The Surprise Question and Identification of Palliative Care Needs among Hospitalized Patients with Advanced Hematologic or Solid Malignancies

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Abstract

Background: Little is known about quality of life (QOL), depression, and end-of-life (EOL) outcomes among hospitalized patients with advanced cancer.

Objective: To assess whether the surprise question identifies inpatients with advanced cancer likely to have unmet palliative care needs.

Design: Prospective cohort study and long-term follow-up.

Setting/Subjects: From 2008 to 2010, we enrolled 150 inpatients at Duke University with stage III/IV solid tumors or lymphoma/acute leukemia and whose physician would not be surprised if they died in less than one year.

Measurements: We assessed QOL (FACT-G), mood (brief CES-D), and EOL outcomes.

Results: Mean FACT-G score was quite low (66.9; SD 11). Forty-five patients (30%) had a brief CES-D score of ≥4 indicating a high likelihood of depression. In multivariate analyses, better QOL was associated with less depression (OR 0.91, $p < 0.0001$), controlling for tumor type, education, and spiritual well-being. Physicians correctly estimated death within one year in 101 (69%) cases, yet only 37 patients (25%) used hospice, and 4 (2.7%) received a palliative care consult; 89 (60.5%) had a do-not-resuscitate order, and 63 (43%) died in the hospital.

Conclusions: The surprise question identifies inpatients with advanced solid or hematologic cancers having poor QOL and frequent depressive symptoms. Although physicians expected death within a year, EOL quality outcomes were poor. Hospitalized patients with advanced cancer may benefit from palliative care interventions to improve mood, QOL, and EOL care, and the surprise question is a practical method to identify those with unmet needs.

Keywords: advance care planning; depression; hospice care; inpatients; palliative care; quality of life

Introduction

QUALITY OF LIFE (QOL) and psychological health are important issues for cancer patients and both have impacts on mortality.[1–3] While much is known about QOL and depression among ambulatory patients with cancer, little is known about these issues among hospitalized patients with advanced cancer.

Hospitalized patients with advanced cancer are at risk for poor outcomes[4] and are commonly suspected to have worse QOL than the ambulatory cancer population. Similarly, there are various published estimates of the prevalence of depression in nonhospitalized cancer patients. In several meta-analyses, the pooled mean prevalence of major depression among cancer patients ranged from 8% to 24%, with greatest prevalence during treatment.[5,6] However, one might expect

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mood to differ among hospitalized patients with advanced cancer. Descriptions of QOL and mood among hospitalized cancer patients are largely absent in the literature.

We aimed to assess QOL and mood among hospitalized patients with advanced cancer, for whom the treating clinician indicated that he/she would not be surprised if the patient were to die within the next year.[7] Evidence suggests that this surprise question has relatively good sensitivity and specificity for identifying patients likely to die in the next year (69.3% and 83.6%, respectively),[8] with a hazard ratio for death of 7.87 among patients with breast, lung, or colon cancer.[9] However, its utility in identifying patients with poor QOL has not been shown, nor has its use been described, to our knowledge, in patients with hematologic malignancies.

We hypothesized that hospitalized cancer patients whose clinicians identified using the surprise question would have poor QOL and high rates of depressive symptoms. Since there is strong evidence that palliative care positively impacts QOL and mood in advanced cancer,[10–12] we also aimed to describe use of these services in this population most likely to benefit. Last, since there is limited research on the psychological burden and palliative care needs of hematologic malignancy patients,[13,14] we specifically included the patients in our analysis and compared their outcomes with those of solid tumor patients.

Materials and Methods

Participants

Between 2008 and 2010, 150 participants were recruited from malignant hematology and solid tumor inpatient units at Duke University Hospital as part of a prospective study of spiritual well-being among patients with advanced cancer.[15] Eligible participants met the following criteria:

(1) Adults (age >18) with advanced cancer of any subtype (stage III or IV solid tumors, stage III/IV lymphoma, or relapsed/refractory acute leukemia or myeloma), for whom the treating clinician indicated that he/she would not be surprised if the patient were to die of their cancer within the next year[7]; (2) receiving care from the hematology/oncology inpatient service; (3) cognitively capable of completing questionnaires; and (4) fluent in English. The inpatient attending physician or advanced practitioner completed the surprise question.

Among 257 eligible patients, 107 declined enrollment and 150 were consented. The reasons cited for declining included not interested (40.1%), health reasons/too sick (33.6%), unknown (13.1%), overwhelmed (5.6%), did not like questions (4.7%), family concerns (1.9%), and the patient was unreachable (0.9%). Of the 107 patients who declined enrollment, 42 (39.2%) were female, 69 (64.4%) were Caucasian, 13 (12.1%) were African American, 1 (0.9%) was Hispanic, and 24 (22.4%) did not report race or ethnicity. Three patients were excluded from the analysis because they did not meet the above study criteria after further quality control review. Our study was approved by the Duke IRB.

Measures

Participants reported their age, sex, ethnicity, race, education level, and cancer diagnosis at enrollment, which occurred at any time during their admission. During the interview, the research nurse assessed physical function using the Karnofsky performance scale (KPS)[16] and comorbidities using a modified version of the Charlson comorbidity index, which does not attribute additional comorbidity points for a cancer diagnosis since all patients in this study had cancer.[17] Education was dichotomized to high school or less versus at least some college. Clinical information was extracted from medical records.

QOL was measured using FACT-G, a validated scale assessing well-being in four domains (physical, functional, emotional, and social) on a 5-point ordinal scale ranging from 0 to 4.[18] Individual subscale scores have a minimally important difference (MID) of 2 to 3 points.[19,20] The total FACT-G MID is 3 to 7 points.[19] MIDs have been shown to be stable across populations.[21,22] There are also published mean FACT scores for ambulatory patients with cancer,[23] which we used as a reference to compare against our cohort.

We measured depressive symptoms using the Center for Epidemiological Studies Depression (CES-D) Symptom Index Short Form. It is a five-item brief version of the 20-item CES-D scale that assesses depressive feelings and behaviors over the last week.[24,25] The five items are as follows: ''I felt that I could not shake off the blues even with help from my family or friends,'' ''I felt depressed,'' ''I felt fearful,'' ''My sleep was restless,'' and ''I felt hopeful about the future.''[24] Each patient response is scored from 0 to 3 (0 = rare, 1 = some or little of the time, 2 = moderately or much of the time, and 3 = most or almost all of the time). The numbers assigned to each question are summed to create the total score. A score of ≥4 indicates high risk of depression. The brief form has similar sensitivity and specificity as the longer scale.[24,26,27] CES-D has been validated in cancer outpatients as well as hospitalized patients with serious illness.[28–32]

Patients also completed the Functional Assessment of Chronic Illness Therapy–Spiritual Well-being (FACIT-Sp) scale, which measures the extent to which medical patients experienced aspects of spiritual well-being in the past week on a 5-point ordinal scale ranging from 0 to 4.[33]

Last, we reviewed charts in November 2014 to assess the presence of advance directives, use of hospice services, and rate of death in the hospital after the index admission.

Statistical analysis

This was a secondary analysis of a prospective study on spirituality in hospitalized cancer patients.[15] We calculated descriptive statistics to assess demographic characteristics. Kruskal–Wallis, Fisher's exact, and chi-squared tests were used as appropriate. Our primary outcomes of interest were FACT-G for QOL and CES-D for depression. To identify associations with these outcomes of interest, we fit a linear regression model for FACT-G and a logistic regression model for CES-D (score of 0–3 vs. ≥4 since 4 is a clinically meaningful threshold indicating high risk of depression). We used stepwise variable selection with an entry and stay threshold of $p = 0.15$ to test the following variables: tumor type (hematologic malignancy vs. solid tumor), KPS, educational status, race (Caucasian vs. not Caucasian), Charlson comorbidity index, FACIT-Spirituality score, sex, and marital status.

To explore the relationship between QOL and depression, we used logistic regression to fit the FACT-G score as the primary predictor without adjustments. As a sensitivity analysis, we tested if the relationship between these clinical

outcomes persisted after adjusting for all selected predictors of depression from our previous model. Higher scores on these QOL and performance status scales represent better QOL or functional status; higher scores on the CES-D represent a higher likelihood of depression. The data were normally distributed and parametric tests were appropriate. We used SAS, version 9.4.

Results

Baseline characteristics

Table 1 gives the following information. Mean age was 58.9 (SD 14.1). More patients had hematologic malignancies (101 of 147) than solid malignancies (46 of 147). Sixty-eight (46.3%) patients were female; most were Caucasian (113; 76.9%). There were no significant differences in age, race, or education by tumor type. There were more female patients in the solid tumor cohort than the hematologic malignancy group (27 of 46, or 58.7%, vs. 41 of 101, or 40.6%; $p = 0.04$). Mean KPS was 63.3%; a score of 60% corresponds to "requires occasional assistance, but is able to care for most of his/her personal needs."

QOL and depression

Mean FACT-G score was 66.9. The hematologic malignancy group had a mean score of 67.7, while the solid tumor group had a mean score of 65.1. See Table 2 for FACT-G subscale scores. Mean brief CES-D score was 3.0. There was no difference in KPS, QOL, or CES-D scores across tumor types. In comparison with a population of ambulatory advanced nonsmall cell lung cancer patients, our inpatient cohort had significantly worse FACT-G scores (66 vs. 80.9, $p < 0.05$).[34]

While solid tumor patients in our study had a higher mean CES-D score compared with patients with hematologic malignancies (4.0 vs. 3.0), this difference was not significant. Twenty-eight (27.7%) hematologic malignancy patients and 17 (36.9%) solid tumor patients had a CES-D score of ≥4, indicating a high likelihood of depression. This difference between groups was not significant. Sex, education, and

TABLE 1. DEMOGRAPHICS

	Total (n = 147)
Age, mean (SD)	58.9 (14.1)
Female	68 (46.3%)
Race	
Native American/Alaskan	3 (2.0%)
Asian	2 (1.4%)
African American	28 (19.0%)
Caucasian	113 (76.9%)
Not reported	1 (0.7%)
Education	
Missing	9
Less than bachelor's degree	80 (58.0%)
Bachelor's degree and above	58 (42.0%)
Diagnosis	
Solid tumor	46 (31.3%)
Multiple myeloma	6 (4.1%)
Lymphoma	33 (22.4%)
Leukemia	62 (42.2%)

FACIT-Sp score were associated with higher QOL. Linear regression analysis showed evidence that higher education (point estimate 4.25, p 0.03) and higher FACIT-Sp scores (point estimate 0.58, $p < 0.0001$) were associated with better QOL (Supplementary Table S1; Supplementary Data are available online at www.liebertpub.com/jpm). There was insufficient evidence to suggest a difference in sex and QOL (point estimate -3.43, p 0.054). Logistic regression showed evidence that a lower FACIT-Sp score was associated with depressive symptoms (OR 0.86, 95% CI 0.81–0.92, $p < 0.0001$).

Patients with solid tumors (OR 1.53, 95% CI 0.65–3.58, p 0.33) had increased odds of depressive symptoms, and patients with more education were less likely to have depressive symptoms (OR 0.61, 95% CI 0.81–0.92, p 0.25), but these differences in odds were not significant. Fitting QOL to depression, we found that patients with better QOL had lower odds of having depressive symptoms (OR 0.91, 95% CI 0.86–0.95, $p < 0.0001$). This association persisted after controlling for tumor type (hematologic vs. solid malignancy), education, and FACIT-Sp.

End-of-life quality outcomes

By November 2014, 127 patients (86%) had died (Table 2). In 101 cases (68.7%), physicians correctly estimated death within 12 months. There was insufficient evidence to suggest a difference in survival between tumor types. Twenty-seven patients (18.4%) had a documented advance directive during the index hospitalization, while 62 (52.1%) had a documented advance directive during a subsequent hospitalization. Twelve (8.2%) died during the index hospitalization; all had hematologic malignancies (p 0.01). In total, 63 patients (43%) died in the hospital. Thirty-seven patients (25.2%) utilized hospice before death. Four patients (2.7%) received a palliative care consultation during the index or subsequent hospitalization (subsequent to this study, our hospital launched a palliative care and solid oncology corounding model that increased palliative care involvement).[35] Comparing across tumor types, there was no significant difference in utilization of hospice benefits, advance directives, death in the hospital, and palliative care consultation.

Discussion

Our study of hospitalized patients with advanced cancer has three key findings. First, QOL was poor. Second, one-third of patients had a CES-D score indicating a high likelihood of depression. Third, end-of-life (EOL) quality outcomes were quite poor. These outcomes did not differ whether a patient had an advanced hematologic or solid organ malignancy. The surprise question identified a cohort with marked unmet palliative care needs.

At a time when patients' QOL should be paramount, hospitalized patients with advanced cancer in our cohort had poor QOL and a high likelihood of depression. Compared with published population normative values from 2236 U.S. cancer outpatients, our cohort had significantly worse QOL in all FACT-G subscales except social well-being, where our cohort had a significantly higher QOL.[23] Mean FACT-G score in our cohort was 14 points worse than in the reference population, far exceeding published MID thresholds for clinical significance.[23]

TABLE 2. PERFORMANCE STATUS, QUALITY-OF-LIFE, AND DEPRESSION SCORES AND END-OF-LIFE OUTCOMES

	Hematologic malignancy (n = 101)	Solid malignancy (n = 46)	Total (n = 147)	p
Karnofsky performance status, mean (SD)	63.0 (21.8)	64.5 (21.3)	63.3 (21.6)	0.75
Modified Charlson comorbidity index				
0	30 (40.5%)	17 (65.4%)	47 (47.0%)	0.03
1	9 (40.5%)	4 (15.4%)	13 (13.0%)	
2	20 (27.0%)	1 (3.8%)	21 (21.0%)	
≥3	15 (20.3%)	4 (15.4%)	19 (19.0%)	
Missing	27	20	47	
Physical, mean (SD)	14.6 (6.7)	12.9 (6.2)	14.1 (6.5)	0.17
Social, mean (SD)	24.6 (3.7)	23.4 (3.9)	24.2 (3.8)	0.05
Emotional, mean (SD)	15.6 (2.1)	15.0 (2.3)	15.4 (2.2)	0.26
Functional, mean (SD)	13.1 (5.1)	13.9 (4.5)	13.4 (4.9)	0.49
FACT-G, mean (SD)	67.7 (11.2)	65.1 (10.4)	66.9 (11.0)	0.18
FACIT-spirituality subscale, mean (SD)	39.6 (7.3)	37.8 (7.0)	39.1 (7.2)	0.10
Depression, mean (SD)	3.0 (1.0, 6.0)	4.0 (2.0, 6.5)	3.0 (1.0, 6.0)	0.11
Depression score ≥4[a]	28/101 (27.7%)	17/46 (36.9%)	45/147 (30.6%)	0.26
End-of-life outcomes				
Correctly estimate patient would die within next 12 months	69 (68.3%)	32 (69.6%)	101 (68.7%)	0.88
DNR during index admission	21 (20.8%)	6 (13.0%)	27 (18.4%)	0.26
DNR during subsequent admission	44 (55.7%)	18 (45.0%)	62 (52.1%)	0.27
Missing	22	6	28	
Died in hospital during index admission	12 (11.9%)	0 (0.00%)	12 (8.2%)	0.01
Died in hospital during subsequent admission	37 (46.3%)	14 (36.8%)	51 (43.2%)	0.33
Missing	21	8	29	
Palliative care consultation during any hospitalization	2 (2.0%)	2 (4.3%)	4 (2.7%)	0.41
Hospice before death	21 (20.8%)	16 (34.8%)	37 (25.2%)	0.07

[a]Indicates high risk of depression.
DNR, do-not-resuscitate order.

These issues are of utmost importance to patients. In a study of 459 patients with advanced cancer, 55% equally valued QOL and length of life, and 27% preferred QOL to length of life.[36] Depressed mood has been found to be an independent risk factor for all-cause mortality in medical inpatients,[37] and several studies show that worse QOL and depressed mood are associated with shorter survival in advanced cancer.[1–3]

Despite the compelling argument that QOL and depression are important, little is known about QOL and depression in hospitalized cancer patients. We found that a lower education level was associated with worse QOL and a lower spirituality score was associated with worse QOL and depression; however, it is still unclear what primarily drives the poor QOL and mood in these patients. It may be a product of acute illness, loss of functionality, the hospital environment, or perhaps a manifestation of their advanced cancer itself. One must wonder whether QOL and mood improve once discharged and whether these poor outcomes are amenable to targeted interventions, including concurrent palliative care, which is known to improve QOL in outpatients with advanced solid tumors.[12,38,39] Further study in this area is needed. Interestingly, our patients had social well-being scores on par with established cancer outpatient norms. This may be because hospitalized patients tend to have extra support from family and staff and suggests that social concerns contribute less to the poor QOL of hospitalized cancer patients.

Notably, QOL and depressive symptoms were similar in hematologic malignancy patients. This counters the usual refrain that hematology patients are fundamentally different in their care needs and in their potential to benefit from palliative care services.[14,40–43] There is limited research exploring psychological symptoms in hematologic malignancy patients compared with solid tumor patients, yet many reasons to believe that hematologic malignancy patients have unmet palliative care needs.[13,14] These patients tend to be concentrated more at academic centers, thus our study presented a unique opportunity to highlight the unmet needs of this underserved population. Furthermore, our findings suggest that the surprise question may have similar utility in identifying hematology inpatients at risk of poor EOL outcomes, depression, and impaired QOL. Additional research exploring these questions is needed.

We found that hospitalized cancer patients infrequently accessed palliative care services, including hospice care, despite the fact that a high proportion died in the hospital and that inpatient hospice care services are readily available at Duke. It is unclear why palliative care was underutilized, especially since the physicians all expected these patients to die within one year, even among those with hematologic malignancies wherein physicians commonly report more difficulty prognosticating.[40,42] It is possible that inpatient physicians were focused only on the acute illness or chose to defer difficult EOL discussions to the outpatient setting. Cultural avoidance of palliative care is another possibility.

Schenker found three main oncologist barriers to palliative care referrals: (1) conceptions that the philosophy of palliative care is incompatible with cancer therapy, (2) a belief that palliative care is the role of the oncologist, and (3) a lack of knowledge about available services.[44] These beliefs may have precluded inpatient palliative care consultation in our cohort. While palliative care consultation is more common today, we reviewed patients' charts up through November 2014, and the rate of referral remained low.

Since this study was completed, several large randomized trials have demonstrated the value of early, concurrent palliative care for patients with cancer.[12,38,39,45,46] In particular, El-Jawahri showed that inpatient palliative care improved QOL among hospitalized stem cell transplant patients.[46,47] Subsequently, a novel, palliative care corounding initiative was implemented on the solid tumor oncology service at Duke University Hospital, resulting in greater palliative care involvement, significantly reduced length of stay, fewer readmissions, and a trend toward more hospice use and less use of intensive care unit services at the end of life.[35] Further research is necessary to determine if concurrent palliative care interventions can improve EOL outcomes, QOL, and mood among inpatients with advanced cancer.

There are several reasons to believe that inpatients with advanced cancer may benefit from concurrent palliative care. Temel showed that early, concurrent palliative care improved QOL and decreased the rate of depression by 58% in patients with advanced non-small cell lung cancer, a difference not attributable to antidepressants.[12] Palliative care also increases the likelihood of in-home death.[12] The majority of cancer patients state that they prefer to die at home rather than in the hospital,[48,49] and cancer patients who die in the hospital experience greater physical and psychological burdens.[10] Furthermore, families have an increased risk of post-traumatic stress and prolonged grief after in-hospital death.[10] Based on our results, hospitalization of cancer patients may be an opportune time to screen for poor QOL, distress, and depression, as well as discuss EOL goals. Screening with the surprise question could lead to interventions such as palliative care or cognitive-behavioral therapy that would improve patients' QOL, mood, and EOL outcomes such as hospice enrollment and at-home deaths.

This study has several limitations. First, this was a cross-sectional single-center study, thus precluding us from studying QOL and mood issues over time. However, we are not aware of any other study exploring QOL, mood, and EOL outcomes among hospitalized patients with advanced cancer, so our findings remain important. Second, there was no control group. If anything, however, our results likely underestimate the poor QOL and rate of depression in hospitalized patients with cancer since many of those who declined to enroll reported feeling too sick to participate. Third, this study was performed at a single academic institution and only included English speakers. More research is needed to determine generalizability of our results; however, we believe our results are particularly useful in their inclusion of many patients with hematologic malignancies, who are excluded from most palliative care studies done to date. In addition, we should also point out that the surprise question was sometimes answered by inpatient clinicians who were not the longitudinal oncologists. On the other hand, evidence suggests that longitudinal relationships may actually reduce

prognostic accuracy,[50] and our results suggest that oncologists overall are relatively good at recognizing the poor prognosis scenarios associated with poor one-year overall survival. Last, the EOL quality assessments were obtained through chart review and thus may slightly underestimate the use of hospice services in the community if this were not documented in the electronic record. Similarly, given that comorbidity information was often missing for patients in the study, these results should be considered exploratory and warrant further testing and replication.

Conclusion

At a time when patients' QOL should be paramount, we found that that hospitalized patients with advanced cancer have poor QOL and a high likelihood of depression. Despite physicians' expectations that these patients would die within a year, hospitalized patients with advanced cancer had poor use of palliative care services, and a high proportion died in the hospital. Hospitalized patients with advanced hematologic or solid tumors may benefit from interventions aimed at improving mood, QOL, and EOL care.

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Author Disclosure Statement

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