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Original Articles

Association of Baseline Platelet Count with Complete Remission, Severe Bleeding, and 24-Month Overall Survival in Patients with Newly Diagnosed Acute Myeloid Leukemia: A Multi-Center Retrospective Cohort Study

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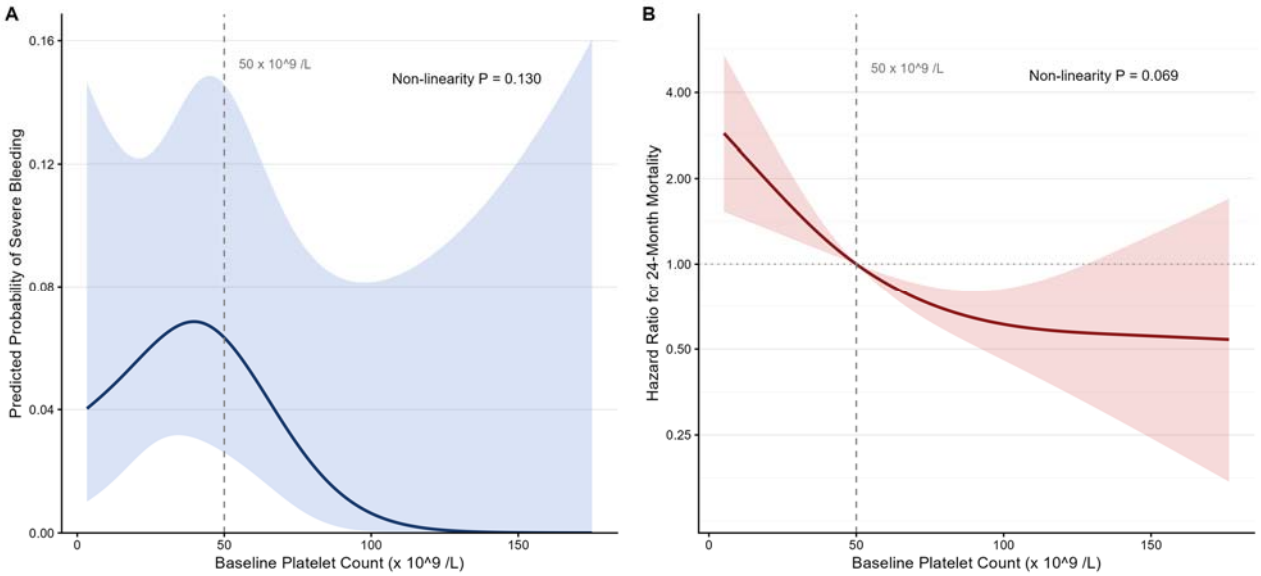
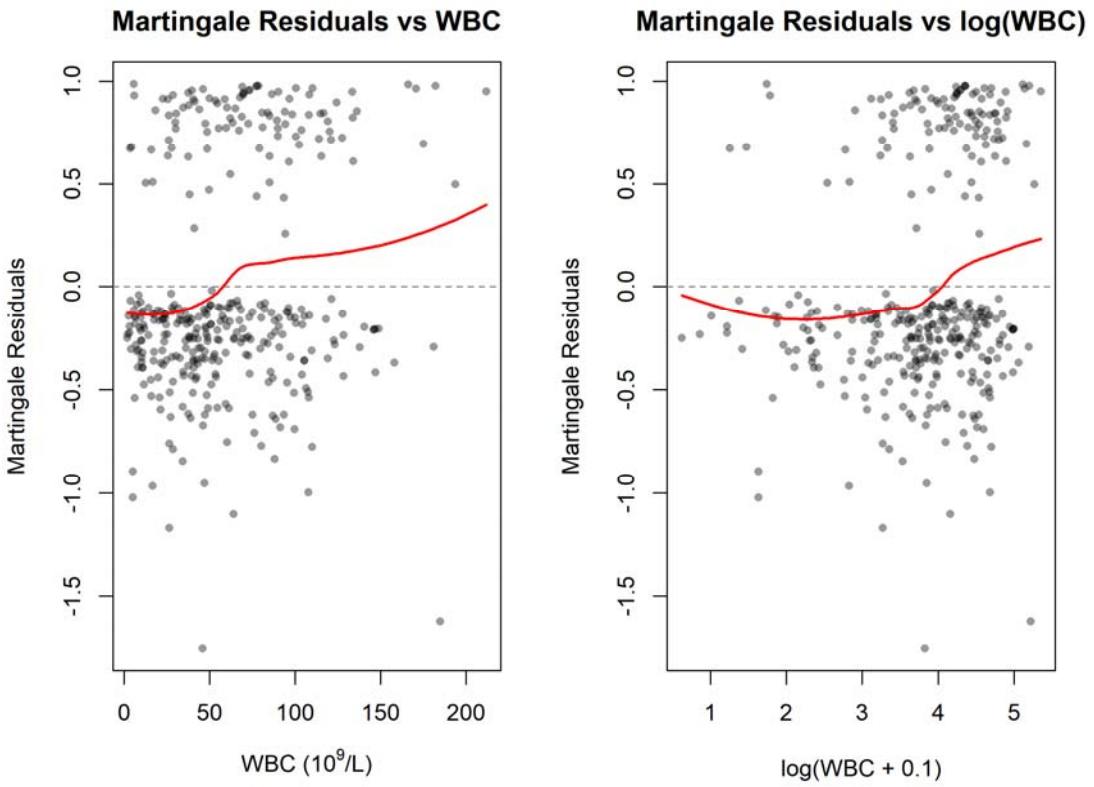
Supplementary Files.



Supplementary Figure 1. Three-knot restricted cubic spline analyses. Adjusted three-knot RCS associations of baseline platelet count with (A) severe bleeding (primary analysis, n=231, excluding patients with bleeding at diagnosis) and (B) 24-month OS (n=356). For severe bleeding, the overall association was not statistically significant (P=0.218) with no evidence of non-linearity (P=0.130). For 24-month OS, the overall association was statistically significant (P<0.001) and approximately linear (non-linearity P=0.069). Shaded areas show 95% CIs. The severe-bleeding RCS was adjusted for DIC and induction treatment class; the OS RCS was adjusted for age, WBC, bone marrow blasts, cytogenetic risk, induction class, ECOG, and AML type.



Supplementary Figure 2. Martingale-residual diagnostics for WBC functional form. Martingale residuals from the 24-month Cox model excluding WBC plotted against (A) WBC on the original scale and (B) log(WBC+0.1). Red curves represent loess smoothers; dashed horizontal lines indicate zero. Mild curvature was observed at higher WBC values, but formal specification tests did not reject the linear form (likelihood-ratio P=0.0996; spline nonlinear-component P=0.0779).

Supplementary Table 1. Univariable and multivariable logistic regression analysis of severe bleeding (CTCAE grade ≥ 3) in the full cohort (sensitivity analysis, n=356, 61 events).

Variable	Type	OR	95% CI	P value
PLT group (Low vs. Normal/High)	Univariable	3.044	1.555–5.962	0.001
WBC, × 10⁹/L	Univariable	1.017	1.011–1.024	<0.001
DIC: No (vs. Yes)	Univariable	0.260	0.133–0.509	<0.001
HMA+VEN (vs. intensive)	Univariable	2.401	1.258–4.582	0.008
Other regimen (vs. intensive)	Univariable	1.673	0.636–4.402	0.297
ECOG ≥2 (vs. 0–1)	Univariable	2.344	1.321–4.158	0.004
Secondary/therapy-related AML	Univariable	2.028	1.054–3.902	0.034
PLT group (Low vs. Normal/High)	Multivariable	2.753	1.318–5.749	0.007
WBC, × 10⁹/L	Multivariable	1.018	1.010–1.025	<0.001
DIC: No (vs. Yes)	Multivariable	0.335	0.156–0.721	0.005
HMA+VEN (vs. intensive)	Multivariable	2.875	1.370–6.034	0.005
Other regimen (vs. intensive)	Multivariable	2.729	0.926–8.042	0.069
ECOG ≥2 (vs. 0–1)	Multivariable	2.579	1.324–5.024	0.005
Secondary/therapy-related AML	Multivariable	2.065	0.961–4.433	0.063

This sensitivity analysis used the original severe-bleeding endpoint (all 356 patients, 61 events) and removed the baseline-bleeding covariate to avoid circularity with the outcome. The model additionally included ECOG performance status and AML type. Low baseline platelet count was associated with severe bleeding (adjusted OR=2.753, 95% CI 1.318–5.749, P=0.007). Abbreviations: OR, odds ratio; CI, confidence interval; DIC, disseminated intravascular coagulation; ECOG, Eastern Cooperative Oncology Group; HMA+VEN, hypomethylating agent plus venetoclax.

Supplementary Table 2. Comparison of baseline characteristics between patients censored before 24 months and those with adequate follow-up.

Variable	Censored <24m (n=88)	Adequate follow-up (n=268)	P value	SMD
Age, years	50.7±13.6	54.6±13.0	0.018	0.292
WBC, × 10⁹/L	61.8±40.6	57.2±39.9	0.347	0.115
Hb, g/L	78.2±18.7	78.2±19.9	0.998	0.000
Baseline PLT, × 10⁹/L	59.9±48.0	55.4±44.0	0.417	0.098
BM blast, %	58.8±16.7	60.0±17.5	0.585	0.068
LDH, U/L	519.8±229.3	513.5±220.2	0.820	0.028
Fibrinogen, g/L	2.6±0.9	2.4±0.9	0.059	0.236
D-dimer, mg/L	5.0±3.1	5.4±2.9	0.234	0.145

Early-censored patients were younger than those with adequate follow-up (50.7 vs. 54.6 years, P=0.018). No other baseline characteristics differed significantly (all P>0.05). Abbreviations: WBC, white blood cell count; Hb, hemoglobin; PLT, platelet count; LDH, lactate dehydrogenase; FIB, fibrinogen; DDimer, D-dimer; SMD, standardized mean difference.

Supplementary Table 3. Common-outcome scenario analyses for the association of low baseline platelet count with 24-month overall survival.

Scenario	HR	95% CI	P (Cox)	P (log-rank)	N	Events
Common-outcome: all-censored died	2.012	1.472–2.750	<0.001	<0.001	356	194
Common-outcome: all-censored survived	2.276	1.469–3.526	<0.001	<0.001	356	106

Common-outcome scenario: all-censored died assumed all 88 patients censored before 24 months died within 24 months (HR=2.012, 95% CI 1.472–2.750, P<0.001). Common-outcome scenario: all-censored survived assumed they all survived to 24 months (HR=2.276, 95% CI 1.469–3.526, P<0.001). Both common-outcome scenarios produced hazard ratios in the same direction as the primary analysis; however, these scenarios do not address differential informative censoring between platelet groups.

Supplementary Table 4. Sensitivity analysis restricted to patients receiving intensive induction (DA or IA regimens, n=264).

Analysis	OR/HR	95% CI	P value	N	Events
Severe bleeding (primary endpoint)	1.821	0.462–10.038	0.407	174	9
24-month OS	2.402	1.273–4.532	0.007	264	67

In patients receiving intensive induction, low baseline platelet count was associated with 24-month overall survival (adjusted HR=2.402, 95% CI 1.273–4.532, P=0.007; 67 deaths). The severe-bleeding association was not statistically significant in this subgroup (OR=1.821, 95% CI 0.462–10.038, P=0.407; n=174, 9 events). Abbreviations: HR, hazard ratio; OR, odds ratio; CI, confidence interval.

Supplementary Table 5. Center and calendar-period sensitivity analyses.

Analysis	Effect measure	OR/HR	95% CI	P value	N	Events
Center-adjusted 24-month OS	HR	1.896	1.192–3.017	0.007	356	106
Center × PLT-group interaction for 24-month OS	Interaction P	—	—	0.186	356	106
2020–2022: 24-month OS	HR	1.614	0.975–2.672	0.063	279	88
2023–2025: 24-month OS	HR	3.048	0.880–10.560	0.079	77	18
2020–2022: severe bleeding	OR	1.253	0.413–4.178	0.696	181	16
2023–2025: severe bleeding	OR	4.994	0.419–1385.252	0.224	50	4

The center-adjusted model added participating center to the prespecified 24-month Cox model. The interaction P value tests whether the platelet-group association varied by center; a non-significant result does not prove homogeneity. Calendar-period analyses were exploratory. Estimates for severe bleeding, particularly in 2023–2025 (4 events), were highly imprecise and should not be interpreted as evidence of no association. OR, odds ratio; HR, hazard ratio; CI, confidence interval; OS, overall survival; PLT, platelet count.