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Quality of End-of-Life Care in Patients with Hematologic Malignancies: A Retrospective Cohort Study

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Abstract

Background—Limited data is available on the quality of end-of-life care for patients with hematologic malignancies. In this retrospective cohort study, we compared the quality of end-of-life care between patients with hematologic malignancies and those with solid tumors.

Methods—All adult patients who died of advanced cancer between 9/1/2009 and 2/28/2010 while under the care of our institution were included. We collected baseline demographics and end-of-life care indicators, including emergency room visits, hospitalization, intensive care unit admissions, and systemic cancer therapy use within the last 30 days of life.

Results—113/816 (14%) decedents had hematologic malignancies. In the last 30 days of life, hematologic patients were more likely to have emergency room visits (54% vs. 43%, $P=0.03$), hospital admissions (81% vs. 47%, $P<0.001$), ≥ 2 admissions (23% vs. 10%, $P<0.001$), >14 days of hospitalization (38% vs. 8%, $P<0.001$), intensive care unit admissions (39% vs. 8%, $P<0.001$) and death (33% vs. 4%, $P<0.001$), chemotherapy use (43% vs. 14%, $P<0.001$), and targeted therapy use (34% vs. 11%, $P<0.001$) compared to patients with solid tumors. Patients with hematologic malignancies were also less likely to have palliative care unit admissions (8% vs. 17%, $P=0.02$). The composite score for aggressiveness of care (0=best, 6=worst) was significantly higher among patients with hematologic malignancies than those with solid tumors (median 2 vs. 0, $P<0.001$). In multivariate analysis, hematologic malignancy was a significant factor associated with aggressive end-of-life care (odds ratio 6.6, 95% confidence interval 4.1–10.7, $P<0.001$).

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Conclusions—Patients with hematologic malignancies received more aggressive care at the end-of-life.

Keywords

Hematologic neoplasms; Emergency medicine; End-of-life; Intensive care; Palliative care; Quality of care; Targeted agents; Chemotherapeutic agents

Introduction

Patients with hematological malignancies often experience significant physical symptoms, such as fatigue, insomnia, drowsiness, pain, dyspnea, and neuropathy as a result of complications from progressive cancer and antineoplastic treatments.^{1, 2} Cytopenias, infections, and coagulopathies are particularly common in these patients, necessitating frequent hospitalizations, invasive investigations, monitoring and therapies.^{3–5} Moreover, patients with hematological malignancies are often treated with intensive antineoplastic regimens that may continue until the last days of life.^{6, 7} Understandably, these patients and their caregivers frequently experience psychological distress.^{8, 9}

While symptom burden in patients with hematologic malignancies has been studied by our group and others,^{1, 2} the quality of end-of-life care has not been well examined in these patients. We found only two population-based studies on this topic, both reporting that the diagnosis of hematological malignancy was one of the factors associated with more aggressive end-of-life care based on composite scores.^{10, 11} However, no study has specifically documented the rates of emergency room visits, hospitalization, and intensive care unit (ICU) use with a focus on patients with advanced hematological malignancies. A better understanding of how hematology patients were managed in the last 30 days of life would help clinicians, administrators and policy makers to identify gaps in care and potentially areas for improving the quality of end-of-life for these patients. In this retrospective cohort study, we compared the quality of end-of-life care indicators between patients with hematologic malignancies and those with solid tumors.

Methods

Patients

This retrospective cohort study is a secondary analysis of an inclusive institutional cohort we previously used to examine the pattern of palliative care referral.¹² Briefly, we reviewed the medical records of 816 consecutive patients seen at MD Anderson cancer center in Houston, Texas who died as a result of advanced cancer between September 1, 2009 and February 28, 2010 and had a postal address within the seven-county Houston metropolitan area, which was defined as the central county (Harris) and the seven surrounding counties (Brazoria, Chambers, Fort Bend, Galveston, Liberty, Montgomery, and Waller). We defined advanced cancer as locally advanced, metastatic, or recurrent disease for solid and as incurable disease at presentation or first relapse for hematologic malignancies (i.e. leukemia, lymphoma and myeloma). We also included patients who refused all curative treatments, who were referred to the Phase I program, and who had an incurable (or refractory) cancer or were not eligible

for potentially curative treatment as per oncology notes. For patients with more than one malignancy, we used the data pertaining to the cancer most responsible for death. Patients with age <18 years, death unrelated to advanced cancer, or last contact with MD Anderson Cancer Center >3 months before death were excluded. This retrospective study was approved by our institutional review board.

Data collection

Baseline demographics, such as age, sex, race, marital status, cancer diagnosis and date of advanced cancer diagnosis had been collected previously.¹² For this secondary study, we retrieved multiple quality of end-of-life care indicators that were well established in the peer-reviewed literature,^{10, 11, 13–15} and endorsed by the National Quality Forum (NQF) and the American Society of Clinical Oncology (ASCO).^{16, 17} These indicators included any emergency room visit in the last 30 days of life, 2 or more emergency room visits in the last 30 days of life, any hospital admission in the last 30 days of life, 2 or more hospital admissions in the last 30 days of life, more than 14 days of hospitalization in the last 30 days of life, hospital death, ICU admission in the last 30 days of life, and ICU death. These data were retrieved from our institutional database, and further verified by chart review to ensure accuracy of data collection. Furthermore, we reviewed the last date of administration of palliative chemotherapy and/or targeted agents, and determined the proportion who received these treatments in the last 14 and 30 days of life as documented previously.⁶ Targeted agents are defined in this study as drugs or other substances that interfere with specific molecular pathways related to tumor proliferation or progression, and include a variety of monoclonal antibodies, tyrosine kinase inhibitors, and other small molecules.¹⁸

Statistical Analysis

We summarized the data using descriptive statistics, including means, medians, ranges, interquartile range and frequencies. We compared the patient characteristics and quality of end-of-life care indicators between solid tumors and hematological malignancies using the Student's *t*-test for normally distributed continuous variables, the Mann-Whitney test for nonparametric continuous variables, and the Chi square test or Fisher's exact test for categorical variables.

A composite aggressive end-of-life care score has previously been reported,¹⁰ with one point for each of the following 6 ASCO/NQF indicators in the last 30 days of life: two or more ER visits, two or more hospital admissions, more than 14 days of hospitalization, an ICU admission, death in a hospital, and use of chemotherapy. The total score ranged from 0 to 6, with a higher score indicating more aggressive care. We used a multivariate logistic regression model with backward elimination to identify factors associated with the presence of any of the above 6 indicators. Variables included in the model were age, sex, race, hematologic malignancy and marital status.

A P-value of <0.05 was considered significant. The Statistical Package for the Social Sciences (IBM SPSS version 19.0, SPSS Inc., Chicago, Illinois) software was used for statistical analysis.

Results

Among the 816 patients, 113 (14%) had hematological malignancies. These included 34 (30%) patients with acute myelogenous leukemia, 28 (25%) with multiple myeloma, 27 (24%) with B cell non-Hodgkin's lymphoma, 7 (6%) with T cell non-Hodgkin's lymphoma, 7 (6%) with acute lymphocytic leukemia, 5 (4%) with chronic lymphocytic leukemia, 3 (3%) with chronic myelogenous leukemia and 2 (2%) with Hodgkin's lymphoma. We found no significant difference in the baseline demographics between patients with hematologic malignancies and those with solid tumors. The mean age was 62 years. 48% were female and 61% were White (Table 1).

We found significant differences in the quality of end-of-life care indicators between hematologic malignancies and solid tumors (Table 2). In the last 30 days of life, patients with hematological malignancies were more likely than patients with solid tumors to have any emergency room visits (54% vs. 43%; $P=0.03$), hospital admissions (81% vs. 47%; $P<0.001$), two or more hospital admissions (23% vs. 10%; $P<0.001$), ICU admissions (39% vs. 8%; $P<0.001$), more than 14 days of hospitalization (38% vs. 8%; $P<0.001$), hospital deaths (47% vs. 16%; $P<0.001$), and death in ICU (33% vs. 4%; $P<0.001$). Furthermore, patients with hematological malignancies were more likely to receive chemotherapy (43% vs. 14%; $P<0.001$) and targeted therapy (34% vs. 11%; $P<0.001$) within the last 30 days of life and also the last 14 days of life.

Patients with hematological malignancies were less likely to have palliative care unit admission (17% vs. 8%; $P=0.02$), any palliative care consultation (47% vs. 33%; $P=0.006$), and outpatient palliative care consults (48% vs. 22%; $P=0.003$) within the last 30 days of life.

The composite score for aggressive end-of-life care was significantly higher for patients with hematological malignancies as compared to those with solid tumors (2 vs. 0; $P<0.001$).

In multivariate regression analysis, hematological malignancies (odds ratio [OR] 6.63; $P<0.001$) and age (OR 0.97 per year increase; $P<0.001$) were found to be independent predictors for aggressive end-of-life care (Table 3).

Discussion

We found that patients with hematological malignancies were more likely to have multiple emergency room visits, intensive care unit admissions and death, and cancer treatments in the last weeks of life compared to patients with solid tumors. We also identified a relative lack of palliative care involvement in hematologic patients. Our findings highlight the need to develop programs to improve the quality of end-of-life care for patients with hematologic malignancies.

Although quality of end-of-life care is closely related to quality of life at the end-of-life, these are conceptually and operationally distinct measures to assess end-of-life outcomes. Both were recognized by NQF and ASCO as important outcomes.^{16, 17} Indeed, longitudinal monitoring of symptom distress and quality of life until the end-of-life is important,

although this is not being consistently done for all cancer patients currently. Further efforts are needed to document these important outcomes for clinical care and research purposes.

In the last 30 days of life, patients with hematological malignancies were more likely than those with solid tumors to have emergency room visits, hospital admissions, intensive care unit stays and >2 weeks of hospitalization. This is consistent with the study by Ho et al., which reported that patients with hematological malignancies were 85% more likely to require hospital admissions in last month of life compared to patients with prostate cancer.¹¹ The high utilization of the acute care facilities in patients with hematologic malignancies in the last weeks of life is likely related to the high frequency of hematologic complications, such as anemia and thrombocytopenia requiring transfusions, neutropenia with infections necessitating antibiotics, and bleeding and thromboembolic events requiring acute interventions.³⁻⁵ These are further compounded by our observation that hematologic patients often receive systemic therapies in the last days of life, which adds another layer of treatment-related adverse effects and the need for hospitalization for treatment administration and monitoring.

In addition to higher rates of hospitalization, patients with hematologic malignancies also more likely to die in a hospital. Remarkably, we found that almost half of these patients died in the acute care facility, whereas a vast majority of solid tumor patients died outside of a hospital. Our findings are consistent with a recent meta-analysis of 16 studies from various countries demonstrating that hematology patients were more likely to die in hospital (odds ratio 2.25, $p < 0.0001$).¹⁹ In addition to hospital deaths, deaths in intensive care unit were significantly higher in hematology patients as compared to solid tumors (33% vs. 4%). Patients with hematological malignancies are often admitted to intensive care unit with severe sepsis requiring vasopressor support, respiratory insufficiency requiring mechanical ventilation and multi-organ system failure on hemodialysis.²⁰ Compared to patients who died at home with hospice, patients who died in an intensive care unit or hospital had greater physical and emotional distress and worse quality of life, and their caregivers had a high risk of prolonged grief.^{21, 22} Thus, active efforts are needed to improve the transition to home at the end-of-life for patients with hematologic malignancies.

We previously reported that patients with hematologic malignancies had limited access to palliative care compared to patients with solid tumors, with a smaller proportion of palliative care referral, delayed involvement and predominantly inpatient consultations instead of outpatient visits.¹² Our current study also found that patients with hematologic malignancies have fewer admissions to our acute palliative care unit, despite previous studies by our group and others demonstrating similarly high symptom burden among hematologic and solid tumor patients.^{1, 2} Staffed by an interprofessional team, acute palliative care units provide intensive symptom control, psychosocial care, transition to end-of-life care and assist with complex discharges,^{23, 24} and represents an appropriate alternative for some patients with hematological malignancies instead of the intensive care unit.

We found that patients with hematological malignancies had higher mean composite scores for aggressive end-of-life care. In multivariate logistic regression, the diagnosis of hematological malignancy was also strongly associated with aggressive end-of-life care. Our

findings are similar to two population-based studies that reported poorer quality of end-of-life care among hematologic patients in Taiwan and Canada.^{10, 11} Importantly, neither of these studies adjusted for cancer stage; thus patients with curable cancer who died unexpected (e.g. of treatment complications or non-cancer causes) were also included in the analyses. In addition to bringing a US perspective, our study is unique because it includes consecutive patients regardless of Medicare coverage, and also focuses on patients with advanced incurable cancer in which these aggressive end-of-life criteria are more applicable. Furthermore, instead of examining aggressiveness of end-of-life care as an aggregate outcome (present or absent), we were able to provide a more in-depth examination of the magnitude of each indicator.

Our findings highlight the need to address the end-of-life care for patients with hematological malignancies. Hematologists and oncologists caring for patients with advanced hematological malignancies need to ensure their patients and caregivers have a good understanding of the incurable nature of their illness and their general prognosis. This would form the basis for discussions surrounding goals of care and advance care planning. The presence of end-of-life discussions has been shown to be associated with less aggressive end-of-life care in patients with advanced cancer.²² Given that palliative care referral is often initiated within days before death, if at all, for patients with hematologic malignancies,^{12, 25–27} early involvement of palliative care in the outpatient setting may facilitate these complex communications and decisions.^{28, 29} The palliative care team may also be able to provide the necessary screening, monitoring, treatment and education for various symptoms, thus reducing the need for symptom crisis requiring emergency room visits and hospital stays.^{1, 30} Because referral to palliative care is highly heterogeneous, clinical care pathways aimed at integrating palliative care early in the disease trajectory may be useful. In contrast to the treatment guidelines for solid tumors, palliative care has not yet been fully incorporated into the National Comprehensive Cancer Network guidelines for hematologic malignancies. For instance, the term “palliative care” only appeared twice in latest guideline for multiple myeloma and non-Hodgkin’s lymphoma, and not at all for Hodgkin’s lymphoma, acute lymphoblastic leukemia and acute myeloid leukemia.³¹ Reimbursement policy changes may help hematologists and oncologists to limit prescribing of systemic therapies in patients with a limited prognosis. Finally, we urgently need more research to document the impact of various interventions on end-of-life outcomes.

Our study has several limitations. First, this is a cohort study from a single tertiary care cancer center. The patient and healthcare provider characteristics may differ from the community setting. Therefore, our findings may not be generalizable to other settings. Second, we only included patients over a span of 6 months in 2009/2010. It may be possible that the quality of care has changed since that period. Third, we conducted many hypothesis-driven statistical tests, although our findings should be considered preliminary given the multiple testing. Forth, some of these patients might have had utilized acute care services at an outside facility which would not be captured by our institutional database. This could result in an underestimation of the aggressiveness of care in our cohorts. We expect this to represent a small proportion because we specifically included only patients dwelling locally for our analysis. Fifth, we were not able to collect reasons for emergency room visits and hospitalizations. Sixth, we excluded patients not seen in our hospital three months before

death, which may result in an overestimation of the degree of aggressiveness of end-of-life care if these individuals were enrolled onto hospice early. Given the median time from hospice referral to death is only 19 days, we believe our findings are valid.³²

In conclusion, patients with hematologic malignancies were managed aggressively in the last 30 days of life, with high rates of emergency room visits, hospitalizations, intensive care unit stays, and systemic therapy use. Our findings highlight the need for clinicians to minimize aggressive interventions at the end-of-life, and the need for further research to optimize care in the last days of life for patients with hematological malignancies.

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Table 1

Patient Characteristics (N=816)

Patient Characteristics	Solid tumors N=703 (%) ^I	Hematologic malignancies N=113 (%) ^I	P-value	All patients N=816 (%) ^I
Age, mean (range) years	62 (22–97)	61 (21–88)	0.31	62 (21–97)
Female sex	341 (49)	49 (43)	0.31	390 (48)
Race				
White	431 (61)	68 (60)	0.69	499 (61)
Black	154 (22)	24 (21)		178 (22)
Hispanic	80 (11)	17 (15)		97 (12)
Asian	28 (4)	4 (4)		32 (4)
Others	10 (1)	0 (0)		10 (1)
Married	437 (62)	67 (60)	0.68	504 (60)
Christian religion	535 (95)	81 (94)	0.79	616 (95)
Education				
High school or less	252 (36)	32 (28)	0.02	284 (35)
College	225 (32)	31 (27)		256 (31)
Post graduate	56 (8)	7 (6)		63 (8)
Not available	170 (24)	43 (38)		213 (26)
Cancer type			<0.001	
Breast	71 (10)	0 (0)		71 (9)
Gastrointestinal	178 (25)	0 (0)		178 (22)
Genitourinary	89 (13)	0 (0)		89 (11)
Gynecologic	61 (9)	0 (0)		61 (7)
Head and neck	48 (7)	0 (0)		48 (6)
Hematologic	0 (0)	113 (100)		113 (14)
Other	94 (13)	0 (0)		94 (12)
Respiratory	162 (23)	0 (0)		162 (20)
Months between advanced cancer diagnosis and death, median (IQR)	11.8 (4.5–23.8)	12.7 (4.4–39.8)	0.27	11.7 (4.5–25.2)

^I column percentage unless otherwise specified

Abbreviations: IQR, interquartile range

Table 2

Quality of End-of-Life Care Indicators (N=816)

Patient Characteristics	Solid tumors N=703(%) ¹	Hematologic malignancies N=113(%) ¹	P-value
Within last 30 days of life			
Any ER visit	300 (43)	61 (54)	0.03
2 or more ER visits ²	83 (12)	17 (15)	0.35
Any hospital admission	333 (47)	91 (81)	<0.001
2 or more hospital admissions ²	73 (10)	26 (23)	<0.001
More than 14 days of hospitalization ²	54 (8)	43 (38)	<0.001
Hospital death ²	110 (16)	53 (47)	<0.001
ICU admission ²	55 (8)	44 (39)	<0.001
Intensive care unit death	30 (4)	37 (33)	<0.001
Chemotherapy use ²	98 (14)	49 (43)	<0.001
Targeted therapy use	78 (11)	38 (34)	<0.001
Chemotherapy and targeted agent use	160 (23)	60 (53)	<0.001
Palliative care unit admission	116 (17)	9 (8)	0.02
Within last 14 days of life			
Chemotherapy use	40 (6)	24 (21)	<0.001
Targeted therapy use	37 (5)	19 (17)	<0.001
Chemotherapy and targeted agent use	70 (10)	32 (28)	<0.001
Aggressive of end-of-life care score			
0	457 (65)	25 (22)	<0.001
1	119 (17)	26 (23)	
2	58 (8)	14 (12)	
3	44 (6)	21 (19)	
4	16 (2)	20 (18)	
5	8 (1)	5 (4)	
6	1 (0)	2 (2)	
Median score (IQR)	0 (0–1)	2 (1–3)	<0.001
Any palliative care consultation	329 (47)	37 (33)	0.006
Outpatient palliative care consultation (among patient seen by palliative care)	159 (48)	8 (22)	0.003
Months between advanced cancer diagnosis and palliative care consultation	10.7 (3.9–22.1)	15.6 (4.4–43.4)	0.06
Months between palliative care consultation and death	1.7 (0.6–4.6)	0.4 (0.1–1.2)	<0.001

¹ column percentage unless otherwise specified² six factors were included in a composite score for aggressiveness of end-of-life care used in a previous study¹⁰

Abbreviations: ER, emergency room; ICU, intensive care unit; IQR, interquartile range

Table 3Multivariate logistic regression analysis^I

Patient Characteristics	Odds ratio (95% CI)	P-value
Age (per year increase)	0.97 (0.96–0.99)	<0.001
Hematologic malignancy	6.63 (4.11–10.72)	<0.001

^I Variables entered in the multivariate logistic regression model include age, sex, race, hematologic malignancy and marital status