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Hepatomegaly as a predictor of disease progression in acute myeloid Leukemia Patients

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Abstract
Background: Acute Myeloid Leukemia (AML) is a heterogeneous and aggressive Hematological malignancy characterized by the rapid proliferation of abnormal myeloid cells. Hepatomegaly, or the abnormal enlargement of the liver, is sometimes observed in AML patients and may have implications for disease progression and patient outcomes. This study investigates the role of hepatomegaly as a predictor of disease progression in AML patients.
Objective: The objective of this study is to evaluate the significance of hepatomegaly as a prognostic indicator in AML, focusing on its association with disease progression, treatment response, and overall survival.
Methods: A retrospective cohort study was conducted, analyzing clinical data from 200 AML patients treated at a major cancer center between 2010 and 2020. Patients were categorized into two groups based on the presence or absence of hepatomegaly at diagnosis. Key outcomes, including disease progression, relapse rates, treatment response, and overall survival, were compared between the two groups using multivariate Cox regression analysis.
Results: The study found that AML patients with hepatomegaly at diagnosis had a significantly higher rate of disease progression compared to those without hepatomegaly. The 3-year progression-free survival (PFS) was 45% in the hepatomegaly group compared to 65% in the non-hepatomegaly group (P=0.02). Additionally, the overall survival (OS) was lower in the hepatomegaly group, with a 5-year OS of 30% versus 50% in the non-hepatomegaly group (P=0.03). Multivariate analysis identified hepatomegaly as an independent predictor of poor prognosis, with a hazard ratio (HR) of 1.8 (95% CI: 1.2-2.7, P=0.01) for disease progression.
Conclusion: Hepatomegaly at diagnosis is associated with an increased risk of disease progression and poorer survival outcomes in AML patients. These findings suggest that hepatomegaly could serve as a valuable prognostic marker, helping to identify high-risk patients who may benefit from more aggressive treatment strategies. Further prospective studies are warranted to validate these findings and explore the underlying mechanisms linking hepatomegaly to disease progression in AML.

Keywords: AML, disease progression, Leukemia Patients, Hepatomegaly, disease progression

1. Introduction
Acute Myeloid Leukemia (AML) is a rapidly progressing hematological malignancy characterized by the clonal expansion of myeloid precursors in the bone marrow, leading to bone marrow failure and systemic complications. Despite advances in treatment, AML remains associated with high morbidity and mortality, particularly due to its heterogeneous nature and the variable response to therapy among different patient subsets. Identifying prognostic markers that can predict disease progression and treatment outcomes is critical for optimizing therapeutic strategies and improving patient survival. Hepatomegaly, or the enlargement of the liver, is an often-overlooked clinical finding in AML patients. It may result from leukemic infiltration, extra medullary hematopoiesis, or other underlying conditions. The presence of hepatomegaly in AML patients has been hypothesized to be a marker of disease burden and aggressiveness, potentially correlating with poorer outcomes. However, its role as an independent predictor of disease progression in AML remains underexplored.
This study aims to investigate the significance of hepatomegaly as a predictor of disease progression in AML patients, examining its association with key clinical outcomes, including progression-free survival (PFS), overall survival (OS), and treatment response.

1.1 Main Objective
The main objective of the paper is to evaluate the role of hepatomegaly as a predictor of disease progression in Acute Myeloid Leukemia (AML) patients.

2. Methods
2.1 Study Design and Population
This retrospective cohort study included 200 adult patients diagnosed with AML and treated at between January 2010 and December 2020. Patients were eligible for inclusion if they had a confirmed diagnosis of AML based on World Health Organization (WHO) criteria and had undergone baseline imaging studies (e.g., ultrasound or CT scan) to assess liver size at the time of diagnosis. Patients with prior liver disease unrelated to AML or those who had received prior chemotherapy for other malignancies were excluded from the analysis.

2.2 Data Collection
Data were extracted from electronic medical records, including demographic information, clinical characteristics, treatment regimens, and outcomes. The presence of hepatomegaly was determined based on imaging studies and was defined as a liver span greater than 15 cm in the mid-clavicular line. Patients were categorized into two groups: those with hepatomegaly (hepatomegaly group) and those without hepatomegaly (non-hepatomegaly group).

2.3 Outcome Measures
The primary outcomes of interest were progression-free survival (PFS) and overall survival (OS). PFS was defined as the time from diagnosis to the first occurrence of disease progression, relapse, or death from any cause. OS was defined as the time from diagnosis to death from any cause. Secondary outcomes included response to induction chemotherapy (complete remission [CR] rate) and relapse rates.

2.4 Statistical Analysis
Descriptive statistics were used to summarize patient characteristics and outcomes. The Kaplan-Meier method was used to estimate PFS and OS, with differences between groups assessed using the log-rank test. Multivariate Cox proportional hazards models were used to identify independent predictors of PFS and OS, adjusting for potential confounders such as age, cytogenetic risk category, and performance status. Hazard ratios (HR) with 95% Confidence Intervals (CI) were reported, and a p-value of < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 26.

3. Results
3.1 Patient Characteristics
The 200 patients included in the study, 60 (30%) had hepatomegaly at the time of AML diagnosis. The median age was 55 years (range 18-78), with no significant differences in age, gender, or baseline white blood cell count between the hepatomegaly and non-hepatomegaly groups. However, a higher proportion of patients in the hepatomegaly group had adverse cytogenetic features.

Table 1: Baseline Characteristics of AML Patients with and without Hepatomegaly

Characteristic	Hepatomegaly Group (N=60)	Non-Hepatomegaly Group (N=140)
Median Age (years)	55	54
Male (%)	58%	56%
Adverse Cytogenetics (%)	45%	30%
Median WBC Count (x10^9/L)	35.0	30.5

3.2 Disease Progression and Survival Outcomes
Patients with hepatomegaly at diagnosis had significantly worse PFS and OS compared to those without hepatomegaly. The 3-year PFS was 45% in the hepatomegaly group versus 65% in the non-hepatomegaly group (P=0.02), while the 5-year OS was 30% in the hepatomegaly group compared to 50% in the non-hepatomegaly group (P=0.03).

Table 2. Survival Outcomes in AML Patients with and without Hepatomegaly

Outcome	Hepatomegaly Group	Non-Hepatomegaly Group	P-Value
3-Year Progression-Free Survival (PFS)	45%	65%	0.02
5-Year Overall Survival (OS)	30%	50%	0.03

Multivariate analysis identified hepatomegaly as an independent predictor of disease progression, with a hazard ratio (HR) of 1.8 (95% CI: 1.2-2.7, P=0.01). Other significant predictors included adverse cytogenetics and high baseline white blood cell count.

3.3 Response to Treatment
The complete remission (CR) rate following induction chemotherapy was lower in the hepatomegaly group (60%) compared to the non-hepatomegaly group (75%), although this difference was not statistically significant ($p = 0.08$). However, the relapse rate was higher in the hepatomegaly group (40% vs. 25%, P=0.04), indicating a higher likelihood of disease recurrence in these patients.

4. Discussion
The findings of this study highlight the prognostic significance of hepatomegaly in patients with AML. The presence of hepatomegaly at diagnosis was associated with an increased risk of disease progression and poorer overall survival. These results suggest that hepatomegaly may serve as a marker of more aggressive disease, potentially due to leukemic infiltration of the liver or other underlying factors. The lower PFS and OS observed in the hepatomegaly group may reflect the increased disease burden and more advanced stage at presentation. The higher relapse rate in this group further supports the notion that hepatomegaly is indicative of a more refractory disease course, which may require more aggressive or alternative therapeutic approaches.

Although the study was limited by its retrospective design and relatively small sample size, the findings provide important insights into the role of hepatomegaly as a prognostic marker in AML. Further prospective studies with larger cohorts are needed to validate these results and to explore the biological mechanisms underlying the association between hepatomegaly and disease progression in AML.

5. Conclusion

The findings of this study underscore the significance of hepatomegaly as a prognostic marker in patients with Acute Myeloid Leukemia (AML). Patients presenting with hepatomegaly at diagnosis were observed to have a higher risk of disease progression, lower progression-free survival (PFS), and reduced overall survival (OS) compared to those without hepatomegaly. The presence of hepatomegaly likely reflects a greater disease burden, possibly due to leukemic infiltration of the liver or other systemic factors, indicating a more aggressive disease course. The association between hepatomegaly and higher relapse rates further suggests that these patients may have a more refractory form of AML, which could require more intensive or alternative therapeutic approaches. While the study provides valuable insights, it is important to acknowledge the limitations inherent in its retrospective design and the relatively small sample size. Nonetheless, these findings highlight the potential utility of hepatomegaly as a clinical marker to identify high-risk AML patients who may benefit from closer monitoring and tailored treatment strategies. Future prospective studies with larger cohorts are necessary to validate these results and explore the underlying biological mechanisms. Understanding the role of hepatomegaly in AML progression could lead to improved risk stratification and personalized treatment approaches, ultimately enhancing patient outcomes.

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