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Development and Validation of a Nomogram for Predicting Anti-Tumor Therapy–Related Hemorrhage in Acute Leukemia

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ABSTRACT

The goal of this work was to identify clinical indicators associated with bleeding episodes among individuals with acute leukemia receiving anticancer regimens and to develop and test a predictive nomogram based on those indicators. Encompassing 468 acute leukemia subjects, with acute promyelocytic leukemia diagnoses omitted, this retrospective cohort investigation drew on records from The Shanghai Fifth People's Hospital and Nanyang Municipal Central Hospital covering January 2013 to December 2023. The primary outcome measure was World Health Organization (WHO) grade 2 or higher hemorrhagic events associated with anticancer treatment. Subjects were randomly split into derivation and validation subsets at a 7:3 ratio. Within the derivation subset, univariable logistic regression and least absolute shrinkage and selection operator (LASSO) regression were applied to identify meaningful predictor variables, which were subsequently used to construct a hemorrhage risk nomogram. The nomogram's utility was assessed using receiver operating characteristic (ROC) curves, calibration curves, and decision curve analysis (DCA). Five independent variables emerged as correlates of bleeding associated with anticancer treatment in patients with acute leukemia. They were used to assemble the predictive nomogram: presence of infection, classes of distinct anti-hemorrhage prophylactic agents and blood derivatives delivered, platelet (PLT) transfusion, hematocrit value, and PLT count. ROC curve evaluation revealed that the nomogram possessed sound discriminatory capacity within both the derivation subset [area under the ROC curve (AUC) = 0.741] and the validation subset (AUC = 0.718). Calibration graphs showed strong concordance between observed and nomogram-estimated probabilities across both subsets, and DCA indicated a solid net clinical benefit. A nomogram to estimate the risk of anticancer treatment-attributable hemorrhage of WHO grade 2 or higher in patients with acute leukemia was developed and validated. Pending corroboration in prospective large-scale cohorts or experimental studies, this nomogram may provide a pragmatic, intuitive aid for bedside use.

Keywords: Hemorrhage, Nomogram, Acute leukemia, Anti-tumor therapy, Predictive model

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Introduction

Representing a swiftly advancing hematopoietic malignancy, acute leukemia stems from the unchecked clonal growth of hematopoietic stem cells [1]. Stratified by the principal cell lineage implicated [2], it splits into acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL). Hallmarks include fast-paced development, a compressed disease trajectory, and discouraging survival prospects [3, 4]. Data from the World Health Organization (WHO) show that globally, 474,500 incident leukemia diagnoses were documented in 2020, accounting for 2.46% of total new cancer diagnoses worldwide [5]. In contrast, inside China, 85,400 people received a new leukemia diagnosis in 2020, forming 1.87% of all incident cancer cases. The condition stands among the 10 deadliest malignancies for Chinese inhabitants and carries the highest tumor-related frequency and fatality rates for children and adults younger than 35 years [6].

Bleeding is a frequent untoward event in leukemic individuals post-chemotherapy or targeted intervention, driven by a range of mechanisms, including platelet (PLT) shortages, diminished coagulation factors, PLT functional defects, and endothelial compromise [7]. It additionally represents a leading contributor to fatal outcomes in this population [8, 9]. To curb the risk of hemorrhage, preventive PLT infusions guided by the patient's measured PLT levels are standard practice in clinical management [10, 11]. Nonetheless, bleeding complications continue to surface at notable rates. Per Stanworth *et al*. [12], among hematologic malignancy patients undergoing chemotherapy who received PLT transfusions, the observed rate of WHO grade 2, 3, or 4 bleeding was 43%. Given this, identifying predisposing factors for anticancer treatment-related hemorrhage is of considerable importance for refining therapeutic effectiveness and long-term patient trajectories.

Earlier scholarly efforts have delved into the contributors to post-treatment hemorrhagic episodes. Research led by Masternak *et al*. [13] demonstrated that mean platelet volume (MPV), a readily measurable hematologic index, shows a tight association with post-chemotherapeutic prognosis and the frequency of untoward events among patients with hematologic neoplasms. Another body of work connected lactate dehydrogenase (LDH)/fibrinogen (FBG) concentrations and FBG dynamics to hemorrhagic complications and death rates specifically in acute promyelocytic leukemia cases [14]. Despite these insights, a reliable prognostic model to estimate hemorrhagic risk in these individuals has remained absent.

Seeking to bridge this evidence deficit, the present inquiry was conceived to identify risk factors for WHO grade 2 or higher bleeding events in acute leukemia patients after anticancer therapies and to develop a risk-stratification model for such events. The findings from this work yield an understanding that can facilitate early flagging of high-risk individuals, thereby supporting hemorrhage avoidance and improving patient outcomes.

Materials and Methods

Study design and data sources

Conceived as a retrospective cohort analysis, this study culled data from Shanghai Fifth People's Hospital and Nanyang Municipal Central Hospital for episodes managed from January 2013 through December 2023. The investigative plan received ethical approval from the Ethical Committee of Shanghai Fifth People's Hospital, Fudan University (2023, ethical approval record No. 076). It was executed in accordance with the Declaration of Helsinki.

Study eligibility criteria

Eligibility for enrollment required meeting all of the following: (1) age of 18 years or older; (2) a freshly confirmed acute leukemia diagnosis; and (3) undergoing initial management with chemotherapy, targeted agents, or both modalities together. Grounds for exclusion were as follows: (1) confirmed acute promyelocytic leukemia (n = 133); (2) a WHO grade 2 or more severe bleeding episode within the fortnight before treatment began (n = 110); (3) any prior diagnosis of hereditary or acquired coagulopathy (n = 2); (4) a separate primary cancer arising in another organ system (n = 3); (5) marked functional compromise of critical organs—heart, liver, or kidneys (n = 8); (6) current pregnancy or breastfeeding (n = 3); and (7) insufficiently complete medical records (n = 2). The last analytical sample consisted of 468 individuals.

Data collection

Outcome variables

The primary study endpoint was anti-tumor therapy-attributable bleeding reaching a severity of WHO grade 2 or higher, characterized as any hemorrhagic manifestation occurring from the time anti-tumor treatment was initiated through the point of marrow recovery (specified by PLT count > 75×10^9/L alongside absolute neutrophil count [ANC] > 1.5×10^9/L) from the myelosuppressive phase of therapy. The WHO classification framework is extensively applied in PLT transfusion trials to rate bleeding severity, sorting hemorrhagic events into these strata: grade 1 (minor), grade 2 (moderate; not warranting prompt red blood cell [RBC] infusion), grade 3 (serious; calling for RBC infusion within a single day), or grade 4 (crippling or posing a threat to life) [15-17]. Secondary endpoints comprised overall survival (OS) and event-free survival (EFS). EFS captured the total days spanning from the launch of treatment to either disease worsening, return of disease, or death, regardless of cause. Return of disease was defined as the detection again of 5% or more blast cells or atypical elements in the bone marrow following achievement of complete remission, and/or leukemic cell spread outside the marrow. Disease worsening

was characterized by a 25% increase in the absolute number of primitive cells in peripheral blood or bone marrow, or by the emergence of extramedullary lesions.

Follow-up

Post-treatment surveillance was carried out at 3-month intervals throughout the initial year and every 6 months afterward. Relevant diagnostic and therapeutic records were pulled from the electronic health record infrastructures of the respective inpatient and outpatient services. For participants who became uncontactable during the study, the last recorded information available was retained. Information on death was collated through rigorous screening of institutional documentation and official death certifications, or through direct outreach to the patient's family members or the physicians managing their care. Observation continued until the earliest of disease worsening, recurrence, death, or the designated cutoff date of December 31, 2023.

Other variables

Broader clinical information was gathered for the cohort. Data captured prior to the launch of anti-tumor treatment included: (1) demographic profile: age, sex, body mass index (BMI, kg/m²), smoking habit, alcohol use history, family background of leukemia, family background of non-hematologic cancer, history of hematologic conditions (such as myelodysplastic syndrome, lymphoma, polycythemia vera, multiple myeloma, hemophilia, disseminated intravascular coagulation [DIC], splenomegaly, and similar), and concurrent medical issues (hypertension, diabetes mellitus, coronary artery disease, cerebrovascular disorders, and autoimmune conditions); (2) illness characteristics: anemia, extramedullary infiltration, bleeding, and infection; (3) bone marrow cell morphologic assessment; and (4) laboratory analyte measurements: white blood cell (WBC) count (10^9/L), absolute neutrophil count (ANC) (10^9/L), lymphocyte (LYM) count (10^9/L), RBC count (10^{12}/L), hemoglobin (Hb, g/L), hematocrit (HCT, %), PLT count (10^9/L), total bilirubin (TBIL, μmol/L), alanine aminotransferase (ALT, U/L), aspartate aminotransferase (AST, U/L), gamma-glutamyl transferase (GGT, U/L), alkaline phosphatase (ALP, U/L), blood urea nitrogen (BUN, mmol/L), creatinine (Cr, μmol/L), mean platelet volume (MPV, fL), platelet distribution width (PDW, fL), platelet–large cell ratio (P-LCR), prothrombin time (PT, s), activated partial thromboplastin time (APTT, s), thrombin time (TT, s), fibrinogen (Fg), D-dimer (D-D), and uric acid (UA). Data collected during the treatment period included: therapeutic approach (including chemotherapy alone, targeted therapy alone, and combined chemotherapy and targeted therapy), categories of anti-hemorrhage prophylactic agents and blood derivatives administered, PLT transfusion, and the number of treatment rounds. Post-treatment data collection included: WBC count, ANC count, LYM count, RBC count, Hb, HCT, PLT count, TBIL, ALT, AST, GGT, ALP, BUN, Cr, MPV, PDW, P-LCR, PT, APTT, TT, Fg, D-D, and UA.

Statistical analysis

Variables where less than one-fifth of observations were absent had their missing entries filled in, while any variable lacking more than 20% of its data points was eliminated from consideration. Analyses testing the sensitivity of results to the imputation process were conducted. Distributional normality of continuous measures was assessed using skewness and kurtosis statistics. The Levene procedure was applied to check variance uniformity. For continuous measures conforming to a normal curve, results were summarized as mean±standard deviation (SD), and between-group contrasts relied on the t-test when variances were equal or the t'-test when they were not. For continuous measures that deviated from normality, medians and interquartile bands [M (Q1, Q3)] were reported, and group contrasts used the Wilcoxon rank-sum test. Categorical measures were shown as frequencies alongside percentages. Fisher's exact test or the Chi-square test was chosen for testing associations among categorical variables. Multiple imputation was performed for variables with a missing rate of less than 20%.

All participating individuals were randomly assigned in a 7:3 ratio to a derivation set and a validation set, and divergences in baseline profiles between the two sets were scrutinized. Within the derivation set, each collected variable was analyzed using univariable logistic regression to assess its association with the emergence of hemorrhagic events. Variables with $P < 0.05$ for bleeding were subsequently entered into the least absolute shrinkage and selection operator (LASSO) regression to identify plausible predictors. A nomogram for forecasting the probability of anti-tumor therapy-linked hemorrhage of WHO grade 2 or greater was then formulated using the uncovered predictors. To test the nomogram's precision and consistency, receiver operating characteristic (ROC) curve evaluation and calibration graph inspection were performed in both the derivation and validation

sets. Clinical net benefit was examined through decision curve analysis (DCA). Kaplan–Meier survival curves, along with the log-rank test, were used to compare overall survival (OS) and event-free survival (EFS) between those who developed WHO grade 2 or higher hemorrhagic events and those who were spared. Odds ratios (OR) estimates with accompanying 95% confidence intervals (CIs) were derived. Two-sided P-values beneath 0.05 were taken to indicate meaningful statistical divergence. The entire data handling and analysis was performed in the R statistical computing platform.

Results and Discussion

Patient characteristics

The present analysis recruited 468 subjects who had received a new acute leukemia diagnosis. Random allocation assigned 328 subjects to a derivation sample and 140 to a validation sample. An analytical comparison revealed no material imbalances in the background profiles between the two samples, confirming that the data partitioning produced comparable groups **(Table 1).**

Table 1. Background profile comparison across the derivation and validation samples.

Variables	P	Statistics	Test set (n = 140)	Training set (n = 328)	Total (n = 468)
Demographic data					
Age, years, mean±SD	0.564	t = -0.577	53.42±13.62	52.58±14.86	53.83±14.49
Sex, n (%)	0.267	χ^2 = 1.233			
Male			69 (49.29)	180 (54.88)	249 (53.21)
Female			71 (50.71)	148 (45.12)	219 (46.79)
Height, cm, mean±SD	0.334	t = 0.967	164.91±8.22	165.69±7.85	165.46±7.96
Weight, kg, mean±SD	0.484	t = 0.701	64.67±11.38	65.49±11.61	65.25±11.54
BMI, kg/m^2, mean±SD	0.756	t = 0.311	23.68±3.21	23.79±3.53	23.75±3.44
History of cancer, n (%)	0.853	χ^2 = 0.034			
No			136 (97.14)	318 (96.95)	454 (97.01)
Yes			4 (2.86)	10 (3.05)	14 (2.99)
History of hematological disease, n (%)	0.084	χ^2 = 2.982			
No			132 (94.29)	321 (97.87)	453 (96.79)
Yes			8 (5.71)	7 (2.13)	15 (3.21)
Smoking, n (%)	0.804	–			
Never			111 (79.29)	266 (81.10)	377 (80.56)
Former			3 (2.14)	9 (2.74)	12 (2.56)
Current			26 (18.57)	53 (16.16)	79 (16.88)
Drinking, n (%)	0.316	–			
Never			125 (89.29)	299 (91.16)	424 (90.6)
Former			3 (2.14)	2 (0.61)	5 (1.07)
Current			12 (8.57)	27 (8.23)	39 (8.33)
Hypertension, n (%)	0.712	χ^2 = 0.136			
No			115 (82.14)	274 (83.54)	389 (83.12)
Yes			25 (17.86)	54 (16.46)	79 (16.88)
Diabetes, n (%)	0.815	χ^2 = 0.055			
No			128 (91.43)	302 (92.07)	430 (91.88)
Yes			12 (8.57)	26 (7.93)	38 (8.12)
Coronary heart disease, n (%)	0.589	χ^2 = 0.291			
No			134 (95.71)	310 (94.51)	444 (94.87)
Yes			6 (4.29)	18 (5.49)	24 (5.13)
Cerebrovascular disease, n (%)	0.356	χ^2 = 0.852			
No			133 (95.00)	304 (92.68)	437 (93.38)
Yes			7 (5.00)	24 (7.32)	31 (6.62)
Autoimmune disease, n (%)	0.888	χ^2 = 0.02			
No			137 (97.86)	322 (98.17)	459 (98.08)
Yes			3 (2.14)	6 (1.83)	9 (1.92)
Comorbidities, n (%)	0.279	χ^2 = 1.171			

No			96 (68.57)	241 (73.48)	337 (72.01)
Yes			44 (31.43)	87 (26.52)	131 (27.99)
Disease features					
Anemia, n (%)	0.679	$\chi^2 = 0.171$			
No			16 (11.43)	42 (12.80)	58 (12.39)
Yes			124 (88.57)	286 (87.20)	410 (87.61)
Extramedullary infiltration, n (%)	0.727	$\chi^2 = 0.121$			
No			128 (91.43)	303 (92.38)	431 (92.09)
Yes			12 (8.57)	25 (7.62)	37 (7.91)
Prior bleeding, n (%)	0.088	$\chi^2 = 2.913$			
No			98 (70.00)	254 (77.44)	352 (75.21)
Yes			42 (30.00)	74 (22.56)	116 (24.79)
Infection, n (%)	0.182	$\chi^2 = 1.781$			
No			70 (50.00)	142 (43.29)	212 (45.3)
Yes			70 (50.00)	186 (56.71)	256 (54.7)
Bone marrow cytomorphology					
Acute leukemia, n (%)	0.65	–			
ALL			30 (21.43)	68 (20.73)	98 (20.94)
AML			105 (75.00)	241 (73.48)	346 (73.93)
Others			5 (3.57)	19 (5.79)	24 (5.13)
Treatment information					
Treatment modality, n (%)	0.135	–			
Chemotherapy			27 (19.29)	61 (18.60)	372 (79.49)
Targeted therapy			113 (80.71)	258 (78.66)	8 (1.71)
Both			0 (0.00)	9 (2.74)	88 (18.8)
Types of hemorrhage prevention drugs and blood products, n (%)	0.781	–			
No			13 (9.29)	26 (7.93)	38 (8.12)
1			108 (77.14)	262 (79.88)	370 (79.06)
≥ 2			19 (13.57)	40 (12.20)	60 (12.82)
Platelet transfusion, n (%)	0.674	$\chi^2 = 0.177$			
No			15 (10.71)	31 (9.45)	46 (9.83)
Yes			125 (89.29)	297 (90.55)	422 (90.17)
Treatment courses, times, M (Q_1, Q_3)	0.547	Z = -0.603	1.00 (1.00, 3.00)	1.00 (1.00, 3.25)	1.00 (1.00, 3.00)
Laboratory tests (post-treatment)					
WBC count, 10^9/L, M (Q_1, Q_3)	0.931	Z = -0.087	1.90 (0.63, 5.75)	1.98 (0.71, 5.01)	1.96 (0.69, 5.21)
NEUT count, 10^9/L, M (Q_1, Q_3)	0.935	Z = -0.082	0.68 (0.17, 2.09)	0.58 (0.12, 2.46)	0.62 (0.14, 2.35)
LYM count, 10^9/L, M (Q_1, Q_3)	0.929	Z = -0.090	0.78 (0.36, 1.45)	0.72 (0.41, 1.37)	0.72 (0.39, 1.39)
RBC count, 10^{12}/L, mean ± SD	0.33	t = 0.975	2.38 ± 0.62	2.44 ± 0.69	2.42 ± 0.67
Hb, g/L, mean±SD	0.345	t' = 0.947	73.27 ± 18.22	75.10 ± 21.04	74.55 ± 20.24
HCT, %, mean±SD	0.579	t = 0.555	22.64 ± 5.81	23.00 ± 6.53	22.89 ± 6.32
PLT count, 10^9/L, M (Q_1, Q_3)	0.398	Z = -0.845	25.00 (10.00, 56.50)	27.00 (11.00, 70.00)	26.00 (11.00, 66.25)
Fg, g/L, mean±SD	0.356	t = 0.923	3.61 ± 1.78	3.80 ± 2.14	3.74 ± 2.04
PT, s, mean ± SD	0.923	t = -0.097	13.30 ± 3.84	13.26 ± 4.32	13.27 ± 4.18
APTT, s, mean±SD	0.886	t = 0.144	29.63 ± 6.67	29.72 ± 6.36	29.70 ± 6.44
TT, s, mean ± SD	0.891	t = -0.137	15.19 ± 2.94	15.14 ± 3.50	15.15 ± 3.34
TBIL, μmol/L, M (Q_1, Q_3)	0.818	Z = -0.230	9.40 (6.90, 13.33)	9.30 (6.90, 13.72)	9.30 (6.90, 13.60)
ALT, U/L, M (Q_1, Q_3)	0.425	Z = -0.798	15.50 (11.00, 25.25)	17.00 (11.00, 29.00)	16.50 (11.00, 29.00)
AST, U/L, M (Q_1, Q_3)	0.366	Z = -0.903	16.00 (12.00, 24.00)	17.00 (12.00, 27.00)	17.00 (12.00, 27.00)

GGT, U/L, M (Q_1, Q_3)	0.132	Z = -1.507	31.00 (19.00, 56.25)	35.00 (21.00, 66.25)	34.00 (20.00, 62.25)
ALP, U/L, M (Q_1, Q_3)	0.711	Z = -0.371	69.50 (58.08, 88.78)	71.35 (55.68, 100.15)	71.00 (56.10, 97.08)
BUN, mmol/L, M (Q_1, Q_3)	0.386	Z = -0.867	4.88 (3.64, 6.21)	5.13 (3.79, 6.29)	5.08 (3.73, 6.26)
Cr, μmol/L, M (Q_1, Q_3)	0.252	Z = -1.145	60.41 (48.63, 72.74)	60.85 (50.98, 75.01)	60.66 (50.00, 74.22)
Outcome					
Bleeding grade, n (%)	0.998	–			
No			39 (27.86)	91 (27.74)	130 (27.78)
Grade 1			16 (11.43)	38 (11.59)	54 (11.54)
Grade 2			69 (49.29)	164 (50.00)	233 (49.79)
Grade 3			13 (9.29)	28 (8.54)	41 (8.76)
Grade 4			3 (2.14)	7 (2.13)	10 (2.14)
WHO grade 2 or higher bleeding, n (%)	0.993	$\chi^2 = 0$			
No			55 (39.29)	129 (39.33)	184 (39.32)
Yes			85 (60.71)	199 (60.67)	284 (60.68)
Treatment efficacy, n (%)	0.337	–			
Complete remission			44 (31.43)	121 (36.89)	165 (35.26)
Complete remission with incomplete hematologic Recovery			1 (0.71)	5 (1.52)	6 (1.28)
Partial remission			4 (2.86)	11 (3.35)	15 (3.21)
No remission			54 (38.57)	94 (28.66)	148 (31.62)
Bone marrow not assessed			37 (26.43)	97 (29.57)	134 (28.63)
Mortality, n (%)	0.409	$\chi^2 = 0.681$			
No			112 (80.00)	251 (76.52)	363 (77.56)
Yes			28 (20.00)	77 (23.48)	105 (22.44)
Recurrence, n (%)	0.551	$\chi^2 = 0.355$			
No			97 (69.29)	218 (66.46)	315 (67.31)
Yes			43 (30.71)	110 (33.54)	153 (32.69)
Progression, n (%)	0.683	$\chi^2 = 0.166$			
No			137 (97.86)	317 (96.65)	454 (97.01)
Yes			3 (2.14)	11 (3.35)	14 (2.99)
EFS, days, M (Q_1, Q_3)	0.214	Z = -1.244	110.50 (41.00, 280.25)	152.50 (39.00, 364.25)	144.50 (39.25, 346.00)
OS, days, M (Q_1, Q_3)	0.183	Z = -1.333	131.50 (41.00, 348.50)	196.50 (39.75, 432.25)	179.00 (41.00, 404.75)

SD, standard deviation; M, median; Q1, 1st quartile; Q3, 3rd quartile. t, Student's t test; t', Satterthwaite t test; Z, Mann–Whitney U test; χ^2, Chi-square test; -, Fisher's exact test.

A detailed summary of the derivation sample is furnished in **Table 2.** Males accounted for 180 of these subjects (54.88%), while females accounted for 148 (45.12%). Looking at past medical backgrounds, a familial cancer burden was documented in 10 subjects (3.05%), previous hematologic pathology in 7 (2.13%), hypertensive disease in 54 (16.46%), diabetes mellitus in 26 (7.93%), established coronary artery disease in 18 (5.49%), cerebrovascular conditions in 24 (7.32%), and a concurrent autoimmune disorder in 6 (1.83%).

Table 2. Derivation sample characteristics contrasted between those who developed WHO grade 2 or higher hemorrhage and those who remained free of such events.

Variables	P	Statistics	WHO grade 2 or higher bleeding		Total (n = 328)
			Yes (n = 199)	No (n = 129)	
Demographic data					
Age, years, mean ± SD	0.021	t = 2.318	51.06 ± 14.75	54.92 ± 14.77	52.58 ± 14.86
Sex, n (%)	0.036	$\chi^2 = 4.374$			
Male			100 (50.25)	80 (62.02)	180 (54.88)

Female			99 (49.75)	49 (37.98)	148 (45.12)
Height, cm, mean ± SD	0.207	t = 1.264	165.25 ± 7.86	166.37 ± 7.83	165.69 ± 7.85
Weight, kg, mean ± SD	0.102	t = 1.641	64.65 ± 11.32	66.79 ± 11.96	65.49 ± 11.61
BMI, kg/m^2, mean ± SD	0.273	t = 1.097	23.62 ± 3.40	24.05 ± 3.73	23.79 ± 3.53
History of cancer, n (%)	0.776	χ^2 = 0.081			
No			193 (96.98)	125 (96.90)	318 (96.95)
Yes			6 (3.02)	4 (3.10)	10 (3.05)
History of hematological disease, n (%)	0.559	χ^2 = 0.341			
No			196 (98.49)	125 (96.90)	321 (97.87)
Yes			3 (1.51)	4 (3.10)	7 (2.13)
Smoking, n (%)	0.263	–			
Never			164 (82.41)	102 (79.07)	266 (81.10)
Former			3 (1.51)	6 (4.65)	9 (2.74)
Current			32 (16.08)	21 (16.28)	53 (16.16)
Drinking, n (%)	1	–			
Never			182 (91.46)	117 (90.70)	299 (91.16)
Former			1 (0.50)	1 (0.78)	2 (0.61)
Current			16 (8.04)	11 (8.53)	27 (8.23)
Hypertension, n (%)	0.4	χ^2 = 0.709			
No			169 (84.92)	105 (81.40)	274 (83.54)
Yes			30 (15.08)	24 (18.60)	54 (16.46)
Diabetes, n (%)	0.925	χ^2 = 0.009			
No			183 (91.96)	119 (92.25)	302 (92.07)
Yes			16 (8.04)	10 (7.75)	26 (7.93)
Coronary heart disease, n (%)	0.969	χ^2 = 0.002			
No			188 (94.47)	122 (94.57)	310 (94.51)
Yes			11 (5.53)	7 (5.43)	18 (5.49)
Cerebrovascular disease, n (%)	0.122	χ^2 = 2.389			
No			188 (94.47)	116 (89.92)	304 (92.68)
Yes			11 (5.53)	13 (10.08)	24 (7.32)
Autoimmune disease, n (%)	0.468	χ^2 = 0.526			
No			194 (97.49)	128 (99.22)	322 (98.17)
Yes			5 (2.51)	1 (0.78)	6 (1.83)
Comorbidities, n (%)	0.841	χ^2 = 0.04			
No			147 (73.87)	94 (72.87)	241 (73.48)
Yes			52 (26.13)	35 (27.13)	87 (26.52)
Disease features					
Anemia, n (%)	0.608	χ^2 = 0.264			
No			27 (13.57)	15 (11.63)	42 (12.80)
Yes			172 (86.43)	114 (88.37)	286 (87.20)
Extramedullary infiltration, n (%)	0.228	χ^2 = 1.456			
No			181 (90.95)	122 (94.57)	303 (92.38)
Yes			18 (9.05)	7 (5.43)	25 (7.62)
Prior bleeding, n (%)	0.014	χ^2 = 6.061			
No			145 (72.86)	109 (84.50)	254 (77.44)
Yes			54 (27.14)	20 (15.50)	74 (22.56)
Infection, n (%)	< 0.001	χ^2 = 19.091			
No			67 (33.67)	75 (58.14)	142 (43.29)
Yes			132 (66.33)	54 (41.86)	186 (56.71)
Bone marrow cytomorphology					
Acute leukemia, n (%)	0.103	–			
ALL			43 (21.61)	25 (19.38)	68 (20.73)
AML			149 (74.87)	92 (71.32)	241 (73.48)
Others			7 (3.52)	12 (9.30)	19 (5.79)

Treatment information					
Treatment modality, n (%)	0.002	–			
Chemotherapy			29 (14.57)	32 (24.81)	61 (18.60)
Targeted therapy			168 (84.42)	90 (69.77)	258 (78.66)
Both			2 (1.01)	7 (5.43)	9 (2.74)
Types of hemorrhage prevention drugs and blood products, n (%)	< 0.001	–			
No			6 (3.02)	20 (15.50)	26 (7.93)
1			165 (82.91)	97 (75.19)	262 (79.88)
≥ 2			28 (14.07)	12 (9.30)	40 (12.20)
Platelet transfusion, n (%)	< 0.001	χ^2 = 17.44			
No			8 (4.02)	23 (17.83)	31 (9.45)
Yes			191 (95.98)	106 (82.17)	297 (90.55)
Treatment courses, times, M (Q_1, Q_3)	0.203	Z = -1.272	1.00 (1.00, 3.00)	1.00 (1.00, 4.00)	1.00 (1.00, 3.25)
Laboratory tests (post-treatment)					
WBC count, 10^9/L, M (Q_1, Q_3)	< 0.001	Z = -5.102	1.10 (0.51, 4.16)	3.32 (1.53, 6.26)	1.98 (0.71, 5.01)
NEUT count, 10^9/L, M (Q_1, Q_3)	< 0.001	Z = -5.447	0.33 (0.07, 1.61)	1.50 (0.33, 3.41)	0.58 (0.12, 2.46)
LYM count, 10^9/L, M (Q_1, Q_3)	< 0.001	Z = -3.497	0.61 (0.34, 1.17)	0.87 (0.53, 1.57)	0.72 (0.41, 1.37)
RBC count, 10^{12}/L, mean±SD	0.029	t = 2.199	2.38 ± 0.65	2.55 ± 0.73	2.44 ± 0.69
Hb, g/L, mean ± SD	0.047	t = 1.993	73.24 ± 19.95	77.96 ± 22.41	75.10 ± 21.04
HCT, %, mean ± SD	0.014	t = 2.474	22.28 ± 6.18	24.10 ± 6.92	23.00 ± 6.53
PLT count, 10^9/L, M (Q_1, Q_3)	< 0.001	Z = -5.61	18.00 (8.00, 41.00)	49.00 (21.00, 119.00)	27.00 (11.00, 70.00)
FBG, g/L, mean ± SD	0.206	t' = -1.268	3.92 ± 2.29	3.62 ± 1.88	3.80 ± 2.14
PT, s, mean ± SD	0.051	t = -1.961	13.63 ± 4.79	12.68 ± 3.41	13.26 ± 4.32
APTT, s, mean ± SD	0.756	t = -0.312	29.81 ± 6.33	29.59 ± 6.42	29.72 ± 6.36
TT, s, mean ± SD	0.964	t = 0.045	15.13 ± 3.72	15.15 ± 3.15	15.14 ± 3.50
TBIL, μmol/L, M (Q_1, Q_3)	0.622	Z = -0.494	9.10 (6.95, 13.40)	9.80 (6.80, 14.00)	9.30 (6.90, 13.72)
ALT, U/L, M (Q_1, Q_3)	0.524	Z = -0.637	18.00 (12.00, 29.00)	16.00 (11.00, 28.00)	17.00 (11.00, 29.00)
AST, U/L, M (Q_1, Q_3)	0.264	Z = -1.117	18.00 (12.40, 29.50)	16.00 (12.00, 25.00)	17.00 (12.00, 27.00)
GGT, U/L, M (Q_1, Q_3)	0.299	Z = -1.04	37.00 (22.50, 69.50)	31.00 (20.00, 59.00)	35.00 (21.00, 66.25)
ALP, U/L, M (Q_1, Q_3)	0.21	Z = -1.255	69.50 (54.60, 97.70)	75.20 (57.00, 101.00)	71.35 (55.68, 100.15)
BUN, mmol/L, M (Q_1, Q_3)	0.592	Z = -0.536	5.15 (3.74, 6.49)	5.12 (3.79, 6.04)	5.13 (3.79, 6.29)
Cr, μmol/L, M (Q_1, Q_3)	0.486	Z = -0.696	59.50 (49.30, 76.20)	62.10 (52.00, 73.80)	60.85 (50.98, 75.01)
Outcome					
Bleeding grade, n (%)	< 0.001	–			
No			0 (0.00)	91 (70.54)	91 (27.74)
Grade 1			0 (0.00)	38 (29.46)	38 (11.59)
Grade 2			164 (82.41)	0 (0.00)	164 (50.00)
Grade 3			28 (14.07)	0 (0.00)	28 (8.54)
Grade 4			7 (3.52)	0 (0.00)	7 (2.13)
Treatment efficacy, n (%)	< 0.001	–			
Complete remission			90 (45.23)	31 (24.03)	121 (36.89)

Complete remission with incomplete hematologic recovery			3 (1.51)	2 (1.55)	5 (1.52)
Partial remission			7 (3.52)	4 (3.10)	11 (3.35)
No remission			53 (26.63)	41 (31.78)	94 (28.66)
Bone marrow not assessed			46 (23.12)	51 (39.53)	97 (29.57)
Mortality, n (%)	0.006	$\chi^2 = 7.521$			
No			142 (71.36)	109 (84.50)	251 (76.52)
Yes			57 (28.64)	20 (15.50)	77 (23.48)
Recurrence, n (%)	< 0.001	$\chi^2 = 17.081$			
No			115 (57.79)	103 (79.84)	218 (66.46)
Yes			84 (42.21)	26 (20.16)	110 (33.54)
Progression, n (%)	0.604	$\chi^2 = 0.269$			
No			191 (95.98)	126 (97.67)	317 (96.65)
Yes			8 (4.02)	3 (2.33)	11 (3.35)
EFS, days, M (Q_1, Q_3)	< 0.001	Z = -6.093	214.00 (84.00, 475.50)	63.00 (24.00, 228.00)	152.50 (39.00, 364.25)
OS, days, M (Q_1, Q_3)	< 0.001	Z = -6.302	256.00 (101.50, 518.00)	67.00 (24.00, 271.00)	196.50 (39.75, 432.25)

SD, standard deviation; M, median; Q1, 1st quartile; Q3, 3rd quartile. t: Student's t test; t': Satterthwaite t test; Z: Mann–Whitney U test; χ^2: Chi-square test; -: Fisher's exact test.

Among the derivation sample participants, bleeding manifestations associated with anti-neoplastic treatment and reaching WHO grade 2 or higher were recorded in 199 individuals. The grade-wise breakdown for this sample was as follows: no bleeding whatsoever, 91 cases (27.74%); grade 1 severity, 38 cases (11.59%); grade 2 severity, 164 cases (50.00%); grade 3 severity, 28 cases (8.54%); and grade 4 severity, 7 cases (2.13%).

Construction of predictive nomogram

When univariable logistic regression was fitted to the derivation sample data, statistically meaningful ties to hemorrhage onset emerged for age, sex, concurrent infection, prophylactic anti-hemorrhagic agents and blood derivative categories administered, PLT transfusion delivery, RBC count, Hb level, treatment approach, HCT level, PLT count, and a background of prior bleeding ($P < 0.05$ for each); **(Table 3).** Following LASSO-based regularization and multivariable logistic adjustment, only five factors retained independent predictive value meriting inclusion in model development: infection presence, prophylactic anti-hemorrhagic agents and blood derivative categories, PLT transfusion, HCT level, and PLT count **(Tables 4 and 5; Figure 1).** Evaluation for multicollinearity and model fit confirmed that the retained predictors did not exhibit problematic intercorrelations and that the overall model demonstrated strong calibration **(Figure 1).** Because HCT showed a linear relationship with the log-odds of the outcome, the most discriminant cutoff was determined by ROC curve inspection and maximization of the Youden index. PLT count followed a curvilinear pattern, prompting application of restricted cubic spline (RCS) modeling. The optimized dichotomization points thus identified equaled 22.55% for HCT and 26.93×10^9/L for PLT count **(Figure 2).** A graphical nomogram was generated to represent the prediction algorithm **(Figure 3)** visually.

Table 3. Univariable logistic regression evaluating clinical determinants potentially related to WHO grade 2 or higher hemorrhage among acute leukemia subjects.

Variables	P	OR (95%CI)	Wald	B
Age	0.022	0.982 (0.967-0.997)	5.237	-0.018
Sex	0.037	0.619 (0.394-0.972)	4.349	-0.480
BMI	0.273	0.966 (0.907-1.028)	1.201	-0.035
History of cancer	0.965	0.972 (0.269-3.512)	0.002	-0.029
History of hematological disease	0.340	0.478 (0.105-2.173)	0.912	-0.737
Smoking	0.266		2.648	
Never		Ref		
Former	0.104	0.311 (0.076-1.271)	2.645	-1.168
Current	0.862	0.948 (0.518-1.733)	0.030	-0.054

Drinking	0.941		0.121	
Never		Ref		
Former	0.756	0.643 (0.04-10.379)	0.097	-0.442
Current	0.870	0.935 (0.419-2.085)	0.027	-0.067
Hypertension	0.401	0.777 (0.431-1.4)	0.707	-0.253
Diabetes	0.925	1.04 (0.457-2.37)	0.009	0.04
Coronary heart disease	0.969	1.02 (0.385-2.703)	0.002	0.02
Cerebrovascular disease	0.127	0.522 (0.226-1.204)	2.324	-0.65
Autoimmune disease	0.278	3.299 (0.381-28.567)	1.175	1.194
Comorbidities	0.841	0.95 (0.576-1.567)	0.04	-0.051
Anemia	0.608	0.838 (0.427-1.645)	0.263	-0.176
Extramedullary infiltration	0.232	1.733 (0.703-4.275)	1.426	0.55
Prior bleeding	0.015	2.03 (1.148-3.589)	5.924	0.708
Infection	<0.001	2.736 (1.733-4.321)	18.642	1.007
Acute leukemia	0.105		4.503	
ALL		Ref		
AML	0.832	0.942 (0.539-1.644)	0.045	-0.06
Others	0.044	0.339 (0.118-0.974)	4.04	-1.081
WBC count	0.296	0.996 (0.99-1.003)	1.091	-0.004
NEUT count	0.246	0.993 (0.981-1.005)	1.344	-0.007
LYM count	0.270	0.992 (0.979-1.006)	1.215	-0.008
RBC count	0.030	0.698 (0.505-0.966)	4.714	-0.359
Hb	0.048	0.989 (0.979-1)	3.896	-0.011
HCT	0.015	0.958 (0.926-0.992)	5.926	-0.043
PLT count	0.002	0.996 (0.993-0.998)	9.934	-0.004
FBG	0.228	1.071 (0.958-1.198)	1.453	0.069
PT	0.062	1.065 (0.997-1.138)	3.483	0.063
APTT	0.755	1.006 (0.971-1.042)	0.098	0.006
TT	0.964	0.999 (0.937-1.064)	0.002	-0.001
TBIL	0.693	0.998 (0.986-1.009)	0.156	-0.002
ALT	0.686	1.001 (0.996-1.006)	0.164	0.001
AST	0.494	1.002 (0.996-1.008)	0.467	0.002
GGT	0.817	1 (0.997-1.002)	0.053	0
ALP	0.377	0.998 (0.994-1.002)	0.78	-0.002
BUN	0.668	1.017 (0.943-1.096)	0.183	0.016
Cr	0.668	1.002 (0.994-1.009)	0.184	0.002
Treatment modality	0.004		10.855	
Chemotherapy		Ref		
Targeted therapy	0.012	2.06 (1.172-3.62)	6.306	0.723
Both	0.170	0.315 (0.061-1.641)	1.88	-1.154
Types of different hemorrhage prevention drugs and blood products	<0.001		14.349	
No		Ref		
1	<0.001	5.67 (2.201-14.605)	12.92	1.735
≥2	<0.001	7.778 (2.498-24.214)	12.534	2.051
PLT transfusion	<0.001	5.18 (2.239-11.985)	14.773	1.645
Number of treatment courses	0.108	0.939 (0.869-1.014)	2.589	-0.063

OR, odds ratio; CI, confidence interval; Ref, reference.

Table 4. Coefficients from LASSO regression and corresponding collinearity diagnostics for hemorrhage-associated factors in acute leukemia.

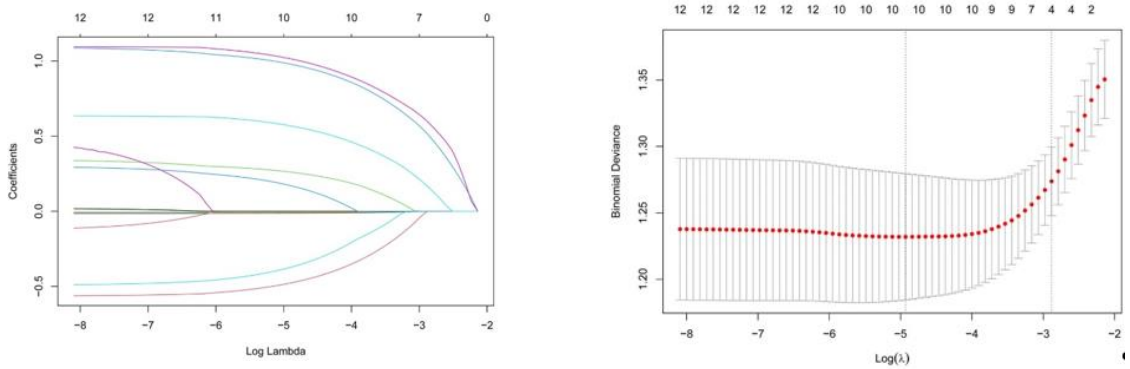
Variables	VIF	Beta
(Intercept)		-0.649799392
Infection	1.024541	0.516647335
PLT transfusion	1.116979	0.599423885
Types of hemorrhage prevention drugs and blood products	1.126291	0.168284131

HCT	1.215247	-0.009589530
PLT count	1.226876	-0.001333247

VIF, variance inflation factor.

Table 5. Multivariable logistic model of features independently associated with WHO grade 2 and above hemorrhage risk following anti-neoplastic treatment for acute leukemia.

Variables	P	OR (95% CI)	Wald	B
Infection	< 0.001	2.979 (1.816-4.888)	18.671	1.092
HCT-binary	0.026	0.585 (0.365-0.938)	4.954	-0.536
PLT count-binary	< 0.001	0.350 (0.204-0.601)	14.502	-1.051
Types of hemorrhage prevention drugs and blood products	0.004		11.250	
No		Ref		
1	0.001	5.439 (1.976-14.967)	10.750	1.694
≥ 2	0.003	6.423 (1.892-21.806)	8.896	1.860
PLT transfusion	0.005	3.674 (1.496-9.022)	8.056	1.301



a) b)

Figure 1. (a) Screening of candidate predictors through univariable logistic modeling; and (b) further regularization-based selection via LASSO regression.

Operating Instructions for the Nomogram: To obtain a patient-specific hemorrhage probability estimate, the clinician performs the following sequence: On the axis belonging to each predictor variable, locate the value that matches the patient under evaluation. Project a vertical line from that point upward to the uppermost "Points" ruler and record the assigned score. After repeating for all five predictors, compute the arithmetic sum of the five scores. Find the summed value along the "Total Points" ruler, position it centrally, then extend a vertical line downward until it meets the "Risk of Hemorrhage" ruler at the base; the number at that intersection is the predicted probability.

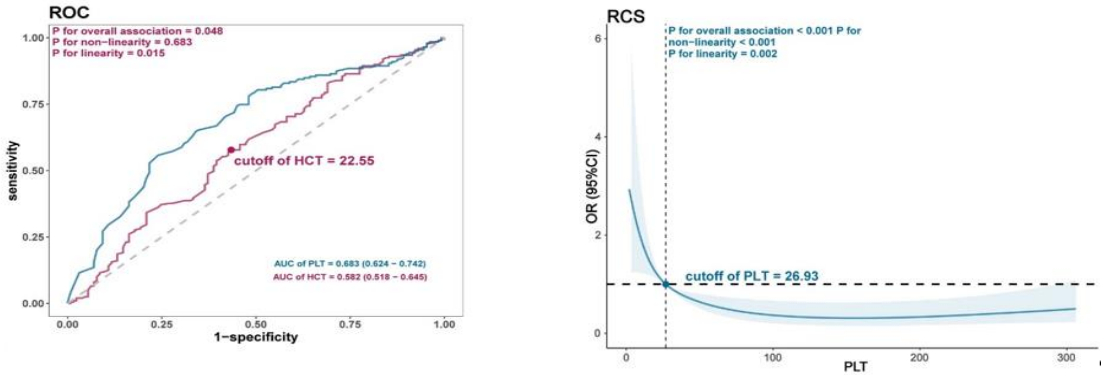


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Figure 2. Determination of optimal binary cut-points through ROC-based Youden index analysis for HCT and RCS curve fitting for PLT count.

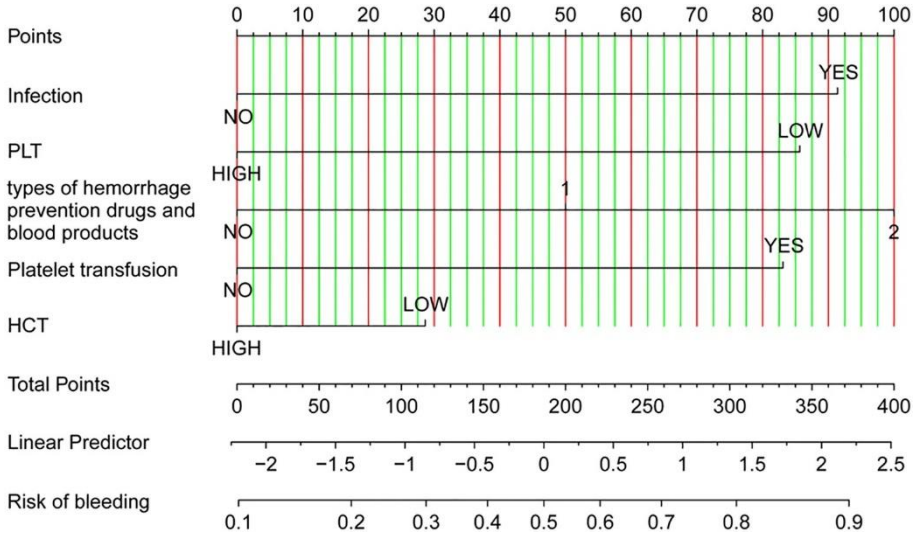
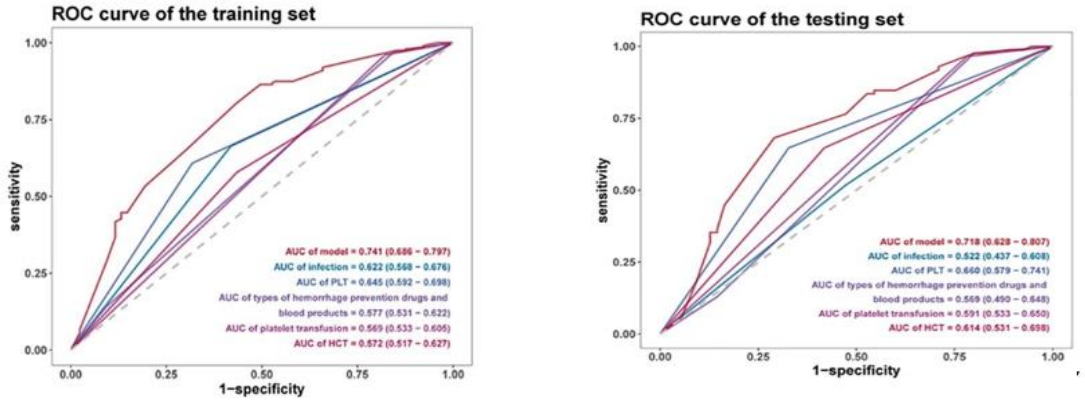


Figure 3. Graphical nomogram estimating individualized probability of WHO grade 2 or higher hemorrhage attributable to anti-neoplastic therapy among acute leukemia patients.

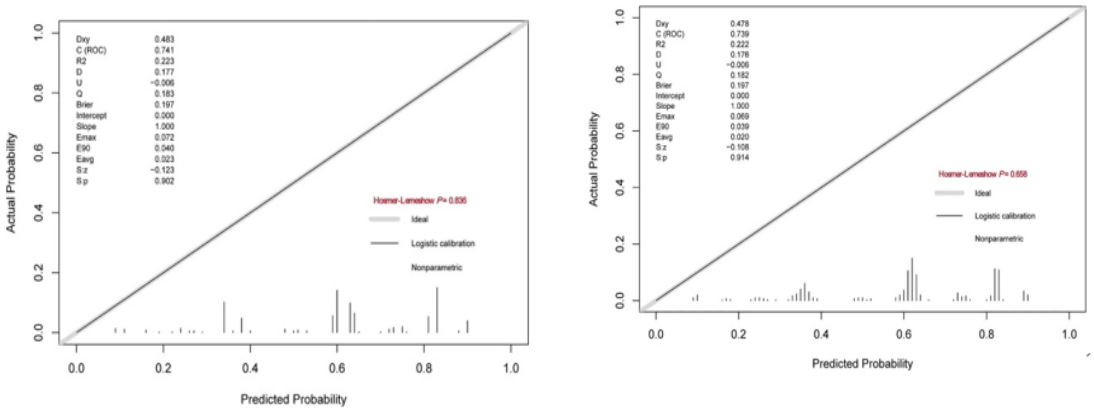
Evaluation of predictive model performance

The nomogram's capacity to discriminate and calibrate was formally tested in both the derivation and validation samples using ROC curves, calibration plots, and DCA. As presented in **Figure 4**, discrimination proved acceptable: the AUC reached 0.741 (95% CI: 0.636–0.797) within the derivation data and 0.718 (95% CI: 0.628–0.807) within the validation data. These values indicate that the nomogram performs adequately in stratifying the likelihood of treatment-emergent hemorrhage of WHO grade 2 or greater in acute leukemia. Calibration graphs further illustrated close concordance between the nomogram-derived risk estimates and the observed hemorrhage rates across the probability spectrum, both in the derivation set **(Figure 5a)** and the validation set **(Figure 5b).** Decision curve analysis revealed that adopting the nomogram to guide clinical action yielded a net positive benefit relative to default strategies of intervening in all or none, supporting its implementation value at the bedside **(Figure 6).**



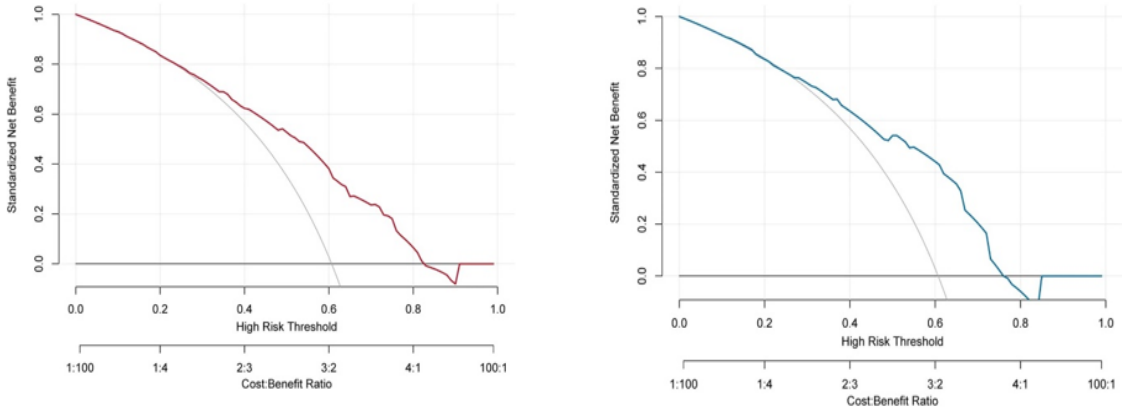
a) b)

Figure 4. ROC-based discrimination assessment of the constructed nomogram applied to the derivation and validation samples.



a) b)

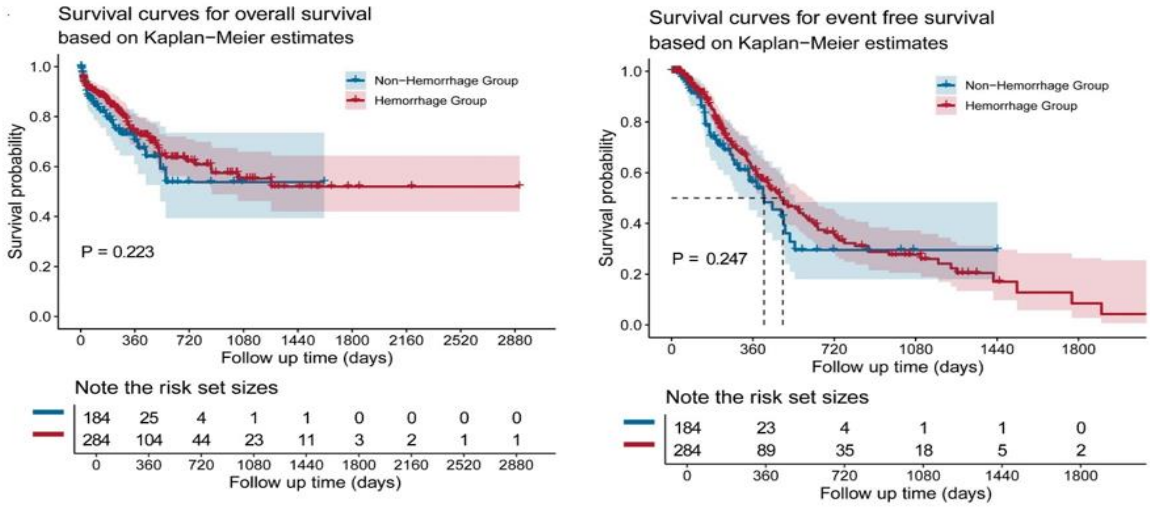
Figure 5. Calibration assessment of the constructed nomogram within the (a) derivation sample and (b) validation sample.



a) b)

Figure 6. Decision curve analysis quantifying the net clinical advantage of the constructed nomogram within the (a) derivation sample and (b) validation sample.

Kaplan–Meier survival curve estimation revealed no statistically significant difference in OS **(Figure 7a)** or EFS **(Figure 7b)** between acute leukemia patients who experienced a WHO grade 2 or higher hemorrhagic event and their counterparts who remained unaffected by such bleeding.



a) b)

Figure 7. Kaplan–Meier survival estimates contrasting (A) OS and (B) EFS for acute leukemia patients stratified by the occurrence versus non-occurrence of WHO grade 2 or higher hemorrhagic events.

What this investigation sought to explore were the potential links that tie the clinical and pathological features of acute leukemia patients to their odds of suffering bleeding events in the setting of anticancer treatment. Five variables emerged from univariable logistic screening followed by LASSO-based regularization. They were found to have significant independent associations with the risk of a hemorrhagic complication rated WHO grade 2 or above. Using this set of factors as building blocks, we assembled an original nomogram tailored to hemorrhage risk estimation in this patient population. Performance metrics derived from ROC discrimination testing, calibration assessments, and decision curve analytics each indicated strong predictive precision and genuine utility in everyday clinical care.

For patients contending with acute leukemia, therapeutic regimens anchored in cytotoxic agents—whether deployed singly or alongside targeted compounds—remain the standard approach [18, 19]. A well-recognized downside of these modalities is chemotherapy-induced thrombocytopenia (CIT), a frequent adverse consequence of both conventional cytotoxic drugs and numerous molecularly targeted therapies, which frequently forces postponement of scheduled cycles, downward dose adjustments, or outright cessation of planned treatment, all while heightening susceptibility to hemorrhagic complications [20]. Within our analytic dataset, five clinical factors demonstrated independent association with treatment-attributable hemorrhage at or above WHO grade 2: concurrent infection, the array of prophylactic hemostatic agents and blood derivatives administered, whether PLT transfusions were given, HCT levels, and PLT counts. Measurable derangements in the coagulation cascade commonly accompany bleeding diatheses, and the seriousness of hemorrhagic manifestations generally mirrors the depth of hemostatic compromise [21]. Against expectations, however, the suite of factors retained in our final model excluded both PT and APTT, which constitute the primary laboratory surrogates for coagulation system integrity. Earlier literature has suggested that it is coagulation failure severe enough to satisfy DIC criteria that principally drives grade 4 (fatal or incapacitating) hemorrhagic events.

In contrast, the evidence tying clotting dysfunction to grade 2–3 bleeding remains tenuous, a discrepancy that implies milder hemorrhagic presentations stem from a more heterogeneous constellation of pathophysiological triggers [22]. Separately, although patient sex met the threshold for significance when examined in isolation through univariable testing, it was eliminated once LASSO regularization was applied, an indication that sex fails to operate as an autonomous contributor within this particular clinical context. Our data further revealed that certain other historical correlates of bleeding liability—among them patient age, Hb concentration, hepatic and renal functional markers, and WBC count—did not retain independent predictive value for WHO grade 2 or higher events in the present sample. Earlier work by Xu *et al*. [23] focused on AML and highlighted infection and respiratory failure as factors independently associated with coagulation system status. Likewise deserving of emphasis is that the specific combination of hemostatic prophylactic measures and blood-derived products that patients received was independently associated with the endpoint of WHO grade 2 or higher anticancer therapy-attributable hemorrhage.

Within the framework of this study, should a subject's PLT count register at $\leq 100\times10^9$/L, the treating team could opt to employ any of the following, singly or in combination: thrombopoietin (TPO), serum interleukin-11 (IL-11), prothrombin complex, plasma, cryoprecipitate, FBG, recombinant activated factor VII, etamsylate, and tranexamic acid. Prior evidence has established that both receiving PLT transfusions and the measured PLT count are associated with intracranial hemorrhage risk in the acute leukemia population; crucially, the relationship between PLT transfusion and intracranial hemorrhage held firm even after statistical correction for PLT count. This elevated hazard tended either to plateau or to climb further in instances where one or more recorded PLT counts fell to $\leq 10\times10^9$/L and in scenarios characterized by a substantial percentage of time with PLT counts residing at $\leq 20\times10^9$/L [24]. Echoing those earlier observations, our own data indicate that PLT transfusion receipt and PLT count each serve as clinically meaningful and statistically independent determinants of the probability of hemorrhagic events graded WHO 2 or above during the anticancer treatment window. The seemingly contradictory nature of this relationship clearly warrants deeper exploration.

Furthermore, HCT may influence platelet functional characteristics, thereby indirectly shaping hemorrhagic tendency in people with leukemia [25]. Erythrocytes, through their effect on HCT, can increase whole-blood viscosity, thus raising resistance to flow. On the opposite end of the spectrum, the low-viscosity milieu of anemia could foster a predisposition to bleeding by reducing the margination of circulating PLTs toward the endothelial surface and by enhancing the local availability of nitric oxide, an endogenous molecule known to dampen platelet reactivity and to relax vascular tone.

As streamlined graphical tools for estimating outcomes, nomograms provide a user-friendly means of computing event probabilities for defined clinical groups [26]. In current oncologic practice, nomograms are widely used to project disease trajectories and survival outcomes [27, 28]. The effort reported here produced a nomogram purpose-built for forecasting the likelihood that a patient with acute leukemia will develop a hemorrhagic event of WHO grade 2 or greater severity during the course of anticancer therapy. The tool's ability to discriminate was corroborated via ROC curve analysis alongside calibration curve inspection. Beyond these measures, decision curve analysis confirmed the tangible clinical benefit and real-world applicability of the newly developed nomogram as an aid in hemorrhage risk forecasting. As such, this body of work offers original insights into the challenge of anticipating WHO grade 2 or higher bleeding episodes associated with anticancer therapeutics in the leukemia arena.

One result of our investigation that warrants particular comment is the absence of any meaningful separation in OS or EFS curves between patients with and without a WHO grade 2 or higher hemorrhagic event. Although at first glance this may seem inconsistent with clinical intuition, a multifactorial explanation is almost certainly at play. The predominant form of bleeding in our cohort was moderate (Grade 2, 50%). In contrast, truly grave Grade 4 events occurred with a frequency of merely about 2%. Compounding this, the near-universal application of prophylactic and interventional supportive measures—PLT transfusions and hemostatic pharmacotherapy—reached over 90% of participants, suggesting that state-of-the-art supportive care successfully neutralized whatever independent contribution bleeding might otherwise have made to mortality. Viewed in this light, within the present cohort, a hemorrhagic event is perhaps best interpreted not as a direct, autonomous harbinger of poor prognosis but rather as a clinical marker reflective of the extent and severity of the backdrop myelosuppressive condition. This nuance stands somewhat at odds with select earlier published accounts and likely mirrors the advances realized through modern transfusion medicine and contemporary supportive algorithms, which together appear to have meaningfully curtailed the lethal sequelae once commonly attendant on treatment-related bleeding.

Based on our review of the existing literature, the present undertaking constitutes the first attempt to forge a hemorrhage risk estimation methodology specific to anticancer treatment in the acute leukemia domain by weaving together diverse clinical characteristics into a unified predictive framework. The nomogram that resulted from this process shows considerable promise as a practical aid for bedside hemorrhage risk stratification in the leukemia population. Nonetheless, this work is not without its shortcomings. To begin with, the cohort was somewhat small. In the second place, our validation process did not extend to testing the nomogram on external, independent datasets, an exercise that is critical to establishing its generalizability and durability; such external verification is needed to strengthen the credibility of the inferences drawn here. A final caveat concerns the well-known heterogeneity in long-term outcomes among acute leukemia patients, which can vary markedly depending on immunophenotypic classification, cellular lineage, and the landscape of molecular genetic aberrations; our study design did not encompass stratified outcome analyses along these dimensions. For the nomogram to gain standing as a validated clinical decision aid, subsequent multi-institutional research programs enrolling substantially larger samples will be required.

Conclusion

This analysis identified five factors as independently predictive of WHO grade 2 or higher hemorrhage arising in the context of anticancer treatment for acute leukemia: infection, the variety of hemostatic prophylactic agents and blood derivatives used, PLT transfusion administration, HCT value, and PLT count. Assembled from these indices, the predictive nomogram demonstrated robust forecasting performance and an accessible format suitable for frontline clinical application. Before it can be adopted with full confidence, however, external corroboration of the nomogram across independent patient series will be necessary.

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