Burden of neutropenia-related hospital readmissions among hematopoietic cell transplant recipients

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INTRODUCTION

- Hematopoietic cell transplantation (HCT) is a potentially curative therapy for many patients with hematologic malignancies.[1]
- The procedure involves conditioning chemotherapy and other immunosuppressive therapies including therapies for opportunistic infections, such as ganciclovir, which frequently result in neutropenia (i.e. a low number of circulating neutrophils in the blood).[2]
- Neutrophils play a vital role in the innate immune response against pathogens and a drop in absolute neutrophil count increases susceptibility to opportunistic infections in patients who receive HCT. [2,3] A quantitative relationship between the severity of neutropenia and the frequency and severity of opportunistic infection is well established.[4]
- HCT recipients who develop acute neutropenia and subsequent opportunistic infection have a high risk of mortality.[2]
- Some studies have evaluated hospital resource use, associated costs, and mortality among cancer patients with acute neutropenia;[5,6] however, there is little information from the hospital perspective for patients who have undergone HCT.

PURPOSE

- The purpose of this study was to examine the occurrence of hospital readmissions involving neutropenia among HCT recipients, as well as associated costs from a hospital perspective.

METHODS

Study population

- Patients who received an HCT between January 2009 and September 2013 were identified from hospital discharge records based on the International Classification of Diseases, Ninth Revision (ICD-9) codes in the Premier Hospital database. The first HCT procedure was defined as the index event. Hospital readmissions related to neutropenia were identified with ICD-9 codes for neutropenia as either primary or secondary hospital discharge diagnosis codes. In the Premier Hospital database only the readmissions to the same hospital or hospital system can be followed longitudinally.

Demographics and clinical characteristics

- Demographics, including age, sex, US region of residence, race/ethnicity, health plan type, urban/rural hospital setting, hospital teaching status, hospital size, and clinical characteristics, including Charlson Comorbidity Index (CCI) score and All Patient Refined Diagnosis Related Group (APR-DRG) severity of illness level were evaluated during the index hospitalizations and during the 12 months prior to HCT.
  - The CCI is a commonly used method to assess the overall comorbidity levels among patients. It is a weighted score based on the diagnosis of 19 specific diseases.
  - APR-DRG is a method designed to identify patients by disease severity level. There are 4 different levels of severity: Level 1–Minor, Level 2–Moderate, Level 3–Major, Level 4–Extreme.

Outcome measurements

- Frequency of hospital readmissions involving neutropenia (documented by diagnostic codes) up to a 12-month period following the discharge date of the index HCT hospitalization (follow-up period) was evaluated.
- Hospital resource utilization, in terms of hospital length of stay (LOS) of readmissions, and costs were determined based on discharge records.

RESULTS

Patients

- Of patients who received allogeneic HCT(allo-HCT) (n=1617), mean age was 42.5 years, 38.5% were ≤40 years of age, and 57.0% were male **(Table 1)**.
  - Mean CCI score was 2.3, indicating the average number of comorbid conditions per patient **(Table 2)**.
  - Greater than one-third of allo-HCT recipients had an APR-DRG illness severity level of 3–Major and 4–Extreme **(Table 2)**.
  - During index HCT hospitalizations 118 deaths occurred, resulting in an evaluable population of 1499 allo-HCT patients.
- Of patients who received autologous HCT (auto-HCT) (n=2776), mean age was 55.0 years, 15.1% were ≤40 years of age, and 58.5% were male **(Table 1)**.
  - Mean CCI score was 3.0, indicating the average number of comorbid conditions per patient **(Table 2)**.
  - The majority (57.0%) of auto-HCT recipients had an APR-DRG illness severity level of 1–Minor **(Table 2)**.
  - During index HCT hospitalizations 39 deaths occurred, resulting in an evaluable population of 2737 auto-HCT patients.

Table 1. Demographics

Demographic	Allo-HCT n=1617		Auto-HCT n=2776	
Age (years)				
Mean (SD)	42.5 (20.7)		55.0 (15.5)	
Median	48		59	
	n	**%**	**n**	**%**
Age group				
0–20 years	325	20.1	125	4.5
21–40 years	297	18.4	294	10.6
41–50 years	262	16.2	352	12.7
51–60 years	367	22.7	769	27.7
≥61 years	366	22.6	1236	44.5
Adult/Pediatric				
Adult (≥18 years old)	1328	82.1	2679	96.5
Pediatric (<18 years old)	289	17.9	97	3.5
Sex				
Female	696	43.0	1152	41.5
Male	921	57.0	1624	58.5
US region				
Midwest	133	8.2	469	16.9
Northeast	909	56.2	1118	40.3
South	554	34.3	989	35.6
West	21	1.3	200	7.2
Race/Ethnicity				
Black	179	11.1	398	14.3
Hispanic	37	2.3	37	1.3
Other	375	23.2	589	21.2
White	1026	63.5	1752	63.1
Urban/Rural hospital				
Rural	92	5.7	152	5.5
Urban	1525	94.3	2624	94.5
Teaching				
No	57	3.5	488	17.6
Yes	1560	96.5	2288	82.4
Number of beds				
<200	127	7.9	116	4.2
200–399	140	8.7	454	16.4
400–599	180	11.1	455	16.4
≥600	1170	72.4	1751	63.1

Allo-HCT: allogeneic hematopoietic cell transplantation; Auto-HCT: autologous HCT; SD: standard deviation.

Table 2. Clinical characteristics

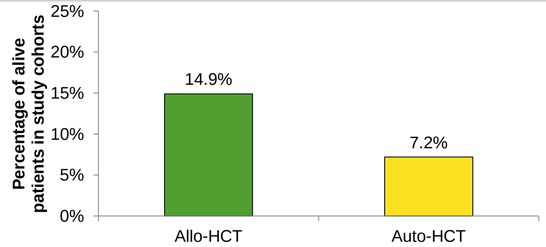
Clinical characteristic	Allo-HCT n=1617		Auto-HCT n=2776	
CCI				
Mean (SD)	2.3 (1.7)		3.0 (1.8)	
Median	2		2	
	n	**%**	**n**	**%**
CCI group				
0	257	15.9	21	0.8
1–2	830	51.3	1540	55.5
3–4	415	25.7	847	30.5
≥5	115	7.1	368	13.3
APR-DRG severity level				
1–Minor	466	28.8	1583	57.0
2–Moderate	551	34.1	968	34.9
3–Major	263	16.3	221	8.0
4–Extreme	337	20.8	4	0.1

Allo-HCT: allogeneic hematopoietic cell transplantation; Auto-HCT: autologous HCT; SD: standard deviation; CCI: Charlson Comorbidity Index; APR-DRG: All Patient Refined Diagnosis Related Group.

Outcomes

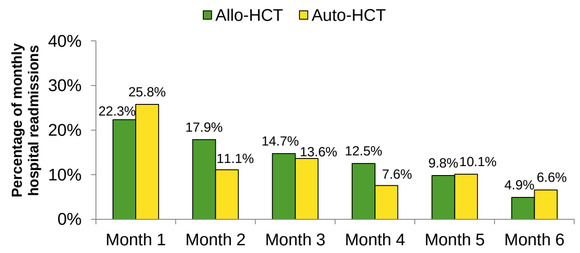
- Among patients alive post discharge who had an allo-HCT and those who had an auto-HCT, 14.9% (n=224) and 7.2% (n=198) had a hospital readmission involving neutropenia, respectively **(Figure 1)**.

Figure 1. Frequency of hospital readmissions involving neutropenia during a 12 month follow-up period



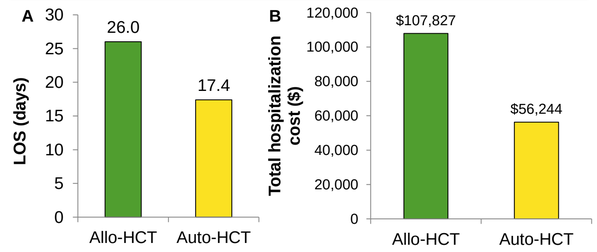
- Among allo-HCT recipients with hospital readmissions involving neutropenia, 22.3% occurred within 1 month and 54.9% occurred within the first 3 months **(Figure 2)**.
- Among auto-HCT recipients with hospital readmissions involving neutropenia, 25.8% occurred within 1 month and 50.5% occurred within the first 3 months **(Figure 2)**.

Figure 2. Percentage* of monthly hospital readmissions involving neutropenia during the follow-up period for months 1–6



*Percentage is calculated as the number of patients with hospital readmissions in each month divided by number of all patients with readmissions in the follow-up period.

Figure 3. A) Mean length of hospital stay (LOS) and B) mean total hospital costs for hospital readmissions involving neutropenia



- The mean LOS for readmissions involving neutropenia per patient were 26.0 days (standard deviation [SD]: ±26.1, median: 19) and 17.4 days (SD: ±17.4, median: 14) for patients who received allo-HCT and auto-HCT, respectively **(Figure 3A)**.
- Mean total hospitalization costs per patient for hospital readmissions involving neutropenia were $107,827 (SD: ±$134,033, median: $59,993, Quartile 3 (Q3): $136,240, Quartile 1 (Q1): $19,187) and $56,244 (SD: ±$75,378, median: $36,265, Q3: $62,345, Q1: $11,622) for patients who received allo-HCT and auto-HCT, respectively **(Figure 3B)**.

LIMITATIONS

- While the Premier Hospital database has information from a large number of hospitals across the United States, it may not be representative of all types of transplant centers. Thus, the study findings may not be representative of all HCT transplant recipients.
- While errors in the hospital administrative data and diagnosis coding could potentially have occurred in the database, the Premier Hospital database is considered a high quality data source that has been widely used in many other real-world research studies.
- In the Premier Hospital database only the readmissions to the same hospital or hospital system can be followed longitudinally and analyzed. Thus, the frequency of hospital readmissions determined in this study is likely to have been underestimated.

CONCLUSIONS

- **Among allo-and auto-HCT recipients approximately 15% and 7%, respectively, had hospital readmissions involving neutropenia.**
- **Hospital readmissions involving neutropenia were associated with substantial hospital resource use (allo-HCT: 26.0 days, auto-HCT: 17.4 days) and were costly, especially among allo-HCT recipients (allo-HCT: $107,827, auto-HCT: $56,244) .**
- **This large scale national study shows that neutropenia continues to present challenges in the clinical management of HCT recipients and represents a substantial healthcare and economic burden to hospitals.**

REFERENCES

1. Brennan TV, et al. *Front Immunol* 2015;6:101; 2. Saria M. *Clin J Oncol Nurs* 2011;15:133–9; 3. Safdar A, et al. *Clin Infect Dis* 2011;53:798–806; 4. Bodey GP, et al. *Ann Intern Med* 1966;64:328–40; 5. Michels SL, et al. *Pharmacoeconomics* 2012;30:809–23; 6. Dulisse B. et al. *J Med Econ* 2013;16:720–35

DISCLOSURES

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