Chapter 2

Real-World Treatment Patterns and Outcomes among Elderly Acute Myeloid Leukemia Patients in the United States

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Additional information is available at the end of the chapter

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Abstract

Over half of patients diagnosed with acute myeloid leukemia (AML) are 65 years or older. Using the linked SEER-Medicare database, we conducted a retrospective cohort analysis to examine patient characteristics, treatment patterns, and survival among the elderly AML patients in routine clinical practice. Out of 29,857 patients with AML in the database, 8336 were eligible for inclusion in the study. The inclusion criteria included a diagnosis with first primary AML between January 1, 2000 and December 31, 2009, >66 years of age, and continuous enrollment in Medicare Parts A and B in the year before diagnosis. Forty percent (N = 3327) of the cohort received chemotherapy within 3 months after diagnosis. The multivariable overall survival analyses showed a lower risk of death among those receiving intensive and hypomethylating agent therapies compared with no therapy. Among the younger cohort, a significant lower mortality was also noted with receipt of allogeneic hematopoietic stem cell transplantation. Over the past decade, about 60% of the elderly AML patients remain untreated in routine clinical practice. Use of antileukemic therapy was associated with a significant survival benefit and provides further support that age alone should not deter the use of guideline-recommended therapies particularly because of the high disparities in outcomes between treatment receipt and palliative care in this elderly cohort.

Keywords: acute myeloid leukemia, immunotherapy, chemotherapy, elderly patients, survival

1. Introduction

The American Cancer Society estimates that about 20,830 new cases of acute myeloid leukemia (AML) will be diagnosed in the United States in 2015 and 10,460 people will die of the disease [1]. Incidence of AML increases with age, with a median age at diagnosis of 66 years making it primarily a disease of the elderly [2]. Survival rates decline with age and AML is the leading cause of mortality from leukemia in the United States [3, 4].

The management of older adults with AML poses a difficult clinical challenge as they are more likely to have comorbidities and poorer performance status which can limit treatment options and tolerability. Treatment efficacy and tolerability have been shown to deteriorate markedly with age [5]. Although intensive combination chemotherapy is frequently chosen to achieve complete remission and long-term survival, fewer than half of elderly patients receive treatment and their outcomes remain dismal [5–7]. Conventional chemotherapy treatments are highly toxic and may increase early death rates in patients 65 and older and these patients are alternatively given low intensity treatment or palliation only [7, 8]. However, without treatment, patients succumb to their illness within weeks to months of diagnosis [9].

For medically fit older patients (>60 years), the National Comprehensive Cancer Network (NCCN) recommend treatment with a combination of an anthracycline and standard dose cytarabine while for medically unfit older adults with poor physical function or unfavorable risk disease, the NCCN recommends less intensive chemotherapy with DNA hypomethylating agents, low-dose cytarabine, or supportive care alone [10]. Allogeneic hematopoietic stem cell transplantation (HSCT) is rarely used in older patients due to significant comorbidities and higher risk of transplant-related morbidity and mortality [11, 12]. Even so, data from the Swedish Acute Leukemia Registry have demonstrated that the majority of patients <80 years are able to tolerate intensive treatment and have shown benefits in spite of deteriorating organ function [8, 13].

Elderly, Medicare aged patients constitute the majority of patients with cancer in the United States, but only 1–2% of them are enrolled in randomized clinical trials (RCTs) providing a limited evidence base in which to evaluate treatment efficacy and safety in this population [14–16]. Advanced age or the presence of significant comorbidity was the most frequently cited factors for clinical trial ineligibility [17]. The incidence of AML is expected to increase due to the aging population, and given the limited treatment options and clinical trial participation among the elderly, we examined Medicare beneficiaries diagnosed with AML from a large population-based cancer registry. The objectives of this analysis were to describe treatment patterns during the study time period, to examine factors predictive of receiving therapy, and to identify factors associated with prognosis among older AML patients in real-world clinical practice.

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2. Methods

2.1. Data sources

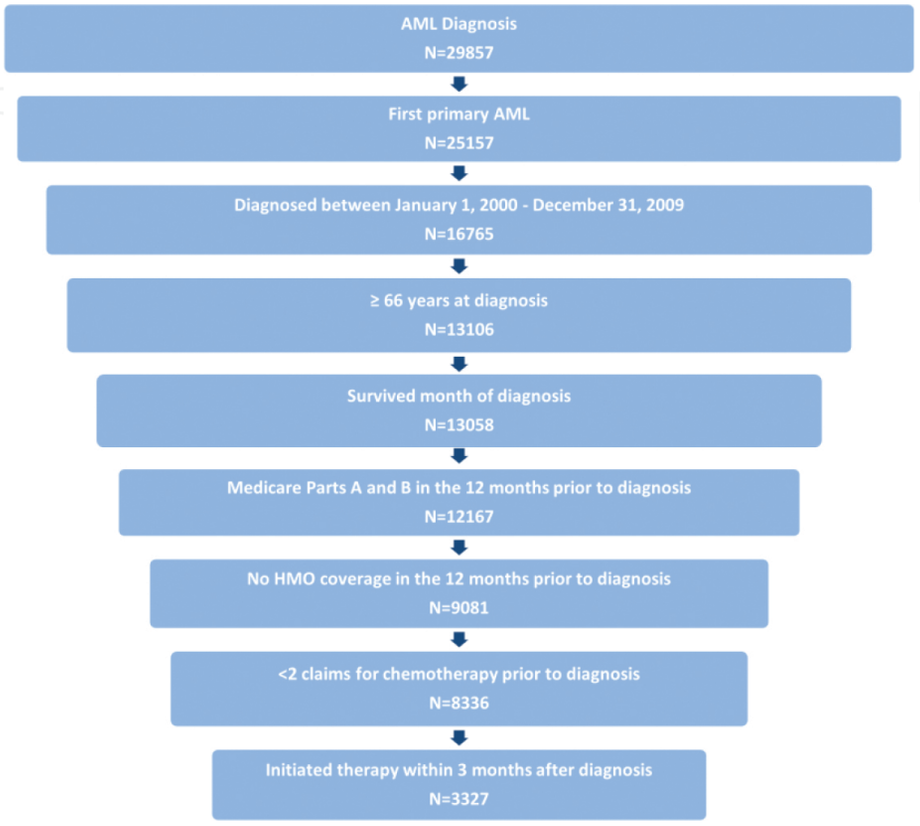

Figure 1. Schematic of inclusion/exclusion criteria.

This study utilized linked data from two large population-based data sources of Medicare beneficiaries with incident cancer identified in the Surveillance, Epidemiology, and End Results (SEER) program tumor registries. The database contains more than 3.3 million persons with cancer. Details of the linked SEER-Medicare database have been published elsewhere [18]. Briefly, the database combines clinical, demographic, cancer diagnosis, survival, and cause of death information with medical claims (hospital, physician, outpatient, home health, and hospice bills) for adults ≥65 diagnosed with cancer and enrolled in Medicare Part A (inpatient care, skilled nursing, home healthcare, and hospice care) and Part B (outpatient and physician services). The SEER is a nationally representative collection of 18 population-based registries of all incident cancers from diverse geographic areas covering approximately 26% of the US population. The registries monitor cancer trends, and provide continuous information on cancer incidence, extent of disease at diagnosis, therapy, and patient survival. A 98% case ascertainment is mandated with annual quality-assurance studies. The majority of persons aged 65 years and older in the SEER are successfully matched to their Medicare enrollment files [18]. All Medicare beneficiaries receive Part A coverage and approximately 95% of beneficiaries subscribe to Part B. The SEER-Medicare linkage used in this study included all

Medicare eligible cancer patients appearing in the SEER data through 2009 and their Medicare claims for Part A and Part B through 2010. Institutional review board approval was waived because the SEER-Medicare data lack personal identifiers.

2.2. Study cohort

The SEER-Medicare dataset contained 29,857 patients with AML. All patients had microscopically confirmed AML diagnosis based on the International Classification of Diseases for Oncology (3rd edition, ICD-O-3) histology codes in the SEER. For inclusion in the study, patients were restricted to those with a first primary AML in order to exclude therapy-related AML, diagnosed within the time period from January 1, 2000 to December 31, 2009, ≥66 years of age, and enrolled in Medicare Parts A and B for a full 12 months before diagnosis date. Study exclusion criteria were as follows: (1) diagnosis at death, (2) enrollment in a health maintenance organization (HMO) any time within the 12 months before diagnosis since HMO claims are unavailable, and (3) receipt of chemotherapy before diagnosis. See **Figure 1** for the schematic of inclusion/exclusion process.

2.3. Study variables

Key study measures include patient demographics (age, race/ethnicity, gender, income, and education level); clinical characteristics (AML diagnosis, tumor characteristics, risk status, comorbidity burden, treatment, and survival time). In the absence of cytogenetic data and molecular abnormalities in the SEER data, prior myelodysplastic syndrome (MDS) or myeloproliferative neoplasm (MPN) was used as a proxy for high-risk patients and was identified using diagnosis codes in Medicare Parts A and B claim files. MDS or MPN that transforms into AML are poor prognostic features of the disease and occur more commonly among elderly patients [19]. Performance status, such as Eastern Cooperative Oncology Group (ECOG), is not available in the dataset so Medicare claims were used to identify poor performance indicators (PPI) which include oxygen and related respiratory supplies, wheelchair and supplies, home health agency services, and skilled nursing facility services occurring in the 12 months before diagnosis [20]. The National Cancer Institute (NCI) comorbidity index [21] is the gold standard in SEER-Medicare to capture comorbidity burden using diagnosis and procedure codes to identify the 15 noncancer comorbidities from the Charlson Comorbidity Index [22] that occurred in the 12 months before cancer diagnosis.

In the Medicare claims files, International Classification of Disease (9th revision) Clinical Modification (ICD-9-CM) procedure codes were used to identify chemotherapy administration while the Healthcare Common Procedural Coding System (HCPCS) "J" codes were used to identify the specific intravenous chemotherapy administered [23]. The first claim for chemotherapy had to appear within 3 months of the AML diagnosis date, and patients were classified into one of three treatment groups using all chemotherapies received during the first 60 days after date of chemotherapy initiation. Those receiving low intensity therapy with a DNA methyltransferase (DNMT) inhibitor such as Azacitidine or Decitabine were classified into the hypomethylating agents or "HMA Therapy" group; and those receiving aggressive induction therapy with Cytarabine + Anthracycline were classified into the "Intensive

http://dx.doi.org/10.5772/63758

Therapy" group. Given that chemotherapy for AML is usually administered during inpatient stays, specific chemotherapy agent identification using J codes was not possible in about 70% of treated patients because inpatient stays are paid according to ICD-9 diagnosis or procedures codes only. Allogeneic HSCT was also identified using ICD-9-CM and HCPCS codes in the patient's Medicare claim files that occurred in the study follow-up period.

2.4. Outcome measures

The primary endpoint was overall survival after the AML diagnosis. Overall survival was measured from date of diagnosis to date of death. To assess the risk of early death (30-day mortality and 60-day mortality) after diagnosis, the "treated" group was limited to patients who received treatment within 30 days after diagnosis to minimize the introduction of immortal time bias into the analysis (period of follow-up time during which death cannot occur) [24]. All patients who were still alive at the end of the follow-up period (December 31, 2010) were censored.

2.5. Statistical analysis

Patient characteristics were compared with treatment status and treatment type using the Chi-square test for categorical variables and ANOVA or *t* test for continuous variables. We considered a *p*-value <0.05 to be statistically significant. Multivariate logistic regression was used to assess factors associated with receipt of treatment.

In the survival analyses, we made comparisons between the treated and Not Treated patients; between treated patients receiving HSCT and those who did not; and between HMA Therapy, Intensive Therapy, and No Treatment groups. The Kaplan-Meier survival analysis was used to plot survival curves. A time-varying Cox regression model with treatment as a time-dependent factor was used to account for variation in treatment initiation between groups. Other independent variables included in the Cox model were selected demographic and clinical characteristics. All statistical analyses were performed using SAS software, version 9.1.3 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Treatment patterns

Treatment rates increased over the study time period from 35% in 2000 to 50% in 2009 (**Figure 2**). Of the 8336 patients who met all study criteria, 3327 (40%) received treatment with chemotherapy within 3 months of diagnosis and 5009 (60%) did not. As age and comorbidity burden increased, likelihood of treatment was found to decrease (**Figures 3** and **4**).

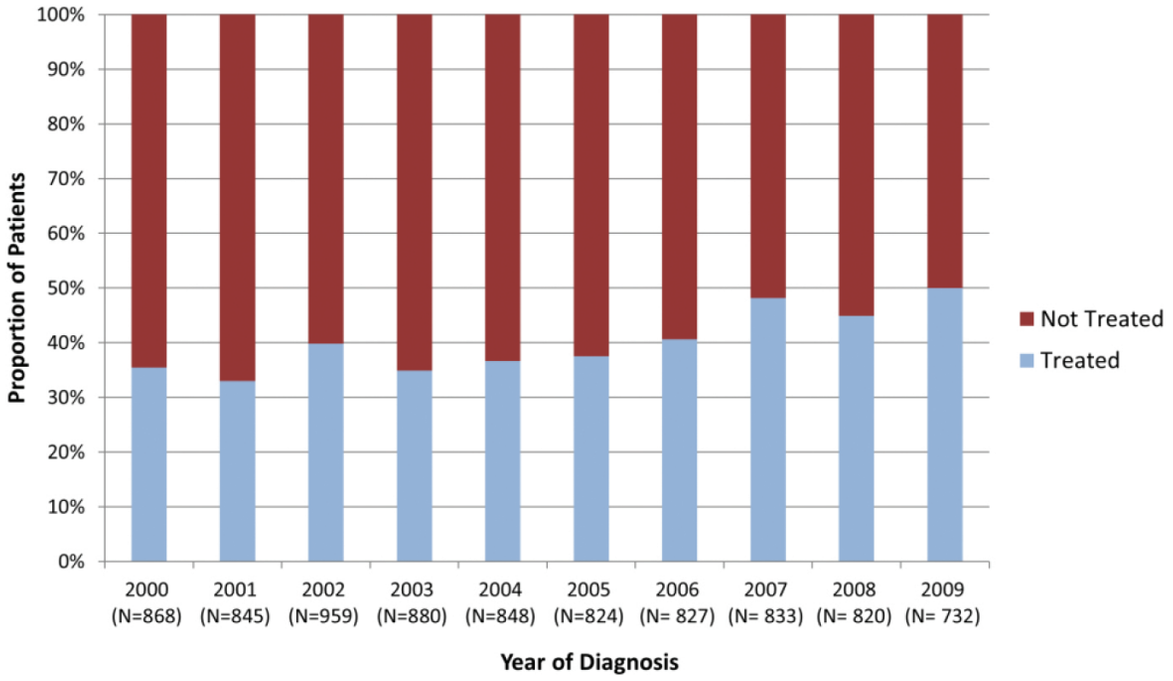

Figure 2. Treatment status by year of diagnosis.

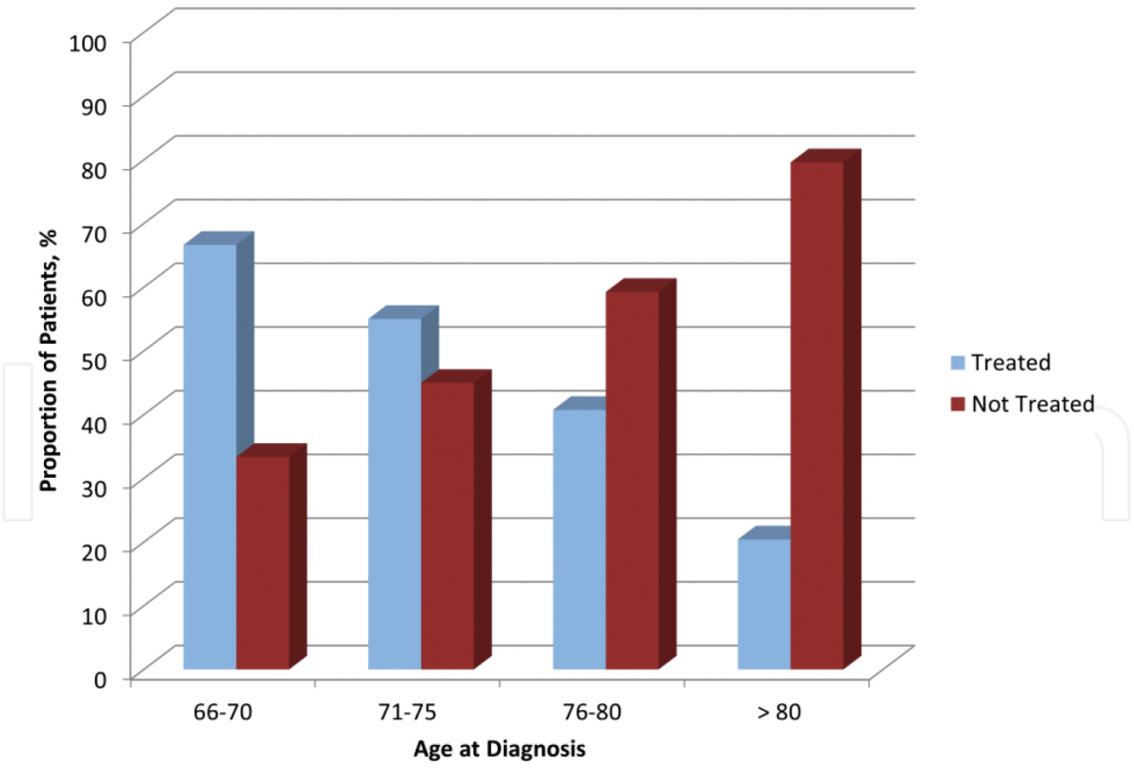

Figure 3. Treatment status by age.

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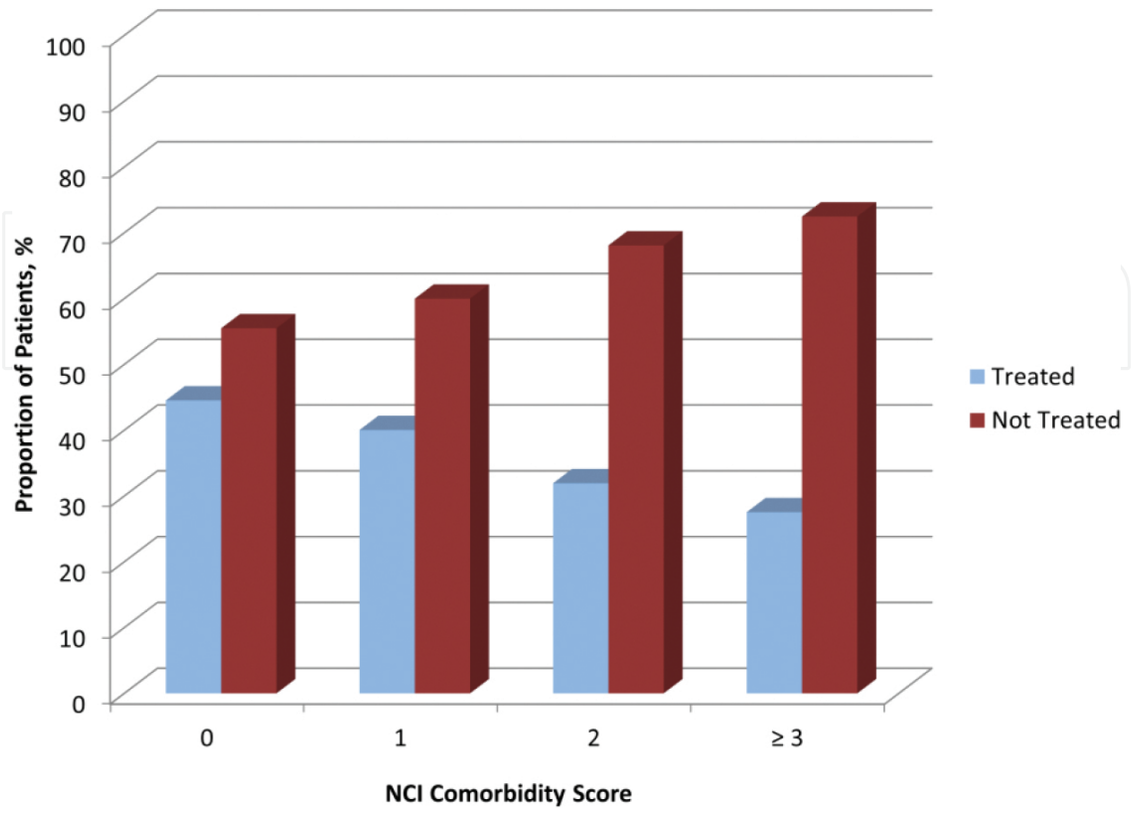

Figure 4. Treatment status by comorbidity burden.

3.2. Cohort characteristics and the odds of treatment receipt

Table 1 shows the baseline patient characteristics of the cohort. Overall, the majority of patients were over 75 years of age (63%), male, white, and married. In the logistic regression model of factors associated with the odds of not receiving treatment with chemotherapy or HSCT, increasing age and increasing comorbidity score were confirmed to significantly decrease the likelihood of receiving treatment. Patients of black or African ancestry were 30% less likely to receive treatment than white patients. Being widowed, separated/divorced, having a history of MDS or presence of PPI significantly decreased the likelihood of receiving treatment.

Table 2 shows the baseline patient characteristics by the type of treatment received. Compared with other treatment groups, patients receiving Intensive Therapy were younger, more likely male, married, less secondary AML (prior MDS), less likely to have PPIs, and had lower comorbidity score. Similarities in age, comorbidity burden, and proportion with high-risk disease were noted in HMA Therapy and Not Treated patients.

Among treated patients, there were 276 (8%) who underwent HSCT therapy and 3051 (92%) who did not (**Table 2**). The HSCT patients were younger at diagnosis with a mean age of 73 compared with the non-HSCT group (75 years; p <0.0001) and were more likely to be male.

Characteristic	Total (N = 8336)		Odds of no treatment		
	n	%	OR[a]	95% CI	*p*-value
Age at diagnosis					
66–70	1322	15.9	ref		
71–75	1774	21.3	1.64	1.41–1.91	<0.0001
76–80	1971	23.6	2.86	2.46–3.32	<0.0001
>80	3269	39.2	7.40	6.36–8.61	<0.0001
Sex					
Male	4331	52.0	ref		
Female	4005	48.0	0.97	0.87–1.07	0.5193
Race/ethnicity					
White	7285	87.4	ref		
Black	502	6.0	1.30	1.04–1.62	0.0045
Other/unknown	549	6.6	0.87	0.71–1.05	0.4119
Marital status					
Married	4373	52.5	ref		
Widowed	2492	29.9	1.29	1.13–1.46	0.0036
Separated/divorced	543	6.5	1.34	1.10–1.64	0.0128
Single	535	6.4	1.21	0.99–1.48	0.0796
Unknown	393	4.7	1.31	1.04–1.66	0.0359
Prior MDS					
No	6896	82.7	ref		
Yes	1440	17.3	1.18	1.03–1.34	0.0151
PPI					
No	7280	87.3	ref		
Yes	1056	12.7	2.02	1.69–2.41	<0.0001
NCI comorbidity score					
0	4266	51.2	ref		
1	2104	25.2	1.07	0.95–1.21	0.1017
2	1018	12.2	1.41	1.20–1.66	0.0326
≥3	948	11.4	1.56	1.31–1.86	0.0004

[a]*Model also includes geographic region, income,and year of diagnosis.*

Table 1. Factors associated with the odds of NOT receiving chemotherapy or HSCT.

http://dx.doi.org/10.5772/63758

Characteristic	Not Treated (*N* = 5009)	HMA Therapy (*N* = 345)	Intensive Therapy (*N* = 124)	*p*	HSCT (*N* = 276)	No HSCT (*N* = 3051)	*p*
	(%)	(%)	(%)	(%)	(%)	(%)	
Age at diagnosis							
66–70	8.8	13.6	39.5	<0.0001	44.6	24.8	<0.0001
71–75	15.9	24.1	31.5		25.4	29.7	
76–80	23.3	25.5	16.1		14.5	25.0	
>80	51.9	36.8	12.9		15.6	20.5	
Sex							
Male	49.9	59.1	62.1	0.0002	61.6	54.5	0.0228
Female	50.1	40.9	37.9		38.4	45.5	
Race/ethnicity							
White	87.2	90.4	87.9	0.2092	88.4	87.6	0.7118
Nonwhite	6.7	9.6	12.1		11.6	12.4	
Marital status							
Married	46.8	61.2	71.0	<0.0001	59.4	61.1	0.0851
Widowed	35.3	21.4	15.3		18.5	22.1	
Separated/divorced	6.5	5.5	13.6[a]		10.1	6.2	
Single	6.4	6.7			7.6	6.4	
Unknown	5.1	5.2			4.3	4.2	
Prior MDS							
No	81.0	79.1	100[a]	0.0026	88.8	85.0	0.0920
Yes	19.0	20.9			11.2	15.0	
PPI							
No	83.2	91.3	100[a]	<0.0001	94.2	93.4	0.6245
Yes	16.8	8.7			5.8	6.6	
NCI comorbidity score							
0	47.3	50.7	55.6	0.1113	55.8	57.2	0.2711
1	25.2	25.8	25.8		22.8	25.5	
2	13.8	11.6	18.5[a]		10.9	9.7	
≥3	13.7	11.9				10.5	7.6

[a]Cells with counts of less than 11 are combined in compliance with the National Cancer Institute data in agreement with small cell sizes.

Table 2. Baseline patient characteristics by type of treatment received.

3.3. Overall survival by chemotherapy type

Covariates	*N*	Total[a] (*N* = 5478)		≤75 years[a] (*N* = 1457)		>75 years[a] (*N* = 4021)	
Treatment		**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Not treated (ref)	5009						
HMA therapy	345	0.52	0.47–0.59	0.54	0.45–0.66	0.50	0.44–0.58
Intensive therapy	124	0.33	0.27–0.41	0.30	0.23–0.39	0.38	0.26–0.54
Age at diagnosis							
66–70 (ref)	537						
71–75	920	1.31	1.17–1.46				
76–80	1276	1.42	1.27–1.58				
>80	2745	1.68	1.52–1.86				
Sex							
Male (ref)	2780						
Female	2698	1.01	0.96–1.08	0.99	0.88–1.11	1.03	0.96–1.10
Race/ethnicity							
White (ref)	4788						
Black	350	0.96	0.86–1.07	1.04	0.85–1.28	0.92	0.80–1.05
Other/unknown	340	0.89	0.79–1.00	0.93	0.74–1.16	0.86	0.75–0.98
Marital status							
Married (ref)	2644						
Widowed	1859	1.12	1.05–1.20	1.33	1.14–1.56	1.10	1.02–1.19
Separated/divorced	349	1.11	0.99–1.25	1.09	0.89–1.33	1.07	0.93–1.23
Single	349	1.18	1.05–1.32	1.31	1.07–1.59	1.12	0.97–1.28
Unknown	277	1.00	0.88–1.13	0.94	0.73–1.20	1.01	0.87–1.18
Prior MDS							
No (ref)	4445						
Yes	1033	0.97	0.91–1.04	1.03	0.89–1.19	0.95	0.88–1.03
PPI							
No (ref)	4605						
Yes	873	1.30	1.20–1.40	1.58	1.32–1.90	1.26	1.16–1.38
NCI comorbidity score							
0 (ref)	2611						
1	1383	1.18	1.10–1.26	1.35	1.18–1.54	1.12	1.03–1.21

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Covariates	*N*	Total[a] (*N* = 5478)		≤75 years[a] (*N* = 1457)		>75 years[a] (*N* = 4021)	
Treatment		**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
2	749	1.29	1.19–1.41	1.43	1.20–1.70	1.25	1.14–1.38
≥3	735	1.38	1.26–1.51	1.40	1.16–1.69	1.35	1.21–1.49

[a]Model also includes geographic region, income, and year of diagnosis.

Table 3. Adjusted overall survival by treatment type.

Patients receiving Intensive Therapy had longer unadjusted median overall survival (18.9 months) compared with patients receiving HMA Therapy (6.6 months) and those Not Treated (1.5 months; log rank p <0.0001). In the multivariable survival analysis (**Table 3**), significantly lower risks of death were noted among patients treated with Intensive Therapy and HMA Therapy compared with Not Treated with similar mortality risk reductions maintained in the younger (≤75) and older (>75) cohorts. Other factors found to be predictive of mortality include increasing age, increasing comorbidity score, and presence of PPIs.

3.4. Overall survival by HSCT

The unadjusted median overall survival was significantly higher for the HSCT (9.7 months) compared with the non-HSCT group (4.7 months; log rank $p < 0.0001$) and this survival benefit was supported in the multivariable survival analysis (**Table 4**), where a statistically significant, 21% lower risk of death in the HSCT group was found compared with the non-HSCT group. Stratifying by age, the lower risk of death among the HSCT group was only supported in the younger cohort (≤75 years old).

Treatment	Treated[a](*N* = 3321)			≤75 years[a] (*N* = 1854)			>75 years[a] (*N* = 1467)		
	HR	**95% CI**	***p***	**HR**	**95% CI**	***p***	**HR**	**95% CI**	***p***
No HSCT (ref)									
HSCT	0.80	0.70–0.92	0.0015	0.63	0.53–0.75	<0.0001	1.21	0.96–1.53	0.1041

[a]Adjusted for age, sex, race, marital status, geographic region, income, year of diagnosis, prior MDS, PPI, and NCI comorbidity index.

Table 4. Adjusted overall survival among treated patients with and without HSCT.

4. Discussion

Treatment for elderly patients diagnosed with AML has increased over time from the 34% reported by Lang et al. between 1991 and 2001 [7] to the 40% reported in our study between 2000 and 2010. However, the 60% of elderly AML patients who remain untreated following

diagnosis represents a large unmet need in this patient population. We observed a significant survival benefit with receiving antileukemic therapy even among the HMA Therapy group who had similar characteristics to the untreated group. Our multivariate analysis demonstrated a greater reduction in mortality among patients receiving Intensive Therapy compared with HMA Therapy, but both therapeutic options appeared to be equally better than supportive measures when the cohorts were properly matched for relevant confounders. Results from prior RCTs also support our findings and have demonstrated not only an improvement in complete remission rate, but also an improvement in overall survival for AML patients aged 65 years or older treated with intensive chemotherapy [25] and HMA Therapy [26] compared with supportive measures only.

The current results also draw attention to the perception that elderly AML is an untreatable disease and conventional chemotherapy is usually withheld due to toxicity and high early death rates. Our results, however, confirm findings from other registry-based analyses that showed elderly AML patients who received treatment exhibited a lower early death rate compared with untreated patients or palliation after adjustment for confounding factors [8, 13, 27]. Despite the overall improvement in early death rates in the treated versus untreated groups, subsets of patients older than 80 years or those with poor performance or higher comorbidity burden did experience higher risks of early death suggesting caution in use of therapy within these subgroups.

The HSCT therapy was associated with a significant lower risk of death compared with patients receiving chemotherapy only and the survival benefit was even more pronounced in the younger cohort (≤75 years) with no benefit in the >75 years old subset. Although our observations are at best hypothesis generating, they raise the question of whether allogeneic HSCT provides therapeutic benefit to AML patients older than 75 years of age. Although use of myeloablative allogeneic HSCT is rare among older unfit patients, reduced-intensity conditioning (RIC) of the allogeneic HSCT has shown encouraging results in the postremission setting [11, 12, 28] and is considered an additional treatment option after complete response from induction therapy among older patients ≥60 years [10]. In fact, a recent uncontrolled study demonstrated that reduced-intensity conditioning HSCT as postremission therapy was well tolerated in selected older patients with AML, and survival compared favorably to historical patients treated without HSCT [29]. However, in the "real world," chronologic age remains a driving factor in receiving HSCT as only 8% of patients in the current study who received chemotherapy underwent subsequent HSCT therapy. The randomized clinical trials are needed to define the role of allogeneic HSCT as postremission therapy in this cohort of patients.

The results show that patients receiving Intensive Therapy were younger, had less secondary AML, were less likely to have indicators of poor performance, and had lower comorbidity burden compared with patients receiving HMA Therapy and No Treatment, and this may be related to physician beliefs that elderly patients are less able to tolerate more aggressive treatments [5, 30–32]. Undertreatment because of age, independent of comorbidities, occurs in other oncology studies, and may be due to patient preferences, physicians' tendencies to treat patients according to their chronologic age, and a lack of evidence-based guidelines for treating older patients [33, 34]. In two prior RCTs where preselection of conventional care regimens

was performed before subjects were randomized, those assigned to aggressive therapies had a median of 5–8 years younger than their counterparts assigned to less intensive regimens [35, 36]. These age disparities in treatment patterns are associated with higher mortality in older AML patients [5, 6] and our results provide further support that demographic factors such as age should not discourage the use of guideline-recommended therapies.

Treatment receipt also varied by gender, socioeconomic factors, geographic region, and marital status, similar to patterns observed in prior oncology research [37–39]. Even after adjustment for known confounders, married patients were more likely to receive treatment and had better outcomes compared with unmarried patients [39] and may indicate that marital status is a surrogate of social-economic support in this patient population. Reducing the disparity of nonclinical factors such as income and geographic region on receipt of cancer therapy may reduce the adverse impact on outcomes among these patients. Further research is warranted to better quantify how nonclinical factors contribute to receipt of cancer therapy and outcomes.

4.1. Strengths and limitations

This unique dataset allowed us to examine all AML patients, both treated and untreated, and provided insight into treatment decisions and effectiveness of therapies in routine oncology practice among this underrepresented elderly patient population. Our analysis has several strengths including the large sample size from a population-based cancer registry, the diverse geographic representation of AML patients in the United States, and comprehensive, longitudinal data with medical claims from the time a person is eligible for Medicare until death regardless of residence or service area.

However, there are some limitations to the analysis that deserve mention. The SEER registry does not collect baseline molecular and cytogenetic information or performance status, and these factors influence clinicians' decisions to treat or the specific regimen to administer. Our proxies for stage (including claims for prior MDS as a marker of disease severity) and performance status (including claims to identify indicators of poor performance) may not adequately assess stage or performance status in all patients and may be subject to bias.

The results of the comparative effectiveness analysis should be interpreted with caution due to the large amount of missing data and resulting small sample size of treatment groups. Conventional chemotherapy treatments for AML are highly toxic [9] and generally require inpatient treatment. Inpatient stays are paid based on ICD-9 diagnosis or procedures codes only and not the specific chemotherapy J code administered. Therefore, we were unable to define the type of chemotherapy received for 70% of the treated cohort without the specific J code. Given that induction chemotherapy with curative intent in the outpatient setting is applied to very select elderly AML patients, our findings may not be representative of the general patient population receiving intensive induction therapy.

Finally, this analysis does not contain information regarding treatment patterns and outcomes of patients enrolled in HMO plans as these claims are not submitted to Medicare. Prior solid tumor studies found that HMO enrollees were diagnosed earlier and had better overall

survival compared with fee-for-service (FFS) plan members [40, 41]. An investigation of how patient characteristics, treatment patterns, and prognosis may differ between these alternative healthcare plans and Medicare enrollees would be a productive area for additional evaluation.

In conclusion, our findings provide an important context for therapeutic selection that occurs in older patients with AML and suggests that age alone should not discourage the use of guideline-recommended therapies particularly because of the high disparities in outcomes between treatment receipt and palliative care. But even with treatment, outcomes remain dismal, and given this important unmet medical need, many new agents are currently in development for older patients with AML [42–45]. Moving forward, it will be important to identify patients less likely to be treated at diagnosis and design clinical trials to address the therapeutic challenges that exist in this cohort of patients.

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