Potential effects of liver dysfunction at the time of diagnosis in patients with acute myeloid leukemia

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Abstract. Whilst severe liver dysfunction is rarely encountered at the time of diagnosis for patients with acute myeloid leukemia (AML), mild elevations aminotransferase (<5 times the upper limit of normal) may be more frequently seen. Liver dysfunction at the time of diagnosis of AML is a parameter that requires investigation and can assist the clinicians in predicting prognosis. The aim of the present study was to investigate liver dysfunction at the time of diagnosis using the assoicated parameters in patients with AML. The present retrospective study included 90 patients diagnosed with AML who were hospitalised in the Hematology Clinic of Dışkapı Yıldırım Beyazıt Training and Research Hospital (Ankara, Turkey). The demographic characteristics of the patients were recorded together with hemogram results, anemia parameters, measurable residual disease positivity (MRD) and risk category, the presence of hepatosplenomegaly, infection, neutrophil recovery time (NRT), platelet recovery time (PRT) and liver dysfunction. The patients were analyzed in two groups following sorting into the liver dysfunction (n=45) and normal liver function test group (n=45). In the analysis of independent quantitative data (age, white blood cell count, hemoglobin, platelet, international normalized ratio, albumin, B12 vitamin, NRT, PRT) the Mann Whitney U-test was used. Independent qualitative data (sex, hepatomegaly, splenomegaly, MRD, risk category, infection) were analyzed using the χ^2 test or the Fischer test. The effect level was investigated using univariate and multivariate logistic regression. A receiver operating characteristic curve was applied to determine the effect level and cut-off values. In the group with liver dysfunction, NRT, PRT, MRD positivity, risk category and the presence of infection were found to be statistically significantly higher. These findings suggest that during the first evaluation of patients diagnosed with AML, liver function tests are simple, rapid and necessary. The results obtained in the present study showed that liver dysfunction at diagnosis can be associated with the high-risk group, in addition to more frequent infection, poorer prognosis and mortality.

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Introduction

Acute leukemia, which is characterised by abnormal cell infiltration into the bone marrow, can be categorised according to cell origin and genotypic characteristics, namely as acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) (1). The most frequently observed subtype in the adult patients is AML, where the mean 5-year survival rate is 28% for patients aged ≥20 years (2).

When the prognostic factors are examined in patients with AML, in addition to various patient-related factors, such as age and comorbidities, there are also the parameters of cytogenic characteristics, treatment-related AML, whether or not there is a response to initial treatment, and measurable residual disease positivity (MRD) (3).

By contrast, ALL is a group formed from T and B cell progenitors that can be sub-classified according to genetic and immunophenotypic characteristics (1). When the prognostic characteristics in the course of ALL are examined, various factors are taken into consideration, such as the initial white blood cell count, age and cytogenetic characteristics (4).

Although severe elevations in the liver function test (LFT) are rarely encountered at the time of diagnosis in patients with acute leukemia, mild elevations occur more frequently (5). Leukemic liver involvement can either emerge as drug-related or associated with a number of other reasons, such as primary liver disease (5). Liver dysfunction is a parameter that is easily accessible, can be detected in the first hours after diagnosis and can predict tissue involvement of the disease outside of blood circulation. Therefore, liver dysfunction at the time of diagnosis of AML is a parameter that requires investigation and can assist the clinician in predicting prognosis. The aim of the present study was to investigate liver dysfunction at the time of diagnosis using the associated parameters in patients with AML.

Materials and methods

Patient recruitment and assessment. The present retrospective study included 90 patients with a diagnosis of AML who were hospitalised in the Hematology Clinic of Dışkapı Yıldırım Beyazıt Training and Research Hospital between April 2020 and August 2022. Patients who were eligible for full-dose standard induction chemotherapy (3+7) (Daunorubicin, 60 mg/m^2/1 to 3 days; Cytarabine (Ara-C), 100 mg/m^2/1 to 7 days) were included in the study (6). All the patients included in the present study received (3+7) standard induction therapy. Since patients with serious liver dysfunction were not included and liver dysfunction was attributed to leukemia as a result of the necessary tests, no dose reduction was made in the treatment and the standard dose was given. The demographic characteristics and descriptive parameters of the patients participating in the prsesent study were analyzed. The patients were then separated into two groups according to the LFT results, namely into the liver dysfunction group and those the normal LFT results group, before parameters were compared between these two groups. The demographic characteristics of the patients were recorded together with hemogram results, anemia parameters, MRD and risk category, the presence of hepatosplenomegaly and infection, neutrophil recovery time (NRT), platelet recovery time (PRT) and LFT results [Alanine amino transferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALP), γ-glutamyl transferase (GGT) and Bilirubin].

Patients would be excluded from the study if they had a history of continuous drug use (especially painkillers), regular smoking and alcohol use-including those who had quit smoking for <1 year, the presence of high plasma cholesterol and triglyceride levels, heart failure, electrocardiographic changes, viral and autoimmune hepatitis diagnosis, body mass index >25, thyroid dysfunction, patients receiving low-intensity therapy and those with comorbidities [for example, old age (>70 years), frailty, sarcopenia] that may affect age- and sex-related prognosis. All the patients underwent routine abdominal ultrasonography to exclude possible diagnoses and patients with normal results were included in the study.

Liver dysfunction would be considered if at least two of the parameters used in the evaluation of liver function tests were elevated simultaneously. Patients with the isolated elevation of one parameter were excluded from the study. Patients with elevated aminotransferases (15X), ALP (4X), GGT (4X) and bilirubin (>3 mg/dl) were considered as severe group and were excluded from the study. For the abdominal ultrasonography measurements, liver size >16 cm was deemed to be hepatomegaly, whereas spleen size >12 cm would be deemed as splenomegaly.

The risk category was determined according to the European Leukemia Network (ELN) 2022 AML risk classification based on cytogenetic results (7). Cytogenetic analysis of the patients was performed on blood samples taken from the bone marrow. Genetic abnormalities were reported using karyotype analysis, fluorescence *in situ* hybridization (FISH) and reverse transcription PCR. Favorable risk category includes the following: t(8;21)/RUNX1:RUNX1T1, inv(16)/CBFB:MYH11, nucleophosmin (NPM1) mutated without FMS-like tyrosine kinase-3 (FLT3)-internal tandem duplication (ITD), and in-frame mutated bZIP CCAAT/enhancer-binding protein α positivity (CEBPA). Intermediate risk category includes the following: mutated NPM1 with FLT3-ITD, t (9;11)/MLLT3:KMT2A and cytogenetic and/or molecular abnormalities not classified as favorable or adverse. Adverse risk category includes the following: t(6;9)/DEK:NUP214, *KMT2A*-rearranged, t(9;22)/BCR:ABL1, t(8;16)/KAT6A:CREBBP, inv(3)/GATA2, *MECOM* (EVI1)-rearranged, del(5q) or -5, abn(17p) or -7, Mutated *ASXL1*, *BCOR*, *EZH2*, *RUNX1*, *SF3B1*, *SRSF2*, *STAG2*, *U2AF1*, *ZRSR2* or *TP53* and complex karyotype, and monosomal karyotype.

NRT and PRT were defined as the time from the beginning of the chemotherapy protocol until the neutrophil count was ≥0.5x10^9/l and the platelet count was ≥20x10^9/l for 3 consecutive days without transfusion support, respectively.

MRD assessment by flow cytometric analysis was performed on bone marrow (BM) samples obtained after standard induction chemotherapy using a standard stain-lyse-wash procedure with ammonium chloride lysis. A total of 1x10^6 cells were stained per analysis tube. MRD was defined by comparison with known antigen expression patterns by normal maturing myeloid precursors and monocytes and then expressed as a percentage of total leukocytes (8).

In the flow cytometric examination, values of ≤1/1,000 were accepted as MRD (-), whereas values of ≥1/1,000 were deemed as MRD (+) (9).

Statistical analysis. The study data were analyzed using the SPSS v.27.0 software (IBM Corp). Descriptive statistical methods were used and the results were stated as the mean ± standard deviation, median, minimum and maximum values, number (n) and percentage (%). The distribution of the variables was measured with the Kolmogorov-Smirnov test and Shapiro-Wilk tests. In the analysis of independent quantitative data, the Mann Whitney U-test was used. Independent qualitative data were analyzed using the χ^2 test or the Fischer test if χ^2 assumptions were not met. The effect level was investigated using univariate and multivariate logistic regression. A receiver operating characteristic (ROC) curve was applied to determine the effect level and cut-off values. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Baseline data. Evaluation was made of 90 patients, comprising of 56 (62.2%) males and 34 (37.8%) females, with a mean age of 52.1±18.3 years. The distribution of the variables was measured using the Kolmogorov-Smirnov test. The results of the analyses of the demographic characteristics and descriptive parameters of the patients in the study are shown in Table I.

The patients were separated into the liver dysfunction (n=45) and those with normal LFT results (n=45). The results of statistical analyses between the groups using the χ^2 test and Mann Whitney U-test showed that NRT and PRT, MRD positivity, risk category and presence of infection were statistically significantly higher in the group with liver

Table I. Descriptive statistics of the data and distribution of the demographic parameters of the patients.

Parameter	Mean ± standard deviation or N (%)
Age, years	52.1±18.3
Sex	
Female	34 (37.8)
Male	56 (62.2)
White blood cell count, $10^3/\mu$l	30.3±58.9
Hemoglobin, g/dl	8.7±2.2
Platelet, $10^3/\mu$l	71.4±118.0
International normalized ratio	1.2±0.2
Albumin, g/dl	3.5±0.6
Ferritin, ml/ng	682.7±576.0
B12 Vitamin, pg/ml	486.5±451.9
Neutrophil recovery time, days	31.7±8.8
Thrombocyte recovery time, days	29.0±9.6
Hepatomegaly	
(-)	56 (62.2)
(+)	34 (37.8)
Splenomegaly	
(-)	60 (66.7)
(+)	30 (33.3)
Measurable residue disease	
(-)	32 (35.6)
(+)	58 (64.4)
Risk Category	
Favorable	47 (52.2)
İntermediate	24 (26.7)
Adverse	19 (21.1)
Infection	
(-)	23 (25.6)
(+)	67 (74.4)

dysfunction compared with those in the normal LFT group (P<0.05; Table II).

Univariate and multivariate model results. In the univariate model, when the patient group with liver dysfunction was compared with the group with normal LFT, the risk category, MRD positivity, presence of infection, and NRT and PRT values were observed to be significant variables for the effect of liver dysfunction on the prognosis of acute myeloid leukemia. (P<0.05; Table III). In the multivariate model, when the patient group with liver dysfunction was compared with the group with normal LFT, the risk category, MRD positivity, and PRT value were observed to be significant-independent variables for the effect of liver dysfunction on the prognosis of acute myeloid leukemia (Table III).

ROC results. The NRT value was seen to have a significant effect [Area under the curve (AUC), 0.640 (0.526-0.754)] in distinguishing patients with and without liver dysfunction (Table IV) The significant effect at the cut-off value of 29.5 for NRT [AUC, 0.622 (0.506-0.739)] was 57.8%, where the negative prediction rate was 63.4% in distinguishing patients with and without liver dysfunction with a sensitivity of 66.7% and the positive prediction rate was 61.2% for specificity (Fig. 1 and Table V).

The PRT value was observed to have a significant effect [AUC, 0.636 (0.522-0.750)] in distinguishing patients with and without liver dysfunction (Table VI). Youden index was used to find the cut-off value. The PRT cut-off value at 25.5 was determined to be statistically significant [AUC, 0.611 (0.494-0.728)] in distinguishing patients with and without liver dysfunction, with a sensitivity of 68.9%, positive prediction of 59.6%, specificity of 53.3% and negative prediction of 63.2% (Fig. 2 and Table VII).

Discussion

Hemolytic anemias, disorders in clotting factors, myeloproliferative neoplasm, multiple myeloma, leukemia and lymphomas are the main hematological diseases affecting the liver (10).

AML is a hematological neoplasm that is characterized by the clonal proliferation of immature cells of myeloid origin, called blasts, in the peripheral blood and/or bone marrow (11). Generally a certain blast ratio (>20%) is required for AML diagnosis (12). The annual incidence of AML is 4.3 per 100,000, with the median age of onset of 68 years in the United States (13). With developing technology, the possibility of early diagnosis and treatment increases, which results in an extended life expectancy. As life expectancy increases, malignancies that increase in frequency with age may also increase the likelihood of being seen in the general population. In addition, with advancements in technology and an increase in genetic studies, the speed, ease and frequency of diagnosis have also increased (14). For the prognosis of patients, although there have been developments in various prognotic evaluation parameters, especially those of the genetic variety (for example NUP98 rearrangement, KMT2A rearrangement), the process remains time-consuming (6,7). Therefore, simple parameters that can provide results within a short period of time at the time of diagnosis would be of benefit for the clinician. LFT are parameters that can be easily accessed and provide results rapidly (within the first 4 h after the patient is admitted) at the time of diagnosis. In the present study, it was investigated whether LFT can be of benefit in terms of overall survival at the time of diagnosis in patients with AML.

Although the main site of hematopoiesis in adult life is the bone marrow, the liver, which is the main site of hematopoiesis in fetal life, also continues this function (15). Therefore, liver dysfunction is one of the most common conditions encountered in hematological disorders (15). Gastrointestinal symptoms are present in ~25% cases of acute leukemias at the time of diagnosis. By contrast, liver and spleen involvement is less common in acute leukemias compared with in chronic leukemia cases (16).

Liver involvement in hematological malignancies and other rheumatological and oncological systemic diseases can be explained by four main mechanisms, namely vascular, toxic, immune and hormonal (17). As a result of such mechanisms, damage is frequently observed in hepatocytes, cholangiocytes

Table II. Comparisons of the parameters between the groups with and without LFT impairment.

Parameters	LFT impairment (-)	LFT impairment (+)	P-values
Age, years	51.9±19.5	52.3±17.2	0.781[b]
Sex			0.192[a]
Female	14 (31.1)	20 (44.4)	
Male	31 (68.9)	25 (55.6)	
White blood cell count, $10^3/\mu$l	34.2±72.1	26.4±42.3	0.744[b]
Hemoglobin, g/dl	8.8±2.48	8.59±1.96	0.958[b]
Platelet, $10^3/\mu$l	85.3±155.7	57.5±59.5	0.744[b]
International normalized ratio	1.25±0.19	1.20±0.20	0.085[b]
Albumin, g/dl	3.51±0.54	3.46±0.65	0.691[b]
Ferritin, ml/ng	629.5±617.0	735.9±533.5	0.145[b]
B12 Vitamin, pg/ml	473.0±444.7	500.0±463.6	0.878[b]
Neutrophil recovery time, days	29.5±8.7	33.8±8.4	0.022[b]
Thrombocyte recovery time, days	26.9±9.1	31.2±9.8	0.026[b]
Hepatomegaly			>0.999[a]
(-)	28 (62.2)	28 (62.2)	
(+)	17 (37.8)	17 (37.8)	
Splenomegaly			0.371[a]
(-)	32 (71.1)	28 (62.2)	
(+)	13 (28.9)	17 (37.8)	
Measurable residue disease			0.008[a]
(-)	22 (48.9)	10 (22.2)	
(+)	23 (51.1)	35 (77.8)	
Risk category			0.030[a]
Favorable	29 (64.4)	18 (40.0)	
İntermediate	11 (24.4)	13 (28.9)	
Adverse	5 (11.1)	14 (31.1)	
Infection			0.008[a]
(-)	17 (37.8)	6 (13.3)	
(+)	28 (62.2)	39 (86.7)	

[a]χ^2 test; [b]Mann-Whitney test. LFT, liver function test.

Table III. Logistic regression analysis.

	Univariate model			Multivariate model		
Parameter	OR	95% CI	P-value	OR	95% CI	P-value
Risk Category	2.084	1.192-3.646	0.010	2.542	1,344-4.806	0.004
Measurable residue disease	3.348	1.342-8.351	0.010	4.249	1.523-11.857	0.006
Infection	3.946	1.381-11.274	0.010			
Neutrophil recovery time	1.060	1.008-1.115	0.023			
Thrombocyte recovery time	1.050	1.003-1.099	0.037	1.060	1.008-1.115	0.024

OR, odds ratio.

and endothelial cells (17). In acute leukemia, these mechanisms underlie hepatocellular necrosis due to infiltration by leukemic cells and lymphocytes (18). Therefore, it is of high importantance to distinguish whether the initial liver dysfunction is due to leukemic infiltration or if it is unrelated to the acute leukosis. Liver dysfunction due to leukemic infiltration improves after induction chemotherapy. Therefore, it is difficult to distinguish at the time of diagnosis (18,19).

Table IV. Receiver operating characteristic curve using NRT cut-off.

Parameter	Area under the curve	95% CI	P-value
NRT	0.640	0.526-0.754	0.022
NRT 29.5 cut-off	0.622	0.506-0.739	0.046

NRT, neutrophil recovery time.

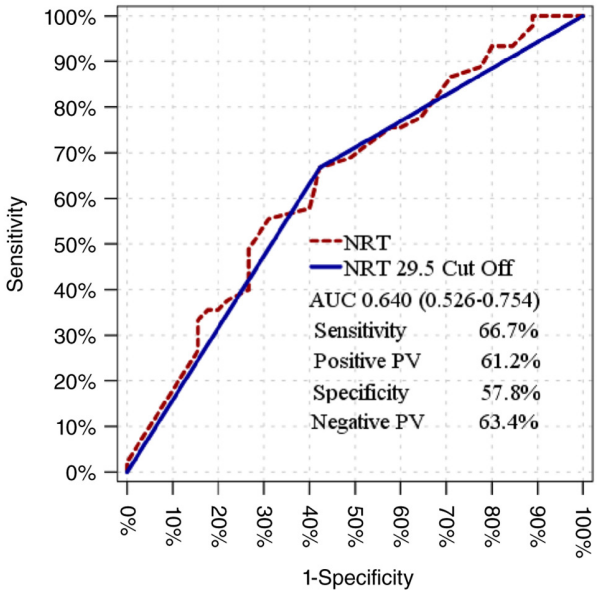

Figure 1. Receiver operating characteristic curve for NRT in distinguishing patients with and without liver dysfunction. The abscissa indicates specificity and the ordinate indicates sensitivity. AUC, 0.640 (0.526-0.754) for NRT value. NRT, neutrophil recovery time; AUC, area under the curve; PV, predictive value.

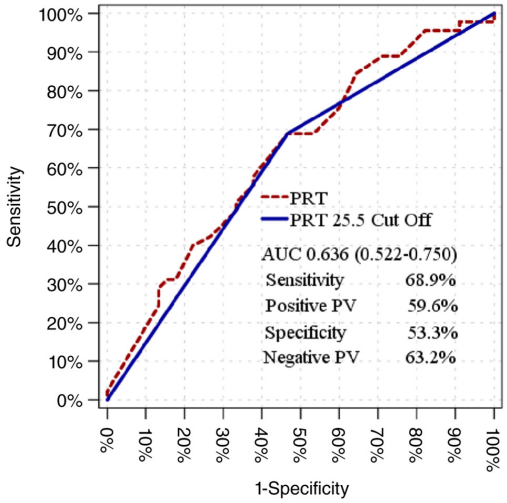

Figure 2. Receiver operating characteristic curve for PRT in distinguishing patients with and without liver dysfunction. The abscissa indicates specificity and the ordinate indicates sensitivity. AUC, 0.636 (0.522-0.750) for PRT value. PRT, platelet recovery time; AUC, area under the curve; PV, predictive value.

By contrast, in cases of chronic lymphocytc leukemia, leukemic cell infiltration, primary and secondary hepatic malignancies, drug-induced hepatotoxicity, immunological effects, infections and Richter transformation are possible causes of LFT disorders (20).

It has been previously shown that mild-to-moderate liver dysfunction can be encountered in patients with newly diagnosed acute leukemia. In paediatric patients diagnosed with ALL, liver dysfunction at the time of diagnosis has been determined at the rate of 34% in Canada (21). In a study by Sandart *et al* (22) on paediatric patients diagnosed with AML, liver involvement at the time of diagnosis was reported at the rate of 29.5% (22).

The present study included a total of 90 patients with newly diagnosed AML who met the study criteria, who were then separated into two groups, namely those with and without liver dysfunction at the time of diagnosis. Since those with age and sex-dependent diseases [for example, old age (>70 years), frailty, sarcopenia] that can potentially confound prognosis were excluded from the study, there was no statistically significant difference in age distribution between the two groups. Age is a parameter that can affect prognosis and causes restrictions in AML treatment protocols. Depending on age, it may be preferable to reduce the dose or apply less intense treatments (23). In the multivariate model, the independent variables of risk category, MRD positivity and PRT value were determined to be significant in the patient group with liver dysfunction compared to the group without.

In patients diagnosed with acute leukemia, there is a number of prognostic factors, such as patient-related (age, lack of physical capacity, etc.) disease-related (WBC >200,000 at diagnosis) and cytogenetic characteristics (adverse risc category: tp53, RUNX etc.). Risk category is one of the most important parameters for determining the prognosis and treatment regimen of patients with acute leukemia (6). In the present study, the ELN 2022 AML risk classification was used to determine the risk category of each patient.

Determining the risk category by performing genetic testing at the time of AML diagnosis, performing diagnostic blast percentage and MRD monitoring with flow cytometry are parameters used in routine practice, which can be used to predict prognosis. In addition, determining the relationship between liver dysfunction at the time of diagnosis and cytogenetic and MRD monitoring can contribute to commenting on prognosis (24). In the present study, patients in the favorable risk category were determined at the rate of 40.0% in the group with liver dysfunction and 64.4% in the group without liver dysfunction, whilst the frequency of patients in the adverse risk category was found to be 31.1% in the group

Table V. Distribution of patients in the group at 29.5 NRT cut-off value

Neutrophil recovery time[ab]	Liver dysfunction (-)	Liver dysfunction (+)
≤29.5	26	15
>29.5	19	30

[a]Defined as the time from the beginning of the chemotherapy protocol until the neutrophil count was ≥0.5x10^9/l for 3 consecutive days without transfusion support. [b]Youden index was used to find the cut-off value.

Table VI. Receiver operating characteristic curve using PRT cut-off.

Parameter	Area under the curve	95% CI	P-value
PRT	0.636	0.522-0.750	0.026
PRT[ab] 25.5 cut-off	0.611	0.494-0.728	0.069

[a]Defined as the time from the beginning of the chemotherapy protocol until the neutrophil count was ≥20x10^9/l for 3 consecutive days without transfusion support. [b]Youden index was used to find the cut-off value. PRT, platelet recovery time.

Table VII. Distribution of patients in the group at 25.5 PRT cut-off value

Platelet recovery time[ab]	Liver dysfunction (-)	Liver dysfunction (+)
≤25.5	24	14
>25.5	21	31

[a]Defined as the time from the beginning of the chemotherapy protocol until the neutrophil count was ≥20x10^9/l for 3 consecutive days without transfusion support. [b]Youden index was used to find the cut-off value.

with liver dysfunction and 11.1% in the group without liver dysfunction. According to these results, the probability of finding patients with adverse risk category is higher in patients with liver dysfunction at the time of diagnosis. These data can also be interpreted as the number of patients who will be given intensive treatment and indications for transplantation may be higher in patients with liver dysfunction, at the time of diagnosis.

MRD is an independent risk factor that can be used to determine the deeper (post-treatment blast rate <5% and MRD negative) remission status, risk classification and treatment plan after diagnosis. It can be measured using flow cytometry, PCR and next-generation sequencing methods (25). In a study by Sandart *et al* (22) of paediatric patients with acute leukemia, liver involvement at the time of diagnosis was reported to be associated with subtype, leukocyte count and patient age. In addition, liver involvement was determined to be associated with minimal residual disease, overall survival and time to relapse (22).

In the present study, there was a high rate of MRD positivity (77.8%) in the group with liver dysfunction. Since MRD positivity is an independent risk factor for prognosis, it may be more likely that MRD positivity will be detected after standard induction chemotherapy in patients with liver dysfunction at the time of diagnosis. Liver dysfunction at the time of diagnosis can be considered to indicate the presence/infiltration of the disease of AML in a solid organ tissue other than the bone marrow. It can be hypothesed that treating abnormal cell death in the liver is more difficult than abnormal cell death in the bloodstream, such that treatment will be less effective in cases of solid organ involvement. As a result, liver dysfunction at the time of diagnosis can be of guidance for assessing prognosis.

In the present study, a statistically significant association was determined between liver dysfunction and MRD positivity. This parameter was also a significant, independent variable in the multivariate model for the effect of liver dysfunction on the prognosis of acute myeloid leukemia. Based on these results, the detection of liver dysfunction at the time of diagnosis can likely be used to predict a high recurrence risk of leukemia, poor prognosis and overall survival.

In patients diagnosed with acute leukemia, the longer the duration of neutropenia and thrombocytopenia after chemotherapy, the greater the risk of complications (26,27). Certain patients will also succumb to various infections due to this prolonged neutropenic period (26). Increasing the duration of thrombocytopenia increases the risk of mild-to-severe bleeding in patients, resulting in the risk of mortality (27). Yamazaki *et al* (28) reported that the recovery of hematopoiesis after induction chemotherapy, especially rapid platelet recovery, was an important determinant of relapse-free survival in patients with AML (28). In another previous

study, it was reported that prolonged NRT was associated with grade 3-4 infection and relapse (29). In the present study, NRT and PRT were statistically significantly higher in patients with liver dysfunction at diagnosis, where subsequent multivariate analysis found PRT to be a significant, independent variable together with MRD positivity and risk category for the effect of liver dysfunction on the prognosis of acute myeloid leukemia.

In patients with liver dysfunction at the time of diagnosis, PRT was found to be longer. This lengthy period causes an increase in the patient's bleeding risk, replacement number and duration. The increase in bleeding risk correspondingly increases the risk of morbidity and mortality. The increase in replacement number may cause transfusion reactions during the later stages of treatment and adverse reactions during transplantation. In addition, NRT was found to be longer in patients with liver dysfunction at the time of diagnosis. This prolonged period increases the patient's exposure to infections, the duration of antibiotic use and the risk of encountering resistant bacteria emergence during the treatment regimen. When all of the aforementioned conditions are taken into consideration, detection of liver dysfunction at the time of diagnosis may be predictive in terms of prognosis. Previous studies have established a relationship between the degree of liver dysfunction and prognosis (10,22,30). Liver dysfunction was detected in 20% patients with hematological malignancies who required intensive care and was found to be an independent risk factor for mortality, where a relationship was found between the degree of liver dysfunction and poor prognosis (30).

LFTs are simple, rapid and potentially beneficial evaluation tools for the first evaluation of patients with newly diagnosed acute leukemia. Liver dysfunction at the time of diagnosis can be a clinical guide for patient follow-up. In a patient with liver dysfunction at the time of diagnosis, the risk of infection, bleeding and the possibility of recurrence should be kept in mind during follow-up.

For the accurate evaluation of the parameters, patients with severe liver dysfunction values were excluded from the study design. Due to the exclusion of such severe cases, the relationship between the degree of liver dysfunction and prognosis in newly diagnosed patients with AML was not evaluated in the present study. Additional comprehensive studies including patients with severe liver dysfunction are needed for this evaluation in the future.

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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

Data collection was performed by DIS and FY. Statistical analysis was performed by BS and MRA. FY, HBAÖ, BS and MRA conducted the literature search, writing of the article and confirm the authenticity of all the raw data. FY, HBAÖ, DIS, AKG and MA analyzed the results and contributed to the final manuscript. The original draft was written by FY, AKG and MA. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The present study was approved by the Ethics Committee of Etlik City Hospital (date, 03.05.2023; approval no. AEŞH-EK1-2023-142; Ankara, Turkey). Patients of Dışkapı Training and Research Hospital Hematology Clinic were transferred to Etlik City Hospital after the closure of Dışkapı Training and Research Hospital Hematology Clinic. The study plan was explained in detail both verbally and in writing to the patients included in the present study. All patients provided a signed informed consent form.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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