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The changing landscape of geriatric care in acute myeloid leukemia: a 5-year analysis of inpatient mortality predictors, trends in mortality, and chemotherapy use

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ABSTRACT

Background: This study examined inpatient mortality factors in geriatric patients with acute myeloid leukemia (AML) using data from the 2016 to 2020 National Inpatient Sample.

Methods: Identifying patients through ICD-10 codes, a total of 127,985 individuals with AML were classified into age categories as follows: 50.58% were 65 to 74 years, 37.74% were 75 to 84 years, and 11.68% were 85 years or older. Statistical analysis, conducted with STATA, involved Fisher's exact and Student's *t* tests for variable comparisons. Mortality predictors were identified through multivariate logistic regression.

Results: Various hospital and patient-level factors, including an increase in age, race, a higher Charlson Comorbidity Index score, insurance status, and specific comorbidities such as atrial fibrillation and protein-calorie malnutrition, independently elevated the risk of inpatient mortality. Asthma, hyperlipidemia, and inpatient chemotherapy were linked to lower mortality. Although there was no statistically significant mortality rate change from 2016 to 2020, a decline in chemotherapy use in the eldest age group was noted.

Conclusion: This study highlights the complexity of factors influencing inpatient mortality among geriatric patients with AML, emphasizing the need for personalized clinical approaches in this vulnerable population.

KEYWORDS Acute myeloid leukemia; comorbidities; geriatrics; inpatient chemotherapy; inpatient mortality; National Inpatient Sample

Acute myeloid leukemia (AML) is a diverse form of blood cancer resulting from genetic and epigenetic alterations in hematopoietic stem and/or progenitor cells, leading to abnormal growth and differentiation. AML is largely a disease of older adults, characterized by disproportionately worse survival associated with increasing age.[1,2] As a result, only 2% of elderly patients are expected to live for 5 years after diagnosis.[3]

Geriatric patients with AML represent a unique and challenging population due to age-related physiological changes, increased vulnerability to treatment-related toxicities, and the presence of multiple comorbidities. Poor survival outcomes in older AML patients can be attributed to the higher prevalence of adverse prognostic factors and comorbidities, as well as a tendency among physicians to opt for less aggressive treatments, anticipating reduced benefits from intensive therapies in this population.[4] Patients with AML may be hospitalized due to diagnosis and initial assessment, induction chemotherapy, treatment-related complications, infections, hematopoietic stem cell transplant, and supportive care.

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Previous studies have demonstrated that the presence of comorbidities is associated with higher mortality rates and resource utilization; however, there is limited data about the impact of comorbidities on all-cause inpatient mortality for AML patients.

The National Inpatient Sample (NIS) database is a valuable resource for investigating population-based health outcomes and disparities.[5] It provides a large sample size and a diverse patient population, allowing for robust analyses of various factors affecting inpatient outcomes. In this retrospective analysis utilizing NIS data from 2016 to 2020, we aimed to explore the impact of multiple patient and hospital-level characteristics, including various comorbidities, on all-cause inpatient mortality rates among hospitalized geriatric patients with AML, while concurrently investigating the 5-year trajectories of inpatient mortality and chemotherapy usage in this group. By identifying the most significant comorbidities and trends, we aim to better inform clinical decision-making, optimize treatment strategies, and ultimately improve patient outcomes.

METHODS

Study design and database description

This retrospective investigation focused on the hospitalization of geriatric patients associated with AML utilizing data from the NIS[6] between 2016 and 2020. Covering 98% of the US population, the NIS is part of the Healthcare Cost and Utilization Project (HCUP), which is sponsored by the Agency for Healthcare Research and Quality.[7] The NIS is the most all-encompassing, deidentified, and publicly accessible inpatient database in the United States. It is designed as a stratified 20% sample of all hospital stays across the country, with each discharge being weighted to achieve a representative national sample.

In this study, patient demographics included factors such as age, sex, ethnicity, median household earnings, and insurance coverage. To address comorbidities, we employed the Charlson Comorbidity Index[8] and took into account various clinically significant comorbid conditions by using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes.

Hospitals were grouped based on characteristics like bed capacity, geographical area, teaching status, and urban or rural location. Moreover, hospital admissions were designated as elective or nonelective, and the day of admission was distinguished as a weekday or weekend occurrence.

The adjusted charges for each year were computed in 2020-equivalent dollars by utilizing consumer price index data to account for inflation.[9]

Study patients

The study included patients hospitalized with AML, as identified by ICD-10-CM codes, which have been in use in the US since October 2015. Patients <65 years of age were excluded from the study. The study population was then divided into three age-based groups, with a comparison of their characteristics outlined in *Table 1*. The specific ICD-10-CM codes employed are available in *Supplementary Table 1*. Although institutional review board approval was sought for this research, it was deemed exempt due to its retrospective nature and the use of previously collected data.

Statistical analysis

We conducted our analyses utilizing STATA MP 14.2 (StataCorp, College Station, TX, USA). NIS data is the product of a multifaceted sampling design that combines stratification, clustering, and weighting. We applied weights to patient-level observations to create estimates for the total population of hospitalizations related to AML patients. To compare proportions, we applied the Fisher exact test, and for continuous variables, we used the Student t test.[10] Multivariate logistic regression analysis was executed to identify potential independent factors predicting all-cause inpatient mortality, incorporating hospital and patient characteristics deemed clinically significant to the outcome from the literature. For trends analysis, we employed a multivariate regression model adjusted for gender and race. All P values were calculated using a two-sided test, and a value <0.05 was considered statistically significant.

RESULTS

Spanning the years from 2016 to 2020, the NIS database registered 174,776,205 weighted discharges. The flowchart in *Figure 1* depicts the process of selecting study participants according to the inclusion criteria. Among these 238,745 patients were classified as having AML not in remission or experiencing a relapse. Upon narrowing this subset by age, we found 127,985 patients who were 65 years or older, aligning with the demographic requirements for our study.

Within this group of elderly patients, the mean length of hospital stay was 9.99 days, resulting in a total of 1,278,725 days of hospitalization of the study population over the period of 5 years. The mean charge amounted to $127,317, while the mean cost was $31,030. This led to a total charge of approximately $16.2 billion and a cost of $3.94 billion over the given period. Moreover, 12.29% (n = 15,720) of these hospitalized individuals did not survive their inpatient stay.

Patient and hospital characteristics

Table 1 provides data on the geriatric patients diagnosed with AML by three age segments (65–74, 75–84, and ≥85), with the groups containing 64,730, 48,300, and 14,955 patients, respectively. A comparative analysis revealed significant statistical disparities among these groups concerning various parameters, including gender, mean age, racial background, Charlson Comorbidity Index, insurance coverage type, average household income, geographic region of the hospital, hospital bed size, the teaching status of the hospital,

Table 1. Patient and hospital characteristics

Variable	Age (years)			*P* value
	65–74	75–84	≥85	
N (%)	64,730 (50.58%)	48,300 (37.74%)	14,955 (11.86%)	
Female, (%)	41.15	39.98	46.53	<0.001
Age, years (mean)	69.60	78.91	87.67	<0.001
Race (%)				<0.001
White	76.99	79.77	80.46	
Black	9.56	7.29	7.88	
Hispanics	6.08	5.78	6.14	
Native Americans/ Pacific Islanders/ Other	7.36	7.16	5.52	
Charlson Comorbidity Index (%)				<0.001
≤2	35.08	30.17	24.74	
3	26.38	24.40	22.03	
4	16.74	18.00	19.73	
≥5	21.81	27.43	33.50	
Insurance status (%)				<0.001
Medicare	83.73	92.47	94.42	
Medicaid	1.61	0.85	0.75	
Private	14.01	6.26	4.56	
Uninsured	0.66	0.41	0.27	
Median household income (quartile) (%)				<0.001
1st (0–25th)	22.67	21.43	19.78	
2nd (25–50th)	25.71	23.90	24.10	
3rd (50–75th)	25.97	26.00	26.70	
4th (75–100th)	25.65	28.67	29.43	
Hospital region (%)				0.006
Northeast	19.69	21.65	23.30	
Midwest	22.23	22.61	23.07	
South	37.55	37.04	33.97	
West	20.53	18.71	19.66	
Hospital bed-size (%)				<0.001
Small	12.45	15.83	18.72	
Medium	20.81	25.09	27.52	
Large	66.74	59.08	53.76	
Teaching status				<0.001
Nonteaching	15.05	22.86	26.71	
Teaching	84.95	77.14	73.29	
Hospital location				<0.001
Rural	3.69	5.35	6.15	
Urban	96.31	94.65	93.85	

(*Continued on next page*)

Table 1. Continued

Variable	Age (years) 65–74	75–84	≥85	*P* value
Admission day (%)				<0.001
Weekday	81.45	78.73	76.73	
Weekend	18.55	21.27	23.27	
Elective versus nonelective (%)				<0.001
Nonelective	80.45	89.18	93.33	
Elective	19.55	10.82	6. 67	
Comorbidities (%)				
COPD	14.52	15.45	13.04	0.007
Asthma	4.58	4.40	3.44	0.036
CKD5/ESRD	6.38	8.24	9.50	<0.001
Liver cirrhosis	1.68	1.25	0.53	<0.001
CHF	14.78	19.76	26.88	<0.001
Atrial fibrillation	16.42	23.60	28.52	<0.001
Hypertension	43.45	39.29	36.91	<0.001
Hyperlipidemia	32.96	37.61	39.79	<0.001
H/O CVA with neurological deficits	1.39	1.17	1.71	0.080
Neutropenia	19.92	16.42	11.57	<0.001
Coagulopathy	0.74	0.90	1.04	0.199
HIV	0.13	0.06	0	0.112
HCV	1.12	0.27	0.33	<0.001
Marijuana	0.39	0.09	0.07	<0.001
Opioid abuse	0.59	0.27	0.13	0.001
Alcohol abuse	1.62	0.90	0.40	<0.001
Protein-calorie malnutrition	13.80	13.19	10.0	<0.001
Obesity	11.11	6.90	3.78	<0.001
Inpatient chemotherapy use	23.71	12.81	5.42	<0.001

CHF indicates congestive heart failure; CKD5, chronic kidney disease stage 5; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; H/O CVA, history of cerebrovascular accident; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

hospital location, day of admission, and the nature of admission (elective or nonelective).

The demographic group aged 65 to 74 years, which we term the "youngest old," had the highest frequency of hospital admissions. The average age within this segment was 69.60 years, with women representing 41.15% of cases. In contrast, those aged 85 or older, referred to as the "oldest old," registered the fewest hospital stays. The mean age in this group was 87.67 years, and females comprised 46.53% of the cases.

Across all age categories, the White population represented the majority. However, their representation was most pronounced in the oldest age group, accounting for 80.46% of the total. With advancing age, there was a shift toward higher Charlson Comorbidity Index scores and increased use of Medicare.

When considering hospital-related characteristics, hospitals in the Northeast and Midwest regions had the greatest proportion of patients in the oldest age group, at 23.3% and 23.07%, respectively. This trend was observed in small hospitals (18.72%), medium hospitals (27.52%), and hospitals located in rural areas (6.15%). Admissions during weekends and under nonelective circumstances were more prevalent among this elderly group.

In the realm of concurrent diseases, the "oldest old" group frequently exhibited chronic kidney disease stage 5/end-stage renal disease (9.5%), congestive heart failure (26.8%), atrial fibrillation (28.52%), and hyperlipidemia

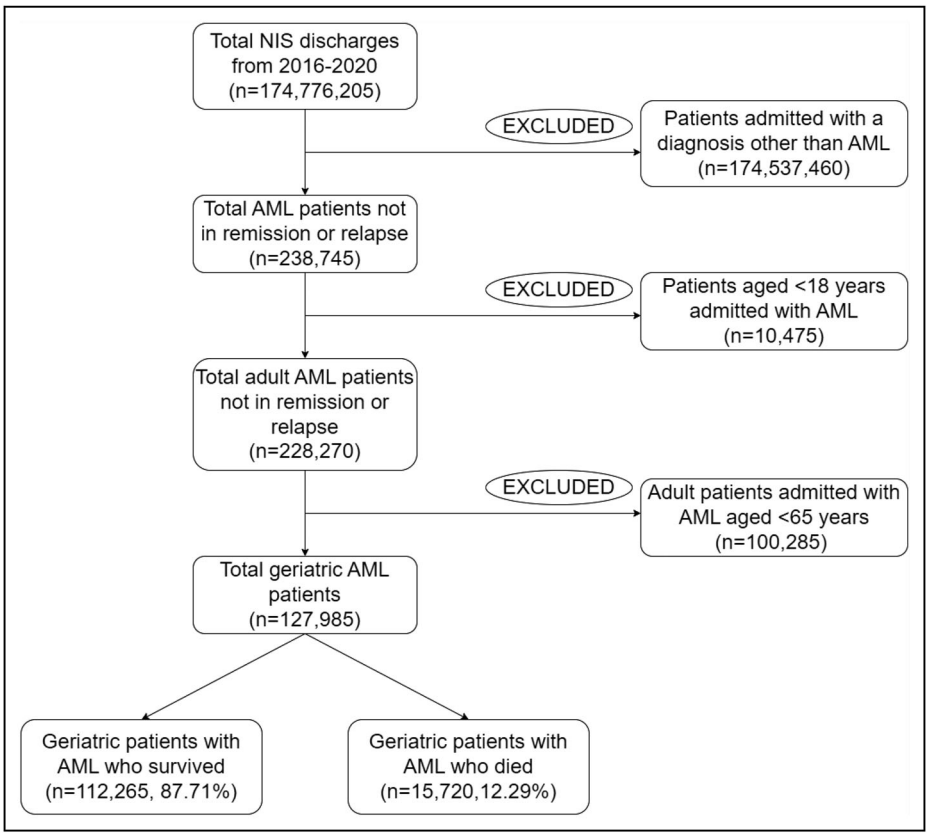

Figure 1. Patient selection flow diagram. AML indicates acute myeloid leukemia; NIS, National Inpatient Sample.

(39.79%). Meanwhile, the "youngest old" group tended to have higher rates of asthma (4.58%), liver cirrhosis (1.68%), hypertension (43.45%), neutropenia (19.92%), HIV (0.13%), marijuana use (0.39%), opioid abuse (0.59%), alcohol abuse (1.62%), obesity (1.11%), and protein-calorie malnutrition (13.8%). Furthermore, this group was the major recipient of inpatient chemotherapy as well.

Predictors of all-cause inpatient mortality

Table 2 summarizes the predictors of all-cause inpatient mortality for geriatric patients with AML. The likelihood of mortality increased with age, with those >85 (odds ratio of 1.27) being significantly more likely to die in the hospital than those aged 65 to 74 ($P < 0.001$).

In terms of race, Native Americans/Pacific Islanders/other races had a significantly higher chance of mortality compared to Whites (adjusted odds ratio [aOR] 1.24, $P = 0.004$). However, there was no significant difference between Whites, Blacks, and Hispanics. Patients with higher Charlson Comorbidity Index scores (a measure of the number and seriousness of comorbid conditions) have a greater mortality risk. Those with scores ≥5 were significantly more likely to die in the hospital (aOR 1.82, $P < 0.001$) than those with scores of ≤2.

Patients with private insurance (aOR 1.52) or those uninsured (aOR 2.19) had a significantly higher adjusted odds of inpatient mortality compared to those with Medicare. The mortality risk decreased with higher household income quartiles, with the fourth quartile having a significantly lower risk than the first quartile (aOR 0.87, $P = 0.03$). Regarding hospital characteristics, patients in large hospitals, admitted over the weekend, or admitted electively had higher odds of mortality. Meanwhile, patients in hospitals in the Midwest, South, or West regions had lower mortality odds than those in the Northeast.

The presence of specific comorbidities, including atrial fibrillation and protein-calorie malnutrition, considerably raised the risk of inpatient mortality, as indicated by their respective aOR of 1.41 ($P < 0.001$) and 1.31 ($P < 0.001$). Conversely, asthma (aOR 0.67, $P < 0.001$) and hyperlipidemia (aOR 0.75, $P < 0.001$) significantly decreased the odds of inpatient mortality by 33% and 75%, respectively. Additionally, inpatient chemotherapy reduced the mortality risk (odds ratio 0.85, $P = 0.009$).

However, after adjusting for other variables, in our multivariate logistic regression model, the impact of other factors lacked statistical significance.

Five-year trends in all-cause hospital mortality and inpatient chemotherapy use in geriatric patients with AML

Figure 2 depicts the 5-year trend for all-cause inpatient mortality in elderly patients with AML, with adjustments for race and gender. While there was a noticeably higher adjusted mortality rate among the oldest compared to the less old group, the 5-year trend did not provide any

Table 2. Predictors of all-cause inpatient mortality for geriatric patients with AML

	Adjusted odds ratio for mortality	Confidence interval	*P* value
Female	0.95	0.88–1.03	0.236
Age (years)			
65–74	Reference		
75–84	1.11	1.02–1.22	0.021
≥85	1.27	1.12–1.44	<0.001
Race			
White	Reference		
Black	1.00	0.86–1.16	0.977
Hispanics	0.96	0.81–1.14	0.669
Native Americans/ Pacific Islanders/ Other	1.24	1.07–1.43	0.004
Charlson Comorbidity Index			
≤2	Reference		
3	1.35	1.20–1.52	<0.001
4	1.50	1.31–1.70	<0.001
≥5	1.82	1.59–2.09	<0.001
Insurance status			
Medicare	Reference		
Medicaid	0.98	0.68–1.41	0.911
Private	1.52	1.34–1.73	<0.001
Uninsured	2.19	1.36–3.55	0.001
Median household income (quartile)			
1st (0–25th)	Reference		
2nd (25–50th)	0.76	0.84–1.06	0.340
3rd (50–75th)	0.77	0.76–0.97	0.013
4th (75–100th)	0.87	0.78–0.99	0.032
Hospital region			
Northeast	Reference		
Midwest	0.76	0.67–0.86	<0.001
South	0.77	0.69–0.86	<0.001
West	0.87	0.77–0.98	0.027
Hospital bed-size			
Small	Reference		
Medium	1.14	0.99–1.30	0.058
Large	1.19	1.06–1.35	0.003
Hospital teaching status			
Nonteaching	Reference		
Teaching	1.03	0.92–1.16	0.607
Hospital location			
Rural	Reference		

(*Continued on next page*)

Table 2. Continued

	Adjusted odds ratio for mortality	Confidence interval	*P* value
Urban	1.16	0.92–1.46	0.204
Admission day			
Weekday	Reference		
Weekend	1.15	1.04–1.27	0.003
Elective versus nonelective			
Nonelective	Reference		
Elective	0.69	0.60–0.80	<0.001
Comorbidities			
COPD	0.97	0.87–1.09	0.619
Asthma	0.67	0.54–0.83	<0.001
CKD5/ESRD	1.14	0.98–1.32	0.079
Liver cirrhosis	1.07	0.78–1.48	0.673
CHF	1.10	0.99–1.22	0.091
Atrial fibrillation	1.41	1.28–1.56	<0.001
Hypertension	0.94	0.85–1.03	0.180
Hyperlipidemia	0. 75	0.68–0.82	<0.001
H/o CVA with neurological deficits	1.17	0.86–1.60	0.327
Neutropenia	1.04	0.94–1.16	0.440
Coagulopathy	1.41	0.95–2.08	0.084
HIV	1.95	0.65–5.89	0.234
HCV	0.95	0.58–1.58	0.855
Marijuana	1.20	0.57–2.52	0.624
Opioid abuse	0.81	0.41–1.59	0.537
Alcohol abuse	0.95	0.65–1.37	0.770
Protein-calorie malnutrition	1.31	1.17–1.46	<0.001
Obesity	0.92	0.80–1.07	0.281
Inpatient chemotherapy	0.85	0.75–0.96	0.009

*Native Americans/Pacific islanders/other races.
CHF indicates congestive heart failure; CVA, cerebrovascular accident; CKD5, chronic kidney disease stage 5; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

statistically significant variations in the mortality rates across all age brackets.

When considering inpatient chemotherapy use, there was a discernible decrease over 5 years in the youngest and middle-aged groups after adjustment for race and gender. The rate of inpatient chemotherapy use fell from 27.77% in 2016 to 19.83% in 2020 ($P < 0.001$), and from 13.59% to 10.83% ($P = 0.005$) in the same periods, respectively. Conversely, the oldest group, despite having a significantly lower adjusted inpatient chemotherapy rate than the other two groups, showed no statistically substantial change from 2016 to 2020. These trends are shown in *Figure 3*.

DISCUSSION

Our retrospective analysis using NIS data offers valuable insights into the key determinants of inpatient mortality among geriatric AML patients. This demographic is marked by extended hospital stays and significant related costs. In our 5-year analysis from 2016 to 2020, we found a sobering mortality rate of 12.29% during hospitalization. Several crucial variables emerged as significant influences on inpatient mortality, encompassing age, race, Charlson Comorbidity Index score, insurance coverage, median household income, hospital region, hospital bed size, and the day of admission. Among these, comorbidities like asthma, hyperlipidemia,

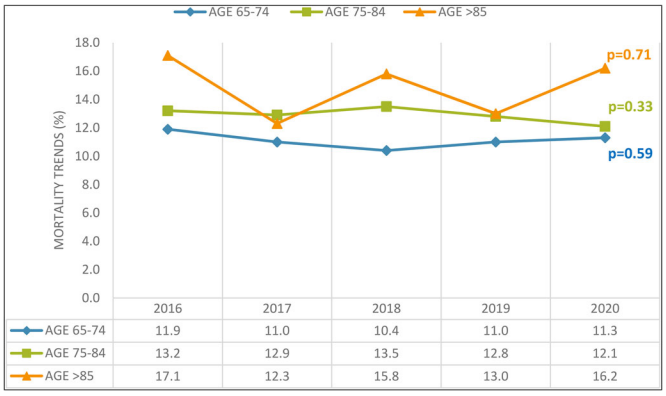

Figure 2. Trends in inpatient mortality for geriatric patients with acute myeloid leukemia.

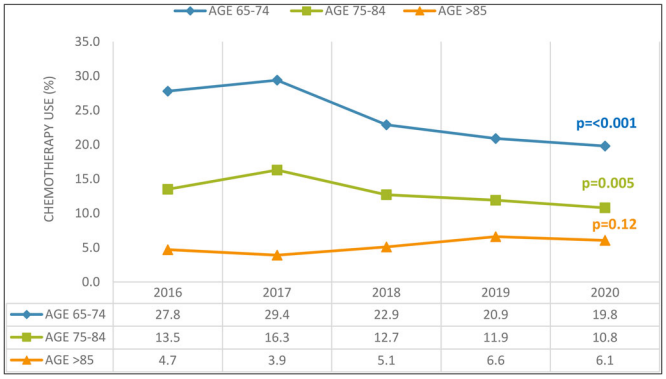

Figure 3. Trends in inpatient chemotherapy use for geriatric patients with acute myeloid leukemia.

atrial fibrillation, protein-calorie malnutrition, and the application of chemotherapy were found to substantially affect inpatient mortality rates.

Previous retrospective research using NIS data revealed an AML-related hospitalization mortality rate of 10.5% in 2018 for patients 60 years and older.[11] However, our analysis, spanning 5 years, demonstrated a marginally higher mortality rate of 12.29%. This discrepancy might be explained by the fact that our study focused on a population aged 65 and above, hence older than the one in the prior study, leading to a higher mortality rate within our specific population. With advancing age and a higher Charlson Comorbidity Index, the risk of inpatient mortality rises in geriatric AML patients due to the cumulative effect of multiple chronic conditions and reduced physiological reserve, which can limit the tolerance to aggressive treatments and increase vulnerability to complications.[12,13] Additionally, an elevated mortality rate among races other than the Black and Hispanic populations, in comparison to Whites, has been noted in earlier studies.[11]

The elevated odds of inpatient mortality seen in uninsured individuals and those with private insurance might be correlated to difficulties in accessing healthcare, disruptions in sustained care, and financial constraints stemming from the expensive nature of cancer treatments. This trend is paralleled in patients residing in low-income areas, possibly linked to the rising expenses of AML treatment, as indicated in past research.[14,15] The increase in inpatient mortality rates in urban and larger hospitals, as displayed in *Table 2*, may be due to their frequent treatment of more complex and advanced-stage cases.

Regarding comorbidities, atrial fibrillation independently elevated inpatient mortality. This comorbidity, potentially linked to chemotherapy,[16] hasn't been thoroughly studied in AML. Additionally, anticoagulation can be complicated by AML and increased fragility with age.[17] Protein-calorie malnutrition in AML patients can weaken the immune system, increase susceptibility to infections, and reduce tolerance to treatment, consequently leading to higher inpatient mortality rates.[18]

Interestingly, our study demonstrated that asthma and hyperlipidemia correlated with a reduced mortality risk in patients with AML. This supports the theory of immune surveillance for asthma.[19,20] As for hyperlipidemia, the reduced mortality odds might be due to the use of HMG-CoA reductase inhibitors, or statins. These drugs may boost the anticancer activity of numerous cytokines and chemotherapy agents, as indicated by multiple clinical trials. However, additional trials are needed to confirm their cancer-preventing and treating efficiency[21] and link to a reduction in inpatient death rates, an outcome attributable either to its capacity to control the disease or the reality that patients with more severe disease or multiple health issues aren't suitable candidates for this treatment.

Conditions like congestive heart failure, chronic kidney disease stage 5/end-stage renal disease, liver cirrhosis, residual effects from strokes, neutropenia, coagulopathy, HIV, and marijuana abuse may increase all-cause in-hospital death risk in AML patients, but they were not standalone mortality predictors in our analysis. Their statistical significance diminished when assessed in combination with other patient characteristics, hospital factors, and comorbidities, as listed in *Table 1*.

The 5-year trend analysis indicated a decrease in inpatient chemotherapy usage, likely resulting from advancements in outpatient care and chemotherapy follow-up procedures. Moreover, lower rates of inpatient chemotherapy are seen in older patients, suggesting a collective decision by physicians and patients to focus on maintaining a good quality of life rather than pursuing intensive treatments due to the heightened risk of comorbidities and decreased chemotherapy tolerance in this demographic.

There are various limitations to our study. The lack of laboratory values, patient history, physical examination records, and imaging outcomes in the HCUP database prevented us from measuring disease severity accurately. However, to address the comorbidity burden, we employed the Charlson Comorbidity Index, a well-accepted and validated prognostic instrument. Additionally, the absence of AML staging information or cytogenetic abnormalities in the HCUP database hindered us from stratifying our data according to the stage of AML. To identify AML patients,

we relied on ICD-10 codes rather than clinical parameters, which may introduce diagnostic misclassification. However, the application of ICD-10 codes to distinguish patients with AML has been validated in prior studies utilizing HCUP data.[11]

In our analysis, mortality was described as all-cause inpatient mortality among geriatric patients with AML who were hospitalized, since the database did not allow us to identify the specific cause of death. Moreover, the observational framework of our study also restricted our capacity to infer a cause-effect relationship between the studied variables and outcomes. Subsequent randomized controlled trials are crucial to address the limitations of our study and to reinforce the robustness of the evidence.

Irrespective of the above limitations, our study has several strengths. We employed the NIS, consisting of deidentified patient information reflecting varied hospital-level characteristics from over 48 states. As a result, our conclusions have a high degree of external validity and generalizability, accurately reflecting the nationwide hospital-admitted patient population. Also, the NIS, as the largest all-payer and publicly available database, circumvents the typical restrictions found in single-center studies due to its extensive scale. The nationwide scope of our data set permitted the utilization of unique hospital and patient variables such as household income and hospital region, among others. These elements would be unattainable in studies centered on a single location. Moreover, this approach helps mitigate biases associated with specific practices observed in studies conducted within single or multiple centers.

CONCLUSION

Our retrospective study provides valuable insights into the inpatient mortality of geriatric patients with AML influenced by various factors such as age, comorbidities, and insurance type. No significant variation was found in the 5-year mortality trends across different age groups. However, a notable decline in inpatient chemotherapy use was observed, except in the "oldest old" group. These findings hold the potential to inform clinical practice, guiding the refinement of treatment strategies, risk stratification, and patient counseling, ultimately enhancing the care of geriatric patients with AML.

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