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Frequency and Reasons for Return to the Primary Acute Care Service among Lymphoma Patients Undergoing Inpatient Rehabilitation

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Abstract

Objective—To assess the frequency and risk factors for return to the primary acute care service among lymphoma patients undergoing inpatient rehabilitation.

Design—Retrospective study.

Setting—Tertiary referral-based cancer center.

Patients—All patients with a history of lymphoma admitted to inpatient rehabilitation between October 1, 2003 and January 30, 2013.

Main Outcome Measures—Items analyzed from patient records included return to the primary acute care service with demographic information, lymphoma characteristics, medications, hospital admission characteristics, and laboratory values.

Results—143 unique patient admissions were analyzed. 54/143 (38%) of lymphoma inpatient rehabilitation admissions returned to the primary acute care service. However, 16/54 (30%) returned due to needing additional chemotherapy. Excluding patients who returned to the primary acute care service for chemotherapy, statistically significant or approaching statistically significant factors ($p < .10$) associated with return to the primary acute care service included a creatinine greater than or equal to 1.3 milligrams/deciliter (mg/dL) ($p = 0.0002$), male sex ($p = 0.001$), history

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of hematopoietic stem cell transplant ($p=0.0355$), and presence of intravenous antifungal agent ($p=0.0717$). Of those transferred back to the primary acute care service; 13/38 (34%) discharged directly home, 10/38 (26%) died in the hospital, 7/38 (18%) transferred to a subacute rehabilitation facility, and 4/38 (11%) transferred to inpatient rehabilitation.

Conclusions—Chemotherapy was the most common reason for return to the primary acute care service. When excluding patients who returned for chemotherapy, lymphoma patients who are male, who have had a hematopoietic stem cell transplant, and have a creatinine greater than or equal to 1.3 mg/dL demonstrated increased risk for return to the primary acute care service.

Keywords

Lymphoma; Inpatient; Rehabilitation; Cancer

INTRODUCTION

Lymphoma, its treatment, and associated complications can lead to significant functional impairment. Cancer patients often suffer from cachexia, nausea, fatigue, lymphedema, deconditioning, myopathy and peripheral neuropathy.^{1,2} Lymphoma patients may require inpatient rehabilitation to enable them to discharge from the hospital and to prepare them for upcoming treatment. Whether a patient can receive radiation or chemotherapy is often dependent upon functional status.³ Studies have shown that inpatient cancer rehabilitation can improve function and symptoms such as fatigue, well-being, and pain.^{4,5} A transfer back to the primary acute care service from inpatient rehabilitation is often due to unexpected medical complications. An uninterrupted inpatient rehabilitation stay with consistent therapy participation is preferred and the most efficient way to utilize these rehabilitation resources.⁶ Because of this, multiple studies have been published that have focused on return to the primary acute care service in a number of patient populations including burn,⁷ stroke,⁸ traumatic brain injury,^{9, 10} and cancer patients. Alam et al. found a return to primary rate of 21% versus 9.7% of non-cancer controls.¹¹ Guo et al. found a return to primary acute care service rate of 35%.¹² In order to further delineate factors for return to the primary acute care service in specific cancer subpopulations, Fu et al. in 2 studies, found a return to primary acute care service rate of 41% and 37% for hematopoietic stem cell transplant and leukemia patients respectively.^{13,14} Lymphoma patients, like other liquid tumor patients, are a medically complex group. Neutropenia puts patients at high risk for infection. Anemia can contribute to fatigue and hypovolemic symptoms. Thrombocytopenia may lead to a higher risk of bleeding. There are two purposes of this study. The primary purpose is to identify risk factors associated with return to the primary acute care service of lymphoma patients. Another purpose is to describe the frequency and reasons for return to the primary acute care service. This is the first study to identify risk factors for return to the acute care primary service specifically among lymphoma patients.

METHODS

Subjects

This retrospective study included all patients with a medical history of lymphoma admitted to the inpatient rehabilitation service at a tertiary referral-based cancer center between October 1, 2003 and January 30, 2013.

Procedure

Institutional review board (IRB) approval was obtained. The IRB granted a waiver of informed consent in compliance with federal and institutional guidelines. Patients admitted after October 1, 2003 were analyzed because their medical records were easily accessible electronically. An experienced physiatrist reviewed medical records and collected data that could be divided into: demographic information, lymphoma characteristics, medications, laboratory values, and hospital admission characteristics. Demographic information included age, gender, race, marital status, insurance type, and date of death (if applicable).

Lymphoma characteristics included type of lymphoma, if there was any pathologic or radiographic evidence of central nervous system or leptomeningeal involvement, if the patient had ever received intrathecal chemotherapy, time since last chemotherapy dose, if the patient had received a bone marrow transplant in the past and whether the patient relapsed. Medication data included the presence of oral and/or intravenous antibacterial agents, antiviral agents, and antifungal agents. Laboratory values consisted of peripheral white blood cell count, platelet count, creatinine, prealbumin, and albumin on the day of transfer to inpatient rehabilitation. Hospital admission characteristics included the patient's location prior to admission, reason for hospitalization, length of hospitalization prior to transfer to rehabilitation, length of inpatient rehabilitation stay, reason for transfer to inpatient rehabilitation, if the patient had returned to the primary acute care service, reason for transfer back to the primary acute care service (if applicable), and if the patient had an indwelling Foley catheter, central venous catheter, or feeding tube at the time of admission to rehabilitation.

Variable frequencies were evaluated. Non-parametric statistical tests on the variables described above including demographics, lymphoma characteristics, medications, bone marrow transplantation status, hospital admission characteristics, and laboratory values were performed. Chi-square analyses was performed on all the data categories with return to the primary acute care service. To remain consistent, a Fisher's exact test was not used in sparse data cells. Due to categorical variables, unequal sample sizes and distribution characteristics, non-parametric statistical techniques were used initially to test the proportional distributions of each category and later the parameter estimates in a logistic regression model. To remain conservative in our model analysis, we used only variables that were statistically significant or near statistically significant with return to the primary acute care service

RESULTS

143 patients with a history of lymphoma were admitted a total of 163 times to inpatient rehabilitation. 1 patient was admitted 4 times, 1 patient was admitted 3 times, and 15

patients were admitted 2 times. Of the patients admitted multiple times, only one admission was randomly selected for analysis. The reason categories for return to the primary acute care service were chemotherapy (16/54, 30%), infectious disease (18/54, 33%), gastrointestinal (5/54, 9%), neurologic (2/54, 4%), renal (2/54, 4%) pulmonary (1/54, 2%), and other reasons (10/54, 19%).

After excluding the 16 patients who returned to the primary acute care service for chemotherapy, the mean age of the remaining 127 patients was 62.6 (sd = 13.4) years. The median age was 65. The range was 24 to 87 years. Patients who did not return to the primary acute care service were 62.2 (sd = 14.4) years of age. Those who did return to the primary acute care service averaged 63.5 (sd = 11.09). A t test did not indicate that the age of patients who returned to primary acute care service significantly differed from patients who did not return to the primary acute care service ($p=.6107$).

Table 1 lists categorical demographic factors and their relationship with return to the primary acute care service while excluding those that returned to the primary acute care service due to chemotherapy.

Table 2 lists select categorical clinical/laboratory factors and their relationship with return to the primary acute care service while excluding those that returned to the primary acute care service due to chemotherapy.

The days since last chemotherapy dose, days in the hospital prior to transfer to rehabilitation, days until death, and days on inpatient rehabilitation were not found to be significantly related to return to the primary acute care service. Table 3 lists select continuous laboratory variables of the lymphoma patients excluding those that returned to the primary acute care service due to chemotherapy. It is notable that the median levels of platelets, prealbumin, and albumin were abnormal.

When excluding patients who returned to the primary acute care service for chemotherapy, 3 variables had a statistically significant relationship with return to the primary acute care service: male sex, creatinine greater than or equal to 1.3 mg/dL, and history of hematopoietic stem cell transplant (BMT). Presence of an intravenous (IV) antifungal agent at the time of inpatient rehabilitation transfer had a near significant relationship. A creatinine of 1.3 mg/dL was used as the cut point because this is the laboratory upper limit of normal.

In Table 4, the odds ratios for male sex and creatinine were much greater than the other 2 variables, IV antifungal and history of BMT. Male sex and elevated creatinine are the strongest independent predictors of return to the primary acute care service.

After returning to the primary acute care service, patients (excluding those who returned to the primary acute care service for chemotherapy) were discharged directly home (13/38, 34.2%), died in the hospital (10/38, 26.3%), transferred to a subacute facility (7/38, 18.4%), returned to acute inpatient rehabilitation (4/38, 10.5%), transferred to hospice (2/38, 5.2%), or transferred to an outside acute care hospital (2/38, 5.2%).

DISCUSSION

The concept of preventative rehabilitation, buffering, or prehabilitation for cancer patients has been gaining increased attention. Optimizing inpatient rehabilitation may impact patient's cancer treatment and thus survival. The primary purpose of this study is to identify risk factors associated with return to the primary acute care service among lymphoma rehabilitation inpatients. Previous studies have looked at other cancer subpopulations including leukemia and hematopoietic stem cell transplant patients. This is the first study to look specifically at another medically challenging cancer group, lymphoma patients.

Patients with many or all of these risk factors may benefit from receiving inpatient rehabilitation at a unit located within a hospital. They would be closer to an intensive care unit (ICU) and many more physician specialists than a freestanding acute rehabilitation facility or post-acute care facility. Patients at a freestanding facility could be miles away from an ICU. In skilled-nursing facilities, which are typically freestanding, patients may be seen by a physician only 1–2 times a week.

We have focused our analysis by excluding patients who returned to the primary acute care service for chemotherapy. Chemotherapy is typically planned and could be interpreted as a successful inpatient rehabilitation stay because a patient's function is improved to allow them to qualify for additional cancer treatment. The purpose of this study is to assist physiatry clinicians in determining which patients are at risk for an unplanned return to the primary acute care service. We feel that the analysis excluding patients who returned to the primary acute care service for chemotherapy patients is more clinically useful. Although in a majority of cases, patients were on a planned chemotherapy regimen, it is possible that some cases where the patient returned to the primary acute care service for chemotherapy could have been unplanned. This was not determined in our study and further research is needed.

There have been prior studies analyzing return to the primary acute care service among cancer patients. Fu et al. developed probability indices for return to the primary acute care service called the Return to Primary-Leukemia (RTP-Leukemia) and Return to Primary-Bone Marrow Transplant (RTP-BMT) scores for those cancer populations.^{13,14} A similar model of a point system for each factor present was not possible in this study. The odds ratios, listed in Table 4, of male sex and creatinine greater than 1.3 mg/dL were much higher than history of hematopoietic stem cell transplant and presence of IV antifungal agent. Therefore equal weight could not be placed on each factor. Table 4 shows male sex and creatinine > 1.3 mg/dL as clear indicators of return to the primary acute care service. The other variables which were independently significant or near significant (IV antifungal agent and history of hematopoietic stem cell transplant), are less prominent in the logistic model. More investigation is needed on the role of these variables and return to the primary acute care service.

An elevated creatinine was found to be associated with return to the primary acute care service in a study of general cancer rehabilitation patients by Guo et al. and Elmi et al. and BMT patients by Fu et al.^{12,13,15} An elevated creatinine could be associated with patients who are more acutely ill. Male gender has not been found to be associated with an increased

rate of return to the primary acute care service in other studies of cancer rehabilitation inpatients. However, some research suggests a lower survival for men in both Hodgkin¹⁶ and Non-Hodgkin Lymphoma. A possible explanation for this is higher levels of rituximab in females.¹⁷ This could be a reason for the increased return to primary acute care in males.

The association of the presence of an intravenous antifungal agent at the time of admission to inpatient rehabilitation and return to the primary acute care service is not surprising. Patients undergoing treatment with intravenous antifungal agents are being treated for an active fungal infection, typically a fungal pneumonia. Fungal pneumonias can be difficult to treat, and patients who are immunosuppressed are more susceptible to them. The presence of an antifungal agent has been associated with return to the primary acute care service in both leukemia and BMT patients. Those studies did not differentiate between intravenous and oral antifungals. This study did make such a differentiation but only found a relationship with IV antifungal agents.^{13, 14}

Fu et al. found 41% of BMT rehabilitation inpatients returned to the primary acute care service and that 38% of those that returned to the primary acute care service died in the hospital.¹³ Given the medical fragility of these patients, it is not surprising that a history of a hematopoietic stem cell transplant was associated with a return to the primary acute care service in our population of lymphoma patients.

Platelet count, presence of antiviral agents, presence of antibacterial agents, low albumin and presence of tube feeding or Foley catheter have been found in prior cancer rehabilitation studies to be associated with return to the primary acute care service. These factors were analyzed in this study as well but no statistically significant associations were identified. Infectious disease was the most common reason for return to primary acute care service. Studies by Alam (general cancer rehabilitation patients) and Fu (hematopoietic stem cell transplant and leukemia patients) found infection to be the most common reason for return to the primary acute care service.^{11,13,14} Older age, involvement of the central nervous system or bone marrow, and relapse after bone marrow transplantation have been implicated with a worse lymphoma prognosis.^{18,19,20} Although their continued relevance in the rituximab/Positron Emission Tomography era has been called into question,¹⁸ the Ann Arbor stage²¹ and Age-adjusted International Prognostic Index²² are tools used to determine lymphoma prognosis. These studies also include age, stage, serum lactate dehydrogenase (LDH) and performance status in their models. LDH is a marker of tumor mass and may reflect tumor burden. Some of these factors were also looked at in our study of return to the primary acute care service.

Study Limitations

The presence of an IV antifungal agent may be influenced by medical care guidelines that are hospital specific. Also National Cancer Institute Comprehensive Cancer Centers are Diagnosis Related Group (DRG) exempt. The patient mix at our DRG exempt institution may be very different from non-DRG exempt institutions. This may affect the generalizability of our findings to community rehabilitation units. Multicenter studies would be needed to address these possibilities. We were unable to analyze functional scores in this study and determine whether there was a relationship with return to the primary acute care

service. Functional scores in the medical records were too incomplete to perform any meaningful analysis. There is little published functional rehabilitation outcomes in the lymphoma population. Performance status has been implicated in the prognosis of lymphoma.¹⁸ Other factors that should be analyzed in future studies could include serum LDH (a serum LDH was not consistently available on the day of admission to inpatient rehabilitation and thus not analyzed) and stage. Other return to primary acute analyses would be useful in other patient populations prone to medical complications.

CONCLUSIONS

Lymphoma rehabilitation inpatients frequently return to the primary acute care service. Excluding those that return for chemotherapy, patients who are male, who have had a history of hematopoietic stem cell transplant and creatinine greater than 1.3 mg/dL may be at higher risk of return to the primary acute care service.

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Table 1

χ^2 Analysis of Select Demographic Variables and Return to the Primary Acute Care Service Lymphoma Rehabilitation Inpatients Excluding Patients That Returned to the Primary Acute Care Service for Chemotherapy

Category	Total Freq (%) or mean (SD)	Return to Primary Acute Care Service		<i>p</i> value
		No Freq(%)	Yes Freq(%)	
Total n (percent)	127 (100)	89(100)	38(100)	
Age *				<i>p</i> =0.6559
65	64 (50.4)	43 (48.3)	20 (52.6)	
>65	63 (49.6)	46 (51.7)	18 (47.4)	
Race				<i>p</i> =0.8224
Asian	4(3.2)	2(2.2)	2(5.26)	
Black	6(4.7)	4(4.5)	2(2.56)	
Hispanic	19(15.0)	13(14.6)	6(15.8)	
White	98(77.2)	70(78.7)	28(73.7)	
Sex				<i>p</i> =0.0014
Male	73(57.5)	43(48.3)	30(78.9)	
Female	54(42.5)	46(51.7)	8(21.1)	
Marital status				<i>p</i> =0.1298
Divorced	10(7.9)	9(10.1)	1(2.6)	
Married	90(70.9)	57(64.0)	33(86.8)	
Separated	1(0.8)	1(1.1)	0	
Single	16(12.6)	13(14.6)	3(7.9)	
Widowed	10(7.9)	9(10.1)	1(2.6)	
Payer source				<i>p</i> =0.4950
County	2(1.6)	1(1.1)	1(2.6)	
Free indigent	3(2.4)	3(3.4)	0	
Medicaid	1(0.8)	1(1.1)	0	
Medicare	60(47.2)	40(44.9)	20(52.6)	
Private ins.	54(42.5)	39(43.8)	15(39.5)	
Self-pay	6(4.7)	5(5.6)	1(2.6)	
Workman's	1(0.8)	0	1(2.6)	
Compensation				

* Age was dichotomized using the median age of 65.

Table 2

χ^2 Analysis of Dichotomized Clinical and Laboratory Variables and Return to the Primary Acute Care Service
Lymphoma Rehabilitation Inpatients Excluding Patients That Returned to the Primary Acute Care Service for
Chemotherapy

Clinical and Lab	Total Freq(%) 127(100%)	Return to Primary Acute Care Service		Pearson χ^2 test of categorical differences
		No Freq(%) 89(70)	Yes Freq(%) 38(29.9)	
Foley				
No	109(85.8)	79(62.2)	30(23.6)	$p=0.1464$
Yes	18(14.2)	10(7.9)	8(6.3)	
Tube feed				
No	122(96.1)	85(66.9)	37(29.1)	$p=0.6211$
Yes	5(3.9)	4(3.2)	1(0.8)	
Central line				
No	27(21.3)	22(17.3)	5(3.9)	$p=0.1448$
Yes	100(78.8)	67(52.8)	33(26.0)	
Antifungal				
No	62(48.8)	42(33.1)	20(15.8)	$p=0.5743$
Yes	65(51.2)	47(27.0)	18(14.2)	
IV Antifungal				
No	108(85.0)	79(62.2)	29(22.8)	$p=0.0717$
Yes	19(14.0)	10(8.9)	9(7.1)	
Antiviral				
No	58(34.7)	42(33.1)	16(12.6)	$p=0.5983$
Yes	69(54.3)	47(37.0)	22(17.3)	
IV Antiviral				
No	116(91.3)	83(65.4)	33(26.0)	$p=0.2391$
Yes	11(8.7)	6(4.7)	5(3.9)	
Antibiotic				
No	37(29.1)	27(21.3)	10(7.9)	$p=0.6479$
Yes	90(70.9)	62(48.8)	28(22.1)	
IV Antibiotic				
No	86(67.7)	64(50.4)	22(17.3)	$p=0.1219$
Yes	41(32.3)	25(19.7)	16(12.6)	
IT Chemo				
No	95(74.8)	65(51.2)	30(23.6)	$p=0.4821$

Clinical and Lab	Total Freq(%) 127(100%)	Return to Primary Acute Care Service		Pearson χ^2 test of categorical differences
		No Freq(%) 89(70)	Yes Freq(%) 38(29.9)	
Yes	32(25.2)	24(18.9)	8(6.3)	
BMT				
No	84(66.1)	64(50.4)	20(15.8)	<i>p=0.0355</i>
Yes	43(33.9)	25(19.7)	18(14.2)	
Total WBC				
<11 K/uL	112(88.2)	80(89.9)	32(84.2)	<i>p=0.3640</i>
<u>>11 K/uL</u>	15(11.8)	9(10.1)	6(15.8)	
Platelet Count				
<140 K/uL	90(70.9)	61(68.5)	29 (76.3)	<i>p=0.3771</i>
<u>>140 K/uL</u>	37(29.1)	28(31.5)	9(23.7)	
Creatinine				
<1.3 mg/dL	102(80.3)	79(88.8)	23(60.5)	<i>p=0.0002</i>
1.3 mg/dL	25(19.7)	10(11.2)	15(39.5)	
Prealbumin *				
<20 mg/dL	76(61.8)	53(60.9)	23 (63.9)	<i>p=0.7578</i>
20 mg/dL	47(38.2)	34(39.1)	13 (36.1)	
Albumin				
<3.5 g/dL	120(95.2)	83(94.3)	37 (97.4)	<i>p=0.406</i>
3.5 g/dL	6(4.8)	5(5.7)	1 (2.6)	

IV=intravenous, IT=intrathecal, mg/dL=milligrams/deciliter, g/dL= grams/deciliter, K/uL=thousands/microliter, BMT=bone marrow transplant, Freq=frequency, %=percentage WBC= white blood cell count

* 4 patients did not have prealbumin checked at inpatient rehabilitation admission

Table 3
Laboratory Values Excluding Patients That Returned to the Primary Acute Care Service for Chemotherapy

Variable at Rehabilitation Admission	Total (N=127)		No Freq(%) 89(70)		Yes Freq(%) 38(29.9)	
	Mean(SD)	Median	Mean(SD)	Median	Mean(SD)	Median
Total WBC (K/uL)	7.1 (8.3)	4.9	6.5(6.0)	5	8.3(12.2)	4.3
PltCount (K/uL)	116.3(108.0)	78	117.3(103.3)	82	113.4(119.7)	71
Prealbumin (mg/dL)	18.4(8.1)	17.5	19.1(8.7)	17.8	16.7(6.1)	14.8
Albumin (g/dL)	2.7(0.5)	2.7	2.8(0.5)	2.8	2.6(0.4)	2.6
Creatinine (mg/dL)	1.0(0.7)	0.8	0.9(0.5)	0.8	1.3(1.0)	1.0

K= 1000's, uL=microliter, mg=milligram, dL=deciliter, g=gram, SD=standard deviation

Table 4

Variable Frequencies and Odds Ratios for Lymphoma Patients' Return to Primary Acute Care Excluding Patients That Returned to the Primary Acute Care Service for Chemotherapy

Factor(Freq,%)	RTP	%	OR [95% CI]
Sex			
Female (54, 42.52)	8	21.05	0.22[0.07, 0.58]
Male (73, 57.48)	30	78.94	4.40[1.7, 12.7]
Creatinine (mg/dL)			
<1.3 (102, 80.3)	23	60.52	0.31[0.10, 0.92]
>1.3 (25, 19.7)	15	39.47	3.14[1.08, 9.27]
BMT			
No (84, 66.1)	20	52.63	0.43[0.14, 1.24]
Yes (43, 33.9)	18	47.36	2.29[0.8, 6.69]
IV Antifungal			
No (108, 85.0)	29	76.31	0.64[0.15, 2.72]
Yes (19, 14.0)	9	23.68	1.55[0.36, 6.28]

Freq=number of patients, %=percentage, RTP=Number who Returned to Primary, CI=confidence interval, OR=odds ratio, BMT=hematopoietic stem cell transplant, IV=intravenous, mg/dL=milligrams/deciliter