



PM R XXX (2017) 1-8

www.pmrjournal.org

Original Research

# Return to the Primary Acute Care Service Among Patients With Multiple Myeloma on an Acute Inpatient Rehabilitation Unit

Jack B. Fu, MD, Jay Lee, PhD, Ben C. Shin, MD, Julie K. Silver, MD,  
Dennis W. Smith, PhD, Jatin J. Shah, MD, Eduardo Bruera, MD

## Abstract

**Background:** Pancytopenia, immunosuppression, and other factors may place patients with multiple myeloma at risk for medical complications. These patients often require inpatient rehabilitation. No previous studies have looked at risk factors for return to the primary acute care service of this patient population.

**Objective:** To determine the percentage of and factors associated with return to the primary acute care service of multiple myeloma rehabilitation inpatients.

**Design:** Retrospective review.

**Setting:** Acute inpatient rehabilitation unit within a National Cancer Institute Comprehensive Cancer Center.

**Participants:** All patients with multiple myeloma admitted to the inpatient rehabilitation unit between March 1, 2004, and February 28, 2015.

**Main Outcome Measures:** Return to the primary acute care service was analyzed with demographic information, multiple myeloma characteristics, medications, laboratory values, and hospital admission characteristics.

**Results:** One hundred forty-three inpatient rehabilitation admissions were found during the study period. After we removed multiple admissions of the same patients and planned transfers to the primary acute care service, 122 admissions were analyzed. Thirty-two (26%) patients transferred back to the primary acute care service for unplanned reasons. Multivariate analysis revealed male gender and thrombocytopenia as significantly associated with return to the primary acute care service. The median survival of patients who transferred back to the inpatient primary acute care service was 180 days versus 550 days for those who did not ( $P < .001$ ).

**Conclusion:** Because of their medical fragility, clinicians caring for rehabilitation inpatients with multiple myeloma should maintain close contact with the primary oncology service. Factors associated with an increased risk of transfer back to the primary acute care service include male gender and thrombocytopenia.

**Level of Evidence:** To be determined.

## Introduction

Hematologic malignancies, including leukemia, myelodysplastic syndromes, lymphoma, and multiple myeloma, are cancers that begin in blood-forming cells. Approximately 26,850 new cases of multiple myeloma are diagnosed in the United States every year, and the disease accounts for more than 11,000 deaths annually [1]. Patients with multiple myeloma, like other patients with hematologic malignancy, are a medically complex group. Leukopenia (from chemotherapy and hematopoietic stem cell transplants) and the use of steroid immunosuppressants increase their risk for infection. Thrombocytopenia increases their risk of bleeding.

Reduced bone strength puts them at risk for fractures and pain. Patients with multiple myeloma often require acute inpatient rehabilitation as the result of complications of their cancer and treatment, including deconditioning, orthopedic long bone fractures, and spinal cord compression from vertebral compression fractures [2-4].

There have been some studies on predominantly outpatient rehabilitation of patients with multiple myeloma [5-8]; however, the published literature regarding rehabilitation inpatients with multiple myeloma is limited to one case series of 8 patients. In that study, 1 of 8 (12.5%) transferred back to the primary acute care inpatient service, 1 of 8 (12.5%)

transferred to a subacute rehabilitation facility, and 6 of 8 (75%) were discharged home [9]. An uninterrupted inpatient rehabilitation stay with ultimate discharge home is the most efficient and preferred outcome. Transfer back to the primary acute care service from inpatient rehabilitation is required when a clinical condition becomes unstable. This requires coordination between the primary acute care and psychiatry team and could contribute to an increase in medical costs. Therefore, identifying the frequency and main reasons for return to the primary acute care service might increase the safety of inpatient cancer rehabilitation and aid providers in triaging appropriate rehabilitation settings for these patients.

There have been published studies identifying risk factors for transfer to the primary acute care inpatient service from inpatient rehabilitation of various populations, including general rehabilitation [10], burn [11], stroke [12,13], and traumatic brain injury [14]. Four previous studies have looked at patients with cancer as a whole. The rate of return to the primary acute care service of general cancer rehabilitation inpatients has been reported to be between 17% and 35% [15-18]. Another 3 previous studies looked at specific hematologic malignancy populations and their risk for return to the primary acute care service, including rehabilitation inpatients with hematopoietic stem cell transplant [19], leukemia [20], and lymphoma [21]. The reported rates of return to the primary acute care service in hematologic malignancy populations have been quite high, between 35% and 41% [19-22]. A better understanding of factors associated with transfer back to acute care could assist in identifying high-risk patients, with potential for more effective care and cost savings.

The primary objective of this study is to identify the percentage of patients with multiple myeloma who transferred to the primary acute care inpatient service from inpatient rehabilitation for unplanned reasons. A secondary objective is to identify risk factors associated with unplanned transfers of patients with multiple myeloma from inpatient rehabilitation to the primary acute care inpatient service.

## Methods

### Subjects

This retrospective study included all patients with a history of multiple myeloma admitted to the inpatient rehabilitation unit within a tertiary referral-based National Cancer Institute Comprehensive Cancer Center from March 1, 2004, through February 28, 2015. If a patient had been admitted multiple times to inpatient rehabilitation during the study period, only one randomly selected admission was analyzed. Because the purpose of this study was to identify factors associated

with unplanned transfer to the primary acute care service, patients with planned transfers (eg, planned chemotherapy) were excluded from the study group.

### Procedure

Institutional review board approval was obtained. The institutional review board granted a waiver of informed consent in compliance with federal and institutional guidelines. A fourth-year medical student and an experienced, board-certified psychiatrist reviewed medical records of patients with a history of multiple myeloma who were admitted to the acute inpatient rehabilitation unit during the study timeframe. A board-certified psychiatrist trained the medical student, who underwent orientation regarding chart review and consulted the psychiatrist at any time if the medical student felt anything was difficult to understand.

Relevant medical records data were recorded and organized into 5 categories: demographic information, multiple myeloma characteristics, medications, laboratory values, and hospital admission characteristics. Demographic information included age, race, gender, marital status, payer source, and date of death (if applicable). Multiple myeloma characteristics included myeloma (M) protein levels, Bence Jones protein levels, if the patient had ever received radiation, date of last chemotherapy, whether the last chemotherapy was intensive or nonintensive, if the patient ever had a plasmacytoma, if the patient had had a bone fracture within 1 year before admission, and if the patient had a history of hematopoietic stem cell transplant.

Intensive chemotherapy is more toxic than non-intensive intravenous and with the goal of eliminating existing bone marrow cells. Nonintensive chemotherapy is typically oral and often offered to older, frailer patients. Medication data included the presence of intravenous (IV) antibiotics, any antiviral agents, and IV antifungal agents at inpatient rehabilitation admission. Laboratory values consisted of peripheral white blood cell count, platelet count, creatinine, pre-albumin, serum calcium, and albumin on the day of transfer to inpatient rehabilitation. Hospital admission characteristics included the patient's location before admission, reason for hospitalization, length of hospitalization before 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 whether the patient had an indwelling Foley catheter, central venous catheter, or feeding tube at the time of admission to rehabilitation. Patients transferred back to the primary acute care service for planned treatment were not included in further analysis.

SAS-JMP version 12 software (SAS Institute, Cary, NC) was used for statistical analysis. The data were

analyzed with the use of descriptive statistics, including frequencies for variables in each of the 5 categories (demographic information, multiple myeloma characteristics, medications, laboratory values, and hospital admission characteristics). Pearson  $\chi^2$  analyses were conducted on all the data categories and the dependent variable "return to the primary acute care service." Data sets were sufficiently large enough that the Fisher exact test was not needed. Significant findings from the univariate analysis were then tested in a logistic regression model, including reporting of odds ratios. The Wald test was used to test the true value of the parameter based on the results we obtained in the development of our statistical model compared with a normal distribution [23].

## Results

During the study period, 128 patients with a history of multiple myeloma were admitted a total of 143 times to the inpatient rehabilitation unit. Twelve patients were admitted 2 times, and one patient was admitted 4 times. Of the patients admitted multiple times, only

one admission was selected randomly for inclusion in the analysis. In addition, 6 of 128 (5%) patients returned to the primary acute care service for planned cancer treatment. After we eliminated planned transfers to the primary acute care service and randomly eliminating multiple admissions of the same patient, 122 unique patient admissions were analyzed.

The primary reason categories (by frequency, percent) for initial acute care hospitalization for the 122 patients were infection (27, 22%), stem cell transplantation (21, 17%), severe pain (19, 16%), neurologic (12, 10%), chemotherapy (10, 8%), failure to thrive (8, 7%), renal (7, 6%), cardiac (6, 5%), orthopedic (5, 4%), altered mental status (2, 2%), dehydration (2, 2%), gastrointestinal (not due to bleeding) (1, 1%), rheumatologic (1, 1%), and pulmonary (1, 1%).

Thirty-two of the 122 total patients (26%) transferred back to the primary acute care service for unplanned reasons. Those categorized reasons were infection (11, 34%), disease progression/unplanned treatment (7, 22%), cardiac (6, 19%), renal (2, 6%), neurologic (2, 6%), gastrointestinal bleed (1, 3%), pulmonary (1, 3%), orthopedic (1, 3%), and insurance (1, 3%).

**Table 1**  
 $\chi^2$  Analysis of categorical demographic variables and unplanned return to the primary acute care service

Demographic Variable	Total (N = 122) Freq (%)	Return to the Primary Acute Care Service		$\chi^2$
		No (n = 90, 73.7%) Freq (%)	Yes (n = 32, 26.3%) Freq (%)	
Age, y				0.755, P = .39
≥ 65	69 (57)	53 (59)	16 (50)	
< 65	53 (43)	37 (41)	16 (50)	
Race				0.607, P = .90
White	71 (58.19)	54 (60.00)	17 (53.12)	
Black	35 (28.68)	25 (27.77)	10 (31.25)	
Hispanic	10 (9.83)	8 (8.88)	4 (12.50)	
Asian	4 (3.27)	3.33 (3.33)	1 (3.12)	
Sex				10.109, P = .002
Male	70 (57.38)	44 (48.89)	26 (81.25)	
Female	52 (42.62)	46 (51.11)	6 (18.75)	
Marital status				9.796, P = .08
Married	92 (75.41)	66 (73.33)	26 (81.25)	
Single	17 (13.93)	13 (14.44)	4 (12.50)	
Divorced	6 (4.91)	6 (6.66)	0 (0)	
Widowed	4 (3.27)	4 (4.44)	0 (0)	
Separated	2 (1.63)	0 (0)	2 (6.25)	
Life partner	1 (0.82)	1 (1.11)	0 (0)	
Payer source				1.285, P = .86
Medicare	74 (60.65)	56 (62.22)	18 (56.25)	
Private				
Insurance	39 (31.96)	27 (30.00)	12 (37.50)	
Self-pay	7 (5.73)	5 (5.55)	2 (6.25)	
County				
Insurance	1 (0.82)	1 (1.11)	0 (0)	
Free care	1 (0.82)	1 (1.11)	0 (0)	
Currently deceased <sup>†</sup>				5.798, P = .02
Yes	82 (67.21)	55 (61.11)	27 (84.38)	
No	40 (32.89)	35 (38.89)	5 (15.63)	

\* P < .05.

<sup>†</sup> Deceased as of June 1, 2015.

No relationship with return to the primary acute care service was found for time since last chemotherapy, patient location before admission, length of acute care hospitalization before rehabilitation transfer, and length of inpatient rehabilitation stay. Table 1 lists the results of  $\chi^2$  analysis of categorical demographic variables, including conversion of age into a binary categorical variable with 65 years as the cutoff. The mean age and standard deviation (SD) for all 122 patients was 65.12 (SD = 10.19). The mean age of patients who did not return to the primary acute care inpatient service was 66.03 (SD = 8.96). The distribution of these patients approximated a normal distribution. Of patients who did return to the primary acute care service, the distribution of age is bimodal. The range of the lower mode is from 35 to 53 (n = 11 patients). The older mode (n = 21) ranged from 57 to 82.

Tables 2 and 3 display the results of  $\chi^2$  analysis of continuous laboratory variables and categorical clinical variables with unplanned return to the primary acute care service, respectively. Being currently deceased as of June 1, 2015, was associated with return to the primary acute care inpatient service while receiving inpatient rehabilitation ( $P = .02$ ). Figure 1 displays the results of a Kaplan-Meier analysis ( $P < .001$ ). Patients who returned to the primary acute care service had a significantly shorter survival time (median = 180 days) than those who did not return to the primary acute care service (median = 550 days).

Initially in our univariate analysis, we were able to find 9 variables with statistically significant associations with unplanned return to the primary acute care service. These included the continuous variables of an elevated Bence Jones protein and a lower platelet count and categorical variables of male gender, presence of Foley catheter, presence of IV antifungal agent, presence of any antiviral agent, presence of IV

antibiotic, history of stem cell transplant, and being deceased as of June 1, 2015.

After a multivariate logistic regression analysis ( $\chi^2 = 33.4327$ ,  $P < .001$ ), however, male gender ( $P = .005$ ) and thrombocytopenia ( $P = .008$ ) were the only 2 that continued to be significant (Table 4). In this multivariate analysis, thrombocytopenia was defined as a platelet count less than 140,000/ $\mu\text{L}$ . The other variables suffered from multicollinearity. A predictive probability scoring system had been developed in previous studies of return to the primary acute care service of other hematologic malignancy populations [19,20]. Having only 2 significant variables, however, did not lend itself well to developing such a system. Figure 2 graphically displays the odds ratios from the multivariate analysis.

## Discussion

Previous published studies have analyzed factors associated with return to the primary acute care inpatient service of patients with lymphoma, leukemia, and hematopoietic stem cell while on inpatient rehabilitation units [19-21]. This study is the first to analyze the factors of patients with multiple myeloma and the last group of hematologic malignancy patient populations to be analyzed. Twenty-six percent of patients with multiple myeloma transferred back to the primary acute care service for unplanned reasons, a rate lower than previous hematologic malignancy populations.

These results are useful for several reasons. By possibly identifying patients at greater risk for unplanned transfer to the primary acute care service, they can guide the consulting psychiatrist in planning the safest inpatient rehabilitation setting for a patient. Patients at high risk also may benefit from closer supervision from the oncology team while on rehabilitation [19]. Minimizing medical complications and

**Table 2**  
 $\chi^2$  analysis of continuous laboratory variables and unplanned return to the primary acute care service

Laboratory Value	Total (N = 122) Mean (SD)	Return to the Primary Acute Care Service		$\chi^2$
		No (n = 90, 73.7%) Mean (SD)	Yes (n = 32, 26.3%) Mean (SD)	
WBC, K/ $\mu\text{L}$	6.10 (4.28)	6.28 (4.12)	5.56 (4.74)	0.612, $P = .43$
Hemoglobin, g/dL	9.5 (1.03)	9.54 (0.97)	9.38 (1.19)	0.559, $P = .45$
Platelet, K/ $\mu\text{L}$	123.48 (90.85)	138.2 (95.07)	81.93 (62.05)	10.827, $P = .001^*$
Pre-albumin, mg/dL	18.63 (8.26)	18.47 (8.39)	19.10 (8.01)	0.123, $P = .73$
Albumin, g/dL	2.80 (0.45)	2.82 (0.47)	2.75 (0.39)	.518, $P = .47$
Creatinine, mg/dL	1.19 (1.05)	1.10 (0.99)	1.46 (1.17)	2.513, $P = .11$
Calcium, mg/dL	9.09 (7.15)	9.30 (8.31)	8.61 (0.95)	.414, $P = .52$
M protein, g/dL	2.73 (16.90)	3.09 (19.5)	1.67 (1.67)	.198, $P = .66$
Bence Jones protein, mg/TV	422.66 (1065.57)	282.05 (695.10)	790.33 (1654.10)	4.446, $P = .04^*$

SD = standard deviation; WBC = white blood cell count; M = myeloma; TV = total volume.

$\dagger\chi^2$  analysis was performed on the mean values of those who returned to the primary acute care service vs those who did not return to the primary acute care service.

\*  $P < .05$ .

**Table 3**  
 $\chi^2$  analysis of select categorical clinical variables and unplanned return to the primary acute care service

Characteristic	Total (N = 122) Freq (%)	Return to the Primary Acute Care Service		$\chi^2$
		No (n = 90, 73.7%) Freq (%)	Yes (n = 32, 26.3%) Freq (%)	
Central line				.250, <i>P</i> = .61
No	58 (47.54)	44 (48.89)	14 (43.75)	
Yes	64 (52.46)	46 (51.11)	18 (56.25)	
Foley				.567, <i>P</i> = .01*
No	106 (86.89)	80 (88.89)	26 (81.25)	
Yes	16 (13.11)	10 (11.11)	6 (18.75)	
Tube feed				.305, <i>P</i> = .05
No	121 (99.18)	89 (98.89)	32 (100)	
Yes	1 (0.82)	1 (1.11)	0 (0)	
IV antifungal				.115, <i>P</i> = .003*
No	112 (91.80)	82 (91.11)	30 (93.75)	
Yes	10 (8.20)	8 (8.89)	2 (6.25)	
Antiviral				.215, <i>P</i> = .003*
No	40 (32.79)	28 (31.11)	12 (37.50)	
Yes	82 (67.21)	62 (68.89)	20 (62.50)	
IV antibiotic				.329, <i>P</i> = .005*
No	97 (79.51)	70 (77.78)	27 (84.38)	
Yes	25 (20.49)	20 (22.22)	5 (15.63)	
BMT				0.454, <i>P</i> = .005*
No	66 (54.10)	51 (56.67)	15 (46.88)	
Yes	56 (45.90)	39 (43.33)	17 (53.13)	
Plasmacytoma				1.310, <i>P</i> = .25
No	103 (84.43)	78 (86.67)	25 (78.13)	
Yes	19 (15.57)	12 (13.33)	7 (21.88)	
Radiation <sup>†</sup>				1.961, <i>P</i> = .16
No	90 (73.77)	75 (83.33)	23 (71.88)	
Yes	32 (26.23)	15 (16.67)	9 (28.13)	
Last Chemotherapy				3.824, <i>P</i> = .15
Intensive	83 (72.17)	58 (68.24)	25 (83.33)	
Nonintensive	30 (26.08)	26 (30.59)	4 (13.33)	
None	2 (1.73)	1 (1.18)	1 (3.33)	
Bone fracture <sup>‡</sup>				.017, <i>P</i> = .90
No	66 (54.10)	49 (54.44)	17 (53.13)	
Yes	56 (45.90)	41 (45.56)	15 (46.88)	

IV = intravenous, BMT = hematopoietic stem cell transplant.

\* *P* < .05.

<sup>†</sup> Any history of previous radiation treatment.

<sup>‡</sup> Bone fracture within last 365 days.

transfers back to the primary service could potentially reduce cost as well. Our close communication with oncologists in the same location was frequent and resulted in return to the primary acute care service in a significant proportion of patients. It also resulted in continuation of rehabilitation after discussion with primary oncologists in other cases. Free-standing rehabilitation facilities might benefit from oncology communication via conferences calls. This should be explored in future research.

When we designed this study, variables previously associated with return to the primary acute care service of rehabilitation inpatients with cancer and variables specific to patients with multiple myeloma were included. Those variables were chosen with the assistance of a multiple myeloma oncologist. Our study focused on unplanned transfers to the primary acute

care inpatient service. Often patients with multiple myeloma have planned upcoming treatments such as another cycle of chemotherapy or hematopoietic stem cell transplantation. We decided to not include these transfers in our analysis.

Severity of thrombocytopenia has been correlated with the severity of multiple myeloma disease [24]. It also is associated commonly with bone marrow involvement and overall health status [25]. Only one patient returned to the primary acute care service due to bleeding. The patient had a platelet count of 24 K/ $\mu$ L and 37 K/ $\mu$ L at the time of admission to the rehabilitation facility and transfer off, respectively. Male gender also was found to be associated with return to the primary acute care service in lymphoma patients, a related population [21]. Male patients are more susceptible to developing multiple myeloma than female patients

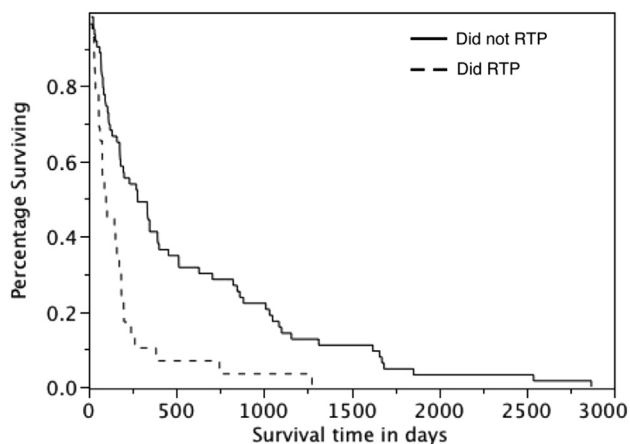


Figure 1. ■ ■ ■

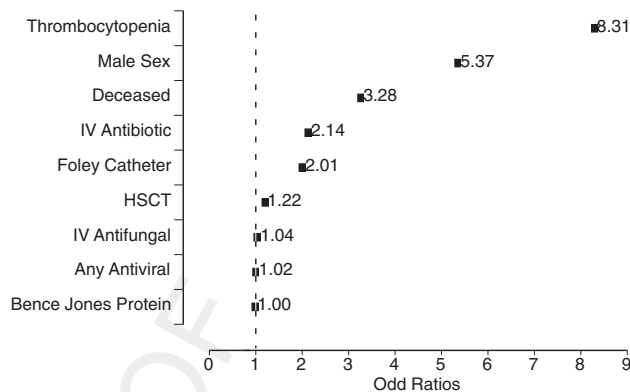


Figure 2. ■ ■ ■

Q4 and our study cohort was also predominantly male (57.4% versus 42.6%) [26]; however, published data have not demonstrated a worse prognosis for male patients [27]. Further study is needed. Patients undergoing hematopoietic stem cell transplant have been found to have a particularly high rate of transfer to the primary acute care service (41%) and death after transfer back (38%) [20].

The variables that were statistically significant after the univariate analysis but not after the multivariate analysis could be of some utility as well. Bence Jones protein is an immunoglobulin light chain found in the urine of patients with multiple myeloma. A greater level is associated with worse disease. The presence of any antimicrobial agents was associated with a greater return risk. Infection was the most common reason for hospitalization and return to the primary acute care service of our patients with multiple myeloma. Clinicians should be vigilant regarding the possibility of infection in this population. Maintaining frequent clinician visits to look for signs of infection may be

Table 4  
Results of a multivariate logistic regression analysis of select variables and return to the primary acute care service

Variable	$\beta$	SE	OR	95% CI	Wald Test
Thrombocytopenia*	1.058	0.399	8.311	1.94-47.47	7.030 <sup>†</sup>
Male gender	0.840	0.299	5.367	1.75-18.89	7.895 <sup>‡</sup>
Deceased <sup>§</sup>	0.593	0.416	3.277	0.74-23.03	2.028
Antibiotic IV	-0.380	0.363	2.141	0.54-10.04	1.095
Foley catheter	0.349	0.344	2.013	0.51-7.97	1.030
HSCT	-0.098	0.314	1.216	0.35-4.25	0.097
Antifungal IV	-0.020	0.494	1.042	0.15-8.98	0.001
Antiviral	0.008	0.309	1.016	0.30-3.53	0.000
Bence Jones protein	-0.000	0.000	0.999	1.00-1.00	0.834

SE = standard error; OR = odds ratio; CI = confidence interval; IV = intravenous; HSCT = history of hematopoietic stem cell transplant.

\* Thrombocytopenia was defined as platelet count < 140,000/ $\mu$ L.

<sup>†</sup> P = .008.

<sup>‡</sup> P = .005.

<sup>§</sup> Deceased as of October 1, 2015.

beneficial. The association of the presence of antimicrobial agents and return to the primary acute care service may reflect patients who were still being treated for an infection at inpatient rehabilitation unit transfer or patients who were on prophylactic antibiotics because of a concern for future infection [28]. Foley catheters also were found by Guo et al [17] to be associated with return to the primary acute care service in a study of general cancer rehabilitation inpatients. Foley catheters are prone to infection and often are used for patients with a lower functional status [29,30]. The shorter survival time of those who return to the primary acute care service is notable. Patients who return to the primary care service should be followed up closely.

Study Limitations

There are limitations to our study. First, this is a retrospective review at one institution. This institution is a Prospective Payment System Exempt - National Cancer Institute Comprehensive Cancer Center. Such centers do not participate in the Center for Medicare and Medicaid Services Prospective Payment System and are therefore exempt from the 60% rule. This could affect the generalizability of our findings. Deconditioning, a rehabilitation diagnosis not within the 60% rule, accounted for 99 of 122 (81.1%) of the admissions. Second, no functional scores were collected because of inadequate records. Functional Independence Measure scores at inpatient rehabilitation admission have been found to be associated with return to the primary acute care service in another study of patients with cancer [18]. Third, a detailed analysis of comorbidities was not performed. Fourth, although some indicators of multiple myeloma status were used in our analysis (eg, calcium, Bence Jones protein, M protein, and the presence of a plasmacytoma), staging was not considered. Future research should take comorbidities, multiple myeloma stage, and functional information into account. Lastly, our analyses were based on only 32 patients who returned to the primary acute care service. This study

was intended to cast a broad net and be hypothesis-generating.

## Conclusions

Because of their medical fragility, patients with multiple myeloma on an inpatient rehabilitation service require attentive medical surveillance and close contact with the primary oncology service. Some factors associated with an increased risk of transfer back to the primary acute care service including male gender and thrombocytopenia. Unplanned transfer back to the primary acute service correlates negatively with survival.

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## Disclosure

J.B.F. Department of Palliative, Rehabilitation and Integrative Medicine, Unit 1414, University of Texas M.D. Anderson Cancer Center, 1515 Holcombe

Boulevard, Houston, TX 77030. Address correspondence to: J.B.F.; e-mail: [jfu@mdanderson.org](mailto:jfu@mdanderson.org)

Disclosure: nothing to disclose

J.L. Department of Exercise and Sports Sciences, New Mexico Highlands University, Las Vegas, NM  
Disclosure: nothing to disclose

B.C.S. Department of Palliative, Rehabilitation and Integrative Medicine, University of Texas MD Anderson Cancer Center, Houston, TX  
Disclosure: nothing to disclose

J.K.S. Department of Physical Medicine & Rehabilitation, Harvard Medical School, Boston, MA  
Disclosures outside this publication: consultancy, Oncology Rehab Partners

D.W.S. Department of Educational Psychology, University of Houston, Houston, TX  
Disclosure: nothing to disclose

J.J.S. Department of Lymphoma/Myeloma, University of Texas MD Anderson Cancer Center, Houston, TX  
Disclosure: nothing to disclose

E.B. Department of Palliative, Rehabilitation and Integrative Medicine, University of Texas MD Anderson Cancer Center, Houston, TX  
Disclosure: nothing to disclose

Supported in part by the M.D. Anderson Cancer Center support grant CA 016672. Eduardo Bruera is supported in part by National Institutes of Health grants RO1NR010162-01A1, RO1CA122292-01, and RO1CA124481-01.

This study was partially presented as a poster presentation at the Association of Academic Physiatrists Annual Meeting in February 2015.

Submitted for publication July 22, 2016; accepted December 16, 2016.

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