Identification of Risk Factors for Chemotherapy-Related 30-Day Readmissions

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Abstract

Purpose: The goal of this study was to develop a method for practitioners to evaluate both quality of care delivered to patients receiving chemotherapy and illicit risk factors for 30-day chemotherapy-related readmissions (CRR). **Methods:** Midas+ DataVision Readmission Tool Pack (Version 2.x) was used to retrospectively identify patients who received inpatient chemotherapy from April 2010 through May 2013. The population was screened for unscheduled admissions within 30 days after discharge. A multidisciplinary team was used to attribute readmissions to chemotherapy administration. Demographic information and oncology-specific characteristics were collected. The CRR rate and relative risk for readmission were calculated for each characteristic. **Results:** A baseline CRR rate of 11.1% was established. Risk factors associated with an increased risk for experiencing a CRR included age of 65 years or older, hematologic cancer diagnosis, first cycle chemotherapy, Medicare coverage, discharge to a skilled nursing facility, and anthracycline administration. **Conclusions:** A baseline CRR rate was established. Institution-specific 30-day CRR risk factors were elucidated. Modifiable risk factors included discharge to a skilled nursing facility and administration of an anthracycline. Further investigation for opportunities for quality improvement in these 2 risk factors is a topic for future research. Expanded research into chemotherapy-related toxicities requiring inpatient admission/readmission outside of clinical trials is warranted. (J Natl Compr Canc Netw 2015;13:748–754)

Background

The American Cancer Society estimates that more than 1.6 million new cancer cases were diagnosed in the United States in 2014.¹ Chemotherapy is often an option for the treatment of cancer either alone or as adjunct to radiation or surgery. It is well documented that chemotherapeutic agents cause adverse drug reactions ranging from minor reactions to severe, life-threatening conditions that may result in hospitalization.² The latter could be of use to medical professionals in identifying patients who are at risk for hospital admission and readmission.

A study completed for the Centers for Medicare & Medicaid Services (CMS) in 2011 evaluated all-condition readmission rates in patients aged 65 years or older across more than 4900 hospitals. The oncology population (n>80,000) had the highest 30-day unplanned and

planned readmission rates (25.0% and 17.7%) when compared with populations such as medicine (18.3% and 2.0%), surgery (12.7% and 2.6%), and cardiovascular (15.4% and 3.1%).² This report excluded cancers with a high mortality rate, which was defined as more patients dying postdischarge without being readmitted than those who were readmitted; examples of high-mortality-risk cancers included breast, colon, lung, and pancreatic. Without these exclusions, the readmission rates may have been even higher. Additionally, exclusion of these cancers highlights the difficulties in assessing readmission quality indicators in the oncology population.

A retrospective cohort study was conducted among the 7 acute care hospitals of the Baylor Health Care System (BHCS), which included adults aged 65 years or older who were admitted from July 2002 through June 2004. The primary outcome was readmission to any of the BHCS hospitals within 30 days of discharge from the patient's first admission. Patients admitted for chemotherapy were not specifically evaluated; however, patients with a diagnosis of metastatic cancer experienced a 30-day readmission rate of 17% with a relative risk (RR) of 1.48.³

At Johns Hopkins Hospital, a prospective study was conducted to determine whether direct communication

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between inpatient and outpatient providers at time of discharge had an impact on 30-day readmissions. The analysis of inpatient services that occurred from September 2010 to December 2011 included 6635 hospitalizations. Although administration of cancer chemotherapeutics occurred in only 8.8% of these index admissions, of the potentially avoidable readmissions, 39.5% were from this group.⁴ The authors concluded that the frequency of interprovider communication did not impact readmission rates.

In the outpatient setting, The North Shore Medical Center Cancer Center (NSMC-CC) published chemotherapy-related admission data from October 2001 to December 2003. Their rate of admissions attributed to treatment in patients receiving outpatient chemotherapy was 32%.⁵ A medical team comprising physicians, nurses, and pharmacists was used to determine which cases were hypothesized to be chemotherapy-related. A strength of this study was the inclusion of all cancers despite mortality risk. Furthermore, the research group looked for trends on a monthly basis and intervened on their population based on their findings. In one such example, the investigators identified several patients receiving high-dose corticosteroids being admitted because of hyperglycemia. The group intervened by checking the blood glucose of patients more frequently and reported reducing the number of admissions from hyperglycemia to zero.⁵

Subsequently, the NSMC-CC reported the results of a follow-up prospective cohort study. The population included adult patients with cancer who received outpatient chemotherapy between January 2003 and December 2006. The authors found that 8.7% of 2068 ambulatory chemotherapy recipients experienced chemotherapy-related hospitalizations, with those who were hospitalized experiencing a 0.9% mortality rate.⁶ An assessment of the risk of chemotherapy-related admissions in this cohort included higher comorbidity scores and higher mean creatinine values. It is unknown how the results of these 2 studies from NSMC-CC in the outpatient setting correlate to the risks of chemotherapy-related readmissions (CRRs) after inpatient chemotherapy administration.

The Hospital Readmissions Reduction Program of the Affordable Care Act of 2010 is starting to affect how hospitals are being reimbursed for hospital stays. In October 2012, CMS began calculating 30-day readmission payment adjustments for the diagnoses of acute myocardial infarction (MI), pneumonia, heart failure, and

stroke. If a hospital exceeds the calculated average readmission rate, they will eventually be penalized up to 1% of their total Medicare reimbursements. Current recommendations call for a multidisciplinary, coordinated effort to identify potential risk factors for readmission.²

With the recent changes to repayment structures by CMS for selected diagnoses and the prospect of that list growing, it is imperative for institutions to take measures to decrease 30-day unplanned readmissions for both patient quality of life and institutional finances. Although the repayment structure as it relates to the oncology population has not been targeted by CMS to date, this does not preclude medical professionals from intervening in meaningful ways to prevent hospital readmissions after administration of chemotherapy. To date, the available literature evaluating the oncology population often excludes major cancer types, focuses on admissions after outpatient administration of chemotherapy, and is not specific to admission/readmission risk based on chemotherapy classes. However, no consensus exists on the best methodology for establishing preventable readmissions.⁷ This study sought to identify readmission risk factors after inpatient chemotherapy administration in a tertiary referral center in a comprehensive cancer population.

Methods

Institution Information

Lakeland Regional Health (LRH) is an 851-bed tertiary referral center located in Lakeland, Florida. LRH contains a 44-bed oncology unit with a daily census of approximately 35 patients consisting of both solid and hematologic tumors. Services for pediatric cancers and bone marrow transplants are not provided at LRH.

Approval of Study Design

This retrospective study was approved by the Institutional Review Board at LRH.

Eligibility

Adult patients aged 18 years and older who received at least one inpatient chemotherapy regimen and were discharged from LRH between April 1, 2010, and May 31, 2013, were eligible for inclusion in the analysis. Patients who received multiple chemotherapeutic regimens were included each time they were admitted and received chemotherapy. Patients were excluded if they underwent surgery during admission for reasons other than biopsy or port placement, left against medical ad-

vice, or were transferred to another facility for care. Readmissions were identified as an unplanned admission within 30 days of initial discharge date.

Patient Identification

Midas+ DataVision Readmission Tool Pack (Version 2.x) was used to identify the index population of patients who received inpatient chemotherapy between April 1, 2010, and May 30, 2013. Midas+ searched all inpatient admissions during the study time frame for encounters with the ICD-9 code V58.11, “encounter for antineoplastic chemotherapy.” The index population was then screened by Midas+ for unscheduled admissions within 30 days after discharge regardless of readmitting diagnosis or ICD-9 code. Criteria for CRR included diagnosis of febrile neutropenia, other known toxicity of administered chemotherapy agent, and documented diagnosis of CRR by the oncologist. A multidisciplinary panel (medical oncologist, oncology nurse, oncology pharmacist) was used to determine which readmissions were attributable to chemotherapy administration; these constituted the CRR population.

Data Collection

Data collected included cancer diagnosis, age, insurance type, distance from hospital, history of chronic obstructive pulmonary disease/MI/congestive heart failure, chemotherapy agents administered, cycle of chemotherapy, line of chemotherapy, length of stay, discharge disposition, days to readmission, readmission diagnosis, length of readmission, readmission discharge disposition, and mortality rate (Tables 1 and 2). Distance from hospital was calculated by entering the patient’s zip code of their home address into Google Maps with LRH as the destination. Midas+ provided baseline characteristics, and those that were not provided were collected through manual chart review.

Statistical Methods

The RR for experiencing a CRR was calculated for each of the collected data points. Differences between patients who experienced a CRR and those who did not were tested using a 2-tailed z-test, with a *P* value less than .05 denoting significance. A 95% CI was also calculated. For nonmutually exclusive data (eg, chemotherapy agent administered), patients who received a given chemotherapy agent were compared against those who did not. Doing so led to a larger sum of admissions tested for all chemotherapy agents than actually occurred (Table 3).

Results

Midas+ identified 618 patients as having received chemotherapy during the study period. Of these, 612 patients met inclusion criteria as index chemotherapy admissions (see Figure 1 for exclusion details). Notably, 4 patients were admitted to receive it but were unable to receive chemotherapy on admission because of poor clinical status. Per protocol, these 4 patients were not assessed as CRRs.

Midas+ was then used to identify unplanned admissions within 30 days for each of the 612 index chemotherapy admissions. This yielded 230 unplanned readmissions for an initial readmission rate of 37.2%. During manual chart review, 112 patients (48.7%) were found to be admissions that were unplanned for chemotherapy administration. These admissions were excluded from the CRR population. Midas+ provided 23 (10%) duplicate results, which were also excluded, yielding a total of 95 readmissions. These readmissions were then screened by the multidisciplinary panel of oncology health care professionals to determine which were attributable to chemotherapy toxicities. In total, 68 patients were found to have experienced a CRR, establishing an overall CRR rate of 11.1%.

Among demographic and admission risk factors, those resulting in a higher rate of readmission included patient age older than 65 years (RR, 1.92; 95% CI, 1.23–2.99; *P*=.003); hematologic cancer diagnosis (RR, 2.47; 95% CI, 1.54–3.94; *P*<.0001), and specifically, diagnosis of leukemia (RR, 2.13; 95% CI, 1.25–3.62; *P*=.005); Medicare coverage (RR, 1.79; 95% CI, 1.14–2.79; *P*=.009); longer primary length of stay of 4 to 6 days (RR, 1.75; 95% CI, 1.12–2.74; *P*=.013); first cycle of chemotherapy (RR, 1.95; 95% CI, 1.24–3.06; *P*<.0037); and discharge to a skilled nursing facility (RR, 3.41; 95% CI, 1.58–8.09; *P*=.004). Table 1 includes a statistical analysis detailing these risk factors. Among classes of chemotherapy agents, the anthracyclines were associated with an increased risk of a CRR (RR, 1.91; 95% CI, 1.21–3.02; *P*=.013). Table 3 includes a statistical analysis of chemotherapy agents.

Febrile neutropenia was the most common primary diagnosis, occurring in 58.8% (*n*=40) of the CRR population. Other adverse effects leading to hospitalization included diarrhea, dehydration, and pancytopenia/thrombocytopenia, but each accounted for less than 10% of all readmission

Chemotherapy-Related Readmissions

Table 1 Demographic and Admission Information

	Chemotherapy Admissions (N=612)	CRR Population (N=68)	Relative Risk (95% CI)	P Value
Age (y)				
≥65	186	31 (16.7%)	1.92 (1.23–2.99)	.003
<65	426	37 (8.6%)	0.52 (0.33–0.81)	.003
Mean	57	58	–	–
Cancer diagnosis ^a				
Hematologic	261	44 (16.9%)	2.47 (1.54–3.94)	<.0001
Solid	351	24 (6.8%)	0.41 (0.25–0.65)	<.0001
Insurance type				
Private	206	25 (12.1%)	1.09 (0.70–1.74)	.70
Medicaid	167	8 (4.8%)	0.34 (0.17–0.70)	.001
Medicare	221	35 (15.8%)	1.79 (1.14–2.79)	.009
Distance from hospital				
<10 miles	271	33 (12.1%)	1.19 (0.76–1.85)	.58
10–25 miles	216	21 (9.7%)	0.82 (0.50–1.33)	.42
>25 miles	125	14 (11.2%)	1.01 (0.58–1.76)	.21
History of COPD				
Yes	71	7 (9.8%)	0.96 (0.46–2.01)	.88
No	584	61 (10.4%)	1.04 (0.48–2.19)	.88
History of myocardial infarction				
Yes	28	5 (17.8%)	1.67 (0.72–3.78)	.25
No	584	63 (10.8%)	0.61 (0.27–1.38)	.12
History of congestive heart failure				
Yes	6	0 (0%)	0 (N/A)	N/A
No	606	68 (11.2%)	^a	^a
Primary admission length of stay (d)				
1–3	317	21 (6.6%)	0.42 (0.25–0.68)	.0002
4–6	206	32 (15.5%)	1.75 (1.12–2.74)	.013
≥7	89	15 (16.8%)	1.66 (0.98–2.82)	.06
Chemotherapy cycle				
First	241	38 (15.8%)	1.95 (1.24–3.06)	.0037
Subsequent	371	30 (8.1%)	0.51 (0.33–0.80)	.0037
Chemotherapy line				
First	532	61 (11.5%)	1.31 (0.62–2.76)	.48
Subsequent	80	7 (8.6%)	0.76 (0.36–1.61)	.48
Discharge disposition				
Home/self-care	571	59 (10.3%)	0.44 (0.23–0.81)	.011
Home-health service	27	5 (18.5%)	1.71 (0.75–3.90)	.19
Skilled nursing facility	11	4 (36.4%)	3.41 (1.58–8.09)	.0004

Abbreviations: COPD, chronic obstructive pulmonary disease; CRR, chemotherapy-related readmission; N/A, not applicable.

^aSee Table 2 for breakdown of cancer diagnoses.

cases (Table 4). One case had a primary admission diagnosis of percutaneous endoscopic gastrostomy (PEG) tube malfunction and methotrexate toxicity listed as a secondary diagnosis. Per protocol, this was labeled with the primary admission (PEG tube malfunction) in Table 4.

The median duration of discharge before a CRR was 11 days (interquartile range [IQR], 5–14), which corresponds with the anticipated time for a chemotherapy nadir. For CRRs, mean

length of stay was 11 days, with a median of 9 days (IQR, 3–8). Most readmitted patients (84%) were discharged to home with self-care. The mortality rate for CRRs was 3% (Table 5).

Discussion

Several baseline characteristics were found to be associated with an increased rate of a CRR: patient age older than 65 years, hematologic cancer diagnosis,

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Table 2 Breakdown of Cancer Diagnoses				
	Chemotherapy Admissions (N=612)	CRR Population (N=68)	Relative Risk (95% CI)	P Value
Hematologic				
Leukemia	64	18 (28.1%)	2.13 (1.25–3.62)	.005
Lymphoma	189	23 (12.2%)	0.42 (0.25–0.70)	.001
Myeloma	8	3 (37.5%)	2.31 (0.91–5.91)	.079
Solid				
Breast	21	3 (14.2%)	2.39 (0.77–7.37)	.13
Colorectal	51	2 (3.9%)	0.63 (0.15–2.89)	.52
Gastric	23	0 (0%)	0.3 (0.02–4.78)	.39
Genitourinary	5	0 (0%)	1.26 (0.08–18.50)	.87
Gynecologic	80	6 (7.5%)	1.20 (0.49–2.93)	.68
Head/neck	49	5 (10.2%)	1.72 (0.67–4.40)	.26
Lung	96	7 (7.3%)	1.17 (0.50–2.73)	.72
Melanoma	6	0 (0%)	1.08 (0.07–16.00)	.96
Pancreatic	6	0 (0%)	1.08 (0.07–16.00)	.96
Peritoneal	8	0 (0%)	0.83 (0.05–12.70)	.89
Sarcoma	5	0 (0%)	1.26 (0.09–18.40)	.87
Testicular	7	1 (14.2%)	2.4 (0.38–15.40)	.35

Abbreviation: CRR, chemotherapy-related readmission.

Medicare coverage, primary length of stay of 4 to 6 days, first cycle chemotherapy, discharge to a skilled nursing facility, and anthracycline administration. Many of these variables may be codependent. Patients older than 65 years commonly have Medicare coverage, and those who are diagnosed with hematologic cancer are commonly treated with anthracyclines.

Patients receiving anthracyclines, and those undergoing first-cycle chemotherapy had a significantly increased risk for 30-day CRRs. The most common readmission diagnosis in our population was febrile neutropenia. Other studies have also demonstrated an increased risk of febrile neutropenia in patients receiving anthracyclines. These studies focused on first cycles where patients were most likely to receive

full-dose chemotherapy. Lyman et al⁸ developed and validated a risk model for neutropenic complications in patients beginning chemotherapy. The authors reported an increased risk of febrile neutropenia in patients receiving anthracyclines. In the validation group, of 1438 patients who received anthracyclines, 37.3% developed severe or febrile neutropenia compared with 2200 patients not receiving anthracyclines, in which 9.6% developed severe or febrile neutropenia ($P<.001$). A significantly lower risk was associated with prophylaxis with a myeloid growth factor. Notably, patients with acute leukemia were excluded. Similarly, Crawford et al⁹ found that the use of an anthracycline-based chemotherapy regimen was the most important independent risk factor

Table 3 Chemotherapy Agents				
	Chemotherapy Admissions (N=612)	CRR Population (N=68)	Relative Risk (95% CI)	P Value
Chemotherapy agents	N=1636 Mean, 2.68/patient	N=184 Mean, 2.7/patient		
Alkylating agents	560	57 (10.2%)	0.48 (0.27–0.86)	.33
Anthracycline	136	24 (17.6%)	1.91 (1.21–3.02)	.013
Antibiotic	24	1 (4.2%)	0.37 (0.05–2.52)	.23
Antimetabolite	322	33 (10.2%)	0.85 (0.54–1.33)	.54
Antimicrotubule	228	23 (10.1%)	0.86 (0.53–1.38)	.56
Topoisomerase inhibitors	171	18 (10.5%)	0.93 (0.56–1.55)	.76
Other ^a	198	28 (14.1%)	1.30 (0.89–1.89)	.17

Abbreviation: CRR, chemotherapy-related readmission.
^aChemotherapy agents not designated by the other listed chemotherapy classes.

Chemotherapy-Related Readmissions

Figure 1 Patient Identification.

Abbreviations: AMA, against medical advice; CRR, chemotherapy-related readmission.

for developing a neutropenic event in the first cycle. The authors concluded that “neutropenic events occur most frequently during the first cycle of cancer chemotherapy, when patients are treated with full-dose chemotherapy without supportive care.” However, the use of primary prophylaxis with a myeloid growth factor was not evaluated in our study and is considered to be a limitation.

Those with a diagnosis of leukemia had a significantly higher risk of experiencing a CRR, with 28.1% of patients returning. These results are similar to the unplanned 30-day readmission rate seen in the CMS study, which showed a 29.5% readmission rate for patients with leukemia.² A diagnosis of leukemia has frequently been used as an exclusion criterion for readmission studies, which highlights the difficulty of assessing the risk of readmission for these patients.

Patients discharged to skilled nursing facilities had an increased risk of CRR. It could be projected that this population represents patients with an anticipated decreased performance status. How policies regarding environmental protection of patients at risk for neutropenia vary between hospitals and skilled nursing facilities is unknown. Although patients and caregivers are routinely educated on measures to prevent infection, patients discharged to skilled nursing facilities may have less control over variables such as environmental contacts and dietary restrictions.

Treatment of solid tumors with chemotherapy frequently occurs in the outpatient setting. However, because of limitations in reimbursement, more doctors may not be able to afford to provide outpatient chemotherapy to Medicaid patients, and these patients are more frequently being treated as inpatients regardless of having good performance status. The high proportion of solid tumors in our study population may be explained by a high number of patients who lacked the financial resources for treatment in the outpatient arena.

Four patients scheduled for chemotherapy administration were too ill to receive chemotherapy on admission. These patients had their chemotherapy orders placed before admission and were found to not have received chemotherapy during manual chart review. Per protocol, these 4 patients were excluded from the primary admission group because they did not receive chemotherapy, but were also not assessed for experiencing a CRR. Subsequent studies should include these patients as potential CRRs.

The Midas+ DataVision Readmission Tool Pack (Version 2.x), was used to screen for unplanned admissions within 30 days after discharge. Using this setting allowed for removal of all scheduled admissions for subsequent chemotherapy administration. However, it was not known a priori exactly how the difference between scheduled and unscheduled admissions would affect the data, specifically in this

Table 4 Readmission Diagnosis

Readmission Primary Diagnosis	CRR Population (N=68)
Febrile neutropenia	40 (58.8%)
Diarrhea	5 (7.4%)
Dehydration	4 (6.2%)
Infective process	3 (4.7%)
Pancytopenia	3 (4.7%)
Thrombocytopenia	3 (4.7%)
Failure to thrive	2 (3.1%)
Hypotension	2 (3.1%)
Acute renal failure	1 (1.6%)
Anemia	1 (1.6%)
Diabetes insipidus	1 (1.6%)
Mucositis	1 (1.6%)
PEG tube malfunction	1 (1.6%)
Peripheral neuropathy	1 (1.6%)

Abbreviations: CRR, chemotherapy-related readmission; PEG, percutaneous endoscopic gastrostomy.

patient population. Patients can be scheduled for admission either on primary discharge or during a follow-up outpatient appointment with their oncologist. Scheduling readmissions ensures bed availability, but not necessarily in the oncology unit. Admitting a patient on an unscheduled basis and listing the admission as “semi-urgent,” “urgent,” or “emergent” will prioritize that patient into a bed on the oncology unit. Because of their unscheduled admission status, many patients falsely appeared as readmissions. Subsequently, the readmission rate was artificially inflated and led to time-consuming manual chart review.

Strengths of this study include repeatable methods, large population size, multidisciplinary team assessing CRR status, and benchmark result establishment. Limitations include an inability to assess admissions occurring at other institutions, inability to assess outpatient mortality, lack of growth factor support data, retrospective study design, and lack of baseline data with which to compare identified risk factors.

Identification of risk factors for 30-day CRRs is achievable. To obtain meaningful results, the factors that may influence the accuracy of data must be considered. For example, unscheduled chemotherapy administration admissions were included in the CRR data set, causing time-consuming manual chart review. Also, readily accessible chemotherapy

Table 5 Readmission Characteristics

CRR Population (N=68)	
Days to readmission	
Mean	11
Range	1–30
IQR	5–14
Length of stay (d)	
Mean	9
Range	1–92
IQR	3–8
Discharge disposition	
Home/self-care	57 (84%)
Home-health service	5 (7%)
Skilled nursing facility	4 (6%)
Hospice	0
Mortality rate	2 (3%)

Abbreviations: CRR, chemotherapy-related readmission; IQR, interquartile range.

administration records are imperative to facilitate administration verification.

The results of this study show that patients receiving anthracyclines, undergoing their first chemotherapy cycle, or having a diagnosis of hematologic cancer, specifically leukemia, are among those at highest risk of experiencing a CRR. To prevent complications secondary to neutropenia, these patients must receive appropriate supportive care, adequate education, and appropriate environmental protection.

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