditioning.

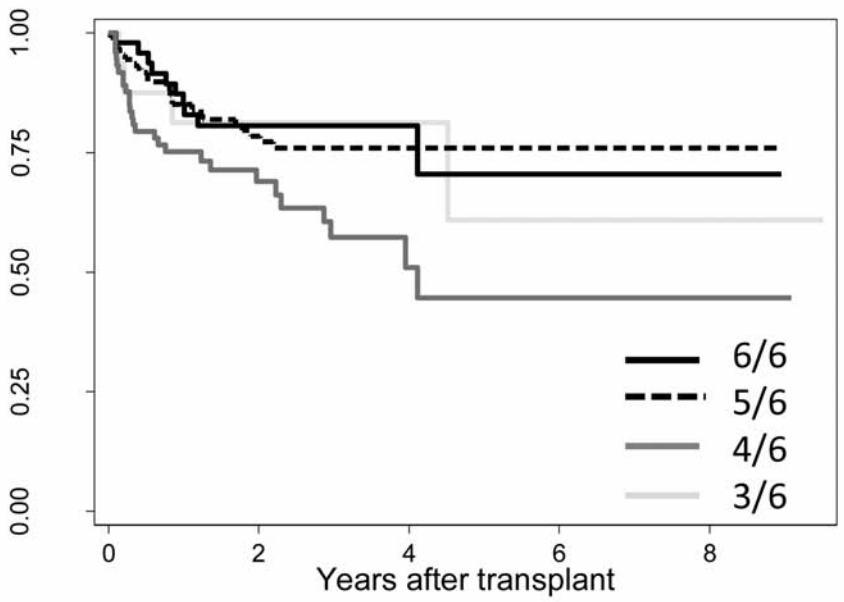
		Overall mortality			Relapse			Transplant-related mortality		
Outcome	N	RR	95%CI	P value	RR	95%CI	P value	RR	95%CI	P value
Adult recipients with standard risk disease status at transplant										
HLA disparity										
Matched (6/6)	29	1.00			1.00			1.00		
5/6	92	0.78	0.42 – 1.46	0.444	0.74	0.32 – 1.73	0.491	1.13	0.46 – 2.77	0.796
4/6	379	0.66	0.38 – 1.15	0.145	0.63	0.29 – 1.34	0.227	0.99	0.44 – 2.24	0.983
5/6	173	0.87	0.49 – 1.54	0.624	0.67	0.30 – 1.48	0.321	1.28	0.55 – 2.97	0.573
Adult recipients with advanced risk disease status at transplant										
HLA disparity										
Matched (6/6)	38	1.00			1.00			1.00		
5/6	196	1.03	0.68 – 1.54	0.905	0.71	0.45 – 1.11	0.131	1.64	0.80 – 3.37	0.176
4/6	610	0.93	0.63 – 1.36	0.695	0.66	0.43 – 1.01	0.057	1.48	0.75 – 2.94	0.256
5/6	283	0.95	0.64 – 1.42	0.807	0.72	0.46 – 1.12	0.147	1.41	0.70 – 2.86	0.336
Adult recipients with acute myeloid leukemia										
HLA disparity										
Matched (6/6)	39	1.00			1.00			1.00		
5/6	172	0.97	0.63 – 1.49	0.888	0.65	0.41 – 1.03	0.069	2.26	0.96 – 5.31	0.061
4/6	618	0.80	0.53 – 1.20	0.276	0.54	0.35 – 0.83	0.005	1.95	0.87 – 4.38	0.106
5/6	286	0.95	0.63 – 1.45	0.827	0.56	0.35 – 0.88	0.012	2.33	1.02 – 5.33	0.045
Adult recipients with acute lymphoblastic leukemia										
HLA disparity										
Matched (6/6)	17	1.00			1.00			1.00		
5/6	76	0.81	0.38 – 1.69	0.566	0.69	0.25 – 1.95	0.488	0.82	0.32 – 2.08	0.673
4/6	218	0.90	0.45 – 1.79	0.758	0.90	0.35 – 2.34	0.828	0.83	0.36 – 1.93	0.673
5/6	107	0.92	0.45 – 1.89	0.827	0.90	0.33 – 2.42	0.833	0.79	0.33 – 1.90	0.597
Adult recipients of myeloablative conditioning										
HLA disparity										
Matched (6/6)	38	1.00			1.00			1.00		
5/6	196	1.04	0.64 – 1.68	0.878	0.69	0.40 – 1.21	0.2	1.88	0.82 – 4.33	0.137
4/6	638	0.91	0.58 – 1.44	0.695	0.73	0.43 – 1.23	0.233	1.36	0.61 – 3.03	0.449
5/6	289	0.86	0.53 – 1.38	0.521	0.64	0.37 – 1.10	0.109	1.47	0.64 – 3.33	0.361
Adult recipients of reduced-intensity conditioning										
HLA disparity										
Matched (6/6)	33	1.00			1.00			1.00		
5/6	112	0.90	0.56 – 1.45	0.677	0.71	0.41 – 1.23	0.225	1.18	0.58 – 2.40	0.65
4/6	385	0.83	0.54 – 1.28	0.398	0.59	0.36 – 0.97	0.039	1.26	0.67 – 2.40	0.474
5/6	185	1.04	0.66 – 1.64	0.854	0.80	0.48 – 1.35	0.407	1.25	0.64 – 2.43	0.521

Online Supplementary Table S3. Multivariate analyses for HLA mismatch types of overall survival, relapse, transplant-related mortality, and acute GVHD in adult recipients of 4/6 cord blood unit.

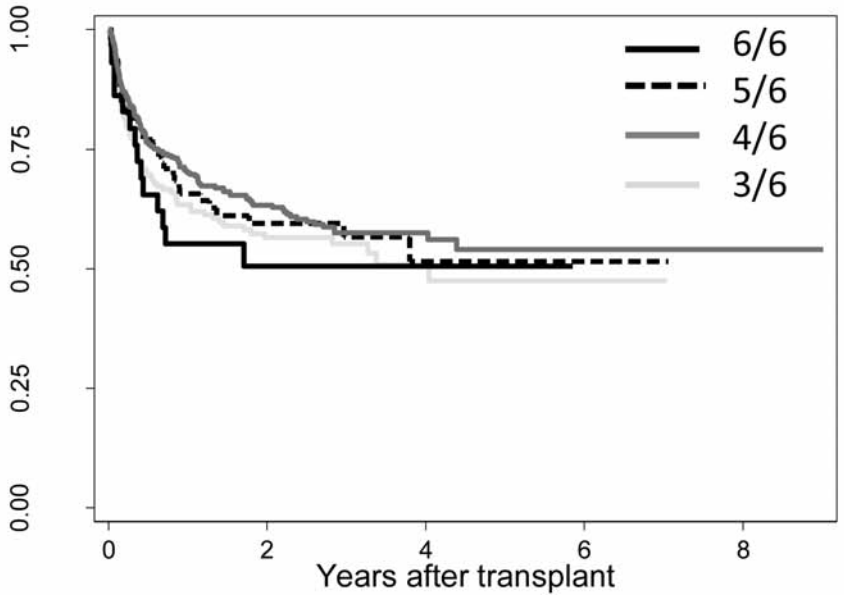
		Overall mortality			Relapse			Transplant-related mortality		
Outcome	N	RR	95%CI	P value	RR	95%CI	P value	RR	95%CI	P value
4/6 matched adult recipients										
HLA-A and -B mimatch	170	1.00			1.00			1.00		
HLA-A double mismatch	7	0.54	0.17 – 1.71	0.294	1.27	0.59 – 2.74	0.542	–		
HLA-A and -DRB1 mismatch	190	0.95	0.71 – 1.26	0.711	0.70	0.50 – 0.99	0.045	1.20	0.77 – 1.86	0.424
HLA-B double mismatch	36	0.60	0.34 – 1.06	0.077	0.97	0.52 – 1.81	0.92	0.44	0.16 – 1.18	0.103
HLA-B and -DRB1 mismatch	581	0.99	0.79 – 1.25	0.95	0.76	0.58 – 1.00	0.047	1.33	0.92 – 1.93	0.128
HLA-DRB1 double mismatch	41	1.12	0.70 – 1.79	0.635	0.46	0.23 – 0.93	0.03	2.06	1.10 – 3.89	0.025

		Grade 2 to 4 acute GVHD			Grade 3 to 4 acute GVHD		
Outcome	N	RR	95%CI	P value	RR	95%CI	P value
4/6 matched adult recipients							
HLA-A and -B mimatch	125	1.00			1.00		
HLA-A double mismatch	7	0.69	0.14 – 3.30	0.643	1.42	0.20 – 10.31	0.726
HLA-A and -DRB1 mismatch	151	1.13	0.78 – 1.64	0.529	1.25	0.67 – 2.35	0.479
HLA-B double mismatch	28	1.22	0.66 – 2.26	0.526	1.36	0.48 – 3.86	0.563
HLA-B and -DRB1 mismatch	428	1.10	0.79 – 1.52	0.581	1.07	0.62 – 1.85	0.804
HLA-DRB1 double mismatch	26	1.37	0.74 – 2.52	0.316	1.38	0.45 – 4.25	0.57

A

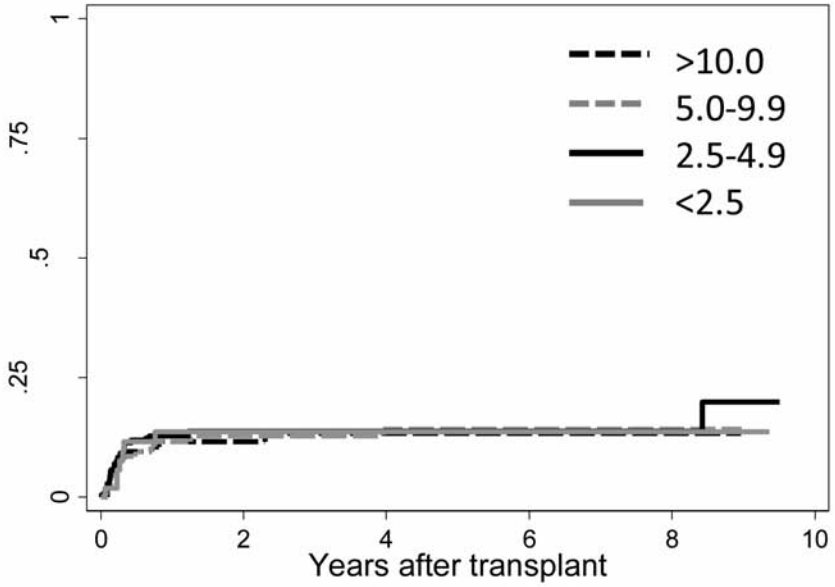


B



Online Supplementary Figure S1. Unadjusted probabilities of overall survival in HLA disparity groups for pediatric (A) and adult (B) recipients with standard-risk disease status leukemia at transplant. In children, the unadjusted probabilities of survival at three years post-transplant were 81% for recipients of HLA-matched (6/6), 76% for one-locus-mismatched (5/6), 57% for two-loci-mismatched (4/6), and 81% for three-loci-mismatched (3/6) single-unit unrelated cord blood (*P*=0.035) (A). For adult recipients, these probabilities were 51%, 57%, 58%, and 55%, respectively (*P*=0.375) (B)

A



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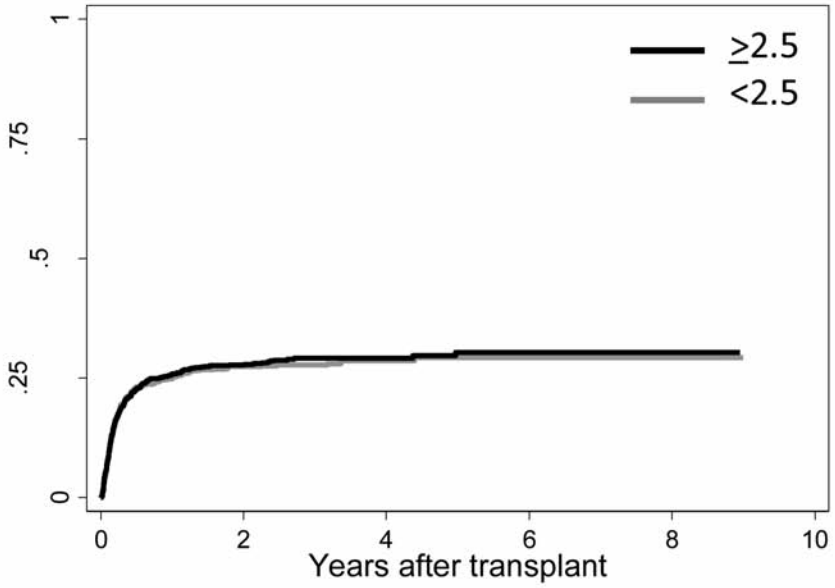
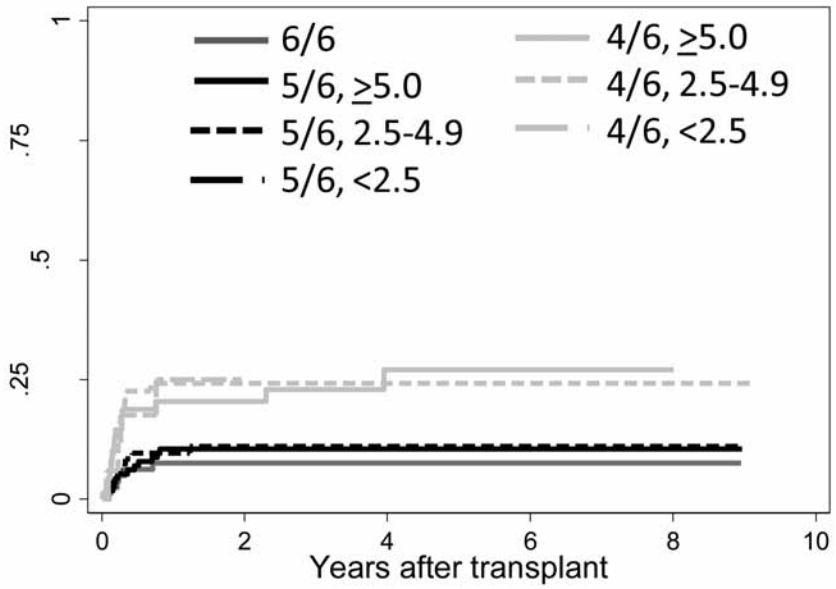


Online Supplementary Figure S2. Unadjusted cumulative incidences of transplant-related mortality in total nucleated cell dose groups for pediatric (A) and adult (B) recipients with leukemia. In children, the unadjusted cumulative incidences of transplant-related mortality at three years post-transplant were 13% for >10x10^7/kg, 14% for 5.0-9.9x10^7/kg, 14% for 2.5-4.9x10^7/kg, and 14% for <2.5x10^7/kg (*P*=0.98) (A). In adults, these incidences were 29% for >2.5x10^7/kg and 28% for <2.5x10^7/kg (*P*=0.77) (B).

A



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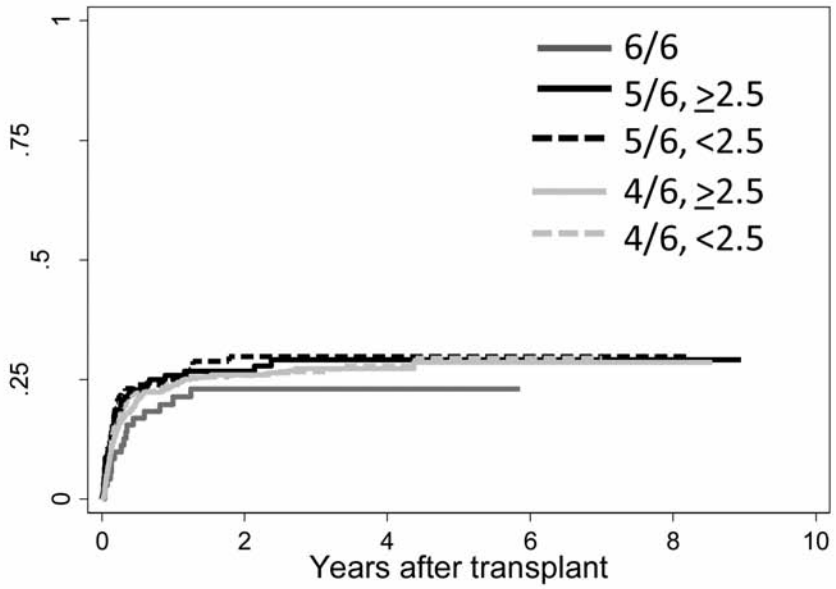

Online Supplementary Figure S3. Unadjusted cumulative incidences of transplant-related mortality in combination groups of HLA disparity and total nucleated cell dose for pediatric (A) and adult (B) recipients with leukemia. In children, the unadjusted cumulative incidences of transplant-related mortality at three years post-transplant were 8% for 6/6, 11% for 5/6 and $\geq 5x10^7$/kg, 11% for 5/6 and 2.5-4.9x10^7/kg, 0% for 5/6 and <2.5x10^7/kg, 23% for 4/6 and $\geq 5x10^7$/kg, 24% for 4/6 and 2.5-4.9x10^7/kg, 25% for 4/6 and <2.5x10^7/kg in children (A). In adults, these incidences were 23% for 6/6, 29% for 5/6 and $\geq 2.5x10^7$/kg, 30% for 5/6 and <2.5x10^7/kg, 27% for 4/6 and >2.5x10^7/kg, 27% for 4/6 and <2.5x10^7/kg (B).