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Original Article

Incidence and prognostic factors for pulmonary infection complications in elderly patients with acute myeloid leukemia

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Abstract: Objective: To investigate the incidence, risk factors, and prognostic effect of pulmonary infections in elderly patients with acute myeloid leukemia (AML), and to provide evidence for optimizing infection prevention and management as well as individualized treatment strategies. Methods: We retrospectively analyzed clinical data from 150 elderly AML patients diagnosed and treated at our hospital between March 2020 and October 2022. Their demographics, laboratory test results, treatment regimens, and follow-up records were collected and analyzed. Logistic regression was used to identify risk factors for pulmonary infections, while Kaplan-Meier survival analysis and Cox regression were employed to assess the effect of infections on survival. Time-dependent ROC curves were applied to evaluate the predictive performance of key laboratory indicators. Results: Among the 150 cases, the incidence of pulmonary infections was 42%. Logistic regression identified low hemoglobin (Hb < 110.5 g/L), elevated C-reactive protein (CRP ≥ 24.01 mg/L), elevated procalcitonin (PCT ≥ 0.255 ng/mL), low neutrophil count (NC < 0.475×10^9/L), and low platelet count (PLT < 84×10^9/L) as independent risk factors for pulmonary infections (all P < 0.05). Kaplan-Meier survival analysis revealed that the median survival of patients with pulmonary infections was significantly lower than that of the non-infected group (P < 0.001). Multivariate Cox regression analysis demonstrated that pulmonary infections were an independent prognostic factor for survival in elderly AML patients (HR = 1.469, P = 0.011). Time-dependent ROC analysis showed that CRP and PCT had the highest predictive efficacy for pulmonary infections, with AUCs of 0.739 and 0.845, respectively. Conclusion: Pulmonary infections are common among elderly AML patients and significantly worsen their prognosis. Low Hb, high CRP and PCT, and low NC and PLT are critical risk factors for infection. Strengthening infection monitoring and initiating early intervention may improve patient survival outcomes.

Keywords: Acute myeloid leukemia, pulmonary infection, risk factors, survival analysis, elderly patients

Introduction

Acute myeloid leukemia (AML) is a highly heterogeneous malignancy originating from hematopoietic stem cells in the bone marrow. It is characterized by the abnormal proliferation of immature cells, blocked differentiation, and suppressed normal hematopoiesis [1, 2]. AML is one of the most common leukemias worldwide, with a striking predominance in the elderly - more than 50% of new cases arise in patients aged 65 years or older [3]. Compared to younger patients, elderly AML patients often present with multiple adverse prognostic factors at diagnosis, including complex chromosomal abnormalities, a high proportion of blast cells, and specific molecular mutations (e.g., FLT3-ITD mutation) [4]. Furthermore, comorbidities such as hypertension, diabetes, and cardiovascular diseases are common in this population, limiting their tolerance for intensive chemotherapy and significantly increasing the risk of treatment-related complications [5].

Pulmonary infections represent one of the most frequent and life-threatening complications in elderly AML patients undergoing chemotherapy, exhibiting both high incidence and mortality rates [6]. These infections are closely associated with chemotherapy-induced myelosuppres-

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sion, immunosuppression, invasive procedures (e.g., central venous catheterization), corticosteroid use, and pre-existing respiratory compromise [7]. Collectively, these factors render elderly AML patients highly susceptible to bacterial, viral, and fungal infections, with pulmonary infections emerging as the predominant type [8]. Pulmonary infections not only pose a direct threat to patient survival but also delay or interrupt chemotherapy, significantly affecting long-term prognosis [9]. Despite this, studies on the incidence and survival effect of pulmonary infections in elderly AML patients are limited, particularly concerning the specific risk factors for these infections.

Existing researches have established the diagnostic and prognostic utility of inflammatory markers, such as C-reactive protein (CRP) and procalcitonin (PCT), in infection management [10]. While elevated CRP and PCT levels demonstrate strong correlations with infection occurrence and severity, their predictive value specifically in elderly AML patients remains insufficiently characterized. Furthermore, hematological data such as hemoglobin (Hb), neutrophil count (NC), and platelet count (PLT) may serve as additional indicators for infection risk assessment [11]. Nevertheless, the specific mechanisms and independent prognostic significance of these biomarkers in elderly AML patients warrant further elucidation.

Pulmonary infections adversely affect both short-term survival and long-term outcomes by impairing immune function [12]. Interestingly, some studies have suggested a survival benefit associated with infections, possibly attributable to intensified anti-infective therapies and enhanced supportive care in these cases [13]. These conflicting observations underscore the need for rigorous evaluation of the net survival effect of pulmonary infections in this population. Moreover, the interactions between infections and other prognostic factors (e.g., age, FAB classification, FLT3-ITD mutation, chemotherapy phase, and bone marrow blast proportion) remain unclear, and how these factors influence patient outcomes requires further investigation.

This retrospective cohort study systematically investigated the incidence, risk factors, and prognostic implications of pulmonary infections in elderly AML patients. Our findings provide critical evidence to optimize infection prevention and personalize therapeutic approaches.

Materials and methods

Case selection

This single-center retrospective study was conducted in the Department of Hematology at The First Affiliated Hospital of Xi'an Medical University. The study included elderly AML patients (≥ 60 years) who were diagnosed and treated between March 2020 and October 2022. According to the Inclusion and Exclusion Criteria, a total of 150 eligible cases were included. This study was approved by the Institutional Medical Ethics Committee of The First Affiliated Hospital of Xi'an Medical University and adhered to the ethical principles of the Declaration of Helsinki for human research.

Inclusion criteria: Patients were included if they met the following criteria: AML diagnosis according to WHO classification [14]; Age ≥ 55 years; Completion of at least one cycle of standard chemotherapy (induction, consolidation, or refractory/relapsed therapy); Availability of complete clinical data and laboratory test results; Follow-up duration ≥ 3 months or confirmation of death outcomes.

Exclusion criteria: Concurrent diagnosis of other malignant hematological diseases or solid tumors; Severe cardiac, pulmonary, hepatic, or renal dysfunction; Presence of active infections at other sites at diagnosis; Loss to follow-up or incomplete clinical data during chemotherapy.

Data collection

Clinical and laboratory data were obtained from the hospital's electronic medical records and patient follow-up records.

Clinical data: Demographics (gender, age, smoking history, hypertension, diabetes, cardiovascular diseases), disease-related information (FAB classification, FLT3-ITD mutation status, and bone marrow blast cell percentage), and treatment-related information (chemotherapy regimen and phase, chemotherapy intensity, invasive procedures, and corticosteroid use).

Laboratory data: Hematologic indicators (hemoglobin [Hb], white blood cell count [WBC], platelet count [PLT], and neutrophil count [NC]), and inflammatory markers (C-reactive protein [CRP] and procalcitonin [PCT]), and other metrics (body weight, height, body mass index [BMI]).

Hematologic tests (Hb, WBC, PLT, NC) were measured using a Sysmex XN-1000 analyzer (Sysmex Corporation, Japan). CRP levels were measured using a Beckman AU5800 analyzer (Beckman Coulter, USA), while PCT was determined using a Roche Cobas e411 analyzer (Roche Diagnostics, Germany). FLT3-ITD mutation status was detected by real-time quantitative PCR using an ABI 7500 instrument (Applied Biosystems, USA).

Follow-up: All follow-up data, including survival status, infection status (especially pulmonary infections), treatment details, and disease recurrence, were collected by phone calls, outpatient visits, and electronic medical records. The follow-up period spanned from initial diagnosis to the study cutoff date (October 31, 2024), with a maximum observation duration of two years.

Primary outcomes: Incidence and risk factors of pulmonary infections, and their effect on survival (evaluated using Kaplan-Meier survival curves and Cox regression analysis).

Secondary outcomes: Predictive efficacy of laboratory indicators (e.g., Hb, CRP, PCT, NC, and PLT) for pulmonary infections, and interaction analysis between infection status and other prognostic factors (e.g., FAB classification, FLT3-ITD mutation, and chemotherapy phase).

Statistical analysis

Statistical analyses were conducted using SPSS 26.0 (IBM Corporation, USA) and R software (version 4.3.3). Descriptive statistics were used to summarize continuous variables (mean ± SD or median [IQR]) and categorical variables (frequencies and percentages). Comparisons between groups were made using t-tests for continuous variables, Mann-Whitney U tests for non-normally distributed variables, and Chi-square or Fisher's exact tests for categorical variables. Risk factor analysis for pulmonary infections was performed with logistic regression, and ROC curves were used to assess the predictive efficacy of continuous variables. Survival analysis included Kaplan-Meier curves and log-rank tests, with univariate and multivariate Cox regression analyses evaluating the independent effects of pulmonary infections and other factors on survival. Time-dependent ROC curves, survival analyses, and interaction analyses were conducted using R 4.3.3. Statistical significance was set at a two-sided *P*-value of < 0.05.

Results

Patient characteristics and pulmonary infection risk factors

Among the 150 patients, no significant differences were observed between those with and without pulmonary infections regarding gender, hypertension, diabetes, cardiovascular diseases, chemotherapy regimen, chemotherapy cycles, central venous catheterization duration, corticosteroid use, or bone marrow blast percentage ($P > 0.05$). However, patients in the infection group had a significantly higher prevalence of smoking history ($P = 0.037$). The infection risk was also significantly higher in patients with FAB classifications M2, M4, and M5 ($P = 0.021$) and FLT3-ITD-positive mutations ($P < 0.001$). High-intensity chemotherapy ($P = 0.003$), induction therapy phase ($P < 0.001$), and invasive procedures ($P < 0.001$) were significantly associated with infection occurrence.

Laboratory results revealed that the infection group had significantly lower hemoglobin (Hb) levels ($P = 0.004$), higher CRP and PCT levels ($P < 0.001$), and reduced platelet count (PLT) and neutrophil count (NC) ($P = 0.005$ and $P < 0.001$, respectively) (**Table 1**).

Risk factor analysis and predictive performance of laboratory indicators

ROC curve analysis identified optimal cut-off values for several laboratory indicators to predict pulmonary infections. CRP and PCT demonstrated strong predictive performance (AUC = 0.739 and 0.845, respectively), with PCT showing high specificity (96.51%) and a high Youden index (60.57%). Hb had lower sensitivity (AUC = 0.637), and PLT showed relatively

Table 1. Baseline characteristics of patients with and without pulmonary infections

Factor	Total	Pulmonary Infection Group (n = 64)	Non-Infection Group (n = 86)	Statistic	*P*-value
Gender					
Male	83 (55.33%)	36 (56.25%)	47 (54.65%)	0.038	0.846
Female	67 (44.67%)	28 (43.75%)	39 (45.35%)		
Smoking History				4.366	0.037
Yes	45 (30%)	25 (39.06%)	20 (23.26%)		
No	105 (70%)	39 (60.94%)	66 (76.74%)		
Hypertension History				0.913	0.339
Yes	59 (39.33%)	28 (43.75%)	31 (36.05%)		
No	91 (60.67%)	36 (56.25%)	55 (63.95%)		
Diabetes History				0.349	0.555
Yes	25 (16.67%)	12 (18.75%)	13 (15.12%)		
No	125 (83.33%)	52 (81.25%)	73 (84.88%)		
Cardiovascular Disease History				0.193	0.661
Yes	11 (7.33%)	4 (6.25%)	7 (8.14%)		
No	139 (92.67%)	60 (93.75%)	79 (91.86%)		
FAB Classification				9.757	0.021
M0	8 (5.33%)	4 (6.25%)	4 (4.65%)		
M2	100 (66.67%)	34 (53.12%)	66 (76.74%)		
M4	12 (8%)	8 (12.5%)	4 (4.65%)		
M5	30 (20%)	18 (28.12%)	12 (13.95%)		
FLT3-ITD Mutation				13.75	< 0.001
Positive	44 (29.33%)	29 (45.31%)	15 (17.44%)		
Negative	106 (70.67%)	35 (54.69%)	71 (82.56%)		
Chemotherapy Regimen				4.694	0.096
IDA + Ara-C	30 (20%)	16 (25%)	14 (16.28%)		
DNR + Ara-C	51 (34%)	25 (39.06%)	26 (30.23%)		
Acla + Ara-C	69 (46%)	23 (35.94%)	46 (53.49%)		
Chemotherapy Season				0.088	0.993
Spring	30 (20%)	13 (20.31%)	17 (19.77%)		
Summer	41 (27.33%)	17 (26.56%)	24 (27.91%)		
Autumn	43 (28.67%)	18 (28.12%)	25 (29.07%)		
Winter	36 (24%)	16 (25%)	20 (23.26%)		
Number of Chemotherapy Cycles				2.32	0.128
≤ 1	83 (55.33%)	40 (62.5%)	43 (50%)		
> 1	67 (44.67%)	24 (37.5%)	43 (50%)		
High-Intensity Chemotherapy				8.93	0.003
Yes	28 (18.67%)	19 (29.69%)	9 (10.47%)		
No	122 (81.33%)	45 (70.31%)	77 (89.53%)		
Chemotherapy Phase				17.987	< 0.001
Induction Therapy	88 (58.67%)	37 (57.81%)	47 (54.65%)		
Consolidation Therapy	40 (26.67%)	10 (15.63%)	34 (39.53%)		
Refractory/Relapsed	22 (14.67%)	17 (26.56%)	5 (5.81%)		
Central Venous Catheterization Time				2.945	0.086
≤ 1 month	84 (56%)	41 (64.06%)	43 (50%)		
> 1 month	66 (44%)	23 (35.94%)	43 (50%)		
Invasive Procedures				19.756	< 0.001
Yes	52 (34.67%)	35 (54.69%)	17 (19.77%)		
No	98 (65.33%)	29 (45.31%)	69 (80.23%)		
Use of Corticosteroids				2.57	0.109
Yes	73 (48.67%)	36 (56.25%)	37 (43.02%)		
No	77 (51.33%)	28 (43.75%)	49 (56.98%)		
Bone Marrow Blast Cell Percentage (%)				2.137	0.144
≤ 50	76 (50.67%)	28 (43.75%)	48 (55.81%)		
> 50	74 (49.33%)	36 (56.25%)	38 (44.19%)		

Age (years)	67.84 ± 4.92	67.86 ± 5.17	67.83 ± 4.76	-0.041	0.967
BMI (kg/m^2)	24.54 [22.84, 25.83]	24.96 [22.70, 26.23]	24.35 [23.11, 25.34]	1.148	0.251
Hemoglobin (Hb) (g/L)	83.50 [62.25, 120.00]	79.50 [64.50, 92.00]	100.00 [58.25, 146.25]	2.867	0.004
White Blood Cell Count (WBC) (×10^9/L)	6.28 ± 2.79	6.63 ± 2.85	6.03 ± 2.74	-1.299	0.196
C-Reactive Protein (CRP) (mg/L)	15.89 [9.63, 26.53]	27.89 [11.65, 41.16]	13.80 [8.98, 17.69]	4.993	< 0.001
Procalcitonin (PCT) (ng/mL)	0.14 [0.08, 0.29]	0.31 [0.18, 0.44]	0.10 [0.05, 0.15]	7.227	< 0.001
Neutrophil Count (NC) (×10^9/L)	0.49 ± 0.21	0.35 ± 0.12	0.59 ± 0.21	8.241	< 0.001
Platelet Count (PLT) (×10^9/L)	108.50 [66.50, 146.00]	92.00 [44.75, 135.50]	122.00 [85.25, 157.50]	2.82	0.005

Note: FAB: French-American-British, FLT3-ITD: FMS-like tyrosine kinase 3 internal tandem duplication, IDA: Idarubicin, Ara-C: Cytarabine, DNR: Daunorubicin, Acla: Aclarubicin, BMI: Body Mass Index, Hb: Hemoglobin, WBC: White Blood Cell count, CRP: C-reactive protein, PCT: Procalcitonin, NC: Neutrophil count, PLT: Platelet count.

weaker predictive efficacy (AUC = 0.635). Logistic regression confirmed that low Hb (< 110.5 g/L), elevated CRP (≥ 24.01 mg/L), elevated PCT (≥ 0.255 ng/mL), low NC (< 0.475×10^9/L), and low PLT (< 84×10^9/L) were independent risk factors for pulmonary infections, with high-intensity chemotherapy and invasive procedures also significantly increasing infection risk (**Figure 1** and **Table 2**).

Logistic regression analysis of risk factors for pulmonary infections

Logistic regression analysis identified significant risk factors for pulmonary infections after converting continuous variables into binary variables based on ROC cut-off values (**Table 3**). Low Hb (< 110.5 g/L) significantly increased infection risk (β = -3.467, P = 0.005, OR < 0.001). Elevated CRP (≥ 24.01 mg/L) and PCT (≥ 0.255 ng/mL) were strongly associated with infection risk (β = 3.188, P = 0.005, OR = 11.704; and β = 3.396, P = 0.004, OR = 13.743, respectively). Decreased NC (< 0.475×10^9/L; β = -2.564, P = 0.007, OR = 0.010) and reduced PLT (< 84×10^9/L) (β = 2.235, P = 0.038, OR = 5.383) were significant risk factors as well. High-intensity chemotherapy (β = 2.841, P = 0.010, OR = 8.897) and invasive procedures (β = 2.327, P = 0.007, OR = 5.823) were also significant risk factors (**Table 4**).

Survival analysis and prognostic factors

During the follow-up, 70 out of 150 patients died (mortality rate of 46.67%), with a median survival time of 10 months. Pulmonary infection was identified as a protective factor for survival (HR = 0.425, P < 0.001), indicating that patients without infections had lower survival rates. Other significant factors affecting survival included age (HR = 1.096, P = 0.001), FAB classification (HR = 1.672, P < 0.001), FLT3-ITD status (HR = 0.461, P = 0.002), chemotherapy phase (HR = 1.810, P < 0.001), and bone marrow blast cell percentage (HR = 1.615, P = 0.046) (**Figure 2**).

Multivariate analysis and key prognostic factors

Multivariate Cox regression analysis showed that infection status (HR = 0.589, P = 0.037), age (HR = 1.076, P = 0.007), FAB classification (HR = 1.571, P = 0.002), FLT3-ITD status (HR = 0.590, P = 0.042), chemotherapy phase (HR = 1.469, P = 0.011), and bone marrow blast cell percentage (HR = 1.738, P = 0.028) were independent prognostic factors for survival (**Tables 5**, **6**).

Time-dependent ROC curve analysis

Time-dependent ROC curve analysis revealed that infection status showed high AUC values at 12 months, indicating strong predictive performance for mid-term survival. FAB classification and FLT3-ITD status had better predictive stability at 24 months. Chemotherapy phase and bone marrow blast cell percentage showed consistently high predictive ability at both 12 and 24 months. Age maintained moderate predictive efficacy, especially at 24 months (**Figure 3**).

Interaction analysis

Interaction analysis between infection and other prognostic factors showed no significant interaction effects, though some trends were observed. Infection appeared to have the most pronounced effect in patients with the M4 subtype (interaction HR = 3.545, P = 0.080), and FLT3-ITD-positive patients also showed a minor interaction effect (interaction HR = 0.769, P = 0.084). The effect of infection on survival in patients undergoing consolida-

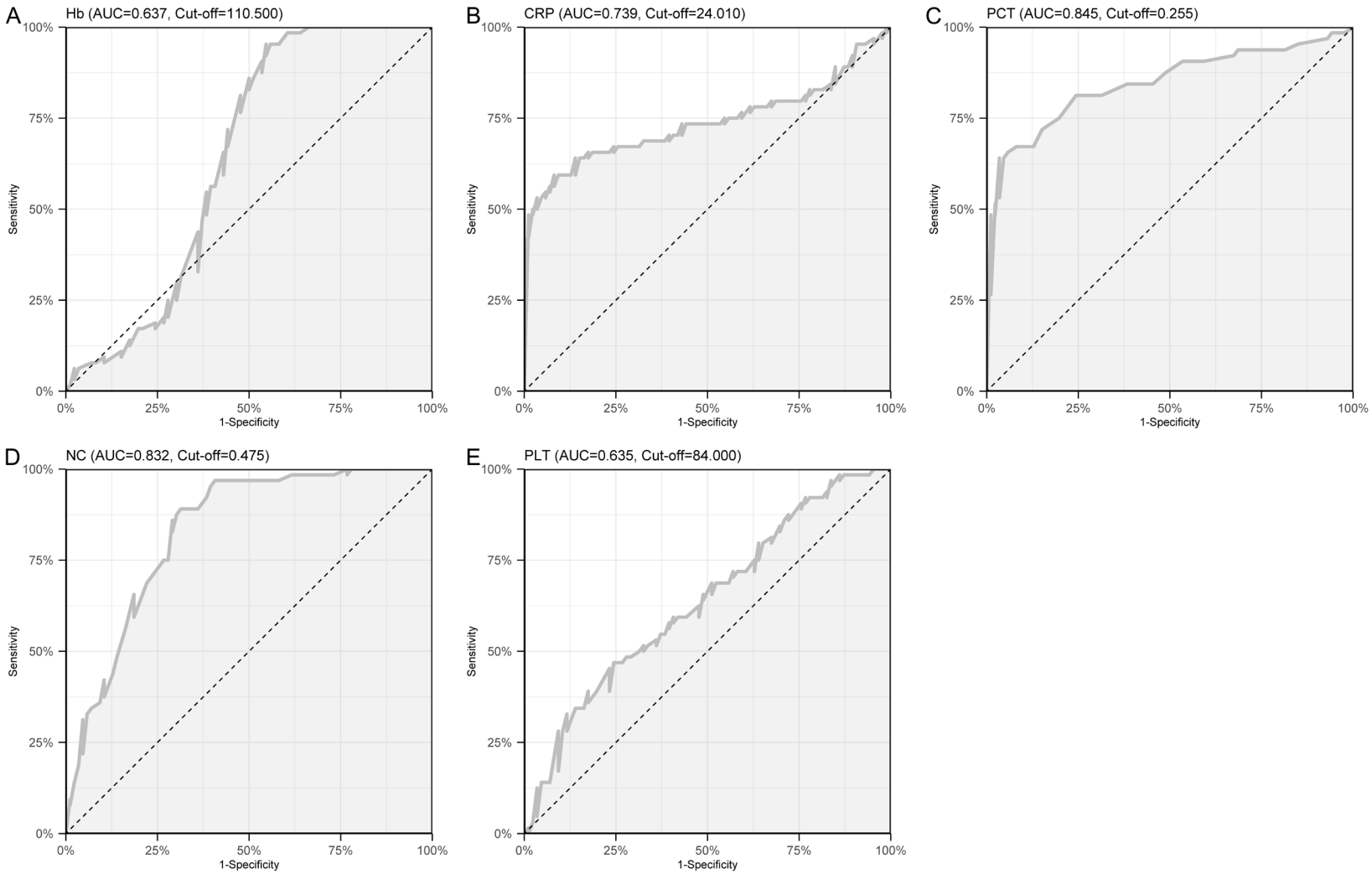

Figure 1. ROC curve analysis of various variables. A. Hemoglobin (Hb) (AUC = 0.637, Cut-off = 110.5). B. C-Reactive Protein (CRP) (AUC = 0.739, Cut-off = 24.01). C. Procalcitonin (PCT) (AUC = 0.845, Cut-off = 0.255). D. Neutrophil Count (NC) (AUC = 0.832, Cut-off = 0.475). E. Platelet Count (PLT) (AUC = 0.635, Cut-off = 84). Note: ROC: Receiver Operating Characteristic, AUC: Area Under the Curve, Hb: Hemoglobin, CRP: C-Reactive Protein, PCT: Procalcitonin, NC: Neutrophil Count, PLT: Platelet Count.

Table 2. ROC curve analysis and optimal cut-off values

Marker	AUC	95% CI	Specificity	Sensitivity	Cut-off	Youden Index
Hb	0.637	0.547-0.727	45.35%	95.31%	110.5	40.66%
CRP	0.739	0.648-0.830	91.86%	59.38%	24.01	51.24%
PCT	0.845	0.777-0.914	96.51%	64.06%	0.255	60.57%
NC	0.832	0.767-0.896	68.60%	89.06%	0.475	57.67%
PLT	0.635	0.545-0.725	75.58%	46.88%	84	22.46%

Note: AUC: Area under the curve, CI: Confidence interval, Hb: Hemoglobin, CRP: C-reactive protein, PCT: Procalcitonin, NC: Neutrophil count, PLT: Platelet count.

Table 3. Variable encoding

Factor	Type	Content
Smoking History	X	Yes = 1, No = 2
FAB Classification	X	M0 = 1, M2 = 2, M4 = 3, M5 = 4
FLT3-ITD	X	Negative = 1, Positive = 2
High-Intensity Chemotherapy	X	Yes = 1, No = 2
Chemotherapy Phase	X	Induction = 1, Consolidation = 2, Refractory/Relapsed = 3
Invasive Procedures	X	Yes = 1, No = 2
Hb (g/L)	X	< 110.5 = 2, ≥ 110.5 = 1
CRP (mg/L)	X	< 24.01 = 2, ≥ 24.01 = 1
PCT (ng/mL)	X	< 0.255 = 2, ≥ 0.255 = 1
NC ($\times 10^9$/L)	X	< 0.475 = 2, ≥ 0.475 = 1
PLT ($\times 10^9$/L)	X	< 84 = 2, ≥ 84 = 1
Pulmonary Infection	Y	Yes = 1, No = 2

Note: Hb: Hemoglobin, CRP: C-reactive protein, PCT: Procalcitonin, NC: Neutrophil count, PLT: Platelet count, FAB: French-American-British classification, FLT3-ITD: FMS-like tyrosine kinase 3 internal tandem duplication.

Table 4. Logistic regression analysis of risk factors for pulmonary infection

Factor	β	Standard Error	Wald	*P*-Value	OR	95% CI for OR
Hb (g/L)	-3.467	3.548	8.035	0.005	< 0.001	< 0.001-0.064
CRP (mg/L)	3.188	2.917	7.734	0.005	11.704	3.581-19.952
PCT (ng/mL)	3.396	3.304	8.311	0.004	13.743	4.466-23.086
NC ($\times 10^9$/L)	-2.564	1.807	7.4	0.007	0.01	< 0.001-0.325
PLT ($\times 10^9$/L)	2.235	1.786	4.311	0.038	5.383	1.158-10.398
Smoking History	1.683	1.259	3.085	0.079	3.341	0.827-6.766
FAB Classification	-1.115	0.744	2.457	0.117	0.392	0.100-1.226
FLT3-ITD	1.344	1.206	1.628	0.202	2.501	0.524-5.658
High-Intensity Chemotherapy	2.841	2.396	6.617	0.01	8.897	2.417-15.670
Chemotherapy Phase	-1.873	1.309	4.145	0.042	0.098	0.007-0.930
Invasive Procedures	2.327	1.488	7.296	0.007	5.823	2.004-10.005

Note: Hb: Hemoglobin, CRP: C-reactive protein, PCT: Procalcitonin, NC: Neutrophil count, PLT: Platelet count, FAB: French-American-British classification, FLT3-ITD: FMS-like tyrosine kinase 3 internal tandem duplication, OR: Odds ratio, CI: Confidence interval.

tion therapy and those with high bone marrow blast percentages was also explored, but none of these effects were statistically significant (**Figure 4**).

Discussion

The incidence of pulmonary infections in this study was 42%, consistent with the 30%-50%

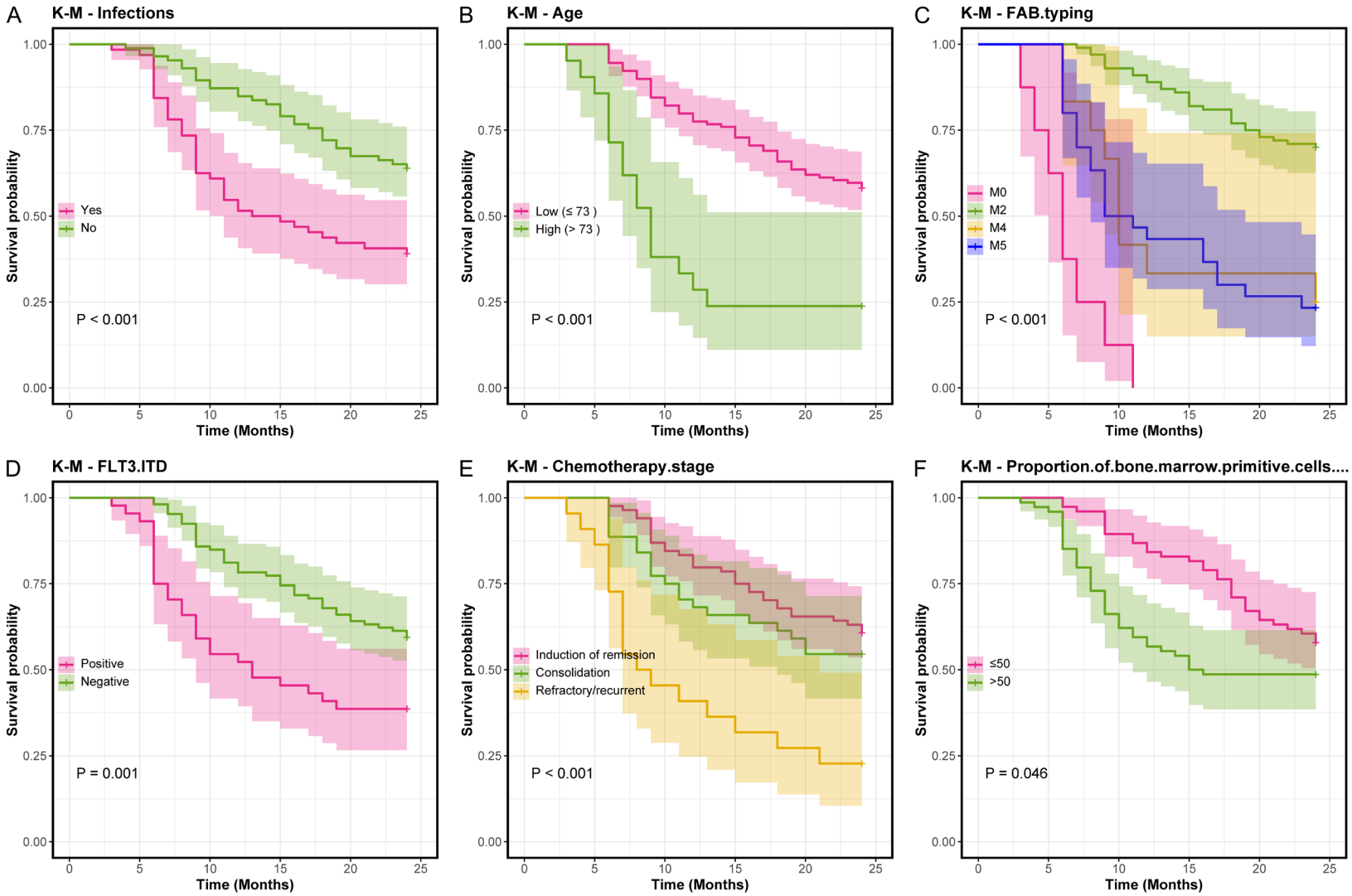

Figure 2. Kaplan-Meier Survival Curve Analysis. A. Effect of Infection Status on Survival Rates. B. Effect of Age on Survival Rates. C. Effect of FAB Classification on Survival Rates. D. Effect of FLT3-ITD Status on Survival Rates. E. Effect of Chemotherapy Phase on Survival Rates. F. Effect of Bone Marrow Blast Cell Percentage on Survival Rates. Note: FAB: French-American-British classification, FLT3-ITD: FMS-like Tyrosine Kinase 3 Internal Tandem Duplication.

Table 5. Univariate Cox regression analysis of survival risk factors

Factor	Beta	StdErr	*P* Value	HR	Lower_95_CI	Upper_95_CI
Infection	-0.855	0.241	< 0.001	0.425	0.265	0.683
Age (years)	0.092	0.028	0.001	1.096	1.038	1.158
BMI (kg/m^2)	0.057	0.058	0.323	1.059	0.945	1.187
Hemoglobin (Hb) (g/L)	< 0.001	0.002	0.937	1	0.996	1.004
White Blood Cell Count (WBC) (×10^9/L)	-0.009	0.043	0.832	0.991	0.912	1.077
C-Reactive Protein (CRP) (mg/L)	0.005	0.007	0.522	1.005	0.991	1.019
Procalcitonin (PCT) (ng/mL)	0.585	0.69	0.396	1.796	0.465	6.94
Neutrophil Count (NC) (×10^9/L)	-0.84	0.599	0.161	0.432	0.133	1.396
Platelet Count (PLT) (×10^9/L)	-0.002	0.002	0.285	0.998	0.993	1.002
Gender	-0.034	0.241	0.887	0.967	0.603	1.549
Smoking History	0.505	0.285	0.076	1.657	0.948	2.896
Hypertension History	0.177	0.25	0.479	1.193	0.732	1.946
Diabetes History	-0.081	0.317	0.798	0.922	0.495	1.717
Cardiovascular Disease History	-0.448	0.399	0.261	0.639	0.292	1.396
FAB Classification	0.514	0.132	< 0.001	1.672	1.29	2.167
FLT3-ITD Mutation	-0.773	0.246	0.002	0.461	0.285	0.747
Chemotherapy Regimen	-0.159	0.149	0.287	0.853	0.637	1.143
Chemotherapy Season	-0.158	0.117	0.178	0.854	0.678	1.075
Number of Chemotherapy Cycles	0.026	0.24	0.915	1.026	0.641	1.642
High-Intensity Chemotherapy	-0.392	0.285	0.169	0.676	0.387	1.181
Chemotherapy Phase	0.593	0.157	< 0.001	1.81	1.329	2.464
Central Venous Catheterization Time	-0.239	0.246	0.331	0.787	0.487	1.274
Invasive Procedures	-0.468	0.243	0.054	0.626	0.389	1.008
Use of Corticosteroids	-0.293	0.24	0.222	0.746	0.466	1.194
Bone Marrow Blast Cell Percentage (%)	0.479	0.24	0.046	1.615	1.008	2.587

Note: Hb: Hemoglobin, BMI: Body Mass Index, WBC: White Blood Cell count, CRP: C-reactive protein, PCT: Procalcitonin, FAB: French-American-British classification, FLT3-ITD: FMS-like tyrosine kinase 3 internal tandem duplication, HR: Hazard ratio, CI: Confidence interval.

Table 6. Multivariate Cox regression analysis of patient survival risk factors

Factor	Beta	Std Err	*P* Value	HR	Lower 95% CI	Upper 95% CI
Infection	-0.529	0.253	0.037	0.589	0.359	0.967
Age (years)	0.073	0.027	0.007	1.076	1.02	1.134
FAB Classification	0.451	0.143	0.002	1.571	1.187	2.077
FLT3-ITD Mutation	-0.527	0.26	0.042	0.59	0.355	0.982
Chemotherapy Phase	0.384	0.152	0.011	1.469	1.091	1.978
Bone Marrow Blast Cell Percentage (%)	0.553	0.252	0.028	1.738	1.008	2.846

Note: HR: Hazard Ratio, CI: Confidence Interval, FAB: French-American-British classification, FLT3-ITD: FMS-like tyrosine kinase 3 internal tandem duplication.

range reported in prior literature, highlighting the substantial infection risk in elderly AML patients. Scamuffa et al. [15] observed a similar pulmonary infection rate of 43.5% in AML patients undergoing hypomethylating agent therapy, suggesting heightened vulnerability in this treatment context. Literature indicates [16] that invasive fungal infections (IFI) in acute leukemia patients occur at a rate of 33.1%, with 76% affecting the lungs, further corroborating the high prevalence of pulmonary infections in AML.

Contributing factors to this elevated incidence include chemotherapy-induced myelosuppression, which significantly reduces NC, impairing

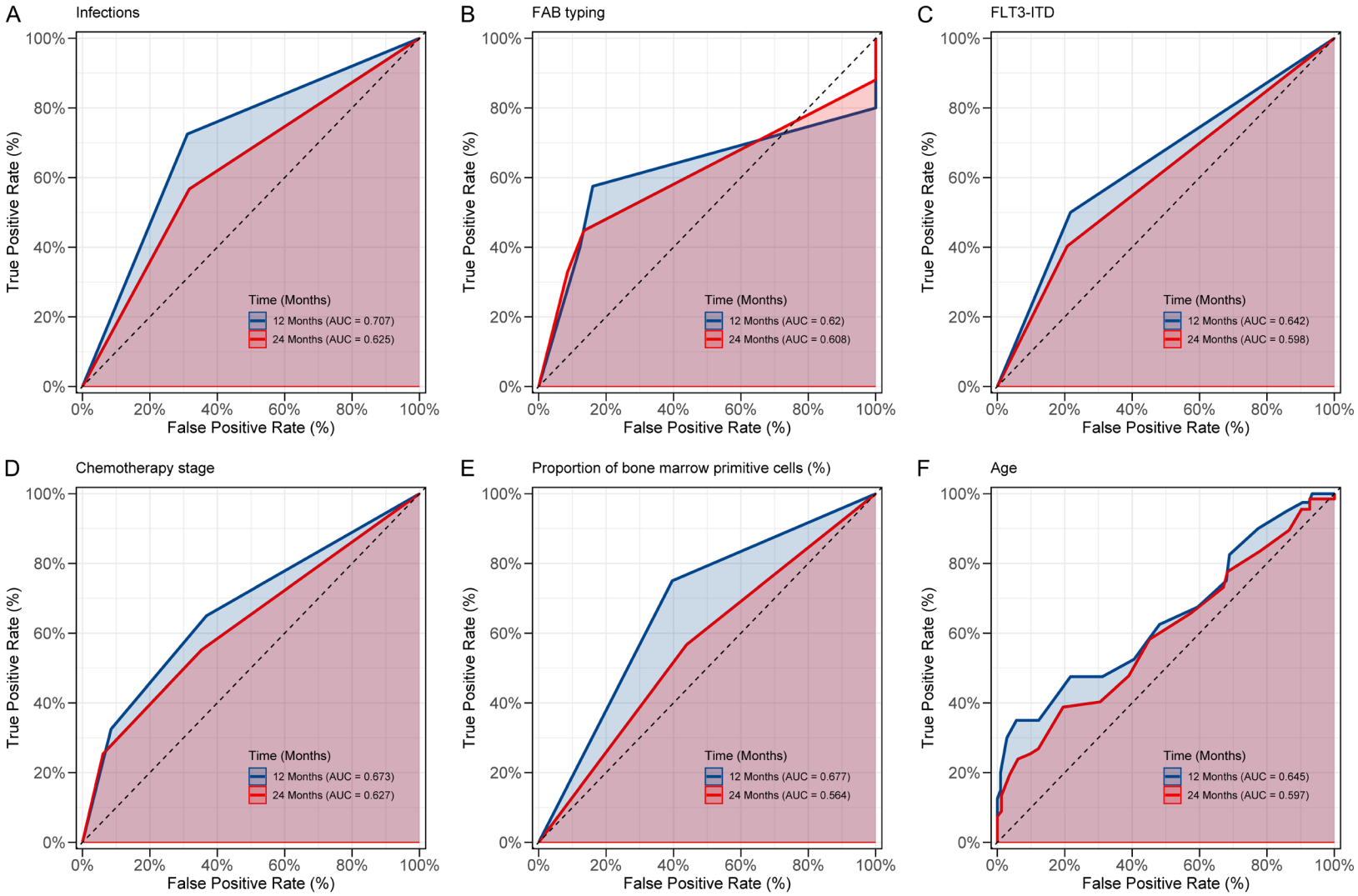

Figure 3. Time-Dependent ROC Curve Analysis of Survival Prediction Performance for Different Prognostic Factors. A. Time-Dependent ROC Curve for Infection Status. B. Time-Dependent ROC Curve for FAB Classification. C. Time-Dependent ROC Curve for FLT3-ITD Status. D. Time-Dependent ROC Curve for Chemotherapy Phase. E. Time-Dependent ROC Curve for Bone Marrow Blast Cell Percentage. F. Time-Dependent ROC Curve for Age. Note: ROC: Receiver Operating Characteristic, FAB: French-American-British classification, FLT3-ITD: FMS-like Tyrosine Kinase 3 Internal Tandem Duplication, AUC: Area Under the Curve.

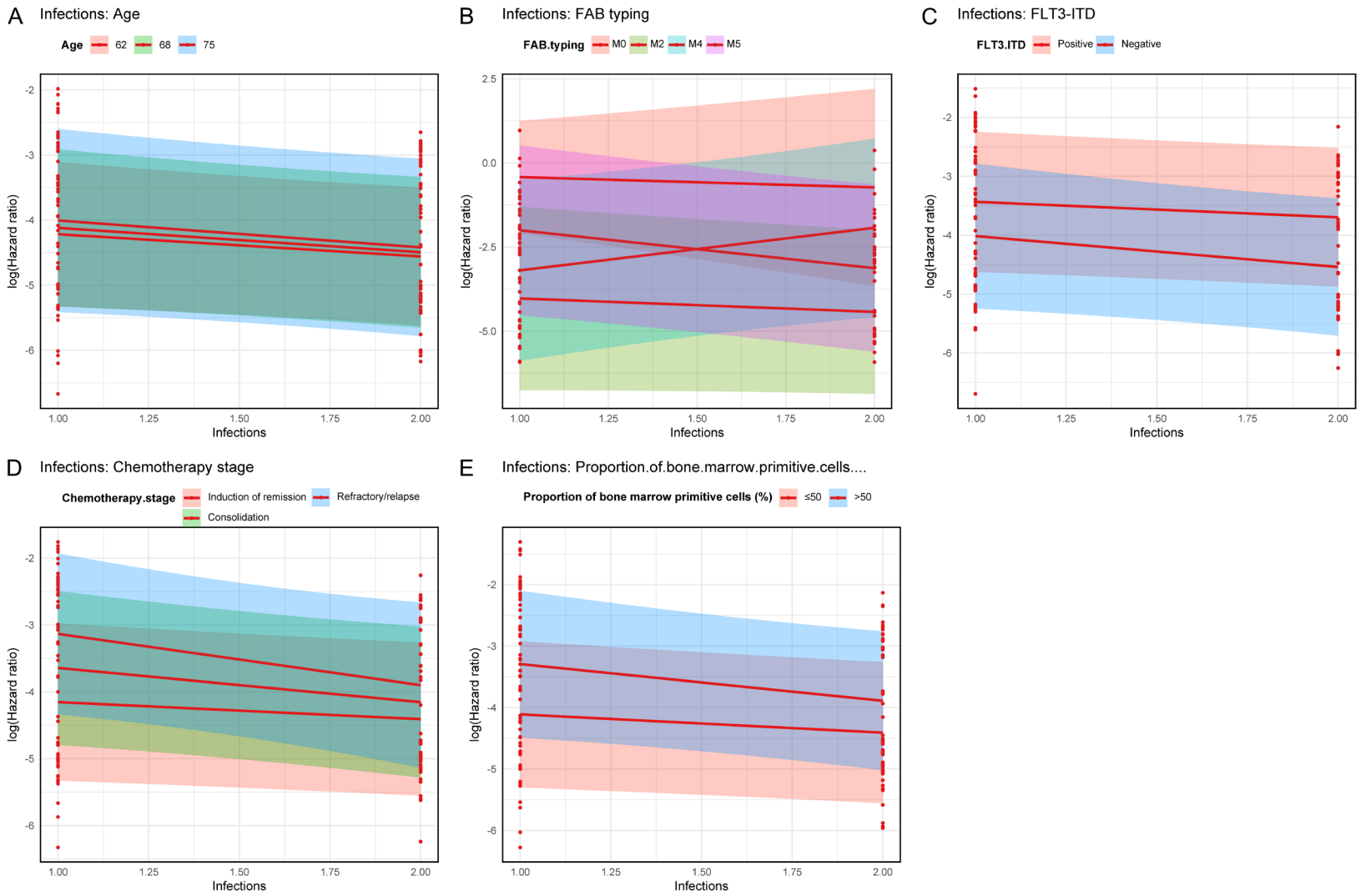

Figure 4. Analysis of Interaction Effects Between Infection and Other Variables. A. Interaction Between Infection and Age. B. Interaction Between Infection and FAB Classification (M0, M2, M4, M5). C. Interaction Between Infection and FLT3-ITD. D. Interaction Between Infection and Chemotherapy Phase. E. Interaction Between Infection and Bone Marrow Blast Cell Percentage. Note: FAB: French-American-British classification (M0, M2, M4, M5), FLT3-ITD: FMS-like Tyrosine Kinase 3 Internal Tandem Duplication, HR: Hazard Ratio, CI: Confidence Interval.

immune defenses. Invasive procedures and corticosteroid use amplify infection risk, while comorbidities such as chronic obstructive pulmonary disease in elderly patients exacerbate susceptibility. Tober et al. [17] reported that elderly AML patients (median age 75 years) on HMA therapy had a lower pulmonary infection rate (8.4%) compared to those on induction chemotherapy (33.3%), yet chronic obstructive pulmonary disease significantly increased risk, supporting the role of comorbidities. Additionally, literature suggests [18] that smoking history, low PLT, low albumin, and prolonged neutropenia are independent risk factors for pulmonary infections, aligning with our findings on smoking history and low PLT (< 84×10^9/L).

In terms of infection characteristics, our study identified higher infection risks in patients with FAB M2, M4, and M5 subtypes and FLT3-ITD-positive mutations, likely due to the aggressive nature of these subtypes and the rapid disease progression associated with FLT3-ITD. The induction chemotherapy phase posed the highest infection risk, attributable to intense treatment and severe myelosuppression. Halpern et al. [19] noted a 20% incidence of invasive fungal infections during induction, with 76% being pulmonary, and identified smoking history and prolonged neutropenia (> 30 days) as significant risk factors, supporting our conclusions. Studies show [20] that newly diagnosed elderly AML patients (≥ 55 years) exhibit a 47.5% infection rate during induction chemotherapy, underscoring high-intensity treatment as a key driver of infection risk. Notably, smoking history was significantly more prevalent in the infection group, suggesting that smoking may compromise lung mucosal barriers or intensify inflammatory responses, thereby increasing infection susceptibility. These findings emphasize the need for enhanced infection monitoring in high-risk subgroups.

Logistic regression analysis confirmed low hemoglobin (Hb < 110.5 g/L), elevated C-reactive protein (CRP ≥ 24.01 mg/L), elevated procalcitonin (PCT ≥ 0.255 ng/mL), low NC (< 0.475×10^9/L), and low PLT (< 84×10^9/L) as independent risk factors for pulmonary infections, alongside high-intensity chemotherapy and invasive procedures. Low Hb significantly increased infection risk, possibly by impairing oxygen transport and immune cell function. Clinical interventions such as transfusion or erythropoietin therapy may mitigate this risk. Ghandili et al. [21] demonstrated that bronchoalveolar lavage (BAL) detected pathogens in 47% of acute leukemia patients, predominantly fungi, supporting the infection susceptibility in patients with low Hb and NC. Among inflammatory markers, CRP (AUC = 0.739) and PCT (AUC = 0.845) exhibited robust predictive performance, with PCT showing 96.51% specificity and a 60.57% Youden index. Kassar et al. [22] reported a 38% positivity rate for galactomannan antigen in acute leukemia patients with pulmonary aspergillosis, reinforcing the diagnostic value of inflammatory markers, consistent with PCT's high specificity in our study. A study suggests [18] that low albumin and PLT were significantly associated with pulmonary infections, further validating our risk factor analysis. These findings advocate for routine CRP and PCT monitoring to facilitate early infection detection.

Neutrophils are critical for infection defense, and NC < 0.475×10^9/L significantly increases infection risk. Similarly, low PLT may compromise coagulation and microvascular integrity, indirectly heightening infection susceptibility. A study showed [23] that cumulative neutropenia (D-index) significantly correlates with pulmonary infection risk, supporting our NC findings. Optimizing supportive care, such as granulocyte colony-stimulating factor or platelet transfusion, is essential for reducing infection risk. High-intensity chemotherapy (OR = 8.897) and invasive procedures (OR = 5.823) also significantly contribute to infection risk by causing severe myelosuppression and providing infection entry points. Agarwal et al. [24] reported an 18% infection incidence during high-dose cytarabine (HiDAC) consolidation, with antibacterial prophylaxis reducing bacterial infection risk (HR = 0.46), highlighting the importance of optimized treatment regimens and preventive measures.

Survival analysis revealed that patients with pulmonary infections had a significantly shorter median survival compared to the non-infected group. Multivariate Cox regression confirmed pulmonary infections as an independent prognostic factor (HR = 1.469). Scamuffa et al. [15] found that early pulmonary infections (cycles 1-2) reduced median survival to 3.3 months compared to 10.5 months in non-early infection cases, reinforcing the adverse prognostic

impact. Literature indicates [17] that elderly AML patients with infections had an overall survival (OS) of 69 days versus 315 days in those without, further validating the prognostic impact. Conversely, univariate analysis suggested a paradoxical protective effect of infection (HR = 0.425), possibly due to intensified anti-infective therapies or enhanced supportive care triggered by infections. Literature suggests [20] that Romyelocel-L intervention reduced infection rates in elderly AML patients (35.6% vs 47.5%, P = 0.09), supporting potential short-term survival benefits of aggressive infection management. However, this protective effect may be limited to short-term outcomes, with long-term prognosis still adversely affected by infections.

Other prognostic factors include age (HR = 1.076), FAB classification (HR = 1.571), FLT3-ITD status (HR = 0.590), chemotherapy phase (HR = 1.469), and bone marrow blast percentage (HR = 1.738), reflecting the interplay of disease biology and patient baseline status. Time-dependent ROC analysis showed that infection status exhibited a high predictive performance at 12 months, while FAB classification and FLT3-ITD status demonstrated better stability at 24 months. Chemotherapy phase and bone marrow blast percentage maintained strong predictive ability at both time points, with age showing consistent moderate efficacy, particularly at 24 months.

To disrupt conventional flow while retaining academic rigor, we note that inflammatory markers like PCT and CRP outperform Hb and PLT (AUC = 0.637 and 0.635, respectively) in predicting infections, likely due to their susceptibility to non-infectious factors such as nutritional status or chemotherapy toxicity. Kassar et al. [22] further validated the utility of galactomannan antigen in diagnosing fungal infections, complementing PCT's diagnostic role. A study showed [21] that BAL-guided treatment adjustments (15%) improve infection management, supporting the integration of diagnostic tools like PCT in clinical practice. Future research could explore multi-marker models combining CRP, PCT, NC, and PLT to enhance infection risk prediction. The predictive stability of FAB classification and FLT3-ITD at 24 months underscores their role in long-term prognosis, while chemotherapy phase and blast percentage remain critical across time points.

This study, being a single-center retrospective analysis with a sample size of 150 patients, may have been subject to selection bias, and the maximum follow-up duration of two years limits insight into long-term prognosis. Additionally, the microbiologic characteristics of pulmonary infections (e.g., pathogen distribution and antimicrobial resistance) and the effect of novel therapies (e.g., targeted therapies or immunotherapies) on infection risk and prognosis were not thoroughly explored, constraining the comprehensiveness of the findings. Future studies should validate predictive models in multicenter, large-sample cohorts, investigate microbiological profiles and resistance mechanisms, and evaluate the effect of novel anti-infective drugs and immunotherapies in managing infections in elderly AML patients to optimize prevention strategies and improve long-term outcomes.

Conclusion

Pulmonary infections are prevalent in elderly AML patients and significantly impair prognosis. Low Hb, elevated CRP and PCT, and low NC and PLT were critical risk factors for infection. Enhanced infection monitoring and early intervention may improve survival outcomes.

Disclosure of conflict of interest

None.

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