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ORIGINAL RESEARCH ARTICLE

Estimating the Incidence-Based Cost of Illness Due to Hematopoietic Stem Cell Transplantation Using One-Year Insurance Claim Data in Korea

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Abstract

Objectives Long-term follow-up data are required for incidence-based cost-of-illness (COI) studies, and it is difficult to carry out such assessments. To overcome this limitation, we estimated the acute and maintenance-state costs of hematopoietic stem cell transplantation (HSCT) using 1-year claim data.

Methods Using Korean National Health Insurance (NHI) data from 2016, 2017, and 2018, we identified patients receiving HSCT based on the procedure code "X5*" (i.e., HSCT). The post-HSCT group was defined as patients without the "X5*" code, but with the code "Z948 (other transplanted conditions)" and indications of HSCT (referring to those who had received HSCT). Mean annual medical use and costs were computed using the monthly values available for each patient.

Results The mean number of hospitalizations/year, outpatient visits per year, hospitalization days/year, and length of stay (LOS)/hospitalization were 8.14, 35.80, 97.16, and 14.72, respectively, for allogeneic HSCT patients (n = 56); 8.08, 33.58, 73.04, and 10.63, respectively, for autologous HSCT patients (n = 89); 2.93, 29.40, 50.95, and 20.84, respectively, for post-allogeneic HSCT patients (n = 40); and 1.72, 16.38, 30.11, and 19.29, respectively, for post-autologous HSCT patients (n = 252). The estimated annual NHI-covered medical costs (US dollars) were $38,833–$40,876 for the allogeneic HSCT group, $1749–$6744 for the post-allogeneic HSCT group, $21,231–$22,863 for the autologous HSCT group, and $3954–$5352 for the post-autologous HSCT group.

Conclusions This study describes an alternative method for conducting incidence-based COI studies using cross-sectional claims data.

1 Introduction

At the national level, medical expenses accounted for a massive portion of the total expenditure, reaching 8.8% of the average total gross domestic product of the Organization for Economic Cooperation and Development (OECD) member countries in 2018 [1]. Accordingly, the need for efficient use of healthcare resources within a limited budget has been increasing. As part of this task, a high

Key Points for Decision Makers

An incidence-based approach to estimate the cost of illness (COI) requires long-term data, and appropriate data sources are often lacking.

This study proposes a methodology for calculating incidence-based COI using 1-year claim data instead of long-term follow-up data.

The methodology used in this study is applicable to health conditions in which acute and maintenance states can be distinguished based on the diagnosis, procedure codes, and prescribed drugs included in the claim records.

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demand for cost-of-illness (COI) studies has been developed for various health conditions. COI studies aim to estimate the economic burden associated with a disease of interest at the patient or national level. These studies are used for various purposes: to assess the economic impact and resources utilized to treat a disease, to provide evidence for prioritizing the allocation of healthcare resources in certain disease areas, and to generate key parameters for conducting cost-effectiveness analyses of healthcare interventions [2, 3].

Methods for estimating COI in a study can be classified as a "prevalence-based approach" or an "incidence-based approach." A prevalence-based study estimates COI over a specific period, usually 1 year, without distinguishing between existing and new patients. In contrast, an incidence-based approach estimates COI over the entire disease cycle, from onset to cure or death [4, 5]. A prevalence-based study is appropriate for estimating the economic burden of a disease at a given point in time. However, an incidence-based study is more appropriate for obtaining information concerning the lifetime costs associated with a disease and considers its natural course and future costs associated with the disease [6].

Hematopoietic stem cell transplantation (HSCT) involves the transplantation of hematopoietic stem cells present in peripheral blood and umbilical cord blood. HSCT can be used to treat various diseases, such as leukemia, hematologic malignancies, aplastic anemia, congenital metabolic abnormalities, congenital immunodeficiency, refractory autoimmune diseases, and solid cancers [7]. HSCT is divided into allogeneic and autologous stem cell transplantation, depending on whether healthy stem cells are collected from a donor or the patient undergoing the procedure. Regardless of the type of transplantation, a pre-treatment process that destroys the patient's existing bone marrow should be carried out through the administration of high doses of anticancer drugs or radiation. Because pre-treatment reduces the patient's cell-mediated or humoral immunity, the probability of infection increases for a certain period. Therefore, increases in the use of healthcare resources and costs are inevitable during this period [8]. Graft-versus-host disease and transplant-related complications following HSCT also contribute to increased use of healthcare services. According to Kwon and Ryu [9], the health status and quality of life of patients undergoing HSCT mainly deteriorated from pre-treatment to 30 days after transplantation, gradually recovered until 100 days after transplantation ("early period after engraftment"), and stabilized over the next 1–4 years ("late period after engraftment").

As healthcare utilization patterns in the early and late stages of transplantation are clearly distinguished for HSCT, an incidence-based approach is desirable for estimating the cost of HSCT. However, the incidence-based approach requires long-term data, and appropriate data sources are often lacking. To overcome this limitation, in this study, we suggest an alternative method for estimating COI for allogeneic and autologous HSCT by combining the acute and maintenance-state costs of HSCT using 1-year cross-sectional claim data.

2 Methods

2.1 Ethical Review

On February 18, 2021, an institutional review board (IRB) waiver of consent was obtained from the Yonsei University IRB (IRB NO: 7001988-202102-HR-1105-01E).

2.2 Data Source

We pooled Korean national patient sample data collected over 3 years (2016–2018), provided by the Health Insurance Review and Assessment Services (HIRA-NPS; data serial numbers: HIRA-NPS-2016-0073, 2017-0044, and 2018-0024), to obtain a sufficient number of patients to perform an analysis of considerable significance. HIRA-NPS data are yearly cross-sectional data composed of claim records for a random sample of 3% of patients stratified by sex and age (5-year age groups), which are part of the population that uses healthcare services covered by the National Health Insurance (NHI) each year [10]. The unit of data is a claim record for individual medical encounters, including outpatient, inpatient, and emergency department services, as well as prescriptions. The data consist of five tables: the first table (Table 20 [11]) comprises the demographic characteristics of patients, such as age and gender, and general information on healthcare services provided, such as primary and secondary diagnoses, whether the patient was an inpatient or outpatient, the date of commencement of medical care, days of hospitalization, the result of treatment including death, and medical expenses. The second table (Table 30 [11]) contains specific information on the healthcare services provided, such as surgeries, diagnostic tests or medical procedures performed, and inpatient prescriptions; the third table (Table 40 [11]) contains all levels of diagnostic information, including primary, secondary, and tertiary diagnoses and beyond. The fourth table (Table 53) contains outpatient prescriptions; and the fifth table (Table of Providers) lists information on the healthcare providers for each medical encounter [11]. The data from each table were merged using a unique claim identification code. In this study, we used data from Tables 20, 30, 40, and 53 [11].

2.3 Patients

Using the HIRA-NPS data from 2016 to 2018, the "HSCT patient group" was constituted to estimate COI during the year of receiving HSCT (i.e., acute-state cost), while the "post-HSCT patient group" was identified to estimate COI after the year of HSCT (i.e., maintenance-state cost). Patients with a claim record with HSCT procedure code X5* (Appendix 1, see the Electronic Supplementary material) were considered to have received HSCT during the year and were included in the HSCT patient group. Furthermore, patients with a claim record with allogeneic HSCT procedure codes (X5051, X5061, X5063, X5131, X5133, X5135, or X5137) were classified into the "allogeneic HSCT group," while those with autologous HSCT procedure codes (X5062, X5064, X5132, X5134, or X5136) were classified into the "autologous HSCT group."

The post-HSCT group was defined as the group of patients who had a claim record (1) with a diagnosis code of Z948, which indicates the condition of other transplanted organs or tissues, including the state of HSCT; (2) with diagnosis codes that are common indications for HSCT (Appendix 2, see the Electronic Supplementary Material); and (3) without the HSCT procedure code X5*. Unlike post-autologous HSCT patients, post-allogeneic HSCT patients may experience acute or chronic graft-versus-host reactions and are usually prescribed immunosuppressants after transplantation [12]. Therefore, among the post-HSCT patients, those who had a claim record of prescribed immunosuppressants were assigned to the post-allogeneic HSCT group, and those without this prescription were assigned to the post-autologous HSCT group. Immunosuppressants included azathioprine (Anatomical Therapeutic Chemical [ATC] code L04AD01), cyclosporine (L04AD01), mycophenolic acid (L04AA06), tacrolimus (L04AD02), sirolimus (L04AA10), everolimus (L04AA18), and other immunosuppressants (L04AX).

To generate a dataset for the HSCT group, claim records with the procedure code X5* were extracted (dataset 1) from Table 30. Dataset 1 was then merged with the data in Table 20 using unique identification codes for the claim records. The merged data were aggregated by patient unit, resulting in claims data for 119 allogeneic and 120 autologous HSCT patients (dataset 2). Patients who died within a year after transplantation were excluded from dataset 2, owing to clinical heterogeneity between those who survived and those who did not survive; consequently, 98 allogeneic HSCT patients and 112 autologous HSCT patients remained. To remove hematopoietic stem cell donors from the allogeneic HSCT group, 29 patients with a diagnosis code of Z523, indicating bone marrow donors, were excluded. Furthermore, patients who underwent transplantation in January or December were excluded to reflect the entire HSCT procedure, resulting in 59 allogeneic HSCT patients and 94 autologous HSCT patients.

One episode of HSCT generally involves the following steps: mobilization for hematopoietic cell collection, peripheral hematopoietic stem cell collection, pre-transplant examination, hospitalization, pre-treatment, HSCT, recovery, and discharge [13]. Among these steps, the pre-transplantation process (i.e., transplantation preparation) takes approximately 1 month [9]. As there were no claim data for the pre-transplantation period of patients undergoing HSCT in January, these patients were excluded from the analysis. As claim records for the initial recovery period may not have been available for patients undergoing HSCT in December, these patients were excluded from analysis. In addition, patients without pre-treatment claim records were removed to reflect the entire procedure, resulting in 56 allogeneic HSCT patients and 89 autologous HSCT patients for the analysis. Finally, only claim records with indications of HSCT (Appendix 2) as the primary diagnosis from Tables 20 and 53 were extracted to analyze the use of inpatient and outpatient healthcare services (Fig. 1).

To generate a dataset for the post-HSCT group, claim records with diagnosis code Z948 from Table 40 were extracted and merged with those from Tables 20 and 30 and then aggregated by patient unit, resulting in claim data for 576 post-HSCT patients. A total of 134 patients who had the HSCT procedure code X5* in Table 30 and 116 patients who did not have diagnostic codes defined as indications for HSCT (Appendix 2) were excluded. Eleven patients who died during the year of data collection were excluded, and 33 patients who took anticancer drugs were excluded to ensure that there were no recurrent patients in the dataset. Consequently, 283 post-HSCT patients were included in this study. The post-HSCT group was divided into a post-allogeneic HSCT group (n = 41) and a post-autologous HSCT group (n = 252), based on the presence of claim records for prescribed immunosuppressants. To remove hematopoietic stem cell donors from the post-allogeneic HSCT group, one patient with a diagnosis code of Z523 (bone marrow donor) was excluded. Finally, only claim records with indications of HSCT (Appendix 2) as the primary diagnosis from Tables 20 and 53 were extracted for data analysis of 40 post-allogeneic HSCT and 252 post-autologous HSCT patients (Fig. 2).

2.4 Data Analysis

To estimate the amount of healthcare services used in the acute and maintenance states of HSCT, we computed the annual average per-capita number of hospitalizations,

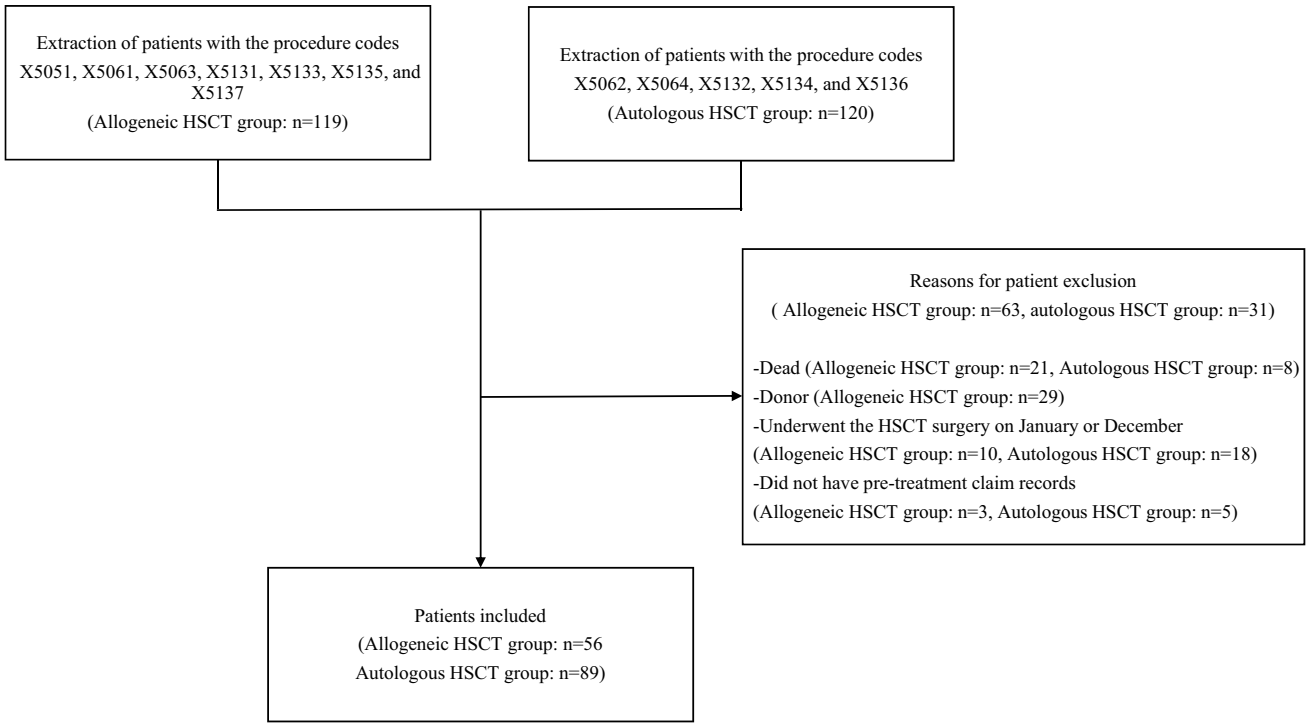

Fig. 1 Process used to identify patients who received HSCT in the current year. *HSCT* hematopoietic stem cell transplantation

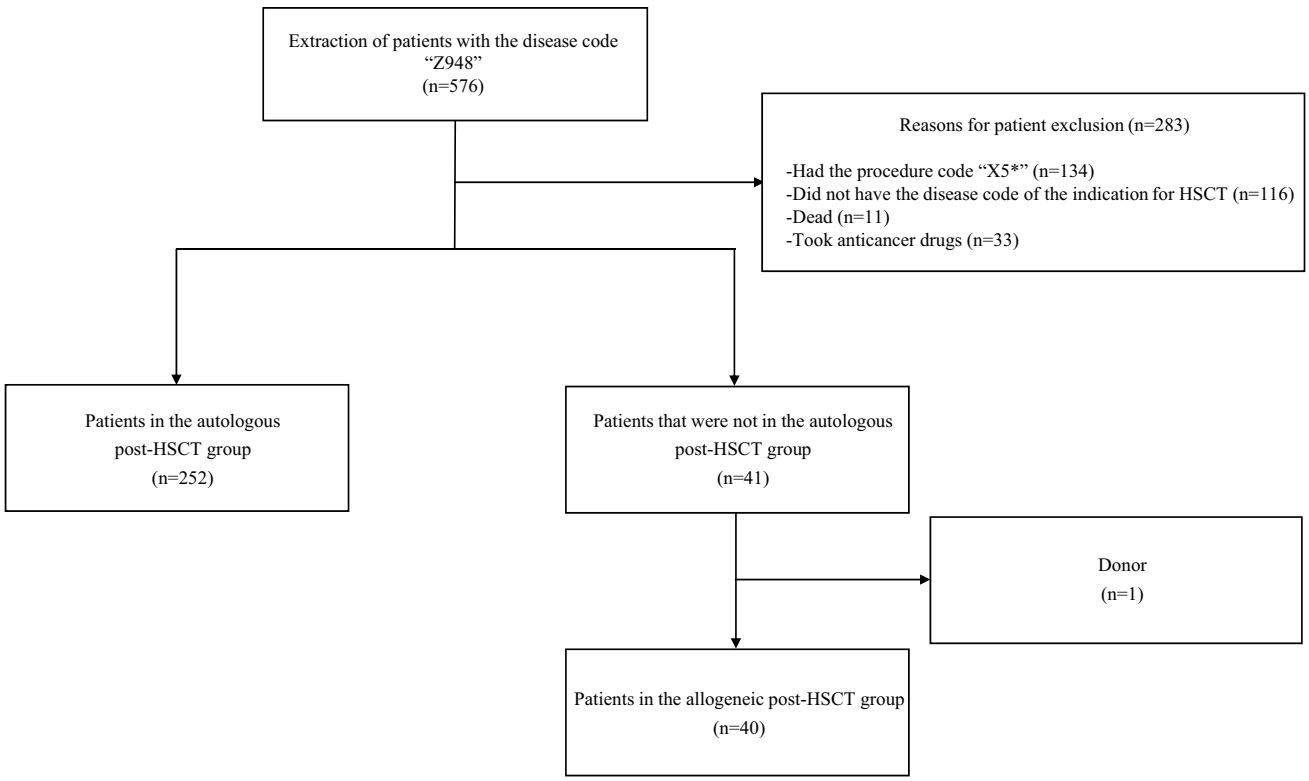

Fig. 2 Process used to identify patients who received HSCT previously. *HSCT* hematopoietic stem cell transplantation

outpatient visits, and inpatient days associated with HSCT for each group. The annual average per-capita costs were also estimated for each group from the insurer's perspective. Expenses for 2016 and 2017 were converted to the present value of 2018 by using the consumer price index in the health sector [14]. All costs were calculated in Korean won and converted to US dollars using the exchange rate of June 29, 2022.

2.4.1 HSCT Group

To calculate the annual healthcare utilization amount and costs for the HSCT group, which covers the 1-month pre-transplantation period to 11 months following transplantation, we defined the index date for each HSCT patient as the date of HSCT (i.e., the date of claim records with the HSCT procedure codes). From the index date, 30-day interval data were built for each patient: 1-month pre-transplantation period (month −1), from 30 days before the index date to 1 day before the index date; first month period (month 1), from the index date to day 30 after the index date; second month period (month 2), from day 31 after the index date to day 60 after the index date; and so on, up to the 11th month period (month 11). As the number of months following transplantation examined in 1-year claim data varies across patients depending on the month of the year in which a patient receives HSCT, not all patients had data for 12 months (i.e., from month −1 through month 11). For example, for those that underwent HSCT in October, claim records in September were used as data for "month −1" and claim records in October, November, and December were used as data for months 1, 2, and 3, respectively. Using the 30-day interval data available for each patient, we calculated the average healthcare utilization amount and costs for each month based on the index date. Subsequently, by summing up the average monthly utilization amount and costs from "month −1" to "month 11," we estimated the average utilization amount and cost of HSCT during the year of HSCT. The numbers of autologous and allogeneic HSCT patients used to compute the average monthly costs by the index date are presented in parentheses for each month in Figs. 3 and 4, respectively.

2.4.2 Post-HSCT Group

The medical expenses for all study participants in the post-HSCT group were estimated from January to December, regardless of when the first claim record was shown during the year. The cost for the month in which no medical use was incurred was estimated to be zero. The annual average utilization and cost were estimated by summing up the average monthly data. All datasets were constructed, and all calculations were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA).

3 Results

3.1 Baseline Characteristics

Table 1 shows the demographic characteristics of the enrolled patients. Regardless of the type of HSCT, male patients accounted for a higher proportion of the cohort than female patients (60.71% vs. 39.29% for allogeneic HSCT and 61.80% vs. 38.20% for autologous HSCT). Patients in their 40s, 50s, and 60s accounted for the largest proportion of the HSCT group. Patients in the post-HSCT group were younger than those in the HSCT group, with more patients in their 10s, 20s, and 30s than those in the HSCT group. Almost no HSCT patients were beneficiaries of the Medical Aid (MA) program, a government-subsidized National Health Security program for the poorest

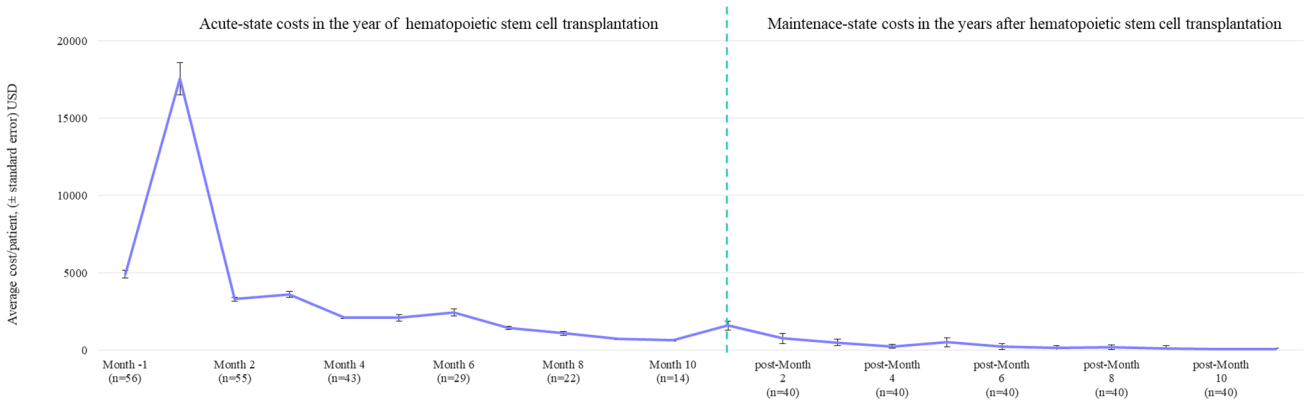

Fig. 3 Monthly healthcare costs for allogeneic HSCT patients. Numbers in parentheses represent the number of allogeneic HSCT patients used to compute average costs for that specific month. *HSCT* hematopoietic stem cell transplantation, *USD* United States dollar

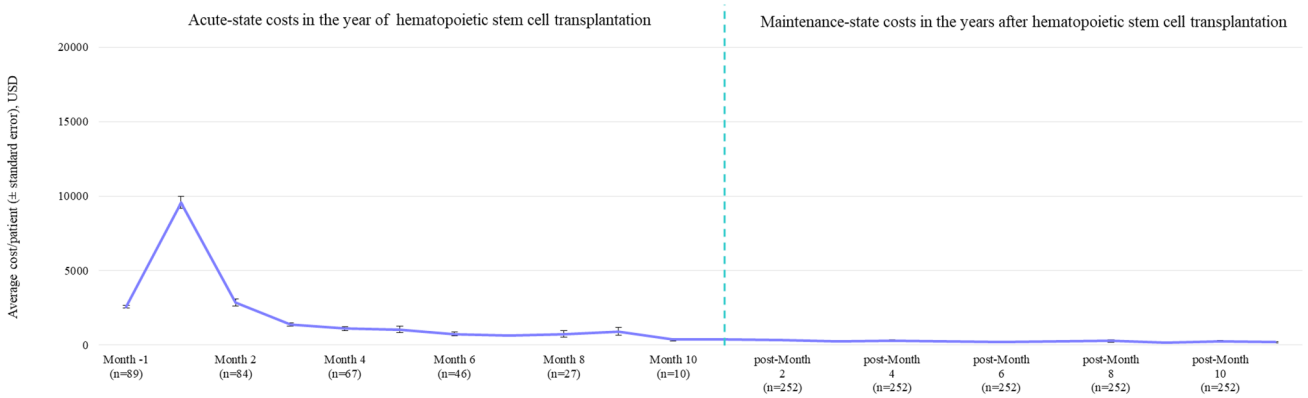

Fig. 4 Monthly healthcare costs for autologous HSCT patients. Numbers in parentheses represent the number of autologous HSCT patients used to compute the average costs for that specific month. *HSCT* hematopoietic stem cell transplantation, *USD* United States dollar

Table 1 Basic characteristics of patients

	Allogeneic HSCT, no. patients (%)		Autologous HSCT, no. patients (%)	
	HSCT group (n = 56 patients)	Post-HSCT group (n = 40)	HSCT group (n = 89)	Post-HSCT group (n = 252)
Gender				
Male	34 (60.71)	23 (57.50)	55 (61.80)	145 (57.54)
Female	22 (39.29)	17 (42.50)	34 (38.20)	107 (42.46)
Age (years)				
< 10	2 (3.57)	4 (10.00)	6 (6.74)	12 (4.76)
10–19	6 (10.71)	7 (17.50)	3 (3.37)	40 (15.87)
20–29	8 (14.92)	3 (7.50)	4 (4.49)	33 (13.10)
30–39	8 (14.92)	11 (27.50)	4 (4.49)	22 (8.73)
40–49	12 (21.43)	7 (17.50)	8 (8.99)	36 (14.29)
50–59	13 (23.21)	6 (15.00)	33 (37.08)	61 (24.21)
60–69	7 (12.50)	2 (5.00)	30 (33.71)	47 (18.65)
≥ 70	0 (0.00)	0 (0.00)	1 (1.12)	1 (0.40)
Type of NHS program enrolled in				
NHI	56 (100.00)	39 (97.50)	88 (98.88)	228 (90.48)
MA	0 (0.00)	1 (2.50)	1 (1.12)	24 (9.52)

HSCT hematopoietic stem cell transplantation, *MA* Medical Aid, *NHI* National Health Insurance, *NHS* National Health Security

class of the population. A higher proportion of MA beneficiaries was observed in the post-HSCT group than in the HSCT group (2.50% and 9.52% in the allogeneic and autologous post-HSCT groups, respectively).

3.2 Healthcare Utilization

During the year of transplantation, allogeneic HSCT patients had an average of 8.14 hospitalizations, 35.80 outpatient visits, and 97.16 hospitalization days (Table 2). The mean length of stay (LOS) per hospitalization was 14.72 days. In the years after allogeneic HSCT, the amount of healthcare utilization decreased to 2.93 hospitalizations, 29.40 outpatient visits, 50.95 hospitalization days, and 20.84 days LOS per hospitalization.

In the autologous HSCT group, one patient had 8.08 hospitalizations, 33.58 outpatient visits, 73.04 hospitalization days, and 10.63 days LOS per hospitalization during the year of transplantation. Similar to the post-allogeneic HSCT group, the amount of healthcare utilization in the post-HSCT period decreased to an annual average of 1.72 hospitalizations, 16.38 outpatient visits, 30.11 hospital days, and 19.29 days LOS per hospitalization.

Table 2 Estimated annual healthcare utilization amount and costs of HSCT

Type of utilization and cost	Annual average per patient (SD)			
	During the year of HSCT (acute state)		During the years after HSCT (maintenance state) [% change from acute state]	
	Allogenic HSCT (n = 56)	Autologous HSCT (n = 89)	Post-allogenic HSCT (n = 40)	Post-autologous HSCT (n = 252)
Healthcare utilization				
No. hospitalizations	8.14 (5.01)	8.08 (6.35)	2.93 (3.58) [−64.00]	1.72 (4.58) [−78.71]
No. outpatient visits	35.80 (20.47)	33.58 (19.47)	29.40 (17.54) [−17.88]	16.38 (20.16) [−51.22]
Hospitalization days	97.16 (60.59)	73.04 (61.16)	50.95 (45.86) [−47.56]	30.11 (49.71) [−58.78]
LOS per hospitalization	14.72 (9.03)	10.63 (5.69)	20.84 (15.52) [+41.58]	19.29 (16.58) [+81.47]
NHI-covered medical costs, USD				
Base-case analysis	40,876	22,863	3660 [−91.05]	3168 [−86.14]
SA1	–	–	2772	3144
SA2	38,776	20,931	6612	4752

HSCT hematopoietic stem cell transplantation, *LOS* length of stay, *NHI* National Health Insurance, *SA* sensitivity analysis, *SD* standard deviation, *USD* United States dollar

3.3 Healthcare Costs: Base-Case Analysis

3.3.1 Allogeneic HSCT

During the year of allogeneic HSCT, the highest cost was incurred in the month of HSCT (i.e., month 1, $17,549/person), and the second highest cost was incurred in the month prior to HSCT (i.e., month −1, $4909/person) (Fig. 3). The monthly medical costs gradually declined after month 3 and became relatively constant from month 7. With no observation in month 11, we assumed that the cost in month 11 was the same as the average monthly costs from month 7 to month 10 ($971/person). Thus, the annual average medical cost in the year of allogeneic HSCT was estimated to be $40,876 per person (the sum of the costs from month −1 to month 10 plus $971 for month 11) (Table 2).

For the post-allogeneic HSCT group, the highest cost was incurred in post-month 1 ($1586/person, Fig. 3); however, the cost remained relatively constant from post-month 3 to post-month 8 (Fig. 3). Assuming that the monthly medical costs incurred in each month of the post-years after allogeneic HSCT are equal to the average monthly costs from post-month 3 to post-month 8 ($305/person), the annual average medical cost in the years after transplantation was estimated to be $3660 per person ($305/person × 12 months) (Table 2).

3.3.2 Autologous HSCT

During the year of autologous HSCT, the highest cost was incurred in month 1 ($9572/person), and the second and third highest costs were incurred in month 2 ($2861/person) and month −1 ($2568/person), respectively. From months 4 to 10, the costs became relatively constant (Fig. 4). Assuming that the medical costs incurred on month 11 were the same as the average monthly costs from month 4 to month 10 ($871/person), the annual average cost in the year of autologous HSCT was estimated to be $22,863 per person (sum of the costs from month −1 to month 10 plus $871 per person for month 11) (Table 2).

For the post-autologous HSCT group, the highest costs were incurred in post-month 1 ($375/person); however, the monthly costs were relatively constant from post-month 1 to post-month 11 (Fig. 4). Assuming that the monthly costs incurred in each month of the post-years after autologous HSCT are equal to the average monthly costs from post-month 1 to post-month 11 ($264/person), the annual average medical costs in the subsequent years after autologous HSCT were estimated to be $3168 per person ($264/person × 12 months).

3.4 Healthcare Costs: Sensitivity analysis

3.4.1 Sensitivity Analysis 1

The monthly medical costs were relatively constant at month 7 in the allogeneic HSCT group (Fig. 3). Therefore, for the post-allogeneic HSCT group, we can assume that the monthly costs stabilized from post-month 6. With this assumption, the monthly medical costs at the post-allogeneic HSCT group would be the same as the medical costs at post-month 6 ($231/person), and the total annual costs were estimated to be $2772 per person based on that value ($231/person × 12 months).

The monthly medical costs of the autologous HSCT group were found to stabilize from month 4 onwards. According to the above logic, it can be assumed that the monthly costs of the post-autologous HSCT group would stabilize after 3 months. Therefore, the monthly costs of the post-autologous HSCT group were assumed to be the same as the medical costs at post-month 3 ($262/person). Thus, the total annual cost was estimated to be $3144 per person ($262/person × 12 months).

3.4.2 Sensitivity Analysis 2

The monthly medical cost of allogeneic HSCT stabilized from month 7 to post-month 11 (Fig. 3). Therefore, it was assumed that $551/person (average from month 7 to post-month 11) was steadily incurred from 7 months after allogeneic HSCT. Thus, the total annual costs were estimated to be $38,776/person (sum of the costs from month −1 to month 6 plus $551/person × 5 months) for the allogeneic HSCT group and $6612/person ($551/person × 12 months) for the post-allogeneic HSCT group.

The monthly medical cost of autologous HSCT was constant between month 6 and post-month 11 (Fig. 4). Accordingly, a cost of $396/person (average from month 6 to post-month 11) can be incurred beyond 6 months after autologous HSCT. Thus, the total annual costs were estimated to be $20,931/person (sum of the costs from month −1 to month 5 plus $396/person × 6 months) for the autologous HSCT group and $4752/person ($396/person × 12 months) for the post-autologous HSCT group.

4 Discussion

Using an incidence-based COI approach, the results of this study revealed a substantial difference in monthly costs based on the time of the HSCT procedure. For the allogeneic HSCT group, the average monthly NHI-covered medical cost per patient was highest during the month of HSCT ($17,549/patient). The cost from 1 month prior to the operation (month −1, $4909/patient) was higher than the monthly cost from month 2 to month 11. The expenses from 1 month before to 3 months after transplantation ($29,357/patient) accounted for approximately 71.82% of the total expenses in the year of allogeneic HSCT ($40,876/person). In the autologous HSCT group, the average cost in the month of HSCT was $9572/patient, which was the highest. The monthly expenses corresponding to 1 month before and after the HSCT ($2568/patient and $2861/patient, respectively) were higher than those in the other months. The costs from 1 month before to 3 months after transplantation ($16,387/patient) accounted for approximately 71.67% of the total cost in the year of autologous HSCT ($22,863/patient).

A significant decline in healthcare utilization and costs occurred after HSCT. In the allogeneic group, the annual average number of hospitalizations, outpatient visits, hospitalization days, and annual cost per patient decreased by 64.00%, 17.88%, 47.56%, and 91.05%, respectively, in subsequent years (Table 2); in the autologous group, these utilization measures decreased by 78.71%, 51.22%, 58.78%, and 86.14%, respectively. However, the average LOS per hospitalization increased by 41.58% and 81.47% in the allogeneic and autologous groups, respectively. These results imply that the frequency of healthcare use in the maintenance phase following HSCT decreases compared to that of the acute state of HSCT; however, once hospitalization occurs, a longer LOS per hospitalization is required.

HSCT is associated with high costs and long hospitalization due to the pre-treatment process, such as systemic radiation or high-dose chemotherapy performed before transplantation. Owing to frequent imaging and diagnostic tests, hospitalization, and medications prescribed immediately after transplantation, medical expenses are inevitably higher in the early period than in the later period following transplantation. In a study conducted in the United States [15], the amount and cost of healthcare use for the first 100 days after HSCT, which accounted for 71.58% and 70.94%, respectively, of the total amount and cost of healthcare use in the year of HSCT, were higher than those in the latter period, regardless of donor type. According to a study conducted in Sweden [16], the annual healthcare cost of allogeneic HSCT was $133,506 per patient, which accounted for approximately 81.57% of the total healthcare costs for 5 years after undergoing the operation. In addition, a cost reduction of 77.40% occurred from the year of transplantation to subsequent years. The results of these previous studies concur with our results, which highlight the appropriateness of our alternative approach of estimating COI for allogeneic and autologous HSCT by combining acute and maintenance-state costs of HSCT based on 1-year cross-sectional claim data.

This study has some limitations. First, owing to the nature of claim records, diagnosis or procedure codes can be omitted or miscoded. Consequently, patients who met the criteria of this study may not have been included or may have been classified into the incorrect patient group. Second, direct medical expenses may have been underestimated as non-insurance-covered costs, and patients who died after undergoing HSCT were excluded. Third, because 1-year data were used, some included individuals may have died within the first year, but after the time of the available data. Fourth, the total hospitalization period of 73–97 days in the HSCT group might have been underestimated as patients who underwent HSCT in January and December were excluded during the HSCT group selection process. Fifth, the post-HSCT group may have included a variety of patients from different periods. In both the post-allogeneic HSCT and post-autologous HSCT groups, the costs in the earlier months were higher than those in the latter months. This finding suggests that in the earlier

months, patients who had undergone HSCT less than a year ago were more likely to be included. To avoid overestimation of the maintenance-state costs of HSCT, a series of sensitivity analyses were performed by assuming the average cost from the time point at which the monthly cost began to be constant, similar to the maintenance-state cost. In addition to sensitivity analyses, further research is needed to test for external validity by comparing the findings with long-term data. Finally, our study could not estimate the total lifetime cost from HSCT initiation to death. If we can incorporate the average survival time in the maintenance state, it may be possible to estimate the total lifetime costs in future studies.

5 Conclusion

Despite the above limitations, this study offers an alternative method for calculating incidence-based COI using 1-year claim data when long-term data are unavailable. According to Figs. 3 and 4, the acute-state and maintenance-state cost graphs are connected. This finding supports the validity of the methodology used in this study. It would be applicable to health conditions such as HSCT, where acute and maintenance states can be distinguished based on diagnosis and procedure codes, and where the prescribed drugs are included in the claim records.

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Declarations

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Conflict of interest The authors declare no conflicts of interest.

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Consent to participate Not applicable.

Consent for publication (from patients/participants) Not applicable.

Availability of data and material The data for these analyses are available upon the researcher's request through the open system of the Health Review and Assessment Service (HIRA) (http://opendata.hira.or.kr). Because HIRA evaluates the research purpose and provides raw data to researchers after their approval, interested researchers can access the data after paying the charge for the data.

Code availability Code for data cleaning and analysis can be provided if it is requested.

Authors' contributions SK constructed the data set, performed the analyses, and wrote the first draft of the manuscript. H-YK reviewed and revised the manuscript accordingly.

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