

Minimal residual disease predicts the outcome of allogeneic hematopoietic cell transplantation in acute myeloid leukemia in the first remission.

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Context

Minimal residual disease (MRD) is an independent prognostic factor for patients with acute myeloid leukemia (AML). The genetic and immunophenotypic diversity of AML is a serious problem for monitoring MRD in daily clinical practice. The most widely used methods for assessing MRD are multiparametric flow cytometry (MFC) and polymerase chain reaction (PCR). There are data on the independent influence of pre-transplant MRD status on the results of allogeneic hematopoietic stem cell transplantation (allo-HSCT).

Objective

To assess the impact of pre-transplant MRD status determined by MFC (MRD MFC) or PCR (MRD PCR) on the long-term results of allo-HSCT.

Materials & Methods

The study included 106 patients with AML in the first complete morphological remission who underwent allo-HSCT at the National Research Center of Hematology from September 2015 to December 2020. The median follow-up was 19.5 (1-50) months.

Table 1. Patient's characteristics.

	MFC (n=106)		PCR (n=46)	
	MRD+ (n=22)	MRD - (n=84)	MRD + (n=16)	MRD - (n=30)
Sex (m/f)	7/15	32/52	6/10	13/17
Age (median, interval)	36 (21-63)	40 (18-66)	30 (19-45)	35 (18-58)
ELN risk				
• favorable	-	19 (22,6%)	4 (25%)	12 (40%)
• intermediate	10 (45,5%)	45 (53,6%)	-	9 (30%)
• adverse	12 (54,5%)	20 (23,8%)	12 (75%)	9 (30%)
Donor type				
• MRD	8 (36,4%)	29 (34,5%)	4 (25%)	11 (36,7%)
• MUD	5 (22,7%)	21 (25%)	4 (25%)	7 (23,3%)
• MMUD	4 (18,2%)	14 (16,7%)	4 (25%)	3 (10%)
• HAPLO	5 (22,7%)	20 (23,8%)	4 (25%)	9 (30%)
Conditioning regimen				
• MAC	6 (27,3%)	26 (31%)	6 (37,5%)	11 (36,7%)
• RIC	16 (72,2%)	58 (69%)	10 (62,5%)	19 (63,3%)

6-color MFC was performed on bone marrow samples obtained before allo-HSCT for all patients. In 46 out of 106 patients, molecular markers such as NPM1, FLT3, RUNX1-RUNX1T1, MLL, and CBFβ-MYH11 were detected at the onset of the disease, which made it possible to determine the MRD status in these patients using PCR.

Results

Out of 106 patients 22 were identified as MRD MFC+, 84 patients were MRD MFC-, 16 patients were MRD PCR+ and 30 patients - MRD PCR-. Statistical analysis revealed significant differences between MRD+ and MRD- patients, regardless of the research method: in patients with MRD+ status had the worst RFS (MRD MFC: 24% versus 64%, $p < 0.0001$; MRD PCR: 37% versus 60%, $p = 0.0151$) and higher PR (MRD MFC: 72% versus 15%, $p < 0.0001$; MRD PCR: 53% versus 19%, $p = 0.0030$).

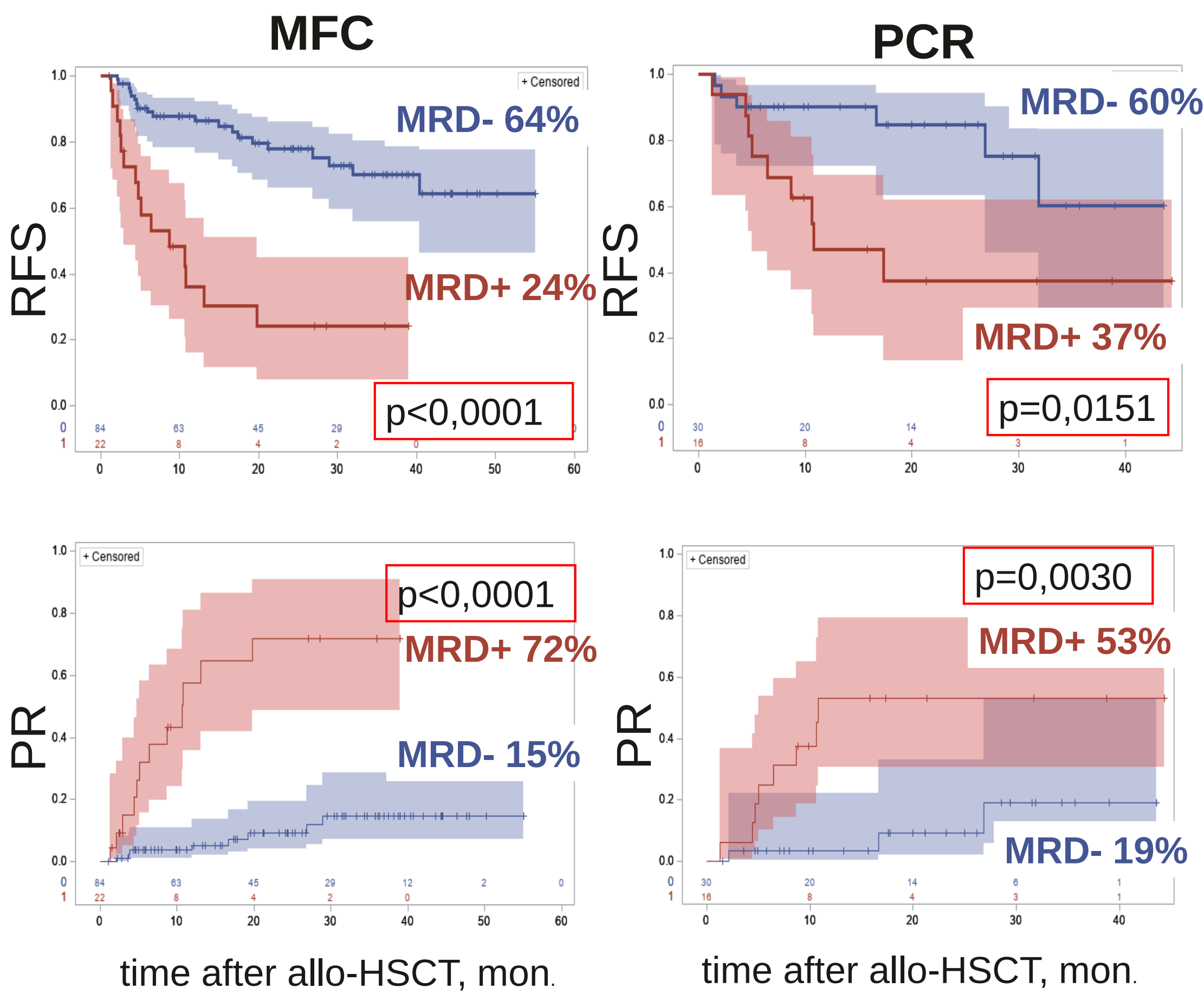


Table 2. Impact of various factors on the probability of relapse (multivariate analysis)

	p	HR	95%CI for HR	
Age (>40y/<40y)	0,0092	7,006	1,682	33,405
Sex	0,2242	0,536	0,198	1,527
ELN risk	0,0023	5,422	1,953	17,444
MRD before allo-HSCT	>0,0001	22,502	6,632	87,714
MAC/RIC	0,096	2,381	0,857	6,617
Donor type	0,1728	4,307	0,592	43,312

In our study, the presence of MRD before allo-HSCT ($p < 0.0001$), ELN risk ($p = 0.0023$) and age $> 40y$ ($p = 0.0092$) were independent factors influencing the probability of relapse.

Conclusions

MRD, regardless of whether it is determined by MFC or PCR, ELN risk, and older age are independent predictors of recurrence risk. The study of MRD in AML patients before allo-HSCT can be used to stratify the risk of allo-HSCT and identify patients who need prophylactic post-transplant therapy in order to prevent disease relapse.