Original Article

Impact of Timing and Setting of Palliative Care Referral on Quality of End-of-Life Care in Cancer Patients

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BACKGROUND: Limited data are available on how the timing and setting of palliative care (PC) referral can affect end-of-life care. In this retrospective cohort study, the authors examined how the timing and setting of PC referral were associated with the quality of end-of-life care. **METHODS:** All adult patients residing in the Houston area who died of advanced cancer between September 1, 2009 and February 28, 2010 and had a PC consultation were included. Data were retrieved on PC referral and quality of end-of-life care indicators. **RESULTS:** Among 366 decedents, 120 (33%) had an early PC referral (>3 months before death), and 169 (46%) were first seen as outpatients. Earlier PC referral was associated with fewer emergency room visits (39% vs 68%; $P < .001$), fewer hospitalizations (48% vs 81%; $P < .003$), and fewer hospital deaths (17% vs 31%; $P = .004$) in the last 30 days of life. Similarly, outpatient PC referral was associated with fewer emergency room visits (48% vs 68%; $P < .001$), fewer hospital admissions (52% vs 86%; $P < .001$), fewer hospital deaths (18% vs 34%; $P = .001$), and fewer intensive care unit admissions (4% vs 14%; $P = .001$). In multivariate analysis, outpatient PC referral (odds ratio [OR], 0.42; 95% confidence interval [CI], 0.28-0.66; $P < .001$) was independently associated with less aggressive end-of-life care. Men (OR, 1.63; 95% CI, 1.06-2.50; $P = .03$) and hematologic malignancies (OR, 2.57; 95% CI, 1.18-5.59; $P = .02$) were associated with more aggressive end-of-life care. **CONCLUSIONS:** Patients who were referred to outpatient PC had improved end-of-life care compared with those who received inpatient PC. The current findings support the need to increase the availability of PC clinics and to streamline the process of early referral. *Cancer* 2014;120:1743–9. © 2014 American Cancer Society.

KEYWORDS: chemotherapeutic agents, inpatients, neoplasms, outpatients, palliative care, quality of care.

INTRODUCTION

Palliative care is an interprofessional discipline that aims at improving the quality of life of patients with advanced diseases and their families by addressing their symptom concerns and their communication and decision-making needs.[1] Growing numbers of studies suggest that palliative care has a positive effect on many clinical outcomes, including symptom distress, quality of life, satisfaction, and survival.[2-4]

The quality of care at the end of life represents another important outcome. Aggressive medical interventions in the last weeks of life, such as emergency room (ER) visits, hospital and intensive care unit (ICU) admission and death, and chemotherapy administration, are generally considered to be indicators of poor-quality care.[5,6] These indicators have now been incorporated into the National Quality Forum and the American Society of Clinical Oncology (ASCO) Quality Oncology Practice Initiative as benchmarks to assess the quality of end-of-life care.[7,8]

A randomized controlled trial of outpatient palliative care referral compared with routine oncologic care revealed that palliative care was effective in improving end-of-life care;[4] however, it is not clear whether inpatient palliative care also offered a similar benefit. To our knowledge, no study to date has specifically examined how the timing and setting of palliative care referral are associated with these end-of-life care indicators. Although early access to palliative care occurs primarily in the outpatient setting, a large proportion of US cancer centers do not have outpatient palliative care clinics.[9] Therefore, the majority of referrals to palliative care occur only in the inpatient setting and late in the disease process.

A better understanding of how the timing and setting of palliative care referral are associated with the quality of end-of-life care may help guide our clinical practice. In this retrospective cohort study, we examined how the timing and setting of palliative care referral were associated with the quality of end-of-life care. We hypothesized that earlier involvement of palliative care in the outpatient setting is associated with positive end-of-life care outcomes.

MATERIALS AND METHODS

Study Setting and Eligibility Criteria

The Institutional Review Board at The University of Texas MD Anderson Cancer Center reviewed and approved this retrospective study and waived the requirement of informed consent. This was a secondary analysis of a study examining the pattern of palliative care referral at our institution.[10] Briefly, we included all adult patients in the Houston area who died of advanced cancer between September 1, 2009 and February 28, 2010; who had received a palliative care referral; and who had contact with our cancer center within the last 3 months of life. Patients were excluded if they transferred care to outside oncologists, relocated to another city, or were lost to follow-up. These criteria were specifically chosen such that we were able to reliably capture their medical information in the last months of life.[10]

The Supportive Care Center operated 5 days per week and saw approximately 25 patients per day. It was staffed by 2 palliative care specialists who were supported by an interdisciplinary team of nurses and a social worker. Upon completion of a standardized, comprehensive assessment, patients received personalized recommendations addressing their symptom distress, psychosocial, communication, and decision-making needs.[11] Patients who were referred to the palliative care mobile team in the inpatient setting were managed similarly by the same team of palliative care specialists following common clinical pathways.

Data Collection

The data retrieval process has been documented previously.[10,12] Briefly, we collected baseline demographics and data on the timing of palliative care referral in relation to death. We also determined whether patients' first palliative care consultation was conducted in the outpatient or inpatient setting, independent of the timing of referral.

We documented the presence or absence of quality-of-care indicators in the last 30 days of life based on the published literature.[13] These included any ER visit, ≥ 2 ER visits, any hospital admission, ≥ 2 hospital admissions, >14 days of hospitalization, hospital death, ICU admission, and ICU death. These data were retrieved from our institutional database and were verified further by chart review to ensure accuracy of data collection. We also manually reviewed the last date of administration of systemic cancer therapy and determined the proportion of patients who received these treatments in the last 14 days and 30 days of life as previously documented.[12]

Statistical Analysis

We summarized baseline demographics using descriptive statistics, including means, medians, ranges, interquartile ranges, and frequencies. We compared the demographics and quality-of-care indicators between patients who had an outpatient palliative care consultation and those who had an inpatient palliative care consultation using the t test for continuous, normally distributed variables (eg, age); the Mann-Whitney test for continuous, nonparametric variables (eg, duration between advanced cancer diagnosis and death); and the chi-square test or the Fisher exact test for categorical variables (eg, proportion of patients with hospital death). We compared the quality of care between early (>3 months between first palliative care consultation and death) and late (≤ 3 months) palliative care referral. This cutoff was chosen because the median time from referral to death to the outpatient clinic was approximately 3 months. A similar analysis also was conducted using the hospice referral criteria of 6 months as a cutoff.

We also compared between outpatient and inpatient palliative care consultations. The inpatient consultation group was a good control because these patients had similar characteristics and received similar interventions from the same team of palliative care professionals as those who were first seen at the outpatient palliative care clinic. It is important to note that the setting of referral is conceptually distinct from the outcome of interest (ie, aggressiveness of end-of-life care in the last 30 days of life). This is because, when clinicians make a palliative care referral, they cannot predict with accuracy that the patient will die in the next 30 days.[14] A palliative care referral is often triggered by symptom distress rather than prognosis. Inpatient palliative care referral is operationally different from our outcome. Inpatient palliative care referral involves only 1 hospital visit, which could occur any time before death (median, 0.7 months; range, 0-17.7 months). In contrast, the outcomes reported here are established by the National Quality Forum and the ASCO and have a higher threshold in terms of severity and timing than a single hospitalization.

A composite aggressive end-of-life care score has previously been reported[13,15] in which 1 point is given for each of the following 6 indicators in the last 30 days of life: ≥ 2 ER visits, ≥ 2 hospital admissions, >14 days of hospitalization, an ICU admission, death in a hospital, and receipt of chemotherapy. The total score ranges from 0 to 6, and higher scores indicate more aggressive care. We used a multivariate logistic regression model with backward elimination to identify factors associated with

TABLE 1. Patient Characteristics (N = 366)

Patient Characteristics	No. of Patients (%)		
	Inpatient Referral, N = 199[a]	Outpatient Referral, N = 169[a]	P
Age: Mean [range], y	59 [23-86]	61 [25-87]	.11[b]
Women	110 (55)	82 (49)	.25[c]
Race			.49[d]
White	117 (57)	111 (62)	
Black	48 (23)	34 (19)	
Hispanic	31 (15)	22 (12)	
Asian	8 (4)	11 (6)	
Others	3 (1)	1 (1)	
Married	129 (65)	112 (67)	.66[c]
Education			.19[c]
≤High school	73 (37)	61 (37)	
College education	63 (32)	61 (37)	
Postgraduate education	10 (5)	14 (8)	
Not available	53 (27)	31 (19)	
Cancer type			.003[d]
Breast	21 (11)	18 (11)	
Gastrointestinal	53 (27)	37 (22)	
Genitourinary	16 (8)	17 (10)	
Gynecologic	21 (11)	19 (11)	
Head and neck	4 (2)	18 (11)	
Hematologic	29 (15)	8 (5)	
Other	18 (9)	16 (10)	
Respiratory	37 (19)	34 (20)	
Time between advanced cancer diagnosis and death: Median [IQR], mo	11.7 [4.7-25.8]	19.6 [10.3-31.3]	< .001[e]
Time between advanced cancer diagnosis and palliative care consultation: Median [IQR], mo	10.6 [3.3-24.3]	12.0 [4.6-24.5]	.40[e]
Time between palliative care consultation and death: Median [IQR], mo	0.7 [0.2-1.6]	3.7 [1.6-9.6]	< .001[e]

Abbreviations: IQR, interquartile range.
[a] Column percentages are indicated unless otherwise specified.
[b] P values were determined with the Student t test.
[c] P values were determined with the chi-square test.
[d] P values were determined with the Fisher exact test.
[e] P values were determined with the Mann-Whitney test.

the presence of any of the above 6 indicators. Variables that were included in the model were age, sex, race, marital status, cancer diagnosis (hematologic or solid tumors), setting of palliative care referral (outpatient or inpatient), timing of palliative care referral (≤3 months or >3 months), time between advanced cancer diagnosis and death, and percentage of advanced cancer diagnoses with palliative care involvement. The data set was complete without missing data.

The Statistical Package for the Social Sciences (IBM SPSS version 19.0; SPSS Inc., Chicago, Ill) was used for statistical analysis. P values < .05 were considered significant.

RESULTS
Patient Characteristics
In total, 366 decedents met the eligibility criteria and were included in this study; 169 (46%) had their first palliative care consultation in the outpatient setting, and 199 (54%) had their first palliative care consultation in the inpatient setting. The median patient age was 61 years (range, 23-87 years). The majority of patients were women (N = 192; 52%), Caucasian (N = 228; 62%), and married (N = 241; 66%). Table 1 lists the baseline patient characteristics at first palliative care consultation, and the results indicate no significant differences between outpatient and inpatient consultations except for cancer diagnosis (P = .003).

Quality of End-of-Life Care by Timing of Palliative Care Referral
Compared with late referrals (≤3 months before death), early palliative care referrals (>3 months before death) were associated with significantly fewer ER visits (P < .001), hospital admissions (P < .001), and hospital

TABLE 2. Quality of End-of-Life Care by Timing of Palliative Care Referral

	Duration Between Palliative Care Referral and Death					
	No. of Patients (%)			No. of Patients (%)		
Patient Characteristics	≤3 Months, N = 246[a]	>3 Months, N = 120[a]	P	≤6 Months, N = 298[a]	>6 Months, N = 68[a]	P
Within last 30 d of life						
Any emergency room visit	168 (68)	47 (39)	<.001[b]	187 (63)	28 (41)	.002[b]
≥2 Emergency room visits	57 (23)	12 (10)	.003[b]	63 (21)	6 (9)	.02[b]
Any hospital admission	200 (81)	58 (48)	<.001[b]	223 (75)	35 (51)	<.001[b]
≥2 Hospital admissions	52 (21)	12 (10)	.01[b]	55 (18)	9 (13)	.38[b]
Hospitalization for ≥14 d	40 (16)	14 (12)	.28[b]	47 (16)	7 (10)	.27[b]
Hospital death	77 (31)	20 (17)	.004[b]	85 (29)	12 (18)	.07[b]
Any ICU admission	28 (11)	7 (6)	.13[b]	30 (10)	5 (7)	.65[c]
ICU death	10 (4)	3 (3)	.56[c]	11 (4)	2 (3)	>.99[c]
Chemotherapy use	42 (17)	17 (14)	.55[b]	50 (17)	9 (13)	.59[b]
Targeted therapy use	36 (15)	13 (11)	.33[b]	39 (13)	10 (15)	.84[b]
Chemotherapy and targeted agent use	67 (27)	29 (24)	.61[b]	77 (26)	19 (28)	.76[b]
Within last 14 d of life						
Chemotherapy use	17 (7)	5 (4)	.36[c]	19 (6)	3 (4)	.78[c]
Targeted therapy use	11 (4)	5 (4)	>.99[b]	13 (4)	3 (4)	>.99[c]
Chemotherapy and targeted agent use	23 (9)	10 (8)	.85[b]	27 (9)	6 (9)	>.99[c]
Aggressive EOL care score						
0	111 (45)	78 (65)	.017[c]	146 (49)	43 (63)	.42[c]
1	52 (21)	19 (16)		59 (20)	12 (18)	
2	32 (13)	11 (9)		37 (12)	6 (9)	
3	29 (12)	8 (7)		33 (11)	4 (6)	
4	17 (7)	3 (3)		17 (6)	3 (4)	
5	5 (2)	1 (1)		6 (2)	0 (0)	
Median score [IQR]	1 [0–2]	0 [0–1]	<.001[d]	1 [0–2]	0 [0–1]	.02[d]

Abbreviations: EOL, end of life; ICU, intensive care unit; IQR, interquartile range.
[a] Column percentages are indicated unless otherwise specified.
[b] P values were determined with the chi-square test.
[c] P values were determined with the Fisher exact test.
[d] P values were determined with the Mann-Whitney test.

deaths ($P = .004$) in the last 30 days of life (Table 2). The composite aggressive end-of-life care score was also significantly lower in the early referral group compared with late referral group (median score, 0 vs 1; $P < .001$). The findings were similar using 6 months as a cutoff for the timing of palliative care referral (Table 2).

Quality of End-of-Life Care by Setting of Palliative Care Referral

The data provided in Table 3 indicate that patients who had outpatient referrals had an improved quality of end-of-life care compared with those who were first referred as inpatients. Specifically, outpatient referral was associated with significantly fewer ER visits ($P < .001$), hospital admissions ($P < .001$), hospital deaths ($P = .001$), ICU admissions ($P = .001$), and a shorter duration of hospital stay ($P = .002$) in the last 30 days of life. In contrast, the proportion of patients who received chemotherapy and targeted therapy in the last 14 days or 30 days of life did not differ significantly between the 2 groups. The composite aggressive end-of-life care score also was

significantly lower in the outpatient referral group (median score, 0 vs 1; $P < .001$).

Factors Associated With Aggressive End-of-Life Care

Figure 1 indicates that outpatient palliative care referrals occurred earlier than inpatient referrals. Moreover, outpatient referrals and earlier referrals were associated with lower aggressive end-of-life care scores. In multivariate regression analysis, palliative care outpatient referral (odds ratio [OR], 0.42; $P < .001$) was associated with less aggressive end-of-life care, whereas men (OR, 1.63; $P = .03$) and hematologic malignancies (OR, 2.57; $P = .02$) were independently associated with more aggressive end-of-life care (Table 4).

DISCUSSION

We observed that almost 50% of decedents who were seen by the palliative care team at our cancer center had at least 1 aggressive end-of-life care indicator. It is noteworthy that patients who were referred to palliative care earlier and as outpatients had improved quality of care compared

TABLE 3. Quality of End-of-Life Care by Setting of Palliative Care Referral

Patient Characteristics	No. of Patients (%)		
	Inpatient Referral, N = 199[a]	Outpatient Referral, N = 169[a]	P
Within the last 30 d of life			
Any emergency room visit	135 (68)	80 (48)	<.001[b]
≥2 Emergency room visits	51 (26)	18 (11)	<.001[b]
Any hospital admission	171 (86)	87 (52)	<.001[b]
≥2 Hospital admissions	47 (24)	17 (10)	.001[b]
Hospitalization for ≥14 d	40 (20)	14 (8)	.002[b]
Hospital death	67 (34)	30 (18)	.001[b]
Any ICU admission	28 (14)	7 (4)	.001[c]
ICU death	10 (5)	3 (2)	.15[c]
Chemotherapy use	34 (17)	25 (15)	.67[b]
Targeted therapy use	29 (15)	20 (12)	.54[b]
Chemotherapy and targeted agent use	55 (28)	41 (25)	.55[b]
Length of hospitalization in last 30 d of life: Median [IQR], d	9 [5-14]	8 [3-11]	.01[d]
Within the last 14 d of life			
Chemotherapy use	14 (7)	8 (5)	.38[b]
Targeted therapy use	9 (5)	7 (4)	>.99[b]
Chemotherapy and targeted agent use	20 (10)	13 (8)	.47[b]
Composite aggressive EOL care score			
0	83 (42)	106 (63)	<.001[c]
1	38 (19)	33 (20)	
2	31 (16)	12 (7)	
3	26 (13)	11 (7)	
4	16 (8)	4 (2)	
5	5 (3)	1 (1)	
Median score [IQR]	1 [0-2]	0 [0-1]	<.001[d]

Abbreviations: EOL, end of life; ICU, intensive care unit; IQR, interquartile range.
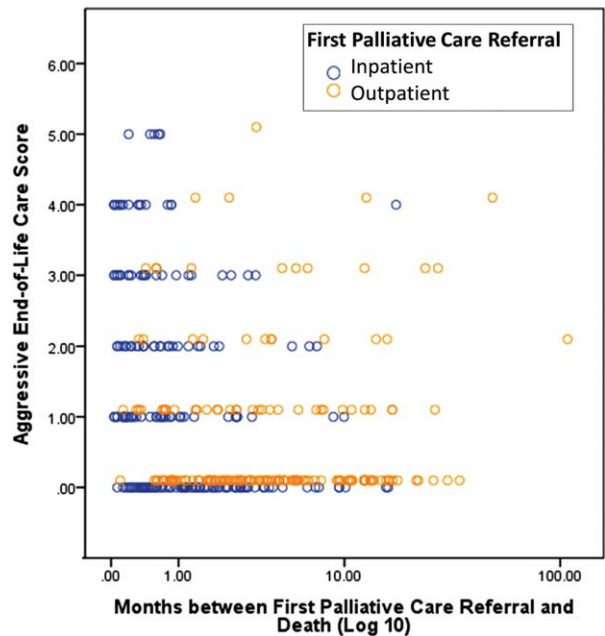[a] Column percentages are indicated unless otherwise specified.
[b] P values were determined with the chi-square test.
[c] P values were determined with the Fisher exact test.
[d] P values were determined with the Mann-Whitney test.

Figure 1. The association between aggressive end-of-life care and the timing and setting of palliative care referral are illustrated. The aggressive end-of-life care score is a previously published composite score with 1 point assigned for each of the following 6 indicators in the last 30 days of life: 2 or more emergency room visits, 2 or more hospital admissions, more than 14 days of hospitalization, an intensive care unit admission, death in a hospital, and receipt of chemotherapy.[13] The total score ranged from 0 to 6, with a higher score indicating more aggressive care. This scatter plot indicates that outpatient consultations (orange circles) occurred earlier in the disease trajectory than inpatient consultations (blue circles) and were more likely to be associated with less aggressive end-of-life care.

with those who were referred late and as inpatients, with lower proportions of patients having ER visits, hospitalizations, and ICU admissions. Outpatient palliative care referral remained an independent factor for improved end-of-life care in multivariate analysis. Our findings support the need to increase outpatient palliative care services in cancer centers and to improve the process of early palliative care referral.

We also noted that a large proportion of our patients received aggressive care at the end of life. How can we improve these outcomes? The Coping with Cancer Study demonstrated that patients who reported having had end-of-life discussions had improved medical use in the last week of life, such as decreased ICU admission, ventilator use, and resuscitation and increased hospice referral.[16] In a noteworthy report, Mack et al indicated that end-of-life

discussions that occurred earlier and in the outpatient setting were associated with improved end-of-life outcomes.[17] The palliative care team plays a key role in facilitating such discussions. Indeed, a landmark randomized controlled trial of palliative care as an intervention demonstrated improved documentation of resuscitation preferences and less aggressive end-of-life care.[4] Our current study expands on this knowledge by demonstrating that early and outpatient involvement of palliative care is associated with improved end-of-life outcomes compared with late and inpatient referrals.

Our observation that early and outpatient palliative care is associated with improved end-of-life outcomes can potentially be explained by multiple mechanisms. First, early involvement allows patients to develop a longitudinal therapeutic relationship with the palliative care team over multiple clinic visits. This may facilitate many important discussions over time, such as goals of care and advance care planning, which may help to minimize

TABLE 4. Multivariate Logistic Regression Analysis for Quality of End-of-Life Care Indicators[a]

Variable	OR (95% CI)	P
Men	1.63 (1.06-2.50)	.027
Hematologic malignancies	2.57 (1.18-5.59)	.018
Palliative care outpatient referral	0.42 (0.28-0.66)	<.001

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Variables that were entered into the logistic regression model with backward selection were age, sex, race, marital status, cancer diagnosis (hematologic or solid tumors), setting of palliative care referral (outpatient or inpatient), timing of palliative care referral (≤3 months or >3 months), time between advanced cancer diagnosis and death, and percentage of advanced cancer diagnoses with palliative care involvement.

aggressive interventions at the end of life. Second, early involvement allows the detection of symptoms such as pain and depression through routine screening, early intervention, and patient education, thus reducing the risk of symptom crisis necessitating ER visits and hospital stays, which are particularly common at the end of life. Third, palliative care can improve access to psychosocial services and introduce resources to the home setting, including hospice referral when appropriate, thus reducing the need for urgent acute care. Finally, oncologists who refer patients to palliative care early in the disease trajectory may be more "palliphilic" and more involved in goals of care discussions with their own patients. Prospective studies are needed to determine the cause-effect relations.

It is important to note that inpatient palliative care services also serve important functions. Studies by our group and others have consistently demonstrated that inpatient palliative care consultation teams can successfully reduce physical and psychological symptom burden and assist with transition of care.[18,19] Acute palliative care units may even be more effective than inpatient consultation teams at relieving patient and caregiver distress.[20-22] However, it would be unreasonable to expect a large impact on the quality of end-of-life care from inpatient palliative care teams when they are involved for the first time weeks or days before death and when many of the catastrophic complications requiring hospitalization have already occurred.

Despite the growing evidence supporting the effectiveness of palliative outpatient clinics, only 59% of the National Cancer Institute-designated cancer centers and 22% of non-National Cancer Institute-designated cancer centers reported having such clinics.[9] This is in contrast to the almost ubiquitous presence of inpatient palliative care consultation teams. Even with a palliative care clinic available, only 46% of patients had their first palliative care

visit in the outpatient setting at our center.[10] Given that oncologic care is predominantly delivered in the ambulatory setting, outpatient palliative care is an ideal setting for cancer patients to access comprehensive symptom management and psychosocial care. ASCO recently published a position paper based on the findings of multiple randomized controlled trials supporting early integration of palliative care in the disease trajectory for patients with advanced cancer and the role of outpatient palliative care clinics.[23,24] Currently, no consensus list of indicators for outpatient palliative care referral exists. Further research is necessary to examine potential barriers for outpatient palliative care referrals and to develop standardized criteria for making such referrals. In addition to increasing the availability of outpatient palliative care clinics, clinical care pathways and increased collaboration are necessary to improve patient access to palliative care.[11,25]

We also observed that men were associated with more aggressive end-of-life care. This finding is consistent with multiple studies demonstrating that women receive fewer medical interventions at the end of life relative to men.[13,26] Possible explanations include the development of terminal illness at an older age among women, differences in acute/chronic medical conditions, and differential treatment preferences and care delivery.[27]

The current study has several limitations. First, the data were based on patients who attended our tertiary care cancer center, who are likely to have different characteristics compared with patients in a community setting and may receive more cancer treatments for their advanced-stage disease. This may limit the generalizability of our results. Prospective studies examining the outcomes of palliative care clinics in both tertiary and community settings are warranted. Second, our sample size was relatively small. In contrast to population-based studies, we were able to verify our data with greater accuracy, and we included non-Medicare patients. Third, we limited our analysis only to patients who received palliative care to ensure that we could compare between 2 groups who had similar needs. Patients who are referred to palliative care often have greater symptom distress and may be more likely to need acute care than patients who are not referred to palliative care. Fourth, we only retrieved outcomes data at our institution. It is possible that some patients received their acute care outside of our institution in the last month of life; however, we believed this represents a minority of patients. In our cohort, 293 of 366 patients (80%) had their last visit within the last 30 days of life. The median time from last institutional follow-up to death was 11 days (interquartile range, 4-25 days). Fifth, because of the

retrospective nature of this study, we were not able to capture other factors that may influence the quality of end-of-life care. For instance, oncologists who refer patients earlier to palliative care may also be more likely to focus on quality of care and discuss goals of care with their patients. The ASCO Quality Oncology Practice Initiative included "referral to palliative care" as 1 of the indicators for assessing care at the end of life. On the basis of our findings, referral to *outpatient* palliative care may be a more appropriate marker.

Our study adds to the body of knowledge by demonstrating that outpatient palliative care consultation is associated with improved quality of end-of-life care compared with inpatient palliative care consultation, independent of cancer diagnosis and other patient characteristics. Our findings support the role of outpatient palliative care clinics in cancer centers and the need to address both the proportion and timing of palliative care referral.

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CONFLICT OF INTEREST DISCLOSURES

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