Original Study

Predictive and Prognostic Markers in Adults With Acute Myeloid Leukemia: A Single-Institution Experience

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Abstract

Outcomes in acute myeloid leukemia (AML) have been correlated with predictive and prognostic factors including age, performance status, comorbidities, cytogenetics, and molecular mutations. Retrospective review of 137 adult AML patients identified 3+7 (3 days of anthracycline and 7 days of cytarabine) induction and absence of monosomal karyotype to positively predict complete remission whereas positive predictors of overall survival were younger age and the absence of monosomal karyotype.

Background: Acute myeloid leukemia (AML) is a heterogeneous malignancy with diverse genetic abnormalities, clinical presentations, and outcomes. Known predictive and prognostic factors in AML include age, performance status, comorbidities, cytogenetics, and molecular mutations. Identifying prognostic and predictive factors can inform the choice of induction therapy and outcomes prediction. **Patients and Methods:** A retrospective review was performed of 137 adult AML patients from 2010 to 2015. Predictors of complete remission (CR) and overall survival (OS) were determined for patients treated with 3+7 (3 days of anthracycline and 7 days of cytarabine) or hypomethylating agent. Variables associated with CR or OS were assessed using univariate Cox regression and a multivariate Cox model. **Results:** The average age was 65 years and 91 patients (66%), sample size is 137 patients had primary AML. Patients in the 3+7 induction group were younger, had a higher bone marrow blast percentage, and more de novo AML compared with those in the hypomethylating agent group ($P < .001$, $P < .001$, $P = .005$, respectively). Univariate logistic regression for CR showed a significant association between age ($P < .001$), choice of induction ($P < .001$), and monosomy ($P = .015$), although only induction with 3+7 ($P < .001$) and absence of monosomy ($P = .042$) remained significant in multivariate analysis. Univariate Cox regression indicated that age ($P = .003$), AML status (de novo or secondary; $P = .0277$), choice of induction ($P = .030$), and monosomy ($P = .010$) had a significant association with OS. Only younger age ($P = .018$) and absence of monosomy ($P = .022$) were predictive of OS in multivariate Cox analysis. **Conclusion:** Positive predictors of CR in adult AML include absence of monosomy and induction treatment with 3+7; whereas positive predictors of OS are younger age and absence of monosomy.

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Introduction

Acute myeloid leukemia (AML) is a highly heterogeneous hematologic malignancy with varying clinical presentation, cytogenetics, and molecular abnormalities as well as a treatment outcome that is dependent on patient- and leukemia-related factors. It is predominantly a disease of older people with average age at diagnosis of 67 years. AML is more common among men than women, but the average lifetime risk in both sexes is <0.5% to 1%. Approximately 2 of 3 AML patients who receive intensive induction chemotherapy with 3+7 (3 days of anthracycline and 7 days of cytarabine) will achieve complete remission (CR). However, the average 5-year survival rate for patients diagnosed with AML is approximately 27%.[1,2] For more

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Table 1 Demographic, Hematologic, and Diagnostic Characteristics According to Treatment Group

	Supportive Care (n = 22)	3+7 (n = 87)	Hypomethylation (n = 27)	*P*
Demographic Characteristics (n = 137)				
Age[a]				<.001
<50 years	0 (0.0%)	19 (21.8%)	0 (0.0%)	
50-70 years	4 (18.2%)	47 (54.0%)	7 (25.9%)	
>70 years	18 (81.8%)	21 (24.2%)	20 (74.1%)	
Sex[b]				.843
Male	16 (72.7%)	47 (54.0%)	14 (51.9%)	
Female	6 (27.3%)	40 (46.0%)	13 (48.1%)	
Race[a]				.652
White	18 (81.8%)	71 (81.6%)	24 (88.9%)	
Black	1 (4.5%)	5 (5.7%)	0 (0.0%)	
Others	3 (13.6%)	11 (12.6%)	3 (11.1%)	
Hematologic Characteristics				
WBC, $\times 10^9$/L[c]	10.6 (1.7-198.1)	6.5 (0.3-167)	4.2 (1.1-84.1)	.509
Platelets, $\times 10^9$/L[c]	39.5 (2-78)	57.0 (7-319)	58.0 (9-217)	.979
Hemoglobin, g/L[d]	92 (19)	95 (18)	91 (15)	.306
Lactate dehydrogenase, U/L	687.5 (183-1744)	264 (133-2618)	250 (176-401)	
Uric acid, µmol/L	434.2 (220-1250)	303.4 (83.3-1100)	345.0 (101.1-606.8)	
Albumin, g/L (n = 132)[d]	33 (6)	37 (5)	36 (6)	.490
Circulating blast, %[c]	6.5 (1-72)	11 (0-95)	10 (0-94)	.705
Marrow blast, %[d]	43.9 (25.4)	54.9 (23.8)	38.2 (18.3)	<.001
Diagnostic Characteristics				
Acute myeloid leukemia[b]				.005
Primary	15 (68.2%)	64 (73.6%)	12 (44.4%)	
Secondary	7 (31.8%)	23 (26.4%)	15 (55.6%)	
Cytogenetics[a]				.128
Favorable	1 (4.8%)	10 (11.5%)	0 (0.0%)	
Intermediate	8 (38.1%)	47 (54.0%)	14 (51.9%)	
Adverse	12 (57.1%)	30 (34.5%)	13 (48.1%)	
Trisomy[b]				.093
No	10 (50.0%)	66 (75.9%)	16 (59.3%)	
Yes	10 (50.0%)	21 (24.1%)	11 (40.7%)	
Monosomy[b]				.188
No	12 (60.0%)	66 (75.9%)	17 (63.0%)	
Yes	8 (40.0%)	21 (24.1%)	10 (37.0%)	

Continuous variables are reported as mean (SD) or median (minimum-maximum), as appropriate. Categorical variables are reported as frequency (%). The *P* value reported corresponds to comparisons or test for association between the 3+7 and the hypomethylation groups. The supportive care group is presented only in a descriptive way. No tests were performed for lactate dehydrogenase and uric acid because of missing observations.
Abbreviation: 3+7 = 3 days of anthracycline and 7 days of cytarabine; WBC = white blood cells.
[a]Fisher's exact test.
[b]Chi-square test.
[c]Wilcoxon rank sum test.
[d]Two-sample *t* test.

than 5 decades, CR in AML has been defined as fewer than 5% leukemic blasts in the bone marrow, the absence of extra medullary AML, and recovery of peripheral blood neutrophil and platelet counts to $>1.0 \times 10^9$/L and 100×10^9/L, respectively.[3,4] It is well established that response to induction therapy is a major independent prognostic factor in AML because it predicts risk of relapse as well as overall survival (OS); this led to the revision of standardized diagnostic and response criteria in 2003.[3,5]

The management of patients with AML has also evolved with growing awareness of the heterogeneity of the disease, as well as incorporation of predictive factors such age, comorbidities, performance status, and the identification of cytogenetic abnormalities.[6-8] Former limitations of cytogenetics as prognostic and predictive markers in the 45% of AML patients with normal karyotypes and others with miscellaneous chromosomal abnormalities have been reduced by the recent recognition of genetic alterations in patients