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Real-World Economic Burden Associated with Transplantation-Related Complications

Miguel-Angel Perales [1], Machaon Bonafede [2], Qian Cai [2,*], Phillip M. Garfin [3], Donna McMorrow [2], Neil C. Josephson [3], Akshara Richhariya [3]

[1] *Adult Bone Marrow Transplant Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, and Department of Medicine, Weill Cornell Medical College, New York, New York*
[2] *Truven Health Analytics, Cambridge, Massachusetts*
[3] *Seattle Genetics, Inc, Bothell, Washington*

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A B S T R A C T

Approximately 20,000 hematopoietic cell transplantation (HCT) procedures are performed annually in the United States. Real-world data on the costs associated with post-transplantation complications are limited. Patients with hematologic malignancies aged ≥18 years undergoing autologous HCT (auto-HCT) or allogeneic HCT (allo-HCT) between January 1, 2011, and June 30, 2014, were identified in the Truven Health MarketScan Research Databases. Patients were required to have 12 months of continuous medical and pharmacy enrollment before and after HCT; patients who experience inpatient death within 12 months post-HCT were also included. Patients with previous HCT were excluded. Potential HCT-related complications were identified if they had a medical claim with a diagnosis code for relapse; infection; cardiovascular, renal, neurologic, pulmonary, hepatic, or gastrointestinal disease; secondary malignancy; thrombotic microangiopathy; or posterior reversible encephalopathy syndrome within 1 year post-HCT. Healthcare costs attributable to these complications were evaluated by comparing total costs in HCT recipients with complications and those without complications. The MarketScan Research Databases were further linked to the Social Security Administration's Master Death File to obtain patient death events in a subset of patients. A total of 2672 HCT recipients were included in the analysis. The mean ± SD age of recipients was 54.5 ± 11.6 years, and the majority of recipients (63.6%) underwent auto-HCT. Complications were identified in 81% of auto-HCT recipients and in 95.5% of allo-HCT recipients. Most complications occurred within 180 days post-HCT. Compared with Auto-HCT recipients without complications, those with complications incurred $51,475 higher adjusted total costs ($P < .01$). Compared with allo-HCT recipients without complications, those with complications incurred $181,473 higher adjusted total costs ($P < .01$). Among the patients with mortality data, auto-HCT recipients with complications had a higher mortality rate (13.4% vs 5.7%, $P < .01$) and a lower probability of survival ($P < .01$) compared with those without complications. In allo-HCT recipients, however, the mortality rate and probability of survival were not significantly different between those with complications and those without complications. HCT recipients with complications were associated with considerable economic burden in terms of direct healthcare costs in a commercially insured population, and in the case of auto-HCT, a higher mortality rate was observed in those with complications.

INTRODUCTION

Hematopoietic cell transplantation (HCT) is a potentially curative treatment for patients with high-risk hematologic malignancies [1,2]. Common indications for HCT in adults include acute myelogenous leukemia, myeloproliferative neoplasms, myelodysplastic syndromes, chronic myelogenous leukemia, chronic lymphocytic leukemia, acute lymphoblastic leukemia, lymphoma, multiple myeloma, Hodgkin lymphoma, non-Hodgkin lymphoma, and certain solid tumors [2].

HCT is associated with potential complications that can have a significant impact on patient outcomes. The frequency and type of complications varies depending on the type of HCT. In general, the most frequently occurring complications include severe infections, malignant relapse, gastrointestinal and pulmonary disease, and, in allogeneic HCT (allo-HCT), graft-versus-host disease [3,4].

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* Correspondence and reprint requests: Qian Cai, MSc, MSPH, Truven Health Analytics, 75 Binney St, 4th floor, Cambridge, MA 02142.
E-mail address: qcai@us.ibm.com (Q. Cai).

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With the rising number of HCTs performed, the financial impact and costs of HCT are increasing [2,5,6]. Based on a report from the Agency for Healthcare Research and Quality, HCT was among the top 10 procedures with the most rapid increase in hospital costs in the United States, even though it is a relatively uncommon procedure [7]. A number of studies have shown the utility of using administrative claims databases to examine costs and resource utilization in patients with hematologic malignancies undergoing HCT [6-9]. A study using 2007 to 2009 administrative claims data reported median costs incurred in the first 100 days post-transplantation of $99,899 in auto-HCT recipients and $203,026 in allo-HCT recipients [6]. However, that study reported only costs incurred in the first 100 days post-HCT, and many recipients continue to have or develop complications beyond day +100. Furthermore, real-world evidence on mortality outcomes and economic burdens associated with post-transplantation complications are limited.

The purpose of the present study was to describe the rate of HCT-related complications, mortality rate, and economic outcomes associated with HCT-related complications among commercially insured patients in the United States who received auto-HCT or allo-HCT.

METHODS

Data Source

This was a retrospective cohort study using patient-level administrative claims databases to identify a sample of the patient population in the United States. Deidentified claims on healthcare utilization, costs, and patient characteristics were extracted from the Truven Health MarketScan commercial and Medicare supplemental databases. The commercial database contains the pharmacy and medical claims of employees and their dependents, and the Medicare supplemental database profiles the healthcare experience of individuals with Medicare supplemental insurance paid for by employers. Both databases provide detailed outcomes measures, including resource utilization and associated costs for healthcare services performed in both inpatient and outpatient settings for approximately 40 million individuals, who were covered annually by a geographically diverse group of self-insured employers and private insurance plans across the United States. The MarketScan research databases were further linked to the Social Security Administration (SSA) Master Death File to obtain patient death events.

All study data were accessed with protocols compliant with US patient confidentiality requirements, including the Health Insurance Portability and Accountability Act of 1996 (HIPAA) regulations. Because the database is fully deidentified and compliant with HIPAA, this study was exempted from Institutional Review Board approval.

Study Patients

Patients who had at least 1 medical claim for inpatient admission with a procedure code for auto-HCT or allo-HCT (International Classification of Diseases, Ninth Revision, Clinical Modification procedure codes 41.01 to 41.09) between January 1, 2011, and June 30, 2014, were identified. The date of the first medical claim for auto-HCT or allo-HCT was designated the HCT date. Patients were required to have at least 2 medical claims for the diagnosis of hematologic malignancies, including acute myelogenous leukemia, myelodysplastic syndromes, myelofibrosis and myeloproliferative disease, acute lymphoblastic leukemia, chronic myelogenous leukemia, multiple myeloma, Hodgkin disease, or lymphoma, of which at least 1 claim was made on or before the HCT date. Patients were also required to be age 18 years or older on the HCT date, with at least 12 months of pre-HCT and 12 months of post-HCT continuous medical and pharmacy enrollment, except for patients who had an inpatient death within the 12-month post-HCT period. Patients with a medical claim for HCT during the 12-month period before the HCT date were excluded.

Auto-HCT and allo-HCT recipients were further classified into 2 comparison cohorts, based on the presence or absence of complications of interest observed during the 12 months post-transplantation. Potential HCT-related complications were defined as medical claims with a diagnosis code for malignant relapse, severe infection, cardiovascular disorder, renal disease, neurologic disorder, pulmonary disorder (including diffuse alveolar hemorrhage, pneumonitis, bronchiolitis, or pneumonia), hepatic disease, gastrointestinal (GI) condition (including graft-versus-host disease and GI bleeding), secondary malignancy, thrombotic microangiopathy, and posterior reversible encephalopathy syndrome [4,5].

Study Variables

Total all-cause direct healthcare costs were defined as the sum of health plan costs and patient-paid costs, including copayment, deductible, and coinsurance, incurred from fully adjudicated claims of prescriptions and medical services associated with any condition. Total costs for healthcare resource utilization within 6 months pretransplantation and 12 months post-transplantation were evaluated for HCT recipients. All dollar estimates were inflated to 2015 US dollars using the Medical Care Component of the Consumer Price Index (CPI).

All-cause medical services were defined as healthcare resource utilization associated with any condition incurred from inpatient admissions and outpatient services, including emergency room visits, physician office visits, and other outpatient services, such as laboratory tests and radiologic exams. All-cause hospital readmissions were evaluated within 12 months after the index hospital discharge. The percentage of patients who underwent a second HCT within 60 days after the index HCT or who had an inpatient readmission associated with the primary diagnosis of infection or GI complication within 30 days after hospital discharge were described as well.

In addition, mortality data were described for the subset of HCT recipients with a link to the SSA Master Death File. The date of death was determined based on the death record from the SSA Master Death File or from the inpatient discharge status of death from the medical claims. Survival time was calculated as the time from the HCT date to the death date. Patients without a death date were censored as of the end of follow-up, that is, continuous enrollment or end of study period, whichever occurred first.

Patient demographic data, including age, sex, geographic region (US Census division), and type of insurance, were recorded on the HCT date. Comorbid conditions were evaluated using the Deyo-Charlson Comorbidity Index, which is an indicator of overall disease burden on the occurrence of at least 1 of 17 comorbid conditions identified using the ICD-9-CM coding manual [10]. The Deyo-Charlson Comorbidity Index score, general comorbid conditions (including cardiac disorders, diabetes, psychiatric disturbances, infection, and heart valve disease), and diagnoses present (including acute myelogenous leukemia, myelodysplastic syndromes, myelofibrosis and myeloproliferative disease, acute lymphoblastic leukemia, chronic myelogenous leukemia, multiple myeloma, Hodgkin disease, lymphoma, solid tumors) during the 12-month preindex period (i.e., the baseline period) were assessed as well.

Statistical Analysis

Descriptive analyses, mean ± SD, and median were reported for all continuous variables, and frequencies and percentages were reported for categorical variables. To compare the difference in patient characteristics and outcomes measures between HCT recipients with complications and those without complications, the *t* test was used for continuous variables and the chi-square test was used for categorical variables. The Kaplan-Meier method of survival analysis was used to display overall survival, and the log-rank test was used to evaluate the difference in survival distributions between comparison groups.

Diagnostic tests were conducted to evaluate the distribution of cost data, and generalized linear models with a gamma distribution were used to estimate the total costs for HCT recipients with complications versus those without complications after adjusting for baseline demographic and clinical characteristics. Differences were considered significant at $P < 0.05$. All data analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Patient Characteristics

A total of 2672 HCT recipients (auto-HCT, n = 1700; allo-HCT, n = 972) met the study criteria (Figure 1). The mean age of auto-HCT recipients was 55.9 ± 10.8 years, and 40.2% were female. The mean age of allo-HCT recipients was 52.1 ± 12.5 years, and 41% were female (Table 1). Multiple myeloma (66.5%) was the most common diagnosis among auto-HCT recipients. Myeloid disorders (acute myelogenous leukemia, myelodysplastic syndrome, myelofibrosis and myeloproliferative disease) were the most common diagnoses for allo-HCT recipients (69.1%). Only .1% of allo-HCT and 1.9% of auto-HCT recipients had a solid tumor only.