



Genetic Signatures and Treatment Outcomes in Acute Myeloid Leukemia with Hyperleukocytosis: A Comprehensive Analysis of 444 Patients



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Introduction

Acute myeloid leukemia (AML) with hyperleukocytosis (HL) presents a significant clinical challenge, yet the relationship between genetic alterations and treatment outcomes remains poorly understood. Comprehensive studies examining the impact of hyperleukocytosis on survival and its genetic associations are limited.

Objective

To evaluate clinical outcomes in AML patients with HL versus non-HL under different treatment intensities and to investigate associated genetic alterations.

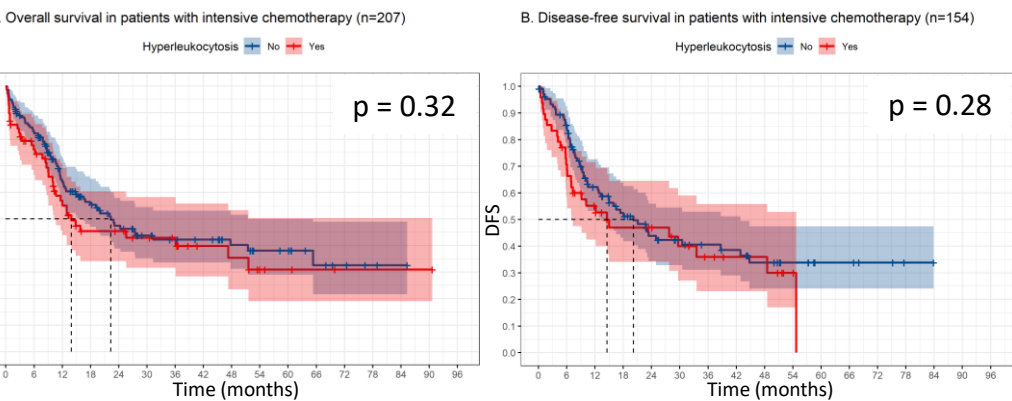
Methods

We analyzed 444 newly diagnosed AML patients, excluding acute promyelocytic leukemia, biphenotypic leukemia, and blastic plasmacytoid dendritic cell neoplasm. Patients received intensive chemotherapy (n=207) or non-intensive treatment (n=237). Hyperleukocytosis (HL) was defined as initial white blood cell count >50,000 cells/ μ L. Clinical outcomes and genetic mutations were compared between groups.

Results

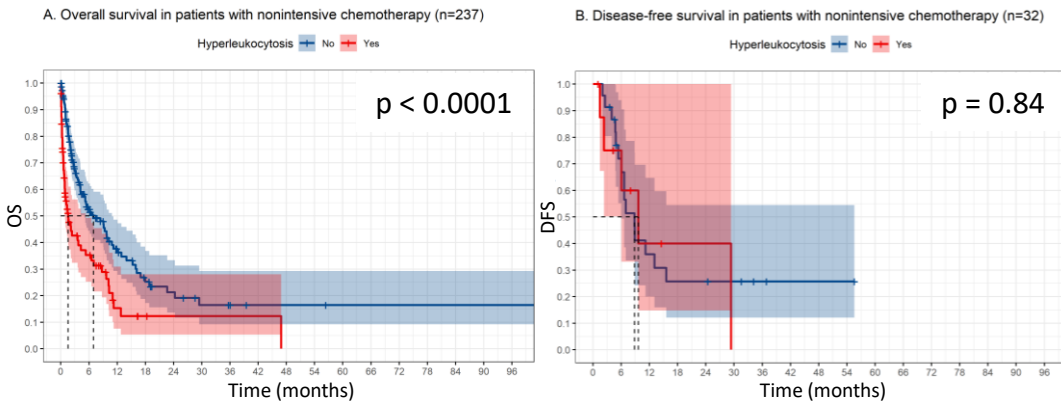
In the intensive chemotherapy group, HL patients showed similar complete remission rates (69.6% vs. 77.5%, p=0.458) and survival outcomes (median OS): 13.9 vs. 22.3 months, p=0.32; median DFS: 14.6 vs. 20.2 months, p=0.28).

Figure 1 Kaplan-Meier survival curves for OS (A) and DFS (B) stratified by HL in AML patients treated with intensive chemotherapy



However, in the non-intensive treatment group, HL patients had significantly higher mortality (69.6% vs. 54.4%, p=0.025) and worse OS but showed similar DFS (median OS: 1.6 vs. 6.9 months, p<0.001; median DFS: 9.7 vs. 8.8 months, p=0.84).

Figure 2 Kaplan-Meier survival curves for OS (A) and DFS (B) stratified by HL in AML patients treated with non-intensive treatment

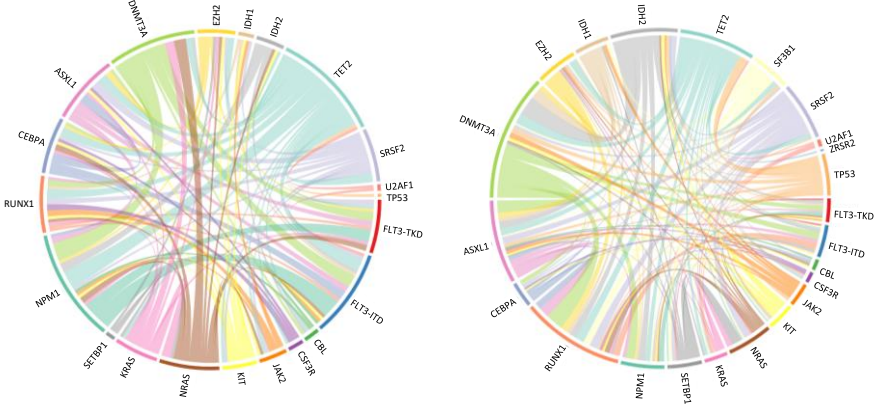


The distributions of genetic alterations in these 2 groups were distinct. HL was strongly associated with specific mutations, including *NPM1* (31.8% vs. 7.8%, p<0.001), *FLT3*-ITD (30.6% vs. 9.3%, p<0.001), and *TET2* (28.2% vs. 12.4%, p=0.001) while showing lower frequencies of *TP53* (2.3% vs. 16.3%, p=0.001) mutations.

Table 1 Association of hyperleukocytosis with genetic alterations (show only in >200 cases)

Mutation	All	HL (%)	Non-HL (%)	P value	Mutation	All	HL (%)	Non-HL (%)	P value
<i>FLT3</i> -ITD	15.6	30.6	9.3	<0.001	<i>IDH2</i>	9.8	9.4	9.9	0.899
<i>FLT3</i> -TKD	8.3	8.2	8.3	0.978	<i>JAK2</i>	4.9	3.5	5.4	0.480
<i>NPM1</i>	14.9	31.8	7.8	<0.001	<i>KIT</i>	5.9	4.7	6.4	0.571
<i>RUNX1</i>	15.3	11.8	16.8	0.277	<i>NRAS</i>	11.1	14.0	9.9	0.317
<i>ANKRD26</i>	0.7	1.3	0.5	0.486	<i>KRAS</i>	7.6	12.8	5.4	0.032
<i>ASXL1</i>	9.1	9.4	8.9	0.893	<i>SETBP1</i>	3.2	1.4	4.0	0.302
<i>CBL</i>	2.8	2.4	3.0	0.772	<i>SF3B1</i>	4.8	0	6.8	0.023
<i>CEBPA</i>	11.8	15.3	10.4	0.241	<i>SRSF2</i>	6.3	5.9	6.4	0.860
<i>CSF3R</i>	2.4	3.5	2.0	0.437	<i>TET2</i>	17.1	28.2	12.4	0.001
<i>DNMT3A</i>	19.4	20.9	18.8	0.678	<i>TP53</i>	12.2	2.3	16.3	0.001
<i>EZH2</i>	6.3	5.8	6.4	0.842	<i>U2AF1</i>	2.4	2.4	2.5	0.951
<i>IDH1</i>	4.5	2.4	5.4	0.250	<i>ZRSR2</i>	0.7	0	1.0	0.357

Figure 3 Co-occurrence of gene mutations patients with HL (n = 61) (left) and non-HL (n = 167) (right)



Conclusion

Our findings demonstrate that HL impacts survival differently based on treatment intensity and is associated with distinct genetic profiles. While not a poor prognostic factor in intensive chemotherapy patients, it significantly worsens outcomes in those receiving non-intensive treatment. These results provide important evidence for risk stratification and treatment selection in AML patients with HL.

References

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