Clinical and sociodemographic predictors of intensive care unit admission following chemotherapy in acute myeloid leukemia

Treatment-related mortality remains a major driver of early death in acute myeloid leukemia (AML). Advances in supportive care have reduced early mortality but fail to benefit patients equitably.[1-3] Our previous work had confirmed Black-White survival disparities in newly diagnosed AML and indicated that intensive care unit (ICU) admission during induction chemotherapy was a significant mediator of these disparities.[4] Current prediction tools to identify the risk of treatment-related mortality (TRM) in AML rely on clinicopathologic variables such as marrow reserve, age, performance status, and organ function, but fail to consider the social determinants of health (SDOH) that are increasingly recognized to impact the success of AML therapy.[5] This represents the first study to include sociodemographic characteristics along with clinicopathologic characteristics as predictors of ICU admission during induction chemotherapy.

The Chicago AML registry provides a unique resource for performing a detailed analysis of the early treatment course in a contemporary, diverse population. Data were collected in Research Electronic Data Capture (REDCap) hosted at the University of Illinois Chicago using an Institutional Review Board-approved protocol and data use agreement at each institution. We examined 950 adult patients consecutively diagnosed with non-promyelocytic AML between January 2012 and 2022 who received intensive induction chemotherapy at one of 6 academic institutions; 32 patients were excluded on the grounds of missing data on ICU admission. The objective was to identify predictors of critical illness in the early period following chemotherapy incorporating self-reported race and census tract measures. To account for missing data, multiple imputation was conducted and the multiply imputed datasets analyzed. Using the method of chained equations, we multiply imputed missing values for each of the patients and clinical risk factors (see Table 1). Binary variables were modeled in logistic regression, whereas multinomial logistic regression was used for variables with multiple categories. Allogeneic stem cell transplantation rates and survival were evaluated to determine the long-term clinical impact of critical illness during initial therapy.

A total of 918 newly diagnosed AML patients were included in this analysis *(Online Supplementary Table S1)*. The patient population comprised 65% Non-Hispanic White (NHW), 12% Non-Hispanic Black (NHB), 13% Hispanic, and 10% Other race/ethnicity. Median age was 57 years (interquartile range [IQR] 47, 65). NHB and Hispanic patients were significantly younger than NHW patients (19% NHB *vs*. 26% Hispanic *vs*. 13% NHW were <40 years). Two-thirds of NHW patients were married compared to 38% of NHB and 57% of Hispanic patients. The NHB and Hispanic patients were over-represented in moderate and high disadvantage tracts, and under-represented in high affluence tracts. Compared to NHW patients, NHB patients were more likely to have public insurance (65% *vs*. 44%) and Hispanic patients were the most likely to be uninsured (20% *vs*. 2% of NHW and 3% NHB).

Comorbities were highest in NHB patients: 39% NHB *vs*. 25% NHW *vs*. 24% Hispanic patients had a Charlson Comorbidity Index (CCI) ≥3. European LeukemiaNet (ELN) 2017 classification differed significantly based on race/ethnicity. Hispanic patients were most likely to have a favorable ELN 2017 risk group (24% *vs*. 18% NHB and 21% NHW patients). Hyperleukocytosis was seen in 17% of patients, and 7% presented with extramedullary disease involvement. The majority of patients had fibrinogen level derangement; 25% had low fibrinogen (<100 mg/dL) while 38% had elevated fibrinogen (>380 mg/dL).

Hispanic patients were most likely to have elevated fibrinogen (46% *vs*. 34% NHW and 44% NHB). Hypoalbuminemia, a known predictor of adverse AML outcomes,[6] was more prevalent in NHB patients (24% *vs*. 15% NHW and 12% Hispanic patients). Rates of primary treatment failure were similar between groups (12-18%) although, numerically, Hispanic patients had the lowest.

A total of 161 patients representing 17.5% of the study population required ICU admission following chemotherapy. Treatment details were available for 143 patients; the majority (N=105) received standard 7+3 based regimens while 37 patients received high-dose cytarabine-containing regimens (e.g., FLAG, cytarabine-mitoxantrone). Twenty percent of ICU patients (N=29) received novel therapies (CPX-351, midostaurin, and investigational agents). For 89 patients with available data on indication for ICU admission, 30 (34%) had infectious complications, 25 (28%) respiratory failure, 16 (18%) cardiovascular complications, 13 (15%) patients had bleeding, and 5 patients had altered mental status. In the 72 patients with available data, the median number of days between start of induction and ICU admission was 22 (IQR:10-57).

We examined patient characteristics associated with ICU admission following chemotherapy. In univariate analysis (Table 1), race/ethnicity was a baseline predictor of ICU admission, with the highest rates of ICU admission in

Table 1. Sociodemographic and clinicopathologic factors associated with intensive care unit admission following high-intensity induction therapy for acute myeloid leukemia.

	N	ICU	%	Missing	*P*
Race/Ethnicity					0.004
NHW	597	86	14		
NHB	117	22	19	-	
Hispanic	123	33	27		
Other	81	20	25		
Age at diagnosis, years					
18-39	151	27	18		
40-59	367	61	17	-	-
60-74	376	68	18		
≥75	24	5	21		
Gender					
Male	429	79	18	-	-
Female	489	82	17		
Married				6	
Yes	576	95	16		-
No	336	65	19		
Tract disadvantage				51	0.09
Low	288	48	17		
Moderate	288	41	14		
High	291	64	22		
Tract affluence				51	
Low	294	55	19		-
Moderate	288	53	18		
High	285	45	16		
Health insurance					
Uninsured	46	10	22	-	-
Public	426	75	18		
Private/Commercial	446	76	17		
Body Mass Index				9	0.10
Underweight	39	2	5		
Normal weight	239	42	18		
Overweight	297	54	18		
Obese I	193	32	17		
Obese II	141	29	21		
Charlson Comorbidity Index				87	0.03
0	325	47	14		
1	154	25	16		
2	130	26	20		
≥3	222	47	21		
ELN 2017 classification				17	0.01
Favorable	165	21	13		
Intermediate	402	66	16		
Adverse	334	71	21		
White blood cell count, $x10^9$/L				41	0.05
<50	727	119	16		
≥50	150	35	23		
Hemoglobin, g/dL				47	
Normal, ≥10	221	35	16		-
Low, 0-10	650	119	18		
Platelets, $x10^9$/L				45	
Very low, 0-19	110	19	17		-
Creatinine, mg/dL				81	
Normal, <1	582	94	16		-
High, ≥1	255	51	20		

Continued on following page.

	N	ICU	%	Missing	*P*
Bilirubin, mg/dL				80	
Normal, 0-1.4	795	137	17		-
High, ≥1.5	43	7	16		
Albumin, g/dL				84	0.03
Low, 0-2.99	131	31	24		
Normal, ≥3	703	110	16		
Lactate dehydrogenase, U/L				110	
Normal, 0-199	152	24	16		-
High, ≥200-1,000	574	95	17		
Very high, ≥1,000	82	20	24		
Fibrinogen, g/dL				247	0.0001
Low, <100	168	14	8		
Normal, ≥100-380	248	44	18		
High, >380	255	58	23		
Bone marrow blasts, %				44	
Lower, 0-20	68	15	22		-
Middle, ≥20-50	324	54	17		
Higher, ≥50-100	482	82	17		
ECOG performance status				533	0.1
0	155	12	8		
1	197	25	13		
≥2	33	5	15		
Extramedullary disease				22	
Yes	67	13	19		-
No	829	144	17		

ECOG: Eastern Cooperative Oncology Group; ELN: European Leukemia Net; ICU: intensive care unit; N: number; NHB: Non-Hispanic Black; NHW: Non-Hispanic White. *P* values >0.10 are suppressed.

Hispanic patients at 27% compared to 19% of NHB and 14% of NHW patients (*P*=0.004). CCI was also associated with ICU admission; a CCI score of 0-1 was associated with an ICU admission rate of 14-16% compared to 20-21% for CCI of 2 or higher (*P*=0.03). Patients with high census tract disadvantage were the most likely to be admitted to the ICU compared to those from intermediate or low disadvantage tracts (61% *vs*. 41% and 48%, respectively, *P*=0.09). Disease-specific characteristics also predicted ICU admission. Patients with a high ELN 2017 genomic risk score were more likely to be admitted to the ICU compared to those with a moderate or low ELN score (21% compared to 16% and 13%, respectively, *P*=0.01). Patients with high disease burden as measured by significant white blood cell (WBC) count elevation (> 50K) were more likely to be admitted to the ICU. Additionally, low albumin (< 3 g/dL) and elevated fibrinogen (> 380 mg/dL) levels at diagnosis were also associated with ICU admission. Interestingly, established factors for mortality in AML, including older age, Eastern Cooperative Oncology Group (ECOG) performance status, and elevated creatinine (>1 g/dL) did not predict ICU admission.

As previously published,[7] elevated Body Mass Index was not predictive of adverse chemotherapy outcomes in AML. Marital status and insurance type were not associated with ICU admission.

Separate multivariable models (Table 2) were constructed for each risk factor, controlling for potential confounding variables. We did not control for variables potentially in the causal pathway from the risk factor of interest to ICU admission (see *Online Supplementary Figure S1*). Compared to NHW patients, Hispanic ethnicity (RR=1.87, 95%CI: 1.31, 2.67, *P*=0.001) and Other race (RR=1.70, 95%CI: 1.10, 2.62, *P*=0.02) were predictors of ICU admission after adjusting for age and gender. Patients with adverse molecular / cytogenetic characteristics defined by ELN 2017 score were more likely to require intensive care (RR 1.85, 95%CI: 1.16, 2.96, *P*=0.01) adjusting for race, age, gender, insurance, and social determinants. Examining lab measures at diagnosis, WBC count, serum albumin and fibrinogen were independent predictors of ICU admission adjusting for race/ethnicity, age, gender, social determinants, insurance, comorbidities, and ELN risk score.

Critical illness during intensive chemotherapy negatively impacted the ability to receive further therapies and served as a surrogate for inferior survival (HR for overall survival=1.88, 95%CI: 1.44, 2.44, *P*<0.0001). Patients admitted to the ICU during induction therapy were less likely to undergo curative therapy with allogeneic stem cell transplant (60% *vs*. 40.5%, RR=0.67, 95%CI: 0.55, 0.82). ICU admission during induction therapy was also associated with a 3.9-fold greater risk of death at 90 days (RR=3.95,

Table 2. Multivariable adjusted predictors of intensive care unit admission following high-intensity induction therapy.

	RR	95% CI	*P*
Race/Ethnicity[1]			
NHW	Ref	-	-
NHB	1.29	0.84, 1.98	-
Hispanic	1.87	1.31, 2.67	0.001
Other	1.70	1.10, 2.62	0.02
Age at diagnosis, years[1]			
18-39	Ref	-	-
40-59	1.01	0.67, 1.52	
60-74	1.15	0.77, 1.74	
≥75	1.33	0.55, 3.22	
Gender, male *vs.* female[1]	0.89	0.67, 1.18	-
Married, Yes *vs.* No[2]	0.88	0.64, 1.20	-
Tract disadvantage[2]			
Low	Ref	-	-
Moderate	0.8	0.55, 1.23	
High	1.15	0.71, 1.86	
Tract affluence[2]			
Low	Ref	-	-
Moderate	1.14	0.78, 1.65	
High	1.04	0.66, 1.65	
Health insurance[3]			
Uninsured	Ref	-	-
Public	1.01	0.54, 1.87	
Private/Commercial	1.14	0.63, 2.09	
ELN 2017 Classification[4]			
Favorable	Ref	-	-
Intermediate	1.44	0.90, 2.30	0.13
Adverse	1.85	1.16, 2.96	0.01
Body Mass Index[5]			
Underweight	0.30	-	0.09
Normal weight	Ref	0.08, 1.18	-
Overweight	1.12	0.78, 1.61	-
Obese I	0.95	0.63, 1.45	-
Obese II	1.15	0.75, 1.76	-
Charlson Comorbidity Index[5]			
0	Ref	-	-
1	1.17	0.74, 1.86	-
2	1.39	0.89, 2.17	0.15
≥3	1.47	1.00, 2.16	0.05
ECOG Performance Status[5]			
0	Ref	-	-
1	1.30	0.66, 2.55	
≥2	1.53	0.61, 3.83	
White blood cell count,[6] ≥50x10^9/L	1.65	1.06, 2.58	0.03
Hemoglobin,[6] <10 g/dL	0.96	0.65, 1.43	-
Platelets,[6] <20x10^9/L	0.99	0.62, 1.56	-
Creatinine,[6] >1 mg/dL	1.13	0.78, 1.62	-
Bilirubin,[6] >1.5 mg/dL	0.79	0.39, 1.61	-
Albumin,[6] <3 g/dL	1.50	1.00, 2.25	0.05
Lactate dehydrogenase,[6] U/L			
<200	Ref	-	-
200-1,000	1.01	0.64, 1.60	
≥1,000	1.29	0.72, 2.32	

Continued on following page.

	RR	95% CI	*P*
Fibrinogen,[6] g/dL <100 100-380 >380	 0.50 Ref 2.45	 0.28, 0.90 - 0.83, 1.84	 0.021 - 0.292
D-Dimer,[6] >0.5 g/dL	1.00	0.49, 2.03	
Bone marrow blasts,[6] % 0-20 >20-50 ≥50	 Ref 0.7 0.69	 - 0.42, 1.31 0.37, 1.30	-
Peripheral blasts,[6] % 0-5 ≥5-25 ≥25	 Ref 1.04 0.73	 - 0.49, 2.21 0.31, 1.74	-
Extramedullary disease[6]	0.93	0.53, 1.66	-

[1]Adjusted for race/ethnicity, age, and gender. [2]Adjusted for race/ethnicity, age, and gender plus tract disadvantage, tract affluence, and marital status. [3]Adjusted for race/ethnicity, age, gender, tract disadvantage, tract affluence, and marital status plus health insurance. [4]Adjusted for race/ethnicity, age, gender, tract disadvantage, tract affluence, marital status, and health insurance plus ELN 2017. [5]Adjusted for race/ethnicity, age, gender, tract disadvantage, tract affluence, marital status, health insurance, and ELN 2017 plus Body Mass Index, Eastern Cooperative Oncology Group (ECOG) performance status, and Charlson Comorbidity Index. [6]Adjusted for all variables shown in the table. CI: Confidence Interval; ELN: European Leukemia Net; ICU: intensive care unit; NHB: Non-Hispanic Black; NHW: Non-Hispanic White; Ref: reference values; RR: relative risk.

95%CI: 2.39, 6.52) and a 54% greater risk of death at one year (RR=1.54, 95%CI: 1.25, 1.90) (Figure 1).

In this well-annotated contemporary cohort of AML patients treated with intensive chemotherapy, over 15% of patients developed critical complications requiring admission to the ICU, similar to previous studies reporting rates of 15-28%.[8,9] In addition to short-term morbidity and 90-day mortality, these ICU patients demonstrated compromised long-term outcomes.

We integrated validated clinical and molecular predictors of outcome in newly diagnosed AML[10] with SDOH and showed for the first time that self-reported race/ethnicity and neighborhood disadvantage are associated with increased incidence of critical illness following intensive chemotherapy. ECOG performance status was not a significant predictor in itself, although this variable was limited by a significant amount (>25%) of missing data which may have underestimated its influence. In multivariable analysis, adjusting for age and gender, Hispanic ethnicity was independently predictive of ICU admission despite younger patient age and more favorable-risk disease. Previous studies have reported inferior AML survival in Hispanic patients,[11] and our results suggest this may be linked to differences in treatment tolerability.

Differences in cumulative front-line organ toxicity may lead to differential treatment at relapse and drive subsequent racial disparities in survival in AML.[12] Our data in adult AML confirm that ICU admission has downstream consequences including a lower likelihood of curative allogeneic stem cell transplant and reduced 90-day and 2-year survival.

Targeted low intensity therapies in AML provide highly effective alternatives to intensive chemotherapy but the latter remains the preferred curative approach for patients under 60 years of age. Recent data demonstrate that within favorable molecular subsets of AML, the survival benefit of chemotherapy is modulated by race.[13] The current findings suggest that the integration of race/ethnicity and allostatic load measures,[14] including albumin and fibrinogen, as prognostic biomarkers into current AML treatment mor-

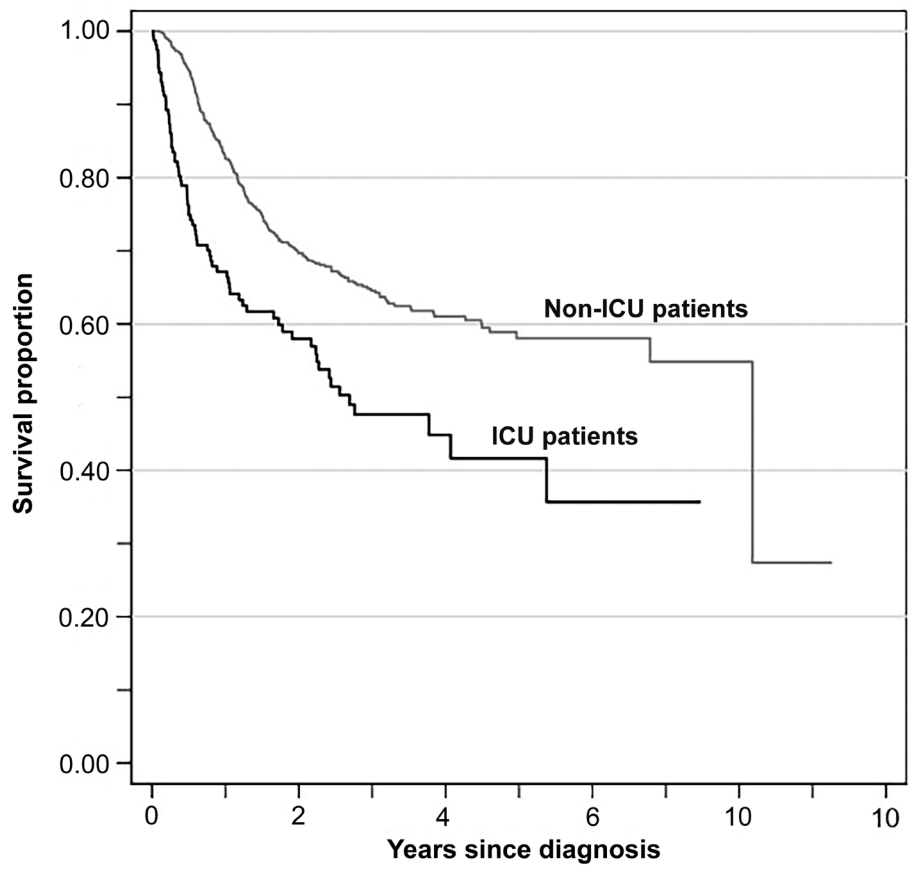

Figure 1. Kaplan-Meier estimates of survival in non-intensive care unit patients and intensive care unit patients with acute myeloid leukemia. HR 1.88 (95%CI: 1.44-2.44, *P*<0.0001)

tality calculators merits further study. Improved selection criteria for intensive therapy incorporating measures and biomarkers of SDOH may reduce early treatment complications and mitigate survival disparities in AML.

Authors

Ivy E. Abraham,[1*] Garth H. Rauscher,[2,3*] Jerry Luo,[4] Sarah Monick,[5] Madelyn Burkart,[6] Peter Doukas,[6] Ahmed Aleem,[7] Nepheli Raptis,[7] Ami Dave,[8] Andrew Wilmington,[8] Mark Debettencourt,[7] Michelle Nwachukwu,[4] Juwairiyyah Fatima,[4] Amani Erra,[9] Gauri Shankar,[7] Stephanie B. Tsai,[7] Melissa Larson,[8] Maryam Zia,[9] John Quigley,[3,4] Jessica K. Altman,[6] Wendy Stock,[5] Anand Patel[5] and Irum Khan[6]

[1]University of Chicago Medicine Ingalls Memorial Hospital, Harvey; [2]University of Illinois at Chicago Division of Epidemiology and Biostatistics, Chicago; [3]University of Illinois Cancer Center, Chicago; [4]University of Illinois at Chicago Department of Medicine, Chicago; [5]University of Chicago, Department of Medicine, Section of Hematology and Oncology, Chicago; [6]Northwestern University Robert H. Lurie Comprehensive Cancer Center, Chicago; [7]Loyola University Medical Center Division of Hematology and Oncology, Maywood; [8]Rush University Medical Center Division of Hematology and Oncology, Chicago and [9]John H. Stroger, Jr. Hospital of Cook County Division of Hematology and Oncology, Chicago, IL, USA

IEA and GHR contributed equally as first authors.

Correspondence:
I. KHAN - irum.khan@northwestern.edu

https://doi.org/10.3324/haematol.2025.288876

Received: August 31, 2025.
Accepted: December 31, 2025.
Early view: January 15, 2026.

Disclosures
No conflicts of interest to disclose.

Contributions
IA, GHR and IK designed the research, analyzed the data, and wrote the paper; IA, GHR, IK, JL, SM, MB, PD, AA, NR, AD, AW, MD, MN, MN, JF, AE, GS, ST, ML, MZ, JQ, JA, WS and AP collected the data and helped edit the paper.

Funding
This work was funded by a grant through the ChicagoCHEC Partnership: U54CA202995, U54CA202997, and U54CA203000 (to GHR and IK).

Data-sharing statement
The data that supports the findings of this study are available from the corresponding author upon reasonable request.

References

1. Larkin KT, Nicolet D, Kelly BJ, et al. High early death rates, treatment resistance, and short survival of Black adolescents and young adults with AML. Blood Adv. 2022;6(19):5570-5581.
2. Halpern AB, Culakova E, Walter RB, Lyman GH. Association of risk factors, mortality, and care costs of adults with acute myeloid leukemia with admission to the intensive care unit. JAMA Oncol. 2017;3(3):374-381.
3. Alam ST, Dongarwar D, Lopez E, et al. Disparities in mortality among acute myeloid leukemia-related hospitalizations. Cancer Med. 2023;12(3):3387-3394.
4. Abraham IE, Rauscher GH, Patel AA, et al. Structural racism is a mediator of disparities in acute myeloid leukemia outcomes. Blood. 2022;139(14):2212-2226.
5. Wuliji N, Jones SMW, Gooley T, et al. Social determinants of health and access to allogeneic hematopoietic cell transplantation for acute myeloid leukemia. Blood. 2025;145(25):3041-3051.
6. Doucette K, Percival ME, Williams L, et al. Hypoalbuminemia as a prognostic biomarker for higher mortality and treatment complications in acute myeloid leukemia. Hematol Oncol. 2021;39(5):697-706.
7. Foran JM, Sun Z, Lai C, et al. Obesity in adult acute myeloid leukemia is not associated with inferior response or survival even when dose capping anthracyclines: an ECOG-ACRIN analysis. Cancer. 2023;129(16):2479-2490.
8. Schellongowski P, Staudinger T, Kundi M, et al. Prognostic factors for intensive care unit admission, intensive care outcome, and post-intensive care survival in patients with de novo acute myeloid leukemia: a single center experience. Haematologica. 2011;96(2):231-237.
9. Zeidan AM, Podoltsev NA, Wang X, et al. Patterns of care and clinical outcomes with cytarabine-anthracycline induction chemotherapy for AML patients in the United States. Blood Adv. 2020;4(8):1615-1623.
10. Sorror ML, Storer BE, Fathi AT, et al. Development and validation of a novel acute myeloid leukemia-composite model to estimate risks of mortality. JAMA Oncology. 2017;3(12):1675-1682.
11. Darbinyan K, Shastri A, Budhathoki A, et al. Hispanic ethnicity is associated with younger age at presentation but worse survival in acute myeloid leukemia. Blood Adv. 2017;1(24):2120-2123.
12. Zheng DJ, Li Y, Huang Y-SV, et al. Racial and ethnic differences in acuity and cumulative frontline organ toxicity at the time of relapse in pediatric acute myeloid leukemia. Blood. 2023;142(Suppl 1):387.
13. Stiff A, Fornerod M, Kain BN, et al. Multiomic profiling identifies predictors of survival in African American patients with acute myeloid leukemia. Nature Genetics. 2024;56(11):2434-2446.
14. Xing CY, Doose M, Qin B, et al. Prediagnostic allostatic load as a predictor of poorly differentiated and larger sized breast cancers among Black women in the Women's Circle of Health Follow-Up Study. Cancer Epidemiol Biomarkers Prev. 2020;29(1):216-224.