Incidence of myelosuppression in AML is higher compared with that in ALL

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Abstract. Acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL) are two subtypes of acute leukemia. However, studies investigating the ability of complete blood count (CBC) parameters to distinguish between patients with AML and ALL remain scarce in the literature. The objective of the present study was to compare the parameters of CBC analysis between Chinese patients with AML and ALL and between patients with M3 AML and non-M3 AML. Prognostic factors for overall survival were also estimated, including sex, age, white blood cell count and hemoglobin. The present study included 147 patients, including children and adults, with newly diagnosed acute leukemia. Information on the age, sex, leukemia subtype, initial CBC results and clinical follow-up findings was recorded and compared between the indicated groups using statistical tests of Mann-Whitney U test and χ^2 test. Leukopenia (white blood cell count $<3.5x10^9$/l), both leukopenia and anemia, both leukopenia and thrombocytopenia and pancytopenia were found to be significantly more frequent among patients with AML compared with that in patients with ALL (P=0.015, 0.016, 0.015 and 0.019, respectively). For patients with ALL, anemia was recognized as a predictor of a favorable outcome (Hazard ratio, 0.185; 95% CI, 0.046-0.747; P=0.018). These findings suggest that normal hematopoiesis is more frequently inhibited in patients with AML compared with that in patients with ALL. Patients with AL with peripheral blood findings indicative of leukopenia, pancytopenia, or both leukopenia and anemia or both leukopenia and thrombocytopenia are more likely to have AML.

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Introduction

Acute leukemia (AL) is a malignancy of hematopoietic progenitor cells and is characterized by excessive numbers of immature cells in the bone marrow (1,2). AL can be classified into two subtypes, namely acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL). AML is more frequently reported in adults aged >40 years old, whilst ALL occurs mainly in children (3,4). The incidence of AML had been higher compared with that of ALL (5,6). The age-adjusted incidence of AML was 4.3 per 100,000 people per year, whilst that of ALL was 1.7, in the United States (5,6). Although the 5-year overall survival (OS) reached 90% in pediatric patients with ALL, the 5-year OS in patients with ALL (≥50 years) and AML were only 25% and 24%, respectively (6-9). Each subtype of AL can be further subdivided into categories as defined by the French-American-British (FAB) system or the World Health Organization (WHO) system (10-12). Specifically, according to FAB system, AML and ALL is divided into eight (M0-M7) and three (L1-L3) subtypes, respectively (10,11). A commonality of AML and ALL is that the multiplication of immature hematopoietic cells leads to the decreased production of normal hematopoietic cells, resulting in a number of pathological conditions, such as anemia, thrombocytopenia and leukopenia (13). However, AML and ALL have differing pathophysiological processes. Myeloid cells proliferate into their mature end cells within the bone marrow, whereas the lymphoid precursors migrate to the lymphoid organs to complete maturation (1). Therefore, the mechanisms underlying the inhibition of normal hematopoiesis will likely differ between these two subtypes of AL, especially the forms of hypocytosis. In particular, to the best of our knowledge, studies investigating the ability of complete blood count (CBC) parameters to distinguish between patients with AML and ALL remain scarce in the literature. Currently, AML and ALL are distinguished mainly by cytological analysis of a bone marrow puncture, based on different cytological features of lymphoblasts and myeloblasts (11,14,15). Lymphoblasts are characterized by small to large sized blasts, moderately condensed to dispersed chromatin, inconspicuous or prominent nucleoli, scant or moderately abundant cytoplasm with variable basophilia and vacuolation, whilst myeloblasts are characteristically large-sized blasts, fine nuclear chromatin, presence of one or more prominent nucleoli, and varying

amounts of cytoplasm with azurophilic granules (11,14,15). Moreover, the presence of 'Auer rods' or 'Phi bodies' is the myeloblast characteristic (11,14,15). Peripheral blood routine examination is simpler, more convenient and safer than bone marrow puncture. Therefore, the present study was undertaken to compare the CBC results between Chinese patients with AML and those with ALL. In addition, CBC parameters between patients with acute promyelocytic leukemia (APL, also named M3), a unique subtype of AML and those with non-M3 AML, were compared. Subsequently, the influence of factors, such as hemocytopenia, sex and age, on the OS of patient were further analyzed.

Patients and methods

Patients. The patients were selected from the Department of Hematology, Zhongshan Hospital of Xiamen University (Xiamen, China), between January 2015 and May 2019. AL was diagnosed according to the 2016 WHO criteria (12). The diagnostic procedures included cytomorphology, cytogenetics, molecular genetics and immunophenotyping of the bone marrow. Clinical follow-up information was obtained by retrospective review of the electronic charts and telephone follow-up. OS was measured from the date of diagnosis to mortality from any cause or the last follow-up, which was used to compare the clinical outcomes. The follow-up of all patients ended in April 2024.

The inclusion criteria were as follows: i) Newly diagnosed with AL (age, 6-90 years); ii) CBC analysis performed before treatment; and iii) availability of all clinical data. The exclusion criteria were as follows: i) Presence of any type of cancer, hyperthyroidism, hemorrhoids, splenectomy, coagulation disorders, chronic cardiopulmonary diseases, combined immune system diseases, infectious diseases, severe organic lesions, mental illness and severe liver or kidney dysfunction; ii) coronary heart disease controlled by oral drugs for 3 years after percutaneous coronary intervention; iii) long-term anemia before AL; iv) treatment with red blood cell (RBC) or platelet (PLT) transfusion before diagnosis; and v) use of any drug that could affect CBC results, such as corticosteroids, antibiotics and diuretics.

Methods. CBC analysis of EDTA-anticoagulated blood samples was performed. CBC counts [numbers of white blood cells (WBCs), neutrophils, eosinophils, basophils, monocytes, lymphocytes, RBCs, PLTs and hemoglobin levels] were measured using an automated blood cell counter (Sysmex XN-9000; Sysmex Corporation). The following data were obtained and analyzed: Age, sex, leukemia subtype, initial CBC counts, CNS involvement and treatments.

In the present study, leukocytosis was defined as any WBC count >$10x10^9$/l (16). Leukopenia was defined as a WBC count of <$3.5x10^9$/l (17). Thrombocytopenia was defined as a PLT count of <$100x10^9$/l (16). In addition, <110 g/l (for women) and <120 g/l (for men) normal hemoglobin levels were used to define anemia (18).

Statistical analysis. All data analyses were performed using SPSS version 26.0 (IBM Corp.). Data for quantitative variables were reported as medians and (interquartile) ranges, whereas data for qualitative variables were reported as numbers and percentages. A Shapiro-Wilk normality test was performed to check if the data were normally distributed. Between-group comparisons of quantitative data were performed using the Mann-Whitney U test if the data were found to be non-normally distributed, and the unpaired independent-samples t-test for normally distributed data. The χ^2 test was used for comparing categorical data. OS curves were drawn by the Kaplan-Meier method and a log-rank test was used to compare OS between the two groups. Univariable Cox proportional hazards models were used to analyze OS-related factors. Among the factors in univariable models, those significant at P≤0.1 were used in a limited backward selection procedure to build multivariable models. P<0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics. In the present study, the CBC results of 147 patients with *de novo* AL were investigated, which included 105 patients with AML and 42 patients with ALL. AML patients was predominant (71.4%) over the ALL patients (28.6%). The median age in patients with ALL (38 years) was lower compared with that of AML patients (54 years). The similar sex ratio was observed in patients with AML and ALL. The AML subgroups included 24 (22.8%) cases of M3, 70 (66.7%) patients with non-M3, and 11 (10.5%) patients with unknown type. Among patients with ALL, there were 35 cases of B-ALL (83.3%), 5 cases of T-ALL (11.9%) and 2 cases of unknown cell type (4.8%). In addition, only 1 patient with ALL at diagnosis suffered from central nervous system (CNS) metastasis. The main clinical characteristics of AL patients are described in Table SI.

CBC results analysis. The results of CBC analysis for patients with AL are presented in Table I. Patients with ALL were found to have significantly higher lymphocyte (P=0.021) and RBC counts (P=0.001) compared with those in patients with AML (Table I). P<0.05 were obtained in both eosinophil count (P=0.022) and eosinophil percentage (P=0.035) between the AML group and the ALL group, however, the same the median value of eosinophil count and eosinophil percentage was observed in the two groups (Table I). In addition, the mean corpuscular volume and mean corpuscular hemoglobin values were significantly increased in AML patients compared with those in patients with ALL (both P<0.001; Table I).

Different forms of hypocytosis analysis. The frequencies of different forms of hypocytosis were next compared between the AML group and the ALL group (Table II). The percentage of patients with leukopenia (WBC count <$3.5x10^9$/l) was found to be significantly higher in the AML group compared with that in the ALL group (P=0.015). In addition, the percentage of patients with both leukopenia and anemia was significantly higher in the AML group compared with that in the ALL group (P=0.016). Similarly, the percentage of patients with both leukopenia and thrombocytopenia was significantly higher in the AML group compared with that in the ALL group (P=0.015). Statistically significant rates of pancytopenia were observed in the AML and ALL groups (P=0.019), with the higher percentage of patients with pancytopenia in the AML group.

Table I. Complete blood count analysis of patients with AL.

Parameter	Reference value	AL (n=147)	Acute myeloid leukemia (n=105)	Acute lymphocytic leukemia (n=42)	P-value
White blood cell count, x10^9/l	3.50-9.50	5.86 (2.21-43.25)	5.39 (1.81-44.19)	5.89 (3.73-21.64)	0.423
Neutrophil count, x10^9/l	1.80-6.30	1.47 (0.42-4.79)	1.26 (0.33-5.02)	1.52 (0.55-3.91)	0.728
Neutrophil percentage, %	40.00-75.00	17.20 (8.00-37.85)	17.90 (8.20-36.90)	16.75 (5.80-47.70)	0.947
Eosinophil count, x10^9/l	0.02-0.52	0.00 (0.00-0.01)	0.00 (0.00-0.00)	0.00 (0.00-0.05)	0.022
Eosinophil percentage, %	0.40-8.00	0.00 (0.00-0.10)	0.00 (0.00-0.00)	0.00 (0.00-0.40)	0.035
Basophil count, x10^9/l	0.00-0.06	0.00 (0.00-0.01)	0.00 (0.00-0.00)	0.00 (0.00-0.01)	0.117
Basophil percentage, %	0.00-1.00	0.00 (0.00-0.10)	0.00 (0.00-0.00)	0.00 (0.00-0.20)	0.073
Lymphocyte count, x10^9/l	1.10-3.20	1.98 (1.02-4.91)	1.57(0.87-4.46)	2.35 (1.53-6.15)	0.021
Lymphocyte percentage, %	20.00-50.00	31.0 (13.00-54.30)	26.00 (10.00-60.00)	36.75 (27.30-52.00)	0.077
Monocyte count, x10^9/l	0.10-0.60	0.19 (0.04-0.92)	0.19 (0.03-1.58)	0.14 (0.05-0.69)	0.386
Monocyte percentage, %	3.00-10.00	4.00 (1.00-14.85)	4.40 (1.00-15.10)	3.25 (1.00-10.00)	0.323
RBC count, x10^{12}/l	4.30-5.80	2.49 (1.97-3.09)	2.38 (1.89-2.92)	2.83 (2.26-3.59)	0.001
Hemoglobin, g/l	130.00-175.00	75.00 (64.50-90.00)	74.00 (62.00-88.00)	78.50 (66.00-104.00)	0.087
Hematocrit, %	40.00-50.00	23.20 (19.65-27.95)	22.80 (18.70-27.60)	23.75 (20.80-30.20)	0.054
Mean corpuscular volume, fl	82.00-100.00	93.90 (87.20-101.05)	96.20 (90.30-102.40)	87.90 (83.80-93.80)	<0.001
Mean corpuscular hemoglobin, pg	27.00-34.00	31.20 (28.95-33.50)	31.90 (30.30-34.60)	29.50 (27.00-30.60)	<0.001
Mean corpuscular hemoglobin concentration, g/l	316.00-354.00	333.00 (319.00-343.00)	332.00 (319.00-344.00)	334.00 (318.00-340.00)	0.722
Red blood cell distribution width, %	0.00-15.00	15.80 (14.25-17.90)	15.80 (14.30-17.60)	15.80 (13.70-19.00)	0.938
Platelet count, x10^9/l	125.00-350.00	40.00 (0.40-500.00)	37.00 (14.00-70.00)	44 (19.00-94.00)	0.301

Values represent median and interquartile range. Comparison between patients with acute myeloid leukemia and acute lymphocytic leukemia was performed using Mann-Whitney U test. AL, acute leukemia.

CBC results analysis in patients with and without M3 AML. Subsequently, the CBC results of patients with *de novo* AML (n=94) were investigated further, including 24 patients with M3 AML and 70 patients with non-M3 AML (Tables SII and SIII). Patients with M3 AML had a lower median age (47 vs. 55 years), compared with that in patients with non-M3 AML. The same gender ratio was observed in patients with and without M3 AML. Notably, WBC count was found to be significantly lower in the M3 group compared with that in the non-M3 group (P=0.003). Both the neutrophil count (P=0.020) and lymphocyte count (P<0.001) were also observed to be significantly lower in the M3 group compared with those in the non-M3 AML group. In addition, the platelet count was lower in the M3 group compared with that in the non-M3 AML group (P=0.031).

Hypocytosis in patients with and without M3 AML. The frequencies of different forms of hypocytosis were also compared between patients with M3 and non-M3 AML (Table SIV). The percentage of patients with leukopenia was found to be significantly higher in the M3 AML group compared with that in the non-M3 AML group (P=0.007). Conversely, the percentage of patients with leukocytosis was significantly higher in the non-M3 AML group compared with that in the M3 AML group (P=0.034). Furthermore, the percentage of patients with both leukopenia and anemia was significantly higher in the M3 AML group compared with that in the non-M3 AML group (P=0.033).

OS analysis. To further understand the influence of various factors, such as hemocytopenia, on the prognosis of patients, their OS was next analyzed. Notably, 84.4% (n=124, including 91 patients with AML and 33 patients with ALL) of patients with AL received chemotherapy treatments, whilst 15.6% (n=23, including 14 patients with AML and 9 patients with ALL) received supportive care (Table SI). In particular, patients with non-M3 AML received fludarabine, cytarabine and mitoxantrone, the standard '3 + 7' regimens or the reduced '3 + 7'-based regimens (19,20). By contrast, patients with M3 AML received treatment regimens containing all-trans retinoic acid (ATRA) + anthracyclines or arsenic trioxide (ATO) + ATRA (21-23). Patients with ALL received corticosteroids alone or in combination with another drug (such as vincristine or cyclophosphamide) (24). Of all patients, 10.9% underwent hematopoietic stem cell transplantation, including 7 patients with AML and 9 patients with ALL (Table SI).

In patients with AL, the median survival was 30 months and 5-year OS was 25.2% (patients with AML: Median survival, 24 months; 5-year survival, 26.7%; ALL patients: Median survival, 33 months; 5-year survival, 21.4%). Among patients with AML, the 5-year survival rates for patients with M3 and non-M3 AML were 50.0% and 18.6%, respectively.

Table II. Comparison of frequencies of different forms of hypocytosis between patients with AML and ALL.

Parameters	AML (n=105)	ALL (n=42)	P-value
Leukopenia [a], N (%)			0.015
Yes	42 (40.0)	8 (19.0)	
No	63 (60.0)	34 (81.0)	
Leukocytosis, N (%)			0.101
Yes	48 (45.7)	13 (31.0)	
No	57 (54.3)	29 (69.0)	
Anemia, N (%)			0.479
Yes	100 (95.2)	38 (90.5)	
No	5 (4.8)	4 (9.5)	
Thrombocytopenia, N (%)			0.219
Yes	89 (84.8)	32 (76.2)	
No	16 (15.2)	10 (23.8)	
Leukopenia[a] and anemia, N (%)			0.016
Yes	39 (37.1)	7 (16.7)	
No	66 (62.9)	35 (83.3)	
Leukopenia[a] and thrombocytopenia, N (%)			0.015
Yes	33 (31.4)	5 (11.9)	
No	72 (68.6)	37 (88.1)	
Anemia and thrombocytopenia, N (%)			0.064
Yes	87 (82.9)	29 (27.6)	
No	18 (17.1)	13 (12.4)	
Pancytopenia, N (%)[b]			0.019
Yes	32 (30.5)	5 (11.9)	
No	73 (69.5)	37 (88.1)	

χ^2 test. [a]Leukopenia in the present study was defined as a WBC count of $<3.5x10^9$/l. [b]Pancytopenia is simultaneous presence of leukopenia, anemia and thrombocytopenia. AML, acute myeloid leukemia; ALL, acute lymphocytic leukemia.

The two common prognostic factors associated with shorter survival in patients with AL (Table III), with AML (Table IV) and non-M3 AML (Table V) were found to be age >60 years and WBC count $>10x10^9$/l. However, OS did not significantly differ between patients with AML and ALL (Fig. 1 and Table III). Among patients with AML, the median OS of patients with M3 AML were not achieved, whilst those with non-M3 AML were 18 months. Patients with M3 AML had significantly longer OS compared with those with non-M3 AML ($P<0.05$; Fig. 2 and Table IV). For patients with ALL, the prognostic factors for survival duration were age and hemoglobin level (Table VI). In addition, patients with ALL aged <60 years and anemia were found to be associated with a favorable outcome (for age ≥60 years: HR, 2.715; 95% CI, 1.069-6.894; P=0.036; for anemia: HR, 0.185; 95% CI, 0.046-0.747; P=0.018).

Discussion

AML is a leukemia subtype that targets the myeloid lineage, whereas ALL occurs when immature lymphoblasts amplify in the bone marrow and inhibit the generation of normal blood cells (25). Regardless of the AL subtype, the immature leukemic cells invade the bone marrow where normal hematopoietic cells are produced, leading to the decreased production of healthy cells in the bone marrow, resulting in decrease of normal mature blood cells in the peripheral blood (13). Therefore, the frequent presentation involves peripheral blood and results in hypocytosis, such as anemia, leukopenia and thrombocytopenia (13). Results from the present study showed that normocytic normochromic anemia and thrombocytopenia are frequent occurrences in both AML and ALL. These findings are consistent with those from Schumacher *et al* (26), which reported that in AML, anemia (normocytic normochromic anemia is the grand majority of cases) occurrence is common whereas thrombocytopenia is also common. In addition, this previous study (26) also reported that in ALL, normocytic normochromic anemia is commonly present and thrombocytopenia is generally severe. However, the difference between AML and ALL in terms of hypocytosis could not be derived from Schumacher *et al* (26) and other previous reports (1,27-30). In order to solve this issue, the present study performed CBC results analysis between patients with AML and ALL.

ALL patients were found to have significantly higher lymphocyte and RBC counts compared with those in patients

Table III. Univariate and multivariable analyses of variables predicting overall survival in the patients with acute leukemia.

Variable	Comparison groups	Univariate analysis			Multivariable analysis		
		Wald	HR (95% CI)	P-value	Wald	HR (95% CI)	P-value
French-American-British system classification	Acute lymphocytic leukemia vs. Acute myeloid leukemia	0.047	0.947 (0.575-1.558)	0.829			
Sex	Male vs. Female	0.021	0.967 (0.615-1.521)	0.884			
Age, years	≥60 vs. <60	18.612	2.725 (1.728-4.297)	<0.001	25.483	3.522 (2.160-5.741)	<0.001
White blood cell count, $x10^9$/l	<3.5 vs. ≥3.5	0.130	0.914 (0.559-1.493)	0.718			
	>10.0 vs. ≤10.0	8.129	1.937 (1.230-3.053)	0.004	17.731	2.826 (1.742-4.583)	<0.001
Hemoglobin, g/l	Male, <120 vs. ≥120; female, <110 vs. ≥110	0.438	1.406 (0.513-3.852)	0.508			
Platelet count, $x10^9$/l	<100 vs. ≥100	1.482	1.452 (0.797-2.648)	0.223			
Pancytopenia[a]	Yes vs. no	0.130	0.914 (0.559-1.493)	0.718			
Received a transplant	Yes vs. no	3.946	0.428 (0.185-0.989)	0.047	2.808	0.485 (0.208-1.130)	0.094

[a]Pancytopenia is defined by the simultaneous presence of leukopenia, anemia and thrombocytopenia. HR, hazard ratio.

with AML in the present study. In addition, the percentage of patients with hypocytosis (including only leukopenia, both leukopenia and anemia, both leukopenia and thrombocytopenia, and pancytopenia) was significantly higher in the AML group compared with that in the ALL group. These data suggest that normal hematopoiesis is more frequently inhibited in AML compared with that in ALL. Therefore, patients with AL with peripheral blood findings of leukopenia, pancytopenia, or both leukopenia and anemia or both leukopenia and thrombocytopenia are likely to have AML. Clinically, patients with AML are more likely to require blood transfusion compared with patients with ALL.

The mechanisms underlying the higher incidence of myelosuppression in AML compared with ALL require further study. However, this difference may be due to different expression of a number of critical regulators of hematopoiesis between AML and ALL. In particular, GATA-1 factor, which is a hematopoietic transcription factor, is required for the proliferation and survival of erythroid precursors and mature cells (31), where it also serves a role in megakaryocytic differentiation (32). Ayala *et al* (33) previously identified GATA-1 expression in 43.9% patients with AML and 66.7% ALL patients, indicating markedly different expression profile between the two diseases. Similarly, the expression of erythroid Krüppel-like factor (EKLF), which is involved in erythroid proliferation and hemoglobinization (34), was noted in 39% patients with AML and 50% patients with ALL (33). These findings indicate that the higher expression of GATA-1 and EKLF in ALL may be associated with a lower probability of myelosuppression.

Consistent with previous studies (35-38), the present findings showed that age <60 years and WBC count <$10x10^9$/l were prognostic factors for longer survival in patients with AML or patients with non-M3 AML, but leukopenia at the time of diagnosis was not associated with the prognosis in AML. Creutzig *et al* (35) previously reported that a WBC count of <$2x10^9$/l was associated with a superior prognosis. Although cut-offs for WBC were set, with counts of <$2x10^9$/l indicating leukopenia, no association between leukopenia and OS was observed in the present study. Patients with M3 AML had significantly longer OS compared with those with non-M3 AML, which is consistent with previous studies (39,40). Sasaki *et al* (39) previously reported that after the introduction of ATRA and ATO in the 1990s, the 5-year survival increased from 20% during the 1980-1989 period to 75% during the 2010-2017 period in patients with M3 AML. However, the 5-year survival rate only increased from 9 to 21% during the same period in patients with non-M3 AML (39). Older age and high WBC counts have been frequently considered to be viable predictors of poor outcome in ALL (41). In the present study, for patients with ALL, the prognostic factors for survival duration were found to be age and hemoglobin level. A WBC count of >$10x10^9$/l was not associated with an unfavorable outcome in patients with ALL. This result may be

Table IV. Univariate and multivariable analyses of variables predicting overall survival in patients with AML.

Variable	Comparison groups	Univariate analysis			Multivariable analysis		
		Wald	HR (95% CI)	P-value	Wald	HR (95% CI)	P-value
French-American-British classification	M3 AML vs. Non-M3 AML	11.470	0.087 (0.021-0.357)	0.001	8.333	0.122 (0.029-0.509)	0.004
Sex	Male vs. Female	0.182	0.889 (0.518-1.525)	0.669			
Age, years	≥60 vs. <60	13.271	2.749 (1.595-4.736)	<0.001	15.441	3.486 (1.870-6.499)	<0.001
White blood cell count, $x10^9$/l	<3.5 vs. ≥3.5	0.178	0.886 (0.505-1.555)	0.673			
	>10.0 vs. ≤10.0	4.965	1.858 (1.077-3.204)	0.026	10.540	2.811 (1.506-5.245)	0.001
Hemoglobin, g/l	Male: <120 vs. ≥120 Female: <110 vs. ≥110	2.018	4.203 (0.580-30.469)	0.155			
Platelet count, $x10^9$/l	<100 vs. ≥100	0.205	1.181 (0.575-2.429)	0.651			
Pancytopenia[a]	Yes vs. no	0.914	1.334 (0.739-2.410)	0.339			
Received a transplant	Yes vs. no	1.231	0.516 (0.161-1.660)	0.267			

[a]Pancytopenia is defined by the simultaneous presence of leukopenia, anemia and thrombocytopenia. AML, acute myeloid leukemia; HR, hazard ratio.

Table V. Univariate and multivariable analyses of variables predicting overall survival in patients with non-M3 acute myeloid leukemia.

Variable	Comparison groups	Univariate analysis			Multivariable analysis		
		Wald	HR (95% CI)	P-value	Wald	HR (95% CI)	P-value
Sex	Male vs. female	0.030	0.948 (0.520-1.728)	0.862			
Age, years	≥60 vs. <60	4.331	1.894 (1.038-3.455)	0.037	8.341	2.680 (1.373-5.233)	0.004
White blood cells count, $x10^9$/l	<3.5 vs. ≥3.5	0.232	1.170 (0.617-2.220)	0.630			
	>10.0 vs. ≤10.0	4.323	1.937 (1.039-3.612)	0.038	11.018	3.213 (1.613-6.402)	0.001
Hemoglobin, g/l	Male, <120 vs. ≥120; female: <110 vs. ≥110	1.726	3.792 (0.519-27.700)	0.189			
Platelet count, $x10^9$/l	<100 vs. ≥100	0.001	1.014 (0.483-2.130)	0.971			
Pancytopenia[a]	Yes vs. no	1.326	1.503 (0.751-3.008)	0.250			
Received a transplant	Yes vs. no	3.343	0.332 (0.102-1.083)	0.068	3.711	0.306 (0.092-1.021)	0.054

[a]Pancytopenia is defined by the simultaneous presence of leukopenia, anemia and thrombocytopenia. HR, hazard ratio.

Table VI. Univariate and multivariable analyses of variables predicting overall survival in patients with acute lymphocytic leukemia.

		Univariate analysis			Multivariable analysis		
Variable	Comparison groups	Wald	HR (95% CI)	P-value	Wald	HR (95% CI)	P-value
Classification	B vs. T	0.810	0.601 (0.199-1.820)	0.368			
Sex	Male vs. Female	0.227	1.226 (0.531-2.832)	0.634			
Age, years	≥60 vs. <60	4.211	2.503 (1.042-6.012)	0.040	4.415	2.715 (1.069-6.894)	0.036
White blood cells count, x10^9/l	<3.5 vs. ≥3.5	0.016	0.933 (0.316-2.759)	0.900			
	>10.0 vs. ≤10.0	4.010	2.413 (1.019-5.716)	0.045	3.757	2.451 (0.990-6.068)	0.053
Hemoglobin, g/l	Male, <120 vs. ≥120; female, <110 vs. ≥110	3.737	0.284 (0.080-1.018)	0.053	5.607	0.185 (0.046-0.747)	0.018
Platelet count, x10^9/l	<100 vs. ≥100	1.783	2.099 (0.707-6.233)	0.182			
Pancytopenia[a]	Yes vs. no	0.103	0.788 (0.184-3.376)	0.748			
Received a transplant	Yes vs. no	2.756	0.354 (0.104-1.206)	0.097	1.258	0.484 (0.136-1.719)	0.262

[a]Pancytopenia is defined by the simultaneous presence of leukopenia, anemia, and thrombocytopenia. HR, hazard ratio.

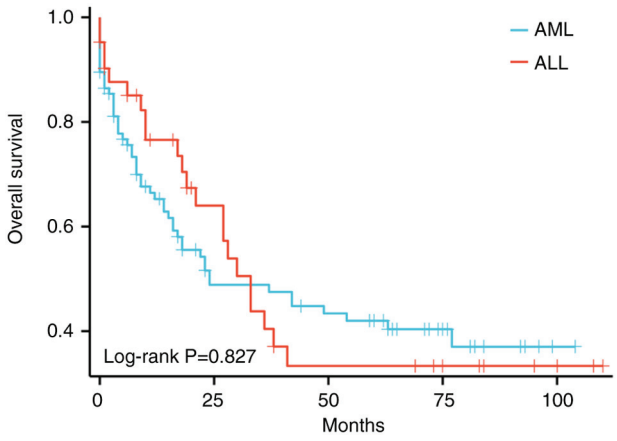

Figure 1. Comparison of overall survival curves between acute myeloid leukemia and acute lymphocytic leukemia patients using the Kaplan-Meier method.

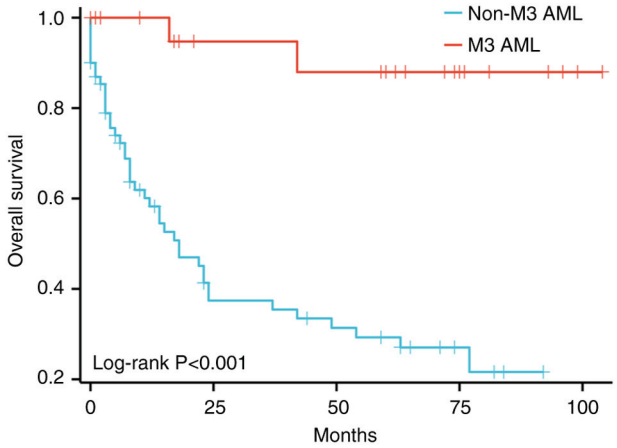

Figure 2. Comparison of overall survival curves between patients with M3 acute myeloid leukemia and non-M3 acute myeloid leukemia patients using the Kaplan-Meier method.

due to the small sample size. In addition, the present findings are not consistent with that of previous study, which reported no association between hemoglobin levels and OS in patients with ALL (42). However, other reports found that the lower hemoglobin levels are associated with a superior outcome in patients with ALL (43,44).

There are some limitations in the present study. Firstly, it was a retrospective study and the data was derived from a single center. Furthermore, only one patient with ALL at diagnosis suffered from CNS metastasis in the present study. Therefore, a comparative analysis of CNS metastasis incidence between patients with AML and ALL could not be performed.

In conclusion, data from the present study suggest that normal hematopoiesis is more frequently inhibited in patients with AML compared with that in patients with ALL. Similarly, amongst patients with AML, the incidence of myelosuppression is higher in patients with M3 AML compared with non-M3 AML patients. To the best of our knowledge, the present study was the first to offer a peripheral blood feature set for distinguishing AML and ALL, where patients with AL

with peripheral blood findings indicative of leukopenia, pancytopenia, or both leukopenia and anemia or both leukopenia and thrombocytopenia are likely to have AML. Nevertheless, this finding needs to be confirmed by studies with a larger cohort in the future. In addition, further research is needed to elucidate the potential mechanisms. It is hoped that these findings can provide clinicians with future research ideas for assessing the difference between AML and ALL, leading to more accurate diagnoses.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

WC and JH designed the project. HW collected clinical data. WC and JH analyzed the data obtained in the present study and generated the tables. WC wrote the manuscript. All the authors have read and approved the final manuscript. WC and HW confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was approved by the Medical Ethics Committees of Zhongshan Hospital of Xiamen University, Xiamen, China (approval no. xmzsyyky2021151) and was conducted in accordance with the guidelines of the institution. The need for informed consent was waived due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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