Original Investigation

Chemotherapy Use, Performance Status, and Quality of Life Near Death

Chemotherapy at the End of Life

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IMPORTANCE Although many patients with end-stage cancer are offered chemotherapy to improve quality of life (QOL), the association between chemotherapy and QOL amid progressive metastatic disease has not been well-studied. American Society for Clinical Oncology guidelines recommend palliative chemotherapy only for solid tumor patients with good performance status.

OBJECTIVE To evaluate the association between chemotherapy use and QOL near death (QOD) as a function of patients' performance status.

DESIGN, SETTING, AND PARTICIPANTS A multi-institutional, longitudinal cohort study of patients with end-stage cancer recruited between September 2002 and February 2008. Chemotherapy use (n = 158, [50.6%]) and Eastern Cooperative Oncology Group (ECOG) performance status were assessed at baseline (median = 3.8 months before death) and patients with progressive metastatic cancer (N = 312) following ≥1 chemotherapy regimen were followed prospectively until death at 6 outpatient oncology clinics in the United States..

MAIN OUTCOMES AND MEASURES Patient QOD was determined using validated caregiver ratings of patients' physical and mental distress in their final week.

RESULTS Chemotherapy use was not associated with patient survival controlling for clinical setting and patients' performance status. Among patients with good (ECOG score = 1) baseline performance status, chemotherapy use compared with nonuse was associated with worse QOD (odds ratio,0.35; 95% CI,0.17-0.75; *P* = 0.01). Baseline chemotherapy use was not associated with QOD among patients with moderate (ECOG score = 2) baseline performance status (odds ratio, 1.06; 95% CI, 0.51-2.21; *P* = 0.87) or poor (ECOG score = 3) baseline performance status (odds ratio, 1.34; 95% CI, 0.46-3.89; *P* = 0.59).

CONCLUSIONS AND RELEVANCE Although palliative chemotherapy is used to improve QOL for patients with end-stage cancer, its use did not improve QOD for patients with moderate or poor performance status and worsened QOD for patients with good performance status. The QOD in patients with end-stage cancer is not improved, and can be harmed, by chemotherapy use near death, even in patients with good performance status.

Invited Commentary

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Physicians have voiced concerns about the benefits of chemotherapy for patients with cancer nearing death.[1-5] In 2012, an American Society of Clinical Oncology (ASCO) expert panel identified chemotherapy use among patients for whom there was no evidence of clinical value[6] as the most widespread, wasteful, and unnecessary practice in oncology. Adequate patient performance status is often used as an indicator of whether the patient will be able to tolerate chemotherapy and respond to treatment. For this reason, performance status is used to gauge whether chemotherapy will offer clinical value.

Specifically, ASCO guidelines recommend against the use of chemotherapy in solid tumor patients who have not benefited from prior treatment and who have an Eastern Cooperative Oncology Group (ECOG)[7] performance status score of 3 or more (ie, bad or more debilitated than "capable of only limited self-care, confined to bed or chair more than 50% of waking hours").[6] This recommendation is supported by studies from the 1980s, which found that chemotherapy administered to patients with poor performance status resulted in low response rates, high rates of toxic effects, and short survival.[8,9] Because patients with good performance status are expected to benefit most from chemotherapy, trials have targeted those patients and have largely excluded cancer patients with poor performance status. As a result, evidence for treatment benefit or harm has rarely been quantified in patients with poor performance status. Research is needed to evaluate the benefits and harms of chemotherapy use among metastatic cancer patients stratified by performance status.

Despite the lack of evidence to support the practice, chemotherapy is widely used in cancer patients with poor performance status and progression following an initial course of palliative chemotherapy.[1,4,10,11] A study of patients with non-small-cell lung cancer (NSCLC) found that 28% of patients had performance status scores of 3 or 4 at presentation and that nearly 40% of these patients were receiving chemotherapy.[12] Available data for patients with NSCLC show a response rate of 2% for third-line and 0% for fourth-line chemotherapy.[13] This situation is not unique to NSCLC. A Norwegian study characterizing patients receiving palliative chemotherapy at a regional cancer center revealed that 53% had a performance status score of 2 and 16%, performance status scores of 3 and 4 at the start of last cancer therapy.[14] Overall, 10% received chemotherapy in the last 30 days of life. Among those patients, 21% had lung cancer; 15%, colorectal; 13%, prostate; and 9%, breast cancer. Of the breast cancer patients, 12% were receiving second-line therapy (associated with 3- to 6-month duration of response)[15] 19%, third-line therapy (2- to 4-month duration of response)[16,17]; and 21%, third-line therapy or higher. Hormone receptor status was not noted in the Norwegian study,[14] but in triple-negative breast cancer patients, duration of response was even shorter: 9 weeks after second-line therapy and 4 weeks after third-line therapy.[18]

The goal of palliative chemotherapy for patients with incurable cancer is to prolong survival and promote QOL. We have shown that chemotherapy use among patients with metastatic cancer whose cancer has progressed while receiving prior chemotherapy was not significantly related to longer survival but was associated with more aggressive medical care in the patient's final week and heightened risk of dying in an intensive care unit.[10] The aim of the current study is to examine the association between patients' performance status and the effect of chemotherapy on QOL in the last week of life. We hypothesize that patients with good performance status who receive additional palliative chemotherapy will have significantly worse QOL at the end of life than those who do not receive chemotherapy, and that patients with poor performance status will not experience QOL improvements with chemotherapy.

At a Glance

- We examined the effect of chemotherapy use on patient quality of life in the last week of life.
- Of cancer patients with progressive metastatic disease, 50.6% were receiving chemotherapy at study entry, a median of 4 months prior to death.
- Chemotherapy use was more frequent in patients with good compared with poorer performance status (chemotherapy patient mean Eastern Cooperative Oncology Group (ECOG) score,1.6 vs nonchemotherapy patient mean ECOG score, 2.0; $P < .001$).
- Among patients with moderate (ECOG score = 2) and poor (ECOG score = 3) performance status at study entry, chemotherapy use was not associated with quality of life improvement near death.
- Among patients with good (ECOG score = 1) performance status at study entry, chemotherapy use compared with nonuse was associated with worse quality of life near death (OR, 0.35; 95% CI, 0.17-0.75).

Methods

Sample

Patients were participants in a federally funded, prospective, multi-institutional cohort study of patients with end-stage cancer and their caregivers. Participants were recruited between September 2002 and February 2008 from cancer clinics at Yale (New Haven, Connecticut), Veterans Affairs (VA) Connecticut Healthcare System (West Haven, Connecticut), Parkland Hospital (Dallas, Texas), Simmons (Dallas, Texas), Dana-Farber (Boston, Massachussetts), and New Hampshire Oncology-Hematology (Hookset, New Hampshire). Patients were required to have a diagnosis of "end-stage cancer" (distant metastases; disease refractory to ≥1 line of chemotherapy), a physician-estimated life expectancy of less than or equal to 6 months, be at least 20 years old, a participating informal caregiver, and adequate stamina for the interview. Patients with serious cognitive impairment[19] or who lacked fluency in English or Spanish were excluded. Participants received $25 per interview. All 6 institutional review boards approved study procedures; all participants provided written informed consent.

Of the 939 eligible patients, 661 (70.4%) participated. Reasons for nonparticipation were "not interested" (n = 106), "caregiver refuses" (n = 32), and "too upset" (n = 21). Partici-

pants were more likely than nonparticipants to be Hispanic (P = .02), but otherwise had similar sociodemographic characteristics.

A majority (384 [58.1%]) died during the study observation period and were more likely to be younger, nonwhite, unmarried, uninsured, less educated, and have had worse performance status at enrollment (all P < .05) than patients who survived. Chemotherapy use at enrollment was unrelated to patients' being in the deceased vs surviving cohort.

Among the 384 patients who died, 33 (8.6%) patients were excluded due to clinical trial participation and 39 (11.1%) due to missing data. Patients excluded due to missing data did not differ from participating patients (N = 312) on age, sex, race/ethnicity, marital status, years of education, baseline performance status, or chemotherapy use.

Measures

Sociodemographic and Baseline Health Status Characteristics

Patients were asked to self-report age, sex, race/ethnicity, years of education, marital status, and health insurance status during baseline interviews conducted at a median of 3.8 months prior to death. Race and ethnicity were classified using National Institute of Health (NIH)-defined categories. The examination of racial/ethnic disparities in cancer care was a stated aim of the NCI-funded Coping with Cancer (CwC) (CA106370) study. Disease information was obtained from medical charts. Information about the number and severity of the patients' comorbid illnesses at the time of enrollment was assessed using the Charlson Comorbidity Index (CCI).[20]

Baseline Performance Status

Eastern Cooperative Oncology Group (ECOG) Performance Status[21] was used to evaluate each patient's performance status at enrollment. An ECOG score of 0 indicated that the patient was fully active, able to carry on all predisease performance without restriction (9 [2.9%]); 1, restricted in physically strenuous activity but ambulatory and able to perform light work (122 [39.1%]); 2, ambulatory and capable of all self-care but unable to perform any work activities, up and about more than 50% of waking hours (116 [37.2%]); 3, capable of only limited self-care, confined to bed or chair more than 50% of waking hours (58 [18.6%]); 4, completely disabled, cannot perform any self-care, totally confined to bed or chair (7 [2.2%]); and 5, dead (0).

Chemotherapy Use

We reviewed medical charts to determine whether patients were receiving chemotherapy at study enrollment: 158 [50.6%] were; 154 [49.4%] were not.

QOD

In a postmortem interview conducted a median of 2.4 weeks after each patient's death, the caregiver most knowledgeable about the health care the patient received in his or her final week of life was asked: "Just prior to the death of the patient (eg, his/her last week; when last seen), how would you rate his/her level of… " "psychological distress?" (0 = none; 10 = extremely upset); "physical distress?" (0 = none; 10 = extremely distressed); "overall QOL in the last week of life/death?" (0 = worst possible; 10 = best possible). Prior studies have validated both the accuracy of the caregiver rating of patient QOL and use of these items to assess patient QOL in the patient's final week.[22,23] Consistent with these studies, ratings for these 3 items were averaged (after reverse coding the psychological and physical distress items) such that greater composite scores represent better QOD on a scale of 0 (worst possible) to 10 (best possible). Taken together, these 3 items were internally consistent (Cronbach's α = 0.76) and represented a single, unidimensional QOD construct. In the present study, this continuous QOD measure was dichotomized based on a median split (QOD ≥ 7 = high QOD, 158 [50.6%]; QOD < 7 = low QOD, 154 [49.4%]) to facilitate analysis and interpretation. Mean (SD) QOD scores in the high and low QOD groups were 8.6 (0.9) and 4.2 (1.8), respectively.

Statistical Analysis

Bivariate associations between sociodemographic, clinical characteristics, and chemotherapy use were assessed using t tests for continuous and χ^2 tests for categorical variables. Characteristics associated (P < .05) with chemotherapy use were included in a multiple logistic regression model to determine which patient characteristics were independently associated with baseline chemotherapy use. Cox proportional hazards models determined if chemotherapy use at enrollment was associated with risk of death, adjusting for confounds (ie, enrollment site, baseline performance status).

Multiple logistic regression analysis tested the hypothesis that performance status modifies an association between baseline chemotherapy use and QOD. Patient QOD was regressed on the main and interactive effects of baseline chemotherapy use and performance status. None of the examined patient sociodemographic and clinical characteristics were significantly associated (P < .05) with patient QOD (**Table 1**). Therefore, none were considered confounding factors.

Associations between chemotherapy use and QOD, in an analysis stratified by baseline performance status, were assessed primarily in terms of odds ratios estimated using logistic regression. The same associations were assessed secondarily in terms of risk ratios estimated using log-binomial regression and between-group differences in QOD scores evaluated using 2-sample t tests. An exploratory model determined whether intensive care near death mediated associations between baseline chemotherapy use and QOD. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc.).

Results

The sample was 54.8% male, averaged 58.6 years of age and 12.4 years of education, and was 61.5% white, 20.5% black, and 16.7% Hispanic. Patients receiving, as opposed to not receiving, chemotherapy at enrollment were younger (56.3 vs 61.0 years, P = .001), more educated (13.1 vs 11.6 years, P = .001), had lower comorbidity (CCI 8.3 vs 9.0, P = .02), better performance scores (ECOG 1.6 vs 2.0, P < .001), were more likely to

Table 1. Baseline Patient Characteristics, Chemotherapy Use, and Quality of Life Near Death

Characteristic	Total (n = 312)	Chemotherapy Use		P Value[a]	Quality of Life Near Death[b]		P Value[a]
		Yes (n = 158)	No (n = 154)		Higher (n = 158)	Lower (n = 154)	
Continuous, mean (SD)							
Age, y	58.6 (12.6)	56.3 (12.1)	61.0 (12.8)	<.01	59.9 (11.6)	57.2 (13.6)	.06
Education, y	12.4 (4.0)	13.1 (3.9)	11.6 (4.1)	<.01	12.2 (4.0)	12.5 (4.1)	.59
Charlson Comorbidity Index[c]	8.6 (2.6)	8.3 (2.3)	9.0 (2.9)	.02	8.6 (2.5)	8.7 (2.8)	.71
Performance status score	1.8 (0.9)	1.6 (0.8)	2.0 (0.9)	<.01	1.8 (0.9)	1.8 (0.9)	.94
Categorical, No. (%)							
Men	171 (54.8)	85 (53.8)	86 (55.8)	.72	85 (53.8)	86 (55.8)	.72
Race/ethnicity							
White	192 (61.5)	101 (63.9)	91 (59.1)	.33	94 (59.5)	98 (63.6)	.55
Black	64 (20.5)	33 (20.9)	31 (20.1)		36 (22.8)	28 (18.2)	
Hispanic	52 (16.7)	21 (13.3)	31 (20.1)		27 (17.1)	25 (16.2)	
Other	4 (1.3)	3 (1.9)	1 (0.6)		1 (0.6)	3 (1.9)	
Married[c]	162 (52.8)	87 (56.5)	75 (49.0)	.19	78 (50.6)	84 (54.9)	.46
Health insurance[c]	165 (54.5)	90 (58.1)	75 (50.7)	.20	81 (52.6)	84 (56.4)	.51
Recruitment site							
Yale, Simmons, DFCI	90 (28.8)	71 (44.9)	19 (12.3)	<.01	48 (30.4)	42 (27.3)	.19
West Haven VA, Parkland	162 (51.9)	74 (46.8)	88 (57.1)		86 (54.4)	76 (49.4)	
NH Oncology-Hematology	60 (19.2)	13 (8.2)	47 (30.5)		24 (15.2)	36 (23.4)	
Cancer diagnosis							
Lung	72 (23.1)	36 (22.8)	36 (23.4)	.01	38 (24.1)	34 (22.1)	.50
Colon	40 (12.8)	24 (15.2)	16 (10.4)		22 (13.9)	18 (11.7)	
Pancreatic	23 (7.4)	15 (9.5)	8 (5.2)		13 (8.2)	10 (6.5)	
Other gastrointestinal	38 (12.2)	12 (7.6)	26 (16.9)		23 (14.6)	15 (9.7)	
Breast	42 (13.5)	28 (17.7)	14 (9.1)		18 (11.4)	24 (15.6)	
Other	97 (31.1)	43 (27.2)	54 (35.1)		44 (27.8)	53 (34.4)	

Abbreviations: DFCI, Dana-Farber Cancer Institute; NH, New Hampshire; QOD, quality of life near death; VA, Veterans Affairs Connecticut Healthcare System.

[a] Reported *P* values based on 2-sample *t* tests for continuous variables and χ^2 tests for categorical variables.

[b] Criteria used to evaluate QOD are detailed in the Methods section.

[c] Data missing for the following variables: Charlson Comorbidity Index (n = 1); married (n = 5); health insurance (n = 9).

be recruited from an academic medical center than other clinical settings, and have pancreatic and breast cancers compared with other cancers (Table 1). In a multiple logistic regression model, patient age (adjusted odds ratio [AOR], 0.96; 95% CI, 0.94-0.99), baseline performance status score (AOR, 0.67; 95% CI, 0.49-0.93), clinical setting (academic medical center vs community clinic AOR, 17.1; 95% CI, 6.6-44.0; hospital vs community clinic AOR, 4.07; 95% CI, 1.70-9.70) and disease (pancreatic cancer vs other cancers AOR, 4.17; 95% CI, 1.30-13.37; breast cancer vs other cancers AOR, 2.45; 95% CI, 1.00-5.99) were independently associated with patients' chemotherapy use.

Patients' risk of death was not significantly associated with chemotherapy use, adjusting for enrollment site and baseline performance status (adjusted hazard ratio, 0.85; 95% CI, 0.65-1.11), nor was it significantly associated with chemotherapy use when examined within each ECOG stratum, adjusting for enrollment site.

Based on the results from a multiple logistic regression model, patient baseline performance status score modified the association between chemotherapy use and QOD (interaction odds ratio [OR], 1.95; 95% CI, 1.13-3.35) and prompted a further analysis of the association stratified by patients' baseline performance status.

Chemotherapy use among patients with good (ECOG score = 1) baseline performance status was associated with lower QOD (OR, 0.35; 95% CI, 0.17-0.75; relative risk, 0.64; 95% CI, 0.46-0.88) (**Table 2**; **Figure**) and lower scores for the continuous QOD measure (chemotherapy group mean, 6.0; 95% CI, 5.3-6.7; nonchemotherapy group mean, 7.0; 95% CI, 6.4-7.6; group difference in means, −1.0; 95% CI, −1.9 to −0.1). Among patients with moderate (ECOG score = 2) and poor (ECOG score = 3) baseline performance status, chemotherapy use was unrelated to patients' QOD. Chemotherapy use remained significantly ($P < .01$) associated with worse QOD among patients with good performance status in models that controlled for receipt of intensive care (ie, ventilation or resuscitation) in the final week of life.

Table 2. Baseline Patient Performance Status, QOD, and Chemotherapy Use

ECOG Score[a]	Patients, No.	QOD	Baseline Chemotherapy Use, No. (%)[b] Yes	No	OR (95% CI)[c]	*P* Value
0	9	Higher	3 (33.3)	0	NE	NA
		Lower	6 (66.7)	0		
1	122	Higher	31 (43.7)	35 (68.6)	0.35 (0.17-0.75)	.01
		Lower	40 (56.3)	16 (31.4)		
2	116	Higher	27 (49.1)	29 (47.5)	1.06 (0.51-2.21)	.87
		Lower	28 (50.9)	32 (52.5)		
3	58	Higher	12 (54.5)	17 (47.2)	1.34 (0.46-3.89)	.59
		Lower	10 (45.5)	19 (52.8)		
4	7	Higher	1 (100)	3 (50.0)	NE	NA
		Lower	0	3 (50.0)		

Abbreviations: ECOG, Eastern Cooperative Oncology Group; NA, not applicable; NE, not estimable; OR, odds ratio; QOD, quality of life near death.

[a] Performance status was measured by ECOG score as follows: 0, asymptomatic; 1, symptomatic, ambulatory; 2, symptomatic, in bed less than 50% of the time; 3, symptomatic, in bed more than 50% of the time; 4, 100% bedridden.

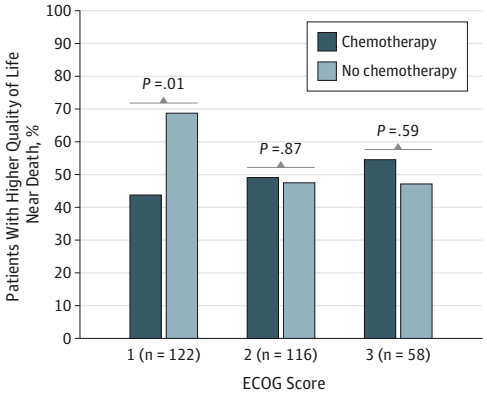
[b] Percentages displayed are column percentages, ie, the percentage of achieving higher (vs lower) quality of death conditioned on baseline chemotherapy (or no chemotherapy).

[c] Odds ratios are from within-stratum (ECOG score) logistic regression models. No significant confounding influences emerged and therefore no adjustments for them were needed or made.

Discussion

Whereas ASCO guidelines in response to the Choosing Wisely campaign[6] focus on the identification of patients with late-stage metastatic cancer most likely to benefit from palliative chemotherapy, our results suggest these guidelines may identify patients most likely to be harmed by it. Consistent with ASCO guidelines, patients with good performance status were the ones most likely to receive chemotherapy near the end of life. However, patients receiving palliative chemotherapy with an ECOG performance status of 0 or 1 had significantly worse QOD than those who avoided chemotherapy. No difference in QOD scores was observed by chemotherapy use among those with ECOG performance status of 2 or 3. Given no observed survival benefit in the studied patients with refractory metastatic disease and the observed significant association between chemotherapy use and worse QOL in the final week of life among those with a baseline ECOG score of 1, these results highlight the potential harm of chemotherapy in patients with metastasic cancer toward the end of life, even in patients with good performance status.

Figure. Patients' Higher Quality of Life Near Death Stratified by Baseline Performance Status and Chemotherapy Use



ECOG indicates Eastern Cooperative Oncology Group. Performance status was measured by ECOG score as follows: 1, symptomatic, ambulatory; 2, symptomatic, in bed less than 50% of the time; and 3, symptomatic, in bed more than 50% of the time. Criteria used to evaluate higher quality of life near death are detailed in the Methods section.

Chemotherapy use in patients with metastatic cancer with chemotherapy-refractory disease is common. Among the patients with end-stage cancer studied, over half were receiving chemotherapy at our baseline assessment a median of 3.8 months before death. Similarly, a recent study found 62% of NSCLC patients received chemotherapy within 60 days of death.[24] The trend toward more aggressive care of terminally ill patients is increasing[25] and has been noted as a serious problem in the Institute of Medicine's 2014 report *Dying in America*.[26] ASCO has attempted to respond to the need to limit widespread, wasteful, and unnecessary treatment practices[6] in formulating guidelines to restrict care only to patients with cancer expected to benefit from it. Our results raise questions about the benefits and use of chemotherapy in patients in the end-stage of their illness regardless of their performance status.

Our findings did not demonstrate that patients who had received chemotherapy at baseline were statistically more likely to survive our study observation period, nor that they had a reduced risk of death adjusting for enrollment site and performance status confounding factors. Nevertheless, the CwC study was neither designed nor powered to test hypotheses about chemotherapy use in relation to patient survival. Lack of evidence of a survival benefit associated with chemotherapy use in the present data should not be interpreted to mean that no such benefit exists. However, our study does highlight the danger of continuing chemotherapy as patients approach the end of life. Notably, in the patients with the highest function (eg, patients most likely to be receiving chemotherapy as in our sample and as per ASCO guidelines), the QOL

in the last week of life was significantly and meaningfully lower than in those not receiving chemotherapy at our baseline assessment.

Our study has several strengths, including the timing and representativeness of our sample. Unlike prior studies that use retrospective data from elderly Medicare patients,[27,28] we examined a prospective cohort of adult patients with cancer of all ages. Patients in this study were identified by their physicians as having a life-expectancy of no more than 6 months, chemotherapy use was documented in real time, patients were followed until they died, and QOL in the last week of life was evaluated by those who knew the patients' experience best. In these ways, our study design had strong external validity (ie, high generalizability)[29] and did not have selection biases that confound retrospective designs[30] and clinical trial data.[31] We also had unusually comprehensive assessments of patient sociodemographic, psychosocial, physical, and clinical characteristics in the months leading up to the patients' deaths. These included validated baseline assessments of patients' performance status, comorbid conditions, and validated assessments of patients' QOL in their final week of life.[22] This unique data set afforded an unusual opportunity to examine naturalistically how chemotherapy affects patient QOD while making adjustments for likely potential confounding factors.

Our study also had limitations, including incomplete information about the dose and duration of the chemotherapy used. We lacked detailed information on prior chemotherapy use and chemotherapy use between the baseline assessment and death. Nevertheless, decisions to start or stop chemotherapy that occurred between the baseline assessment and death would be expected to minimize differences in chemotherapy outcomes because those with good QOL would be more likely to start treatment; and those with poor QOL would be more likely to stop it. Another limitation is that patients were not randomly assigned to a chemotherapy arm, and no minimally important difference has been validated for our QOL measure. However, we examined a comprehensive set of likely potential confounding factors and those identified were included in the multivariable models. Future research will need to address more thoroughly biases inherent in treatment selection (eg, through randomization, propensity weighting, or matching) and also include repeated, more comprehensive and standardized QOL assessments to determine how QOL in the months, not just the week, before death is affected. In addition, an optimal study design would have followed all patients enrolled in the study from the initiation of chemotherapy until they died to confirm the effects of chemotherapy on survival and QOD.

Although use of a validated QOD measure is a strength of the present study, there is need for further refinement of this measure of QOD. For example, the wording of 2 of the items in the QOD measure suggest that psychological and physical distress may be assessed independently, but we only had a single item to assess each domain. These items were too closely correlated to represent 2 distinct factors that could be analyzed separately. In future studies, it might be helpful to differentiate between patients' psychological and physical well-being at the end of life to determine if either or both are affected by chemotherapy use among patients with chemotherapy-refractory metastatic disease.

Future studies are needed to identify underlying mechanisms of action to determine precisely why chemotherapy intended to palliate is detrimental to QOD. Given that our prior report[10] demonstrated that patients who received palliative chemotherapy were more likely to receive QOL-impairing, life-prolonging care, we explored whether the receipt of more aggressive care was a potential mechanism and/or mediator. Results indicated that the association between chemotherapy use and worse QOL in the final week of life for patients with good performance status (ECOG score = 1) at time of enrollment remained statistically significant even after adjustment for receipt of aggressive life-prolonging care. Thus, chemotherapy appears to contribute directly to worse QOD, presumably through adverse and toxic effects that impair the QOL of those who are initially feeling well. Prospective studies of chemotherapy use in patients with end-stage cancer are needed and should include repeated assessments of adverse effects of treatment and designate QOL and QOD as primary study endpoints. Identifying better predictive biomarkers to select patients who are most likely to benefit from chemotherapy, especially in the palliative setting, is also of paramount importance.

Conclusions

Results of this study suggest that chemotherapy use among patients with chemotherapy-refractory metastatic cancer is of questionable benefit to patients' QOL in their final week. Not only did chemotherapy not benefit patients regardless of performance status, it appeared most harmful to those patients with good performance status. ASCO guidelines regarding chemotherapy use in patients with terminal cancer may need to be revised to recognize the potential harm of chemotherapy use in patients with progressive metastatic disease.

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