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Patient beliefs that chemotherapy may be curative and care received at the end of life among patients with metastatic lung and colorectal cancer

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Abstract

Background—Many patients with incurable cancer inaccurately believe that chemotherapy may cure them. We know little about how such beliefs affect choices for care at the end of life. We assessed whether patients with advanced cancer who believe chemotherapy may offer cure are more likely to receive chemotherapy in the last month of life and less likely to enroll in hospice care before death.

Methods—We studied patients diagnosed with stage IV lung or colorectal cancer in the Cancer Care Outcomes Research and Surveillance Consortium, a population- and health system-based prospective cohort study. Among 722 patients who completed a baseline survey and died during the study period, we used logistic regression to assess the association of understanding goals of chemotherapy with chemotherapy use in the last month of life and hospice enrollment before death, adjusting for patient and tumor characteristics.

Results—One-third (33%) of patients recognized that chemotherapy was "not at all" likely to cure their cancer. After adjustment, such patients were no less likely than other patients to receive end-of-life chemotherapy (OR=1.32, 95%CI=0.84-2.09), but they were more likely than other patients to enroll in hospice (OR=1.97, 95%CI=1.26-2.66).

Conclusions—Understanding of the purpose of chemotherapy for incurable cancer is a critical aspect of informed consent. Still, advanced cancer patients who were well-informed about chemotherapy's goals received late life chemotherapy at similar rates to other patients.

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Understanding of the incurable nature of cancer, however, is associated with increased hospice enrollment before death, suggesting important care outcomes beyond chemotherapy use.

Introduction

Cancer patients should have the opportunity to make choices for care that incorporate both realistic expectations for the outcomes of therapy and personal values and goals, principles affirmed in recent guidelines.[1] Yet Weeks et al recently demonstrated that most patients with incurable lung and colorectal cancer inaccurately believe that chemotherapy could be curative.[2] This work raised concerns about the adequacy of informed consent for chemotherapy among such patients, who may experience palliation or life prolongation as a result of chemotherapy, but not cure.

These findings emerged in a broader context of work suggesting that decision-making for patients with advanced cancer can be problematic. Many patients have a limited understanding of prognosis [3, 4] and have discussions about end-of-life care late or not at all.[5, 6] Perhaps as a result, aggressive end-of-life care is prevalent and on the rise.[7, 8]

The patients studied by Weeks had already chosen to use initial chemotherapy for their metastatic cancers, and we do not know whether more realistic expectations would have changed their initial choices. However, given their incurable disease, more choices lay ahead for these patients, especially about the care they wish to receive at the end of life. Using follow-up data on the medical care of patients in the Cancer Care Outcomes Research and Surveillance (CanCORS) study, we assessed the extent to which early perceptions about whether chemotherapy might be curative were associated with care received by patients with metastatic lung and colorectal cancer at the end of life, including chemotherapy use near death and hospice enrollment. We also evaluated the extent to which patient preferences for symptom-directed or life-prolonging care were associated with end-of-life care choices.

Methods

The CanCORS study enrolled approximately 10,000 patients with lung or colorectal cancer diagnosed between 2003 and 2005. Patients were enrolled from five geographic regions (Northern California, Los Angeles County, North Carolina, Iowa, or Alabama), five participating health maintenance organizations (HMOs), and 15 Veteran's Affairs (VA) medical centers.[9, 10] Each site identified incident cases using a comprehensive, rapid case ascertainment protocol using either population-based or institutional cancer registries. The study was approved by the human subjects committees at all participating institutions.

Patients (or surrogates of patients who were deceased or too ill to participate) were interviewed at baseline, approximately 4-6 months after diagnosis, in English, Spanish, or Chinese. Medical records were abstracted for the time period beginning 3 months before diagnosis. Medical record abstraction was carried out in two phases; abstraction under the original CanCORS protocol was performed through 15 months or death for those who died sooner. For patients surviving beyond 15 months, additional medical record abstraction was conducted subsequently under the CanCORS II protocol. The date of last abstraction under CanCORS II varied slightly by site; the earliest completion date at any site was October

2010. Both rounds of data collection assessed chemotherapy use within the last 30 days of life and hospice enrollment.

For this analysis, we focused on patients with lung and colorectal cancer who had stage IV cancer at the time of initial diagnosis (N=2671), were living at the time of baseline survey administration with a survey completed by the patient or a surrogate (N=1333), reported having had a discussion with a physician about chemotherapy and answered questions about whether chemotherapy might be curative and about care preferences (N=1189), had medical records available for abstraction (N=946), and died within the medical record abstraction period. The final cohort included 722 patients, 477 with lung and 245 with colorectal cancer.

Outcomes included receipt of chemotherapy within the last month (30 days) of life and any hospice utilization, determined from medical record abstraction.

Additional variables of interest included survey data on perceptions about whether chemotherapy might be curative, elicited by asking, "After talking with your doctors about chemotherapy, how likely did you think it was that chemotherapy would cure your cancer?" [2, 11] Response options were "very likely," "somewhat likely," "a little likely," "not at all likely," and "don't know." Patient preferences for care were ascertained with the question, "If you had to make a choice now, would you prefer treatment that extends life as much as possible, even if it means having more pain and discomfort, or would you want treatment that focuses on relieving pain and discomfort as much as possible, even if it means not living as long?"[3] Five questions modified from the Consumer Assessment of Healthcare Providers and Systems survey were used to assess patients' perceptions of patient-physician communication.[2, 12, 13] Score means were transformed into a 0-100 scale. Surveys also assessed sex, race/ethnicity, age, marital status, education, number of months able to live at current standard if income lost, performance status (based on the EQ-5D, with performance status defined as "good" for patients with no mobility problems, no self care problems, and no or some problems with their usual activities [14]), and comorbidity (adapted from the self-administered Charlson index and the comorbidity questions from the Prostate Cancer Outcomes Study[15, 16]). Additional data from medical record abstraction included vital status, date of death, and insurance type.

Statistical analyses

Descriptive analyses included the prevalence of outcomes (chemotherapy in the last 30 days of life and hospice use) according to the presence of independent variables (eg, sex, race/ethnicity). Multivariable analyses were conducted using logistic regression on the outcomes of chemotherapy use in the last 30 days of life and hospice use. Variables were included in analyses based on *a priori* hypotheses about possible influences on end-of-life treatment choices, including sociodemographic variables (sex, race/ethnicity, marital status, age, education, wealth, insurance, and membership in an integrated provider network); health attributes (comorbidity, performance status, cancer type, and length of survival from diagnosis to death); our independent variables of interest, understanding of whether chemotherapy might be curative and preferences for care; and physician communication ratings, which were previously shown to be negatively associated with understanding of the

purpose of chemotherapy.[2] All variables were retained in multivariable models regardless of statistical significance.

Perceptions about whether chemotherapy might be curative were categorized as accurate if the patient or surrogate responded that chemotherapy was "not at all likely" to cure. Following conduct of the main analyses, we also evaluated the effect of expanding our definition of accurate expectations about chemotherapy, first examining the effect of considering a response of "don't know" or refusal as accurate, and second considering only responses of "very likely" to cure as inaccurate.

Due to item non-response, a multiply-imputed data set was created using standard statistical methods.[17, 18] Imputed values were used for covariates in bivariable and multivariable analyses, but not for chemotherapy use or hospice care, and not for perceptions about chemotherapy or care preferences, for which no data were missing based on cohort selection. Statistical analyses were conducted using Stata version 12 (StataCorp LP, College Station, TX.)

Results

This cohort of stage IV lung or colorectal cancer patients who were alive at 4-6 months after diagnosis but died during follow up survived a median of 13 months between diagnosis and death (Table 1). Physician communication scores were generally favorable, with 51% of patients offering the highest possible rating. Only 33% of patients recognized that chemotherapy was "not at all" likely to cure their cancer. Care preferences at baseline were divided between preferences for life-prolonging (44%) versus symptom-directed care (43%); 13% of patients did not state a preference.

Overall, 128 patients (18%) received chemotherapy in the last month of life, including 21.7% of those who recognized that chemotherapy was not at all likely to cure their cancer, and 15.8% of those who did not. In adjusted analyses assessing factors associated with chemotherapy use in the last month of life, patients who recognized that chemotherapy was not at all likely to cure them were no less likely to receive end-of-life chemotherapy (OR=1.32, 95% CI=0.84-2.09, P=.23) than those who believed chemotherapy offered some possibility of cure (Table 2). A preference for symptom-directed over life-prolonging care was also not associated with receipt of end-of-life chemotherapy (OR=.71, 95% CI=0.44-1.14, P=.15). Non-white patients were less likely than white patients to utilize late chemotherapy (OR=.52, 95% CI=0.30-0.90, P=.02, Table 2), as were patients who lived longer after their cancer diagnosis (OR=.93, 95% CI=0.91-0.96, per month of survival post-diagnosis, P<.001).

Overall, 255 patients (35%) enrolled in hospice before death. Nearly half (49.2%) of patients who recognized that chemotherapy was not at all likely to cure their cancer enrolled in hospice before death, versus 28.4% of those who held inaccurate expectations about chemotherapy. In adjusted analyses, patients who recognized that chemotherapy was not at all likely to cure their cancer were more likely to enroll in hospice (OR=1.97, 95% CI=1.37-2.82, P<.001), as were those who preferred symptom-directed versus life-

prolonging care (OR=1.83, 95% Ci=1.26-2.66, P=.002.) Non-white patients were less likely than white patients to enroll in hospice (OR=.60, 95% CI=0.40-0.90, P=.02, Table 3.) Patients aged   80 versus <60 (OR=2.47, 95%=CI 1.16-5.23, P=.02) and patients with lung versus colorectal cancer (OR=2.08, 95% CI=1.40-3.09, P<.001) had higher rates of hospice use, whereas patients who lived longer after diagnosis were less likely to use hospice before death (OR=.99, 95% CI=0.98-0.995 per month of survival from diagnosis, P=.001).

In sensitivity analyses that expanded our definition of accurate expectations about whether chemotherapy might be curative, results of multivariable models were similar, with accurate expectations associated with hospice use, but not end-of-life chemotherapy (results not shown).

Conclusions

Previous work by Weeks et al demonstrated that most patients with metastatic lung and colorectal cancer do not know that chemotherapy will not cure them.[2] This work raised concerns about the adequacy of fully informed decision making for cancer treatment among patients with incurable cancer. We sought to understand another possible dimension of this work–whether patients who believe that chemotherapy might cure them make different choices about care near death.

Our findings present a complex picture. On one hand, chemotherapy utilization in the last month of life was not a function of baseline expectations that chemotherapy might be curative. Instead, although overall use of late life chemotherapy in our cohort was relatively low (18%), patients who recognized that chemotherapy would not cure them were no less likely to use chemotherapy near death. (In fact, their absolute odds of chemotherapy use were higher, although not statistically so). In addition, late chemotherapy use was not associated with care preferences; those who wanted care directed at comfort were just as likely to receive chemotherapy near death as patients who preferred life-prolonging care, although our study was underpowered to detect small differences in use of late chemotherapy.

On the other hand, patients who recognized that chemotherapy was not curative were more likely to enter hospice, as were patients who preferred comfort-directed care. Previous work has shown that recognition of a poor prognosis is associated with less aggressive care at the end of life,[3] and end-of-life discussions are associated with more and earlier hospice use. [5, 19] Thus it seems reasonable that patients who recognize that chemotherapy will not cure them may similarly wish to receive hospice care, which is considered a marker of high quality end-of-life care[20, 21] and is associated with better quality of life near death.[5, 22, 23] Hospice enrollment may therefore be an important outcome of realistic expectations about chemotherapy, even if late life chemotherapy use is not impacted.

Is it counterintuitive that chemotherapy use at the end of life would not reflect understanding of its efficacy, or care preferences? Only if we assume that chemotherapy would be chosen for a single purpose- to cure- and not to palliate. Although end-of-life chemotherapy use was relatively infrequent, many of those who used it in the last month of life were aware it would

not cure them, and wished to receive care focused on alleviating symptoms. The increasing use of targeted therapy may make chemotherapy more tolerable and therefore more appealing to patients who want to avoid highly toxic regimens. While late life use of chemotherapy is often considered a marker of aggressive care, our findings suggest that at least some users of chemotherapy at the end of life have other goals, including palliation.

We should not minimize the potential impact of late life chemotherapy on patients, who may experience side effects without benefit, or on the health care system, where late life interventions may drive up the cost of care. Our study cannot tell us whether end-of-life chemotherapy achieved palliative goals for patients, and previous literature suggests that end-of-life chemotherapy is associated with use of other measures of aggressive end-of-life care.[24] Of note, work by Greer et al has found that early integration of palliative care is associated with decreased use of intravenous chemotherapy at the end of life, but not oral chemotherapy.[25] Taken together, this work and ours suggests that not all late life chemotherapy is the same, and decision-making about chemotherapy is complex, not purely based on hopes for cure. This area deserves more study, as does the framing of such conversations by physicians.

In addition, as we have noted, chemotherapy use late in life was relatively infrequent among all patients, not just those who recognized early in the course of the disease that it would not cure them. Despite the fact that many patients had hopes of cure soon after diagnosis, many may have reached more realistic expectations over time and decided to forgo treatment as a consequence. Nonetheless, even some well-informed patients may choose to receive chemotherapy until the end of life.

Other findings deserve special mention. Non-white patients were less likely to use hospice than whites, a finding consistent with prior work suggesting greater use of aggressive measures and lower hospice use among minorities.[26-28] However, non-white patients were also less likely to use late life chemotherapy; further study of this issue would be useful. In addition, despite the potential that different incentives or provider practice types could influence late life care utilization, we found no relationship between either chemotherapy use or hospice and insurance type or enrollment in an integrated provider network.

Our findings should be considered in light of limitations. Of note, patient reports about expectations for chemotherapy and care preferences were typically ascertained 4 to 6 months after diagnosis. Patient expectations and goals of care, however, can be dynamic. It is possible that end-of-life chemotherapy use would be more closely tied to expectations and preferences if they were assessed in the last month of life. However, changing goals and expectations may be more likely to shift toward palliative goals and expectations than away from them,[29] and it therefore seems unlikely that patients who recognized early that chemotherapy would not cure them would then develop more optimistic beliefs as they approached death. If anything, we may have underestimated the number of patients who reached an understanding near the end of life that treatment was not curative. Also, our cohort included patients with advanced cancer who lived at least 4-6 months (thus participating in the baseline survey) and discussed chemotherapy with a physician; the

patients also had relatively poor performance status. We cannot be certain if our findings would generalize to patients who die soon after diagnosis. Of note, hospice utilization was lower in our cohort of longer-surviving patients, but rates of end-of-life chemotherapy use were similar to those we have reported among all CanCORS decedents with stage IV cancer. [19] In addition, we focused this analysis on patient beliefs that chemotherapy might be curative. Because most patients believed chemotherapy might be curative, we felt it was important to understand the outcomes of such beliefs. However, future work might be enriched by an understanding of the full spectrum of goals of chemotherapy, including life prolongation and/or palliation of symptoms. Finally, our study was subject to nonresponse bias; however, other evidence has found the CanCORS cohort to be representative of patients diagnosed with lung and colorectal cancer in the United States.[30]

Despite high rates of early beliefs that chemotherapy may be curative, even some patients who recognized that chemotherapy would not cure them received chemotherapy in the last month of life. One possible explanation is that, at least for some patients, late chemotherapy use may be an informed decision based on realistic expectations that it will not be curative. Yet conversations about the incurable nature of the disease are associated with higher rates of hospice utilization, suggesting that informed decisions about the goals of chemotherapy can have a broader impact on care, well beyond initial decisions about treatment.

Acknowledgement

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Table 1

Patient characteristics. Data are given as frequency (percentage).

	N=722
Sex	
Male	457 (63.3)
Female	265 (36.7)
Race/Ethnicity[3]	
White	507 (70.2)
Non-White	215 (29.8)
Marital status3	
Married/living as married	426 (59.0)
Non-married	296 (41.0)
Age at diagnosis (years) [3]	
21-59	264 (36.6)
60-69	224 (31.0)
70-79	175 (24.2)
80	59 (8.2)
Comorbidity score at diagnosis[2]	
None/Mild	437 (60.5)
Moderate/Severe	285 (39.5)
Survival between diagnosis and death, median months (interquartile range)	13.0 (8.5, 24.7)
Physician communication score	
0-79	152 (21.1)
80-99	202 (28.0)
100	368 (51.0)
Education[1]	
<High school	143 (19.8)
High school/some college	439 (60.8)
college degree	140 (19.4)
Number of months able to live at current standard of living if lost income[1]	
<1 month	157 (21.8)
1-2 months	97 (13.4)
3-12 months	122 (16.9)
1 year	346 (47.9)
Insurance[3]	
Veterans Affairs	106 (14.7)
Private	250 (34.6)
Supplemental	237 (32.8)
Public	83 (11.5)
None	46 (6.4)

	N=722
Poor performance	
Yes	544 (75.4)
No	178 (24.7)
Integrated provider organization member	
Yes	281 (38.9)
No	441 (61.1)
Cancer type	
Lung	477 (66.1)
Colorectal	
Accurate understanding about whether chemotherapy might cure	
Yes	240 (33.2)
No	482 (66.8)
Care preference	
Life-prolonging care	318 (44.0)
Symptom-directed care	310 (42.9)
Missing/not asked	94 (13.0)

[1] Data obtained from baseline or follow-up interviews

[2] Based on the self-administered Charlson index and comorbidity questions from the Prostate Cancer Outcomes Study (PCOS)

[3] Data obtained primarily from baseline interview; if non-response, then data obtained from medical record abstraction; if both sources missing, then data obtained from administrative data (or tracking records)

Table 2

Patient factors associated with chemotherapy use in the last 30 days of life. Odds ratios and p-values are from multivariable logistic regression.

	Chemotherapy use in the last 30 days of life	Chemotherapy use in the last 30 days of life	
	Unadjusted %	Odds Ratio (95% CI)	P Value
Sex			
Male	17.7	Reference	
Female	17.7	0.77 (0.48, 1.26)	0.30
Race/Ethnicity			
White	19.7	Reference	
Non-white	13.0	0.52 (0.30, 0.90)	0.02
Marital status			
Married/living as married	17.8	0.86 (0.55, 1.36)	0.53
Non-married	17.6	Reference	
Age at diagnosis (years)			
21-59	20.8	Reference	
60-69	15.2	0.69 (0.39, 1.24)	0.22
70-79	17.1	0.95 (0.45, 2.02)	0.90
80	15.3	0.95 (0.36, 2.49)	0.91
Comorbidity score at diagnosis			
None/Mild	17.2	Reference	
Moderate/Severe	18.6	1.01 (0.64, 1.60)	0.96
Physician communication score			
0-79	15.8	0.68 (0.38, 1.21)	0.19
80-99	18.3	0.75 (0.45, 1.23)	0.25
100	18.2	Reference	
Education			
<High school	20.3	0.97 (0.47, 2.02)	0.94
High school/some college	16.6	0.87 (0.49, 1.54)	0.63
college degree	18.6	Reference	
Number of months able to live at current standard of living if lost income			
<1 month	18.5	1.01 (0.49, 2.09)	0.97
1-2 months	21.7	1.50 (0.75, 2.98)	0.26
3-12 months	18.0	1.27 (0.69, 2.34)	0.44
1 year	16.2	Reference	
Insurance			
Veterans Affairs	10.4	0.42 (0.17, 1.02)	0.06
Private	20.0	Reference	
Supplemental	15.2	0.62 (0.30, 1.27)	0.19
Public	24.1	1.32 (0.60, 2.89)	0.49

	Chemotherapy use in the last 30 days of life	Chemotherapy use in the last 30 days of life	
	Unadjusted %	Odds Ratio (95% CI)	P Value
None	23.9	0.93 (0.37, 2.31)	0.88
Performance status			
Poor	18.4	1.00 (0.59, 1.69)	1.00
Good	15.7	Reference	
Integrated provider organization member			
Yes	13.2	0.72 (0.42, 1.25)	0.24
No	20.6	Reference	
Cancer type			
Lung	20.6	1.04 (0.62, 1.75)	0.88
Colorectal	12.3	Reference	
Survival from diagnosis, months		0.93 (0.91, 0.96)	<0.001
<13 months	6.7		
13 months	28.8		
Accurate understanding about whether chemotherapy might cure			
Yes	21.7	1.32 (0.84, 2.09)	0.23
No	15.8	Reference	
Care preference			
Life-prolonging care	19.2	Reference	
Symptom-directed care	17.1	0.71 (0.44, 1.14)	0.15
Missing/not asked	14.9	0.79 (0.40, 1.56)	0.49

Table 3

Patient factors associated with hospice use. Odds ratios and p-values are from multivariable logistic regression.

	Hospice Use	Hospice Use	
	Unadjusted %	Odds Ratio (95% CI)	P Value
Sex			
Male	36.3	Reference	
Female	33.6	0.77 (0.52, 1.14)	0.19
Race/Ethnicity			
White	39.5	Reference	
Non-white	25.6	0.60 (0.40, 0.90)	0.02
Marital status			
Married/living as married	34.5	0.93 (0.65, 1.35)	0.72
Non-married	36.5	Reference	
Age at diagnosis (years)			
21-59	31.4	Reference	
60-69	36.6	1.23 (0.78, 1.96)	0.37
70-79	34.9	1.35 (0.74, 2.46)	0.33
80	41.2	2.47 (1.16, 5.23)	0.02
Comorbidity score at diagnosis			
None/Mild	34.1	Reference	
Moderate/Severe	37.2	0.73 (0.51, 1.14)	0.09
Physician communication score			
0-79	40.1	0.96 (0.62, 1.49)	0.86
80-99	31.7	0.73 (0.48, 1.10)	0.14
100	35.3	Reference	
Education			
<High school	37.8	1.53 (0.83, 2.80)	0.17
High school/some college	37.6	1.72 (1.07, 2.76)	0.03
college degree	27.7	Reference	
Number of months able to live at current standard of living if lost income			
<1 month	46.5	1.82 (1.11, 2.99)	0.02
1-2 months	34.0	1.09 (0.57, 2.08)	0.80
3-12 months	27.9	0.84 (0.47, 1.51)	0.58
1 year	33.2	Reference	
Insurance			
VA	43.4	0.88 (0.46, 1.66)	0.69
Private	32.4	Reference	
Supplemental	35.9	0.77 (0.44, 1.35)	0.37
Public	33.7	0.88 (0.45, 1.72)	0.71
None	32.6	0.62 (0.28, 1.41)	0.26

	Hospice Use	Hospice Use	
	Unadjusted %	Odds Ratio (95% CI)	P Value
Performance status			
Poor	37.7	1.38 (0.91, 2.09)	0.13
Good	28.1	Reference	
Integrated provider organization member			
Yes	38.1	1.09 (0.72, 1.65)	0.69
No	33.6	Reference	
Cancer type			
Lung	42.4	2.08 (1.40, 3.09)	<0.001
Colorectal	21.6	Reference	
Survival from diagnosis, months		0.99 (0.98, 0.995)	0.001
<13 months	52.4		
13 months	18.3		
Accurate understanding about whether chemotherapy might cure			
Yes	49.2	1.97 (1.37, 2.82)	<0.001
No	28.4	Reference	
Care preference			
Life-prolonging care	27.0	Reference	
Symptom-directed care	43.6	1.83 (1.26, 2.66)	0.002
Missing/not asked	36.2	1.51 (0.89, 2.57)	0.13