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ARTICLE

Reimbursement, Utilization, and 1-Year Survival Post-Allogeneic Transplantation for Medicare Beneficiaries With Acute Myeloid Leukemia

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Abstract

Background: The economics of allogeneic hematopoietic cell transplantation (alloHCT) for older patients with acute myeloid leukemia (AML) affects clinical practice and public policy. To assess reimbursement, utilization, and overall survival (OS) up to 1 year post-alloHCT for Medicare beneficiaries aged 65 years or older with AML, a unique merged dataset of Medicare claims and national alloHCT registry data was analyzed.
Methods: Patients diagnosed with AML undergoing alloHCT from 2010 to 2011 were included for a retrospective cohort analysis with generalized linear model adjustment. One-year post-alloHCT reimbursement included Medicare, secondary payer, and beneficiary copayments (no coinsurance) (inflation adjusted to 2017 dollars). Cost-to-charge ratios were applied to estimate department-specific inpatient costs. Cox proportional hazards regression models were utilized to identify risk factors of 1-year OS post-alloHCT.
Results: A total of 250 patients met inclusion criteria. Mean total reimbursement was $230 815 (95% confidence interval [CI] = $214 381 to $247 249) 1 year after alloHCT. Pharmacy was the most- costly inpatient service category. Adjusted mean total reimbursement was statistically higher for patients who received cord blood grafts ($P = .01$), myeloablative conditioning ($P < .0001$), and alloHCT in the Northeast and West ($P = .03$). Mortality increased with age (hazard ratio [HR] = 1.08, 95% CI = 1.0 to 1.17), poorer Karnofsky performance score (<90% vs ≥90%, HR = 1.60, 95% CI = 1.08 to 2.35), and receipt of myeloablative conditioning (HR = 1.88, 95% CI = 1.21 to 2.92).
Conclusions: This merged dataset allowed adjustment for a richer set of patient- and HCT-related characteristics than claims data alone. The finding that nonmyeloablative conditioning was associated with lower reimbursement and improved OS 1 year post-alloHCT warrants further investigation.

Acute myeloid leukemia (AML) is prevalent in older individuals; in the United States, AML prevalence is 2.0 cases per 100 000 individuals aged less than 65 years and 20.1 cases per 100 000 for those aged 65 years and older (1). Treatment of older patients with AML presents challenges because they are more likely to have poor-risk cytogenetic disease and worse survival than younger patients, with 5-year survival rates less than 15% (2). Given the adverse prognosis and outcomes associated with older age, older patients with AML can benefit from allogeneic hematopoietic cell transplantation (alloHCT) as consolidation therapy after achieving complete remission. The number of alloHCTs for treatment of malignant diseases in patients aged 60 years or older has increased steadily; from 2007 to 2013, 22% of alloHCT recipients were aged 60 years or older compared

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with approximately 2% in 1993–1999 (3). To date, however, a significant knowledge gap remains regarding health-care costs for older populations post-alloHCT.

HCT has been identified as one of the most rapidly growing categories of health-care expenditure in the United States (4). Between 2004 and 2007, total HCT-associated hospital costs increased by 85%, from $694 million to $1.3 billion, related to increases in both the number of HCT hospitalizations and average cost per hospitalization. Early studies of HCT costs have been largely based on single-center experiences and are not generalizable (5,6), limiting their usefulness for payers and policy makers who are interested in the utilization and cost impact of HCT. As the need to assess medical costs related to HCT continues to grow, especially from a population-based perspective, administrative claims datasets have been utilized and become an increasingly important source of "real-world evidence" (7–12). Given the limited amount of clinical information present in claims data, the effects of disease status, functional status, graft source, conditioning intensity, and transplant-related factors on costs cannot be fully evaluated using administrative claims data alone (7). Especially reduced-intensity or nonmyeloablative conditioning regimens now routinely allow for alloHCT in older patients with hematologic malignancies who have acceptable risks of morbidity and nonrelapse mortality (13–18). The economic effect of conditioning intensity on HCT cost has not been fully evaluated.

This study is based on a unique dataset merging traditional Medicare fee-for-service (FFS) claims data from the Centers for Medicare & Medicaid Services (CMS) with Center for International Blood & Marrow Transplant Research (CIBMTR) registry outcomes data, providing comprehensive information on alloHCT recipient– related and transplant-related characteristics and survival. The primary objective was to assess reimbursement, service utilization, and overall survival (OS) at designated time points up to 1 year after alloHCT for Medicare FFS beneficiaries aged 65 years or older with AML in the United States.

Patients and Methods

Study Design and Data Sources

This was a retrospective cohort study based on the merged dataset of CMS-Medicare claims data and CIBMTR datasets (Medicare-CIBMTR dataset). Medicare claims for autologous and allogeneic transplant procedures and associated service utilized from 2010 to 2012 were used. The dataset included 100% of Medicare FFS patients who underwent alloHCT, as indicated by HCT-related International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis/procedure codes (V42.21, V42.82, 41.00–41.09) and/or Healthcare Common Procedure Coding Systems codes (38240, 38241) (19). Medicare files for reimbursement and service utilization analyses included Medicare Part A institutional (inpatient, outpatient, skilled nursing, home health, and hospice) claims and Medicare Part B physician or supplier claims. Inpatient service utilization was evaluated by the Medicare Provider and Analysis Review files, which contain records for 100% of Medicare FFS beneficiaries who use inpatient hospital and/or skilled nursing facility services. Each Medicare Provider and Analysis Review record represents a summary of inpatient hospital or skilled nursing facility stays and may represent one or multiple claims (20).

To enrich administrative claims data with additional disease and transplant-related characteristics and survival information, the Medicare dataset was merged with the CIBMTR transplant and outcomes data. CIBMTR recipient and donor baseline and follow-up outcomes data include information on 100% of allogeneic and approximately 80% of autologous transplants that take place in the United States (21).

Matching Process

Patient social security number, date of birth, sex, and transplant date and type (alloHCT vs autologous HCT) were used as primary matching criteria. If the social security number was missing in the CIBMTR dataset, the state in which the transplant center was located was applied as an additional matching criterion. Of Medicare FFS patients who underwent alloHCT, 89% were matched to CIBMTR data (22). The present study was considered exempt by the National Marrow Donor Program Institutional Review Board.

Study Population and Patient Selection

The study focused on Medicare FFS beneficiaries aged 65 years or older who underwent alloHCT for AML between 2010 and 2011. Inclusion and exclusion criteria were applied to finalize the study cohort (Supplementary Figure 1, available online). Patients were excluded who received alloHCT before March 1, 2010, or after December 31, 2011 (to allow for a claims window of 2 months prior and 1 year post-HCT follow-up); had received a prior autologous or alloHCT; or were not enrolled in both Parts A and B 60 days before and on the date of HCT. Of note, any variable or criterion with a count of less than 11 cannot be displayed due to CMS policy.

Patient-, Disease-, and Transplant-Related Characteristics

Patient characteristics included age at transplant date, sex, year of transplant, and the state where the transplant center was located. States were classified into four regions: Midwest, Northeast, South, and West.

Disease- and transplant-related characteristics from the CIBMTR data were included to allow examination of their association with outcome measures: Karnofsky performance score ($<$90 and $\geq$90%), disease status (first complete remission [CR1], second CR, third CR or higher, relapse, or primary induction failure), donor type (unrelated, human leukocyte antigen-identical sibling, or other), graft source (bone marrow, peripheral blood, or umbilical cord blood), Sorror comorbidity score (0, 1–2, $\geq$3), cytomegalovirus serostatus (negative, positive), conditioning intensity (myeloablative or nonmyeloablative), graft-versus-host disease prophylaxis, and antithymocyte globulin or alemtuzumab use.

Reimbursement, Service Utilization, and OS

The total reimbursement for 1-year post-alloHCT care included Medicare payment, secondary payer payments, and patient responsibility for deductibles, coinsurance, and copayments from the inpatient admission date or 2 days before the outpatient infusion date (to identify conditioning regimen) until 1 year after alloHCT or death date. Cumulative reimbursement was calculated at designated time points up to 1 year after alloHCT (100, 180, 270, and 365 days), inflation-adjusted to 2017 dollars using CMS Market Baskets (23). The cumulative reimbursement at 365 days is total reimbursement at 1 year post-alloHCT. For

patients who died within 1 year, cumulative reimbursements were calculated at the time of death and included as part of the total reimbursement within 1 year post-alloHCT.

Service utilization was measured by total hospitalization service days and total distinct service day counts of outpatient clinic visits at the same designated time points after alloHCT as for cumulative total reimbursement. Additionally, cost-to-charge ratio (CCR) analysis was used to estimate inpatient costs and further identify department-specific categories of services during hospitalization (24–26).

OS at 100 days and 1 year after alloHCT was calculated. The index period of alloHCT for reimbursement and service utilization included day of admission for HCT through transplant date and discharge date. When alloHCT occurred in an outpatient setting, the index period was day 2 through HCT date to identify the conditioning regimen.

Statistical Analysis

Descriptive analysis of alloHCT patient characteristics was performed. Inflation-adjusted mean reimbursement and observed service utilization were calculated. Medicare hospital-specific CCRs were applied to department-specific inpatient charges (by cost centers), allowing us to investigate service-specific inpatient costs (24–25). Patients who underwent alloHCT at centers with missing Medicare hospital-specific CCRs were excluded from CCR analysis (n = 71). The total amount of 1-year post-alloHCT inpatient costs generated by CCR analysis is an estimation of department-specific total expenditures during hospitalization.

Univariate and multivariable generalized linear models (GLMs) (gamma family with log link) were performed to evaluate effects of selected parameters individually and simultaneously. A multivariable model was used to identify predictors of 1-year total reimbursement post-alloHCT adjusting for age, sex, transplant center region, year of transplant, Karnofsky performance score disease status, donor type, graft source, Sorror comorbidity score, cytomegalovirus serostatus, conditioning intensity, graft-versus-host disease prophylaxis, antithymocyte globulin or alemtuzumab use, and 2-month total reimbursement before the index alloHCT hospitalization or outpatient alloHCT claim. Adjusted total reimbursement 1 year post-alloHCT was calculated by patient characteristics significantly associated with total reimbursement, including transplant center region, graft source, and conditioning intensity.

The Kaplan-Meier method was used to estimate cumulative probability of OS, stratified by disease stage and conditioning intensity. Univariate and multivariable Cox proportional hazards regression models were used to identify factors predicting 1-year OS post-alloHCT. Time-dependent covariates were applied to ensure the assumption of proportionality was not violated. Potential effects of pre-alloHCT service utilization on OS at 1 year post-alloHCT were adjusted by 2-month total reimbursement before alloHCT. Hazard ratios (HRs) and 95% confidence intervals (CIs) were generated. All analyses were conducted using SAS Enterprise Guide 6.1 (SAS Institute, Inc., Cary, NC).

Results

Patient-, Disease-, and Transplant-Related Characteristics

A total of 250 patients met inclusion criteria. The median age at transplant date was 68.1 years (Table 1). Most patients were white men and received alloHCT in CR1 using peripheral blood as the graft source. More than 70% of the patients received reduced-intensity or nonmyeloablative conditioning regimens.

Inflation-Adjusted Reimbursement and Observable Service Utilization

Inflation-adjusted cumulative reimbursement by designated time point for the entire cohort is presented in Figure 1. The mean cumulative reimbursement was $166 032 (95% CI = $153 931 to $178 133) at 100 days and $230 815 (95% CI = $214 381 to $247 249) at 1 year after alloHCT, with inpatient reimbursement accounting for more than 80% of the total at each designated time point. The mean total reimbursement was $186 254 (95% CI = $166 765 to $205 744) for patients who survived 1 year after alloHCT (n = 131) and $279 869 (95% CI = $255 453 to $304 285) for patients who died within 1 year (n = 119).

Counts of total service days by service setting and time point are shown in Supplementary Figure 2 (available online). On average, patients with AML had three inpatient admissions within 1 year after alloHCT, with means of 50 inpatient service days and 33 outpatient visits associated with 45 outpatient service days.

Department-Specific Inpatient Costs for 1-Year Post-AlloHCT

The total 1-year post-alloHCT inpatient cost generated by CCR analysis indicated that pharmacy (medication, dispensing fees, and administrative support) accounted for 34% of mean inpatient costs 1 year after alloHCT ($63 117), followed by intensive care (15%, $28 585), laboratory (13%, $24 470), organ acquisition (donor search and graft acquisition costs; 9%, $16 283), and all others (combined all service categories accounting for <2% of inpatient costs; 6%, $11 980) (Figure 2). Total estimated inpatient cost via CCR analysis for 1 year post-alloHCT was $188 747, similar to the 1-year post-alloHCT reimbursement of $186 960 for inpatient services.

Predictors of Total Reimbursement 1-Year Post-AlloHCT

The multivariable GLM results indicated that region, graft source, and myeloablative conditioning were significantly associated with total reimbursement 1 year after alloHCT (Supplementary eTable 1, available online). Table 2 shows results of the GLM model performed to determine the adjusted total reimbursement by each predictor. Adjusted total reimbursement was higher ($P = .01$) for patients who received cord blood than for those who received peripheral blood stem cells ($313 077, 95% CI = $229 255 to $427 548 for cord blood; $222 013, 95% CI = $182 445 to $270 161 for peripheral blood). Myeloablative conditioning was associated with higher reimbursement ($273 754, 95% CI = $213 951 to $350 272) than nonmyeloablative conditioning ($187 976, 95% CI = $149 284 to $236 697, $P < .001$). Adjusted total reimbursement by region was higher in the Northeast ($248 393, 95% CI = $192 403 to $320 675, $P = .03$) and West ($249 892, 95% CI = $190 048 to $328 580, $P = .03$) compared with the Midwest ($200 661, 95% CI = $155 637 to $258 710).

Table 1. Patient Characteristics*

Characteristic	No. (%)
No. of patients	250
No. of centers	81
Age, y	
65–69	157 (62.8)
70–79	93 (37.2)
Mean age (SD), y	68.7 (2.7)
Median age (IQR), y	68.1 (66–70)
Sex	
Male	163 (65.2)
Female	87 (34.8)
Race	
White	238 (95.2)
All other	12 (4.8)
Transplant center region	
Midwest	57 (22.8)
Northeast	66 (26.4)
South	78 (31.2)
West	49 (19.6)
Transplant year	
2010	105 (42)
2011	145 (58)
Karnofsky performance score, %	
<90	114 (45.6)
>90	136 (54.4)
Disease status	
CR1	140 (56)
CR2	44 (17.6)
CR3+/relapse	24 (9.6)
Primary induction failure	42 (16.8)
Donor type	
Unrelated donor	182 (72.8)
HLA-identical sibling	<60
Other	<11
Graft source	
Bone marrow	11 (4.4)
Peripheral blood	218 (87.2)
Umbilical cord blood	21 (8.4)
Sorror comorbidity score	
0	68 (27.2)
1–2	80 (32)
3+	102 (40.8)
Cytomegalovirus serostatus	
Negative	64 (25.6)
Positive	186 (74.4)
Conditioning intensity	
Myeloablative	70 (28)
Nonmyeloablative	180 (72)
Graft-versus-host disease prophylaxis	
Cyclosporine ± others	59 (23.6)
Tacrolimus ± others	167 (66.8)
Cyclophosphamide and others	24 (9.6)
Antithymocyte globulin/alemtuzumab	
Antithymocyte globulin alone	>80
Alemtuzumab alone	<11
Neither	160 (64)

*Cells with counts less than 11 cannot be displayed due to Centers for Medicare & Medicaid Services data use agreement. CR1 = first complete remission; CR2 = second complete remission; CR3 = third complete remission; HLA = human leukocyte antigen; IQR = interquartile range (25–75%).

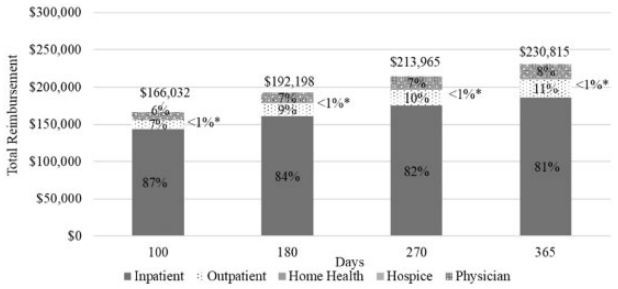

Figure 1. Distribution of cumulative mean reimbursement by time point up to 1 year post-allogeneic hematopoietic cell transplantation (alloHCT). Each time point includes the entire study cohort. For patients who died within 1 year of observation post-alloHCT, cumulative reimbursements were calculated until the time of death and considered part of the total reimbursement within 1 year post-alloHCT. *Home health and hospice services accounted for less than 1% of total reimbursement, respectively, for each designated time point.

Cumulative Probability and Predictors for 1-Year Post-alloHCT OS

Cumulative probability of OS at 100 days post-alloHCT was 84% (95% CI = 79% to 88%); OS at 1 year after alloHCT was 52% (95% CI = 46% to 59%). Survival probabilities varied by disease status ($P = .0220$) and conditioning intensity ($P = .0067$) (in Supplementary Figures 3 and 4, available online, respectively). After adjusting for patient- and disease- or transplant-related characteristics, mortality risk within 1 year post-alloHCT was higher for patients who were older (HR = 1.08, 95% CI = 1.00 to 1.17), had lower functional status (Karnofsky performance score <90% vs ≥90%, HR = 1.60, 95% CI = 1.08 to 2.35), received alloHCT at the third CR+/relapse (vs CR1; HR = 1.78, 95% CI = 0.99 to 3.20), or received myeloablative conditioning (vs reduced-intensity or nonmyeloablative conditioning regimens; HR = 1.88, 95% CI = 1.21 to 2.92) (Table 3).

Discussion

Utilizing a unique merged dataset of Medicare claims data and CIBMTR transplant and outcomes data, we identified key factors of Medicare reimbursement and OS for older patients with AML. Factors associated with reimbursement were region, graft source, and conditioning intensity. Medicare reimbursement is known to be adjusted for geographic variation (27–29). Total 1-year reimbursement was higher in the Northeast and the West than in the Midwest.

Although graft source was not significantly associated with 1-year OS post-alloHCT, cord blood was found to be a driver of reimbursement. This is unsurprising and is most likely due to increased acquisition costs, prolonged time to engraftment, and subsequent hospitalizations (27). An internal post hoc analysis revealed that cord blood had the highest mean costs for acquisition and related services ($36 321), followed by peripheral blood ($14 855) and bone marrow ($5876) derived from the present CCR analysis. The association of donor type with reimbursement could change due to recent increased use of haploidentical-HCT (30,31). However, very few patients (<11) received haplo-HCTs during the study period (2010–2011).

Reduced intensity or nonmyeloablative conditioning was associated with lower 1-year post-alloHCT reimbursement and

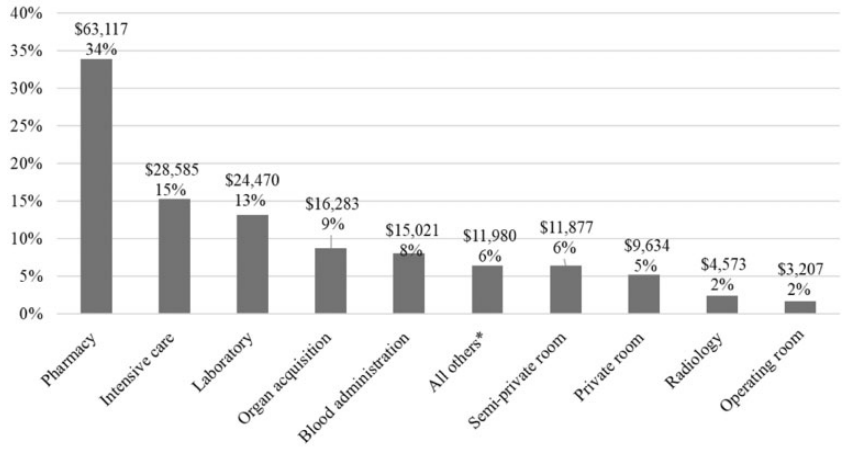

Figure 2. Department-specific inpatient costs 1-year post-alloHCT: Estimated by application of cost-to-charge ratios. The y-axis: percent of contribution to total inpatient costs 1 year post-alloHCT; the x-axis: department-specific cost center. *All others individually equate to less than 2% of cost categories, including magnetic resonance imaging, coronary care, physical therapy, end-stage renal disease services, emergency department, occupational therapy, anesthesia, speech pathology, clinic visit, outpatient services, blood, durable medical equipment, ambulance, lithotripsy, professional fees, used durable medical equipment, ward, inhalation therapy, other services, and cardiology.

Table 2. Generalized linear regression model: adjusted total reimbursement 1 year post-alloHCT by region, graft source, and conditioning intensity*

Parameter	Estimate	Adjusted mean (95% CI)	*P*
Transplant center region			
Midwest (ref)	0	$200 661 ($155 637–$258 710)	—
Northeast	0.213	$248 393 ($192 403–$320 675)	.03
South	0.058	$212 604 ($168 352–$268 488)	.55
West	0.219	$249 892 ($190 048–$328 580)	.03
Graft source			
Peripheral blood (ref)	0	$222 013 ($182 445–$270 161)	—
Bone marrow	−0.279	$167 944 ($117 047–$240 974)	.10
Umbilical cord blood	0.344	$313 077 ($229 255–$427 548)	.01
Conditioning intensity			
Nonmyeloablative (ref)	0	$187 976 ($149 284–$236 697)	—
Myeloablative	0.376	$273 754 ($213 951–$350 272)	<.0001
Scale	4.104		

*Generalized linear regression model was adjusted for age, sex, region, transplant year, Karnofsky performance score, disease status, donor type, graft source, Sorror comorbidity score, cytomegalovirus status, conditioning intensity, antithymocyte globulin or alemtuzumab use, and total reimbursement 2 months before alloHCT. alloHCT = allogeneic hematopoietic cell transplantation; CI = confidence interval.

better survival (15–18). The association of conditioning regimen intensity with total reimbursement might originate from underlying factors for undergoing myeloablative vs nonmyeloablative conditioning, such as age, graft source, disease status, and comorbidity index. Additional investigation using a prospective randomized study design may be warranted to specify indirect and/or direct effects of conditioning intensity on long-term clinical outcomes and reimbursement. Further, patients who died within 1 year post-alloHCT had higher observable mean total reimbursement than those who survived for a full year or longer post-alloHCT in the study cohort. As a study from Korea found, monthly inpatient costs for AML treatment increased significantly in the last month before death (32), possibly due to transplant and/or post-alloHCT service utilization, such as use of intensive care (33).

The Sorror comorbidity score did not predict OS in this patient population. Previous studies have confirmed the association of the comorbidity score with treatment-related mortality, not OS (34–35). The comorbidity status may have been taken into account to select the regimen intensity to reduce treatment-related mortality. It is also possible that patients with higher comorbidity scores had more poor risk disease features, with the disease-related features being more important determinants of OS than the comorbidities scores.

Administrative claims data may serve as the most relevant source of information on health-care costs from the payer's perspective (7). The total amount of Medicare reimbursement calculated within 1 year after alloHCT reflects only adjudicated claims paid to facilities and providers. The hospital-specific CCR analysis was used to estimate inpatient costs 1 year post-alloHCT, allowing us to stratify post-alloHCT inpatient services into department-specific expenditures for hospitalization and to specify pharmacy costs (medication, dispensing fees, and administrative support), intensive care, laboratory, and graft acquisition are key categories of 1-year post-alloHCT inpatient costs. Total estimated inpatient cost via CCR analysis for 1 year post-alloHCT ($188 747) was similar to 1-year post-alloHCT reimbursement for inpatient services ($176 870), possibly due to

Table 3. Overall survival 1 year post-alloHCT: univariate and multivariable analyses*

Parameter	No.	Univariate		Multivariable	
		HR (95% CI)	P	HR (95% CI)	P
Age	250	1.05 (0.98 to 1.12)	.18	1.08 (1.00 to 1.17)	.05
Sex					
Male	163	1.00 (referent)		1.00 (referent)	
Female	87	0.83 (0.57 to 1.23)	.35	0.72 (0.47 to 1.10)	.12
Transplant center region					
Midwest	57	1.00 (referent)		1.00 (referent)	
Northeast	66	1.17 (0.70 to 1.97)	.55	1.32 (0.73 to 2.39)	.35
South	78	1.24 (0.75 to 2.05)	.40	1.26 (0.69 to 2.28)	.45
West	49	1.07 (0.60 to 1.90)	.81	1.32 (0.70 to 2.49)	.39
Year of transplant					
2010	105	1.00 (referent)		1.00 (referent)	
2011	145	0.81 (0.56 to 1.16)	.24	0.78 (0.53 to 1.13)	.19
Karnofsky performance score, %					
≥90	136	1.00 (referent)		1.00 (referent)	
<90	114	1.36 (0.95 to 1.95)	.09	1.60 (1.08 to 2.35)	.02
Donor type					
Unrelated donor	182	1.00 (referent)		1.00 (referent)	
HLA-identical sibling	<60	0.77 (0.49 to 1.20)	.25	0.84 (0.52 to 1.37)	.49
Other	<11	1.09 (0.40 to 2.97)	.87	0.84 (0.28 to 2.50)	.75
Graft source					
Peripheral blood	218	1.00 (referent)		1.00 (referent)	
Bone marrow	11	1.82 (0.84 to 3.91)	.13	1.55 (0.62 to 3.84)	.35
Umbilical cord blood	21	1.51 (0.84 to 2.68)	.17	1.67 (0.87 to 3.19)	.12
Disease status					
CR1	140	1.00 (referent)		1.00 (referent)	
CR2	44	0.81 (0.46 to 1.39)	.44	0.82 (0.46 to 1.46)	.50
CR3+/relapse	24	1.83 (1.06 to 3.18)	.03	1.78 (0.99 to 3.20)	.05
PIF	42	1.59 (1.00 to 2.53)	.05	1.26 (0.77 to 2.07)	.36
Sorror comorbidity score					
0	68	1.00 (referent)		1.00 (referent)	
1–2	80	0.88 (0.55 to 1.42)	.61	0.76 (0.46 to 1.27)	.30
3+	102	1.00 (0.64 to 1.55)	.99	0.92 (0.57 to 1.50)	.75
Cytomegalovirus serostatus					
Negative	64	1.00 (referent)		1.00 (referent)	
Positive	186	1.28 (0.83 to 1.96)	.27	1.32 (0.83 to 2.11)	.25
Myeloablative preparative regimen					
No	70	1.00 (referent)		1.00 (referent)	
Yes	180	1.67 (1.15 to 2.44)	.01	1.88 (1.21 to 2.92)	.01
Antithymocyte globulin/alemtuzumab					
Antithymocyte alone	>80	1.00 (referent)		1.00 (referent)	
Alemtuzumab alone	<11	1.30 (0.46 to 3.69)	.62	1.25 (0.42 to 3.67)	.69
Neither	160	1.55 (1.03 to 2.34)	.03	1.49 (0.96 to 2.32)	.08
Total reimbursement 2 mo before transplant	250	1.00 (1.00 to 1.00)	.47	1.00 (1.00 to 1.00)	.94

*Cells with counts less than 11 cannot be displayed due to Centers for Medicare & Medicaid Services data use agreement. CI = confidence interval; CR1 = first complete remission; CR2 = second complete remission; CR3 = third complete remission; HLA = human leukocyte antigen; HR = hazard ratio; PIF = primary induction failure.

application of Medicare hospital-specific CCRs that Medicare used to calculate outlier payments and Diagnosis Related Group cost weighting for reimbursement (ResDac) (24). It also supports the fact that Medicare reimbursement is often used as a proxy for health sector costs under the assumption that Medicare reimbursement is set at a level such that providers make minimal long-run economic profit (26). For future research, a costcenter–specific CCR is recommended to estimate costs of inpatient care more accurately (25).

The existing knowledge gaps regarding medical costs for older populations with AML and cross-culture differences in health-care systems make international comparison on AML treatment costs challenging. Inpatient services were found to be a major cost driver in costs of initial AML treatment in the Netherlands (36). A Belgian single-center study evaluated medical costs and survival for AML by treatment group and found that HCT and autologous dendritic cell therapy cost more than chemotherapy only, but produced better survival (37). Further cost-effectiveness analysis of HCT and alternative treatments with quality-adjusted life-years will be critical.

This study has several limitations. The study cohort included patients who received alloHCT in 2010–2011. Although the estimation of total reimbursement 1 year after alloHCT was converted to 2017 dollars, changes in Medicare reimbursement rates over the observation years could not be evaluated. The reimbursement for outpatient drugs covered by Part D plans was

Table 4. Recommendations for future research*

Study design	A prospective randomized study
Analyses	Costcenter–specific CCR analysis
	Cost-effectiveness of alloHCT and alternative treatments (such as chemotherapy only)
Outcome measures	Long-term post-alloHCT costs and treatment-related mortality
	Patient responsibility and other post-alloHCT out-of-pocket costs

*alloHCT = allogeneic hematopoietic cell transplantation; CCR = cost-to-charge ratio.

not included because less than half of patients were enrolled in Part D coverage during the study period. Due to lack of complete data for Medicare beneficiaries enrolled in Medicare Advantage plans or health maintenance organization programs, our analysis was limited to Medicare beneficiaries enrolled in Part A and Part B under FFS programs. Future studies comparing costs and service utilization by Medicare plans (FFS vs non-FFS) and Medicare vs commercially insured populations are suggested. Patient responsibility was limited to copayment, coinsurance, and deductibles, which accounted for 3% of total payments for inpatient services to the providers, 14% for outpatient services, and 17% for physician services. Clinical outcome was measured as 1 year OS post-alloHCT as the timeframe was limited by the available CMS dataset; a longer follow-up to additional years post-HCT would identify additional events that may affect post-alloHCT costs and service utilization. A further limitation of the dataset in its present form is the relatively small final sample size, which provided a better cohort homogeneity but posed challenges for multivariable modeling using a large number of predictors (Supplementary eTable 1, available online). Larger sample sizes obtained by merging additional years of data could allow for more effective estimation of the relationship between these predictors and outcomes. Finally, the majority of recipients were white men, likely reflecting the higher incidence of AML in men, the availability of donors, and the population of Medicare overall (3,21). Recommendations for future research are shown in Table 4.

The present study is the first application of a CIBMTR-Medicare merged dataset facilitating an analysis of patient- and HCT-related factors of Medicare reimbursement and survival in an AML population for addressing economics of alloHCT and models of care. This unique merged dataset provides an opportunity to improve the usefulness of Medicare claims data. Future investigations are warranted to specify indirect and/or direct effects of disease- and HCT-related variables on reimbursement and outcomes in specified patient populations.

Notes

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