

Contribution of measurable residual disease status to prediction accuracy of relapse and survival in adults with acute myeloid leukemia undergoing allogeneic hematopoietic cell transplantation

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SUPPLEMENTARY TABLE 1. Multivariate Cox regression models in the pre-HCT MRD cohort

Covariate	Relapse		RFS		OS		NRM	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Pre-HCT MRD status								
MRD ^{reg}	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD ^{pos}	3.6 (2.73-4.76)	<0.001	2.61 (2.08-3.29)	<0.001	2.05 (1.61-2.60)	<0.001	1.34 (0.87-2.07)	0.19
Age at HCT (per 10 years)	0.98 (0.88-1.09)	0.73	1.04 (0.96-1.14)	0.34	1.06 (0.96-1.16)	0.24	1.19 (1.02-1.38)	0.029
Type of AML								
De novo	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Secondary	0.71 (0.52-0.96)	0.028	0.85 (0.68-1.08)	0.18	0.95 (0.75-1.21)	0.69	1.13 (0.79-1.62)	0.49
2017 ELN cytogenetic risk*								
Favorable	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Intermediate	2.71 (1.26-5.84)	0.011	1.84 (1.10-3.08)	0.021	2.01 (1.14-3.55)	0.015	1.25 (0.61-2.56)	0.53
Adverse	4.62 (2.13-9.98)	<0.001	2.42 (1.43-4.09)	<0.001	2.66 (1.50-4.72)	<0.001	1.01 (0.47-2.14)	0.99
Missing/Not reported	4.67 (1.78-12.24)	0.002	2.56 (1.26-5.20)	0.009	2.84 (1.34-5.98)	0.006	1.26 (0.40-3.92)	0.70
Disease status at HCT								
First remission	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Second remission	1.46 (1.07-2.00)	0.016	1.38 (1.08-1.76)	0.011	1.46 (1.13-1.87)	0.0031	1.30 (0.87-1.96)	0.20
Days between CR and HCT	1.00 (1.00-1.00)	0.29	1.00 (1.00-1.00)	0.90	1.00 (1.00-1.00)	0.91	1.00 (1.00-1.00)	0.38
ANC recovery before HCT**								
Yes	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
No	1.45 (0.98-2.15)	0.06	1.41 (1.04-1.92)	0.028	1.31 (0.95-1.81)	0.10	1.35 (0.82-2.23)	0.24
Pre-HCT Cytogenetics HCT								
Normalized karyotype	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Abnormal karyotype	1.67 (1.19-2.34)	0.003	1.53 (1.16-2.01)	0.002	1.39 (1.04-1.86)	0.026	1.26 (0.79-2.02)	0.34
Non-informative karyotype***	1.02 (0.72-1.46)	0.90	1.00 (0.77-1.31)	0.97	1.07 (0.81-1.42)	0.62	0.93 (0.62-1.40)	0.72
Karnofsky score	1 (0.99-1.02)	0.87	0.99 (0.98-1.00)	0.16	0.99 (0.98-1.01)	0.28	0.98 (0.97-1.00)	0.02
Conditioning intensity								
MAC	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Non-MAC	1.69 (1.26-2.27)	<0.001	1.77 (1.40-2.23)	<0.001	1.62 (1.27-2.08)	<0.001	1.83 (1.25-2.68)	0.002

* Risk stratification according to the presence of cytogenetic abnormalities only. **ANC \geq 1,000/ μ L. ***Normal cytogenetics in cytogenetically-normal AML or missing cytogenetics at diagnosis. Abbreviations: AML, acute myeloid leukemia; ANC, absolute neutrophil count; CI, confidence interval; ELN, European LeukemiaNet; HCT, hematopoietic cell transplantation; HR, hazard ratio; MAC, myeloablative conditioning; MRD, measurable residual disease; NRM, non-relapse mortality; OS, overall survival; RFS, relapse-free survival.

SUPPLEMENTARY TABLE 2. Multivariate Cox regression models in the peri-HCT MRD dynamics cohort

Covariate	Relapse		RFS		OS		NRM	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Peri-HCT MRD dynamics								
MRD ^{neg} /MRD ^{neg}	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD ^{pos} /MRD ^{neg}	3.64 (2.64-5.02)	<0.001	2.64 (2.03-3.44)	<0.001	2.23 (1.70-2.92)	<0.001	1.42 (0.88-2.29)	0.15
MRD ^{pos} /MRD ^{pos}	9.25 (6.09-14.05)	<0.001	6.35 (4.37-9.22)	<0.001	3.00 (2.01-4.49)	<0.001	2.34 (0.91-6.03)	0.077
MRD ^{neg} /MRD ^{pos}	-	-	-	-	-	-	-	-
Age at HCT (per 10 years)	0.98 (0.88-1.10)	0.79	1.07 (0.98-1.18)	0.15	1.07 (0.97-1.19)	0.16	1.29 (1.09-1.52)	0.003
Type of AML								
De novo	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Secondary	0.66 (0.48-0.92)	0.015	0.81 (0.63-1.03)	0.091	0.94 (0.73-1.21)	0.64	1.10 (0.75-1.61)	0.62
2017 ELN cytogenetic risk*								
Favorable	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Intermediate	2.60 (1.09-6.24)	0.032	1.74 (0.99-3.03)	0.052	1.92 (1.04-3.52)	0.036	1.27 (0.60-2.69)	0.54
Adverse	4.30 (1.78-10.36)	0.001	2.12 (1.19-3.75)	0.01	2.37 (1.28-4.40)	0.006	0.85 (0.38-1.93)	0.70
Missing	4.48 (1.54-13.03)	0.006	2.49 (1.17-5.27)	0.017	2.72 (1.24-5.99)	0.013	1.45 (0.45-4.65)	0.53
Disease status at HCT								
First remission	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Second remission	1.29 (0.92-1.79)	0.14	1.28 (0.99-1.66)	0.061	1.37 (1.04-1.79)	0.023	1.38 (0.90-2.11)	0.14
Days between CR and HCT	1.00 (1.00-1.00)	0.20	1.00 (1.00-1.00)	0.79	1.00 (1.00-1.00)	0.87	1.00 (1.00-1.00)	0.31
ANC recovery before HCT**								
Yes	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
No	1.67 (1.11-2.52)	0.015	1.60 (1.16-2.21)	0.004	1.41 (1.00-1.98)	0.049	1.52 (0.90-2.56)	0.12
Pre-HCT Cytogenetics HCT								
Normalized karyotype	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Abnormal karyotype	1.72 (1.20-2.46)	0.003	1.62 (1.22-2.17)	0.001	1.42 (1.04-1.94)	0.028	1.41 (0.86-2.31)	0.17
Non-informative karyotype***	1.13 (0.78-1.65)	0.51	1.10 (0.83-1.46)	0.53	1.16 (0.86-1.56)	0.34	0.97 (0.63-1.49)	0.88
Karnofsky score	1.00 (0.99-1.02)	0.63	0.99 (0.98-1.01)	0.34	1.00 (0.98-1.01)	0.59	0.98 (0.97-1.00)	0.042
Conditioning intensity								
MAC	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Non-MAC	1.39 (1.02-1.90)	0.039	1.58 (1.24-2.02)	<0.001	1.53 (1.18-1.99)	0.001	1.81 (1.21-2.72)	0.004

* Risk stratification according to the presence of cytogenetic abnormalities only. **ANC $\geq 1,000/\mu\text{L}$. ***Normal cytogenetics in cytogenetically-normal AML or missing cytogenetics at diagnosis. Abbreviations: AML, acute myeloid leukemia; ANC, absolute neutrophil count; CI, confidence interval; ELN, European LeukemiaNet; HCT, hematopoietic cell transplantation; HR, hazard ratio; MAC, myeloablative conditioning; MRD, measurable residual disease; NRM, non-relapse mortality; OS, overall survival; RFS, relapse-free survival.

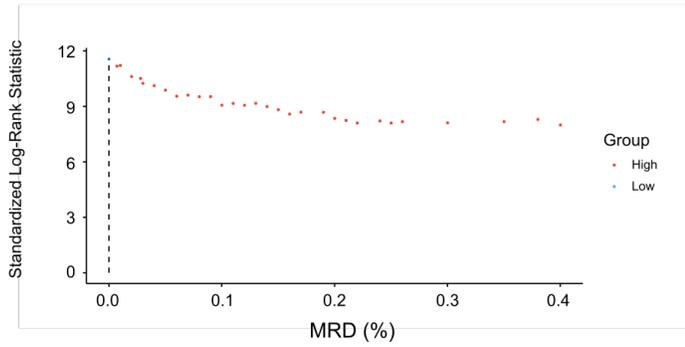
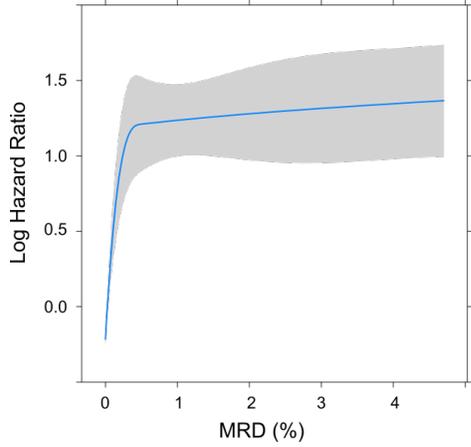
SUPPLEMENTARY FIGURE LEGEND

Supplementary Figure 1

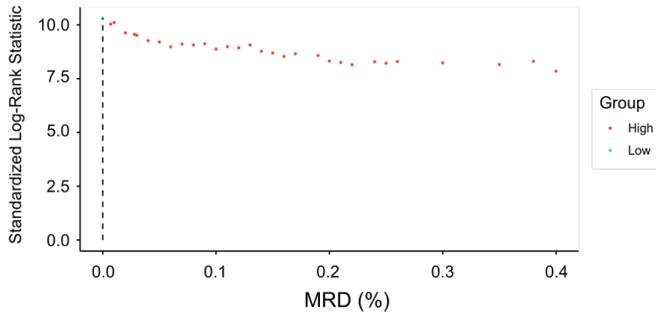
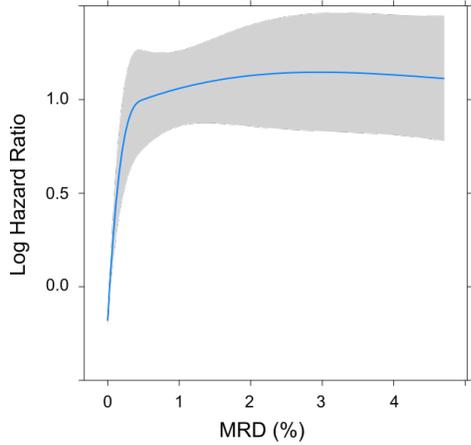
Restricted cubic spline functions (left panels) and maximally selected rank statistics (right panels) for pre-HCT MRD levels and (A) time to relapse, (B) relapse-free survival, and (C) overall survival.

SUPPLEMENTARY FIGURE 1

A



B



C

