Chemotherapy use and patient treatment preferences in advanced colorectal cancer: a prospective cohort study

S. Yousuf Zafar[1,2,*], **Jennifer L. Malin**[3,4], **Steven C. Grambow**[2,5], **David H. Abbott**[2], **Jane T. Kolimaga**[2,7], **Leah L. Zullig**[2,8], **Jane C. Weeks**[9], **John Z. Ayanian**[10], **Katherine L. Kahn**[11], **Patricia A. Ganz**[12], **Paul Catalano**[13], **Dee W. West**[14], and **Dawn Provenzale**[2,7] **for the Cancer Care and Outcomes Research and Surveillance (CanCORS) Consortium**

[1]Duke Cancer Institute, Durham, NC

[2]Center for Health Services Research in Primary Care, Durham VA Medical Center, Durham, NC

[3]Greater Los Angeles VA Healthcare System, Los Angeles, CA

[4]Division of Hematology and Medical Oncology, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA

[5]Department of Biostatistics & Bioinformatics, Duke University Medical Center, Durham, NC

[6]Dana-Farber Cancer Institute, Boston, MA

[7]Division of Gastroenterology, Department of Medicine, Duke University Medical Center, Durham, NC

[8]University of North Carolina - Chapel Hill, Department of Health Policy and Management, Chapel Hill, NC

[9]Department of Health Policy and Management, Dana Farber Cancer Institute, Boston, MA

[10]Department of Health Care Policy, Harvard Medical School, and Division of General Medicine, Brigham and Women's Hospital Boston, MA

[11]RAND Corporation, Santa Monica, CA; and Divisions of General Internal Medicine & Health Services Research, Department of Medicine, University of California Los Angeles, Los Angeles, CA

[12]School of Public Health, University of California, Los Angeles, CA

[13]Department of Biostatistics & Computational Biology, Dana Farber Cancer Institute, Boston, MA

[14]Northern California Cancer Center, Fremont, CA; and Stanford School of Medicine, Stanford, CA

Abstract

BACKGROUND—Our objective was to determine how patient preferences guide the course of palliative chemotherapy for advanced colorectal cancer.

METHODS—Eligible patients with metastatic colorectal cancer (mCRC) were enrolled nationwide in a prospective, population-based cohort study. Data were obtained via medical record abstraction and patient surveys. Logistic regression was used to evaluate: patient

[*]Corresponding author: S. Yousuf Zafar, MD, MHS, Duke Cancer Institute, DUMC 3505, Durham, NC 27710, Office: 919.684.0138, Fax: 919.613.5228, yousuf.zafar@duke.edu.

characteristics associated with seeing medical oncology and receiving chemotherapy; and patient characteristics, beliefs and preferences associated with receiving >1 line of chemotherapy and receiving combination chemotherapy.

RESULTS—Among 702 patients with mCRC, 91% saw a medical oncologist, and among those, 82% received chemotherapy. Patients 65-75 and 75 years were less likely to see an oncologist, as were patients who were too sick to complete their own survey. In adjusted analyses patients 75 years and with moderate or severe comorbidity were less likely to receive chemotherapy, as were patients who were too sick to complete their own survey. Patients received chemotherapy even if they believed chemotherapy would not extend their life (90%), chemotherapy would not likely help with cancer-related problems (89%), or preferred treatment focusing on comfort even if it meant not living as long (90%). Older patients were less likely to receive combination first-line therapy. Patient preferences and beliefs were not associated with receipt of >1 line of chemotherapy or combination chemotherapy.

CONCLUSIONS—The majority of patients received chemotherapy even if they expressed negative or marginal preferences or beliefs regarding chemotherapy. Patient preferences and beliefs were not associated with intensity or number of chemotherapy regimens.

Keywords

BACKGROUND

A growing body of evidence has demonstrated the value of patient-centered care. Patients involved in decision-making are more knowledgeable about their care and more satisfied with their care.[1, 2] Patient dissatisfaction with treatment-related decision-making may negatively impact the quality of cancer care.[3] Patient preferences should be particularly emphasized in the setting of advanced cancer, where the treatment is palliative. For example, while chemotherapy for patients with advanced colorectal cancer can modestly extend survival, it is associated with risk of significant toxicity.[4] This balance between possible benefit versus probable risk necessitates a patient-centered approach to treatment decision-making. However, studies suggest improper use of chemotherapy near the end of life may reflect inadequate shared decision-making between patient and physician.[5] Physicians may find it easier to offer chemotherapy for the patient with advanced cancer rather than engaging in challenging end-of-life discussions.[6] For their part, patients might prefer to take a passive decision-making role when considering therapy for advanced cancer.[7, 8] What remains unclear is how patient preferences guide the course of palliative chemotherapy for advanced cancer.

To evaluate the quality of patient-centered care for patients with advanced cancer, an important question must be answered: do patient preferences play a role in treatment-related decision-making for palliative chemotherapy? We conducted a multiregional cohort study of patients with advanced colorectal cancer to assess factors associated with seeing a medical oncologist and receipt of chemotherapy, specifically addressing the effect of the patient's role in decision-making, quality of communication with their physician, overall quality of care, preferences for treatment, and their beliefs and concerns regarding treatment. We hypothesized that patient preferences would play a role in treatment-related decision-making.

METHODS

Patients

Study participants were enrolled by the Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium. CanCORS is a prospective, observational, population- and healthcare systems-based cohort study to determine how characteristics and beliefs of cancer patients, providers, and health care organizations influence treatments and outcomes.[9] Patients 21 years or older with colorectal cancer were enrolled from one of the following: five geographic regions, five integrated health care systems in the NCI-funded Cancer Research Network, or fifteen Veterans Administration (VA) Hospitals from September, 2003 to January, 2006 within three months of diagnosis. Patients were followed for 15 months past enrollment. Only patients with stage IV colorectal cancer (n=702) were included in this analysis.

Data collection

Primary data were collected from medical records, patient surveys, and surrogate surveys.[9-11] Trained abstractors at each of the data-collection sites abstracted medical records data, including cancer diagnosis, initial tumor location, and stage. Medical record data were also used to verify medical oncology visits, determine the first line of chemotherapy delivered (defined as the first chemotherapy regimen used to treat the patient's metastatic colorectal cancer), and determine whether the first line of therapy was single agent or combination therapy (more than one chemotherapeutic agent). Comorbidity was abstracted from the medical record and scored using the Adult Comorbidity Evaluation 27 (ACE-27), a 27-item index developed to provide prognostic information for cancer patients.[12]

Patient surveys were completed in English, Chinese, and Spanish using computer-assisted telephone interviews. A surrogate (relative or household member) familiar with the patient's cancer care was interviewed for patients who had died or were too ill to be interviewed. The surveys (available at www.cancors.org/public) used previously validated items and scales whenever possible and assessed patients' sociodemographic characteristics (age, race/ethnicity, annual income), insurance coverage, comorbid conditions, and beliefs about cancer care; survey development has been previously described.[11] Surveys also assessed quality of communication with their physician (5 items),[11] overall quality of care (2 items), preferences for treatment (2 items), and beliefs and concerns regarding treatment (9 items).[13] For patients who were too ill (n=60) or had died (n=140), a survey was administered to a surrogate when available. Most patients completed the survey after treatment was started. Human subject committees approved the study protocol at each participating site.

Statistical analysis

We calculated descriptive statistics summarizing sociodemographic characteristics, comorbidity, treatment, and survey-based patient preferences and beliefs. We used logistic regression to assess factors associated with seeing a medical oncologist and receipt of chemotherapy. Four analytic models were developed to assess factors associated with: (1) seeing a medical oncologist anytime prior to survey completion; (2) receipt of chemotherapy; (3) receipt of combination vs. single-agent first-line therapy; and (4) receipt of only one vs. more than one lines of therapy. In models 3 and 4 we considered the variables addressing role in chemotherapy decision-making, quality of communication with their physician, overall quality of care, preferences for treatment, and beliefs and concerns regarding treatment. These variables were not included in model 1 since not all of those patients completed a survey. These variables were not included in model 2 since they are

available only for patients seeing an oncologist and completing full surveys (n=409). Among patients completing a full survey, only 23 patients did not receive chemotherapy. An effective sample of 23 was too small to produce reliable results in logistic regression.

A consistent model building approach was used for all outcomes. Four variables were included unconditionally in all models: age, comorbidity, gender, and race. Survey respondent (patient vs. surrogate) was included as a variable in models 1 and 2. Step-wise model refinement was applied with p=0.20 criterion for entering variables into the models and p=0.10 criterion for removing them from the models. If necessary to prevent overfitting, the least significant variables were removed to attain model degrees of freedom to effective sample size ratio of 7[14]. Multiple imputation was used to address item nonresponse for survey-based variables and was performed centrally by the CanCORS Statistical Coordinating Center.[15] Results from multivariable models incorporate formal imputation adjustments.[16]

Data analysis was conducted at the Durham VA Medical Center, the coordinating site for VA hospitals participating in CanCORS. This analysis used CanCORS core data (version 1.9), medical record data (version 1.9), and patient survey data (version 1.8). Statistical analyses were performed using SAS for Windows Version 9.2 (SAS Institute, Cary, NC).

RESULTS

Cohort characteristics

Seven hundred two patients were included in this analysis (Figure 1). Patient characteristics are summarized in Table 1.

Medical oncology visits

Ninety-one percent of 702 patients had at least one visit with a medical oncologist (n=640, Figure 1). In multivariable analysis (Figure 2), age was associated with seeing an oncologist: patients 65-74 years old and 75 years old were less likely than those <55 years old to see an oncologist. Survey type (self-completion vs. completion by a surrogate) was significantly associated with seeing a medical oncologist, reflecting the greater severity of illness and functional decline among patients who were unable to fully participate in the survey. Patients who had their surveys completed by a surrogate or patients without any survey data were less likely to see a medical oncologist than patients who completed their own surveys. Variables addressing role in chemotherapy decision-making, quality of communication with their physician, overall quality of care, preferences for treatment, and beliefs and concerns regarding treatment were not included in this model since they are available only for patients seeing an oncologist and completing full surveys (n=409).

Chemotherapy regimens

Of those who consulted an oncologist (n=640), 527 (82%) received chemotherapy. Figure 3 illustrates the most common first-, second-, and third-line chemotherapy regimens. For their first-line chemotherapy regimen, 32% of patients received only single-agent therapy (e.g., fluorouracil or capecitabine). Among 477 patients with available chemotherapy regimen data, 63% received more than one line of chemotherapy. The regimens used for first-line therapy were generally in concordance with those listed in the National Comprehensive Cancer Network's colorectal cancer guidelines between 2003-2006, the period inclusive of patient enrollment.

Receipt of chemotherapy

Unadjusted analyses are presented (Table 2). Among those seeing an oncologist, patients who reported a preference for extending their life were more likely to receive chemotherapy than those focusing on comfort (99% vs. 90%, p<0.001). Patients who believed chemotherapy would extend their life were more likely to receive chemotherapy than those who thought it unlikely that chemotherapy would extend their life (99% vs. 90%, p=0.008). Patients who believed that chemotherapy might help with cancer-related problems were more likely to receive chemotherapy than those who thought chemotherapy would be unlikely to help (100% vs. 89%, p<0.001).

In multivariable analysis (Figure 4) age, comorbidity, and survey respondent were significantly associated with receipt of chemotherapy. The oldest patients (age 75 years) were least likely to receive chemotherapy when compared to those <55 years old. Patients with moderate or severe comorbidity were less likely to receive chemotherapy than those with no comorbidity. Patients who had their surveys completed by a surrogate were less likely than patients who completed their own surveys to receive chemotherapy. Patients without any survey data had a similarly lower likelihood of receiving chemotherapy. Variables addressing role in chemotherapy decision-making, quality of communication with their physician, overall quality of care, preferences for treatment, and beliefs and concerns regarding treatment were not included in this model since they are available only for patients seeing an oncologist and completing full surveys (n=409). Among this group only 23 patients did not receive chemotherapy; the effective sample of n=23 would have been too small to produce reliable results in logistic regression models.

Intensity of first-line chemotherapy

Multivariable analysis examined the association between characteristics, preferences, beliefs and intensity of first-line chemotherapy, as defined by receipt of combination therapy (more than one drug) versus single-agent therapy (Figure 5). The oldest patients were less likely to receive combination therapy as a part of their first-line regimen. Role in decision-making, quality of communication with their physician, overall quality of care, preferences for treatment, beliefs, and concerns regarding treatment were assessed but were not significantly associated with receipt of combination first-line therapy.

Number of chemotherapy regimens

Multivariable analysis examined the association between characteristics, preferences, beliefs and number of chemotherapy regimens received. Patient characteristics, role in decision-making, quality of communication with their physician, overall quality of care, preferences for treatment, beliefs, and concerns regarding treatment were assessed, but none were significantly associated with receipt of combination first-line therapy (data not shown).

DISCUSSION

Given the substantial toxicity and personal costs associated with modest survival gains from metastatic colorectal cancer treatment, we hypothesized patient preferences would play an important role in receipt of palliative chemotherapy. We found patients with beliefs and preferences favoring chemotherapy were statistically more likely to receive treatment. Nonetheless, the vast majority of patients who expressed a preference for comfort-oriented care believed that chemotherapy would be unlikely to extend their life, or did not believe that chemotherapy would help with cancer-related problems still received chemotherapy. Patient preferences, beliefs, concerns about treatment, actual and preferred role in decision-making, and the quality of communication with their physician were not associated with intensity or number of chemotherapy regimens delivered.

Patient preference in palliative chemotherapy decision-making

Why did the majority of patients receive chemotherapy despite reporting beliefs and preferences that would seem incongruent with this treatment choice? Patients who offered negative or marginal views about chemotherapy in our survey might have still elected to receive treatment in the hopes that they fall in the group of patients who experience a meaningful benefit with minimal harm. This sense of optimism might have played a role in our findings since patients who were a "little likely" to expect benefit might have considered the risks of treatment reasonable. Patients with advanced cancer are often more willing than their providers to accept greater risk of harm for smaller benefit.[17] In addition, patients might disregard their own negative views of treatment if they are in conflict with their doctor's view.[3, 18, 19]

In the metastatic setting where the benefit of treatment is limited, patients may be more likely to defer treatment decision-making to their physician.[7] Hence, clinical factors rather than patient preference appear to have a disproportionate role in the treatment decision-making process. Our study indeed suggests that clinical factors, in particular age and comorbidity, influence the receipt of chemotherapy. These findings are consistent with a substantial body of literature showing that older, sicker patients are less likely to receive chemotherapy,[17, 20-23] including the analysis by Kahn et al which focused on stage III colorectal cancer patients enrolled in the same study described here.[10] Furthermore, completion of the survey by a surrogate rather than the patient likely serves as a proxy for poor performance status.[10] We found that completion of a surrogate survey was negatively associated with seeing a medical oncologist, receiving any chemotherapy, and receiving more than one line of chemotherapy. Older patients diagnosed with metastatic colorectal cancer had lower odds of being referred to a medical oncologist. While older patients are at higher risk of being diagnosed with colorectal cancer, our cohort includes patients who have already been diagnosed. Furthermore, our model adjusted for comorbidity, race, and gender. Hence, age remains an independent predictor of referral to medical oncology.

Appropriateness of palliative chemotherapy use

Multiple studies suggest underuse of adjuvant chemotherapy for stage III colorectal cancer.[10, 21, 23-27] Though the same degree of evidence is not available for the palliative setting in the US, though several studies have described low rates of palliative chemotherapy use for advanced colorectal cancer outside the U.S.[28-32] However, appropriate use of palliative chemotherapy for advanced cancer is difficult to discern without detailed clinical information. Since guidelines do not recommend treatment of patients with poor performance status, some patients are not candidates for chemotherapy from the time of diagnosis. Our analysis does not suggest an underuse of chemotherapy for advanced colorectal cancer in the U.S. We found that among patients who reported a preference for chemotherapy or favored quantity over quality of life, virtually all received chemotherapy. Additionally, the first-line chemotherapy regimens prescribed were largely those included in clinical guidelines available at the time of data collection. Taken together, these data suggest concerns regarding potential underuse of chemotherapy in patients with metastatic colorectal cancer can largely be put to rest.

Our findings are subject to limitations. We were unable to model the association between preferences, beliefs, and receipt of chemotherapy due to small effective sample sizes. However, unadjusted results are presented and are informative. Additionally, we assessed associations between those variables, intensity of chemotherapy, and number of lines of chemotherapy. We did not collect data detailing the conversation between patient and provider, so we cannot determine how that conversation might have colored patient preferences or beliefs about chemotherapy. Most patients completed the survey after their

treatment decisions had been made. Their preferences or beliefs might have been different if measured prior to treatment decision-making. However, over the course of cancer care, patient preferences tend to shift in favor of treatment,[33] and the majority of patients who expressed negative opinions towards chemotherapy still received treatment. Furthermore, we were unable to assess the impact of online, print, nursing, or navigation resources in patient decision-making. We did not focus on the use of chemotherapy at the very end of life and cannot comment on overuse in that setting, as has been extensively reported in the literature.[5] Our data were collected between 2003-2006, and the focus on shared decision-making has evolved over time. Finally, some survey items pertaining to preference and beliefs were created specifically for CanCORS. Their validity has not been tested, but the survey tool was thoroughly piloted.[11]

This study has several strengths. Our analyses are supported by both medical record and patient self-reported data. Patients were enrolled from multiple geographic regions and health care settings, and few exclusion criteria were applied. Patients enrolled in CanCORS have been shown to be demographically representative of the geographic regions in which they were enrolled.[34]

In summary, treatment decisions in the palliative setting were not always congruent with stated preferences and beliefs regarding chemotherapy. The vast majority of patients who expressed negative or marginal preferences or beliefs regarding chemotherapy still received chemotherapy. Patient preferences and beliefs were not associated with intensity or number of chemotherapy regimens delivered. Additionally, underuse of palliative chemotherapy was not evident. These findings shed new light on the patient experience and decision-making in the use of palliative chemotherapy, and can shift the focus of health services research in advanced cancer from investigating underuse of treatment to the inclusion of patient preferences in decision-making. Research should focus on tailoring delivery of care based on patient preferences and beliefs.

Acknowledgments

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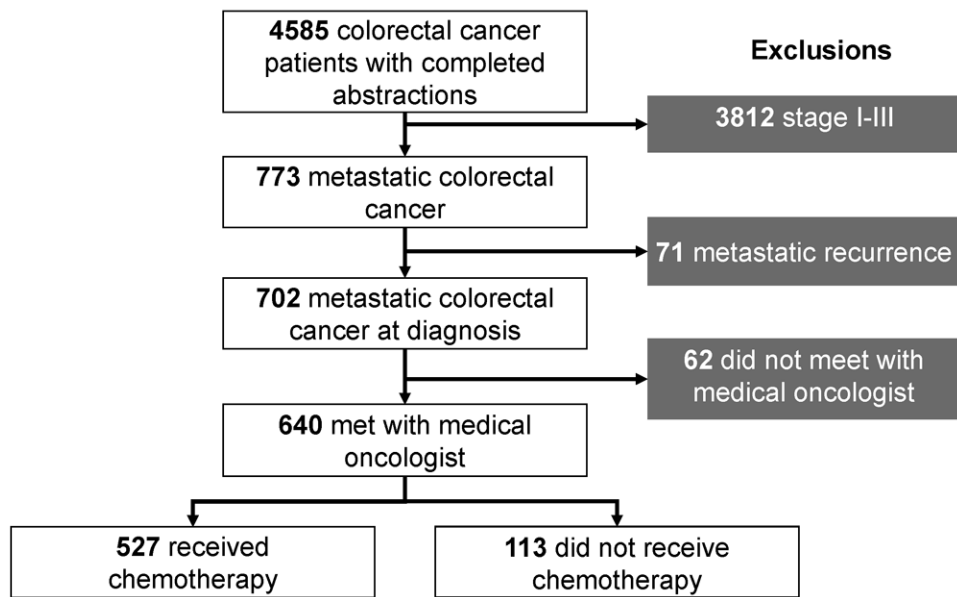
Figure 1.
Derivation of study cohort. Of the 640 who met with a medical oncologist, 409 completed a full patient survey. Of those who completed a full survey, only 23 patients did not receive chemotherapy.
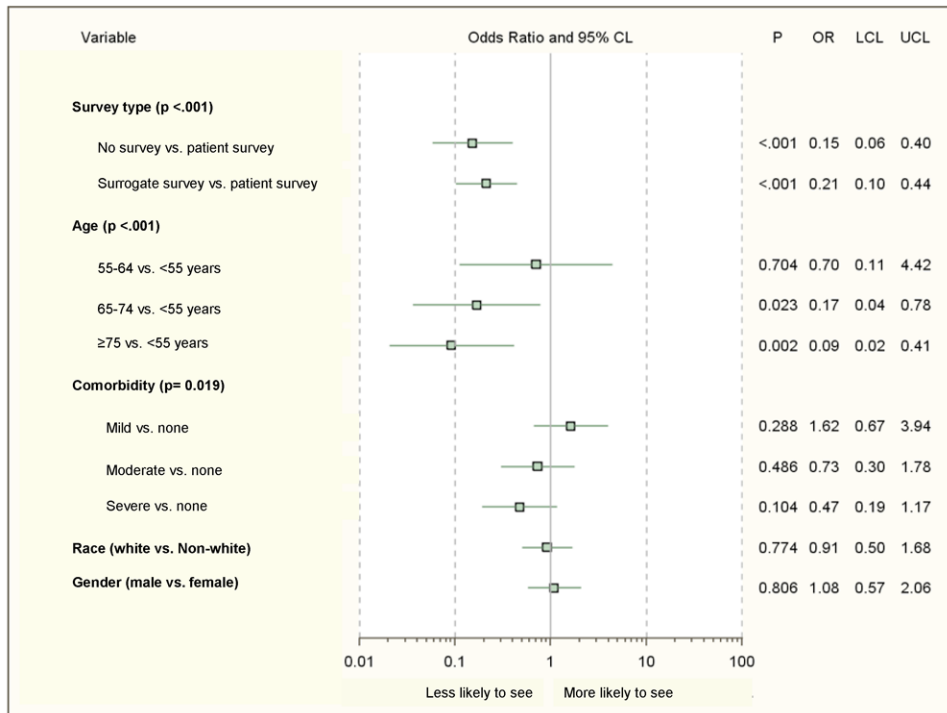
Figure 2.
Factors associated with seeing a medical oncologist (n=702).
CL, confidence limit; OR, adjusted odds ratio; LCL, lower confidence limit; UCL, upper confidence limit
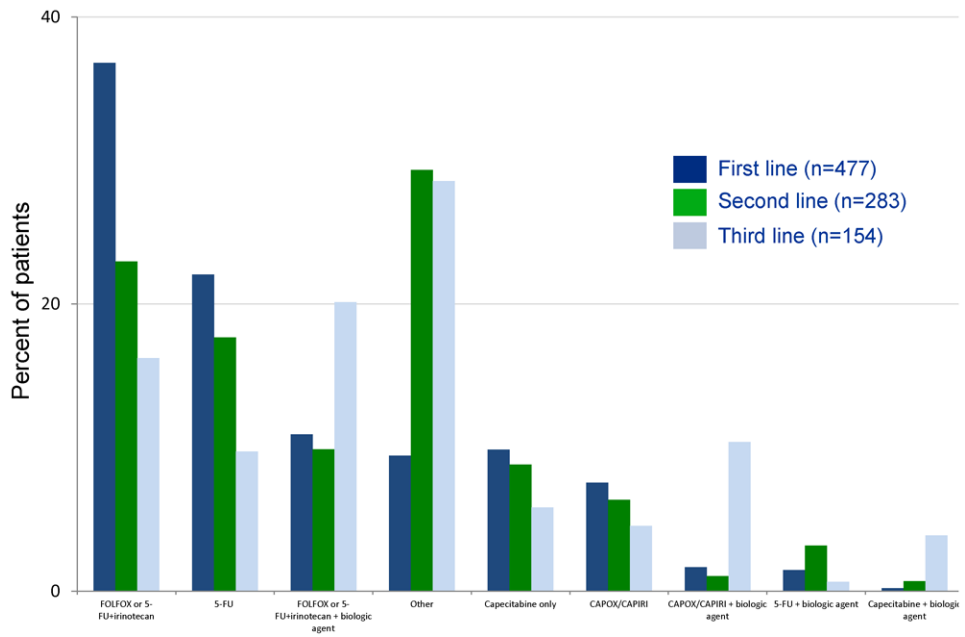
Figure 3.
Chemotherapy regimens used in the first, second, and third lines.
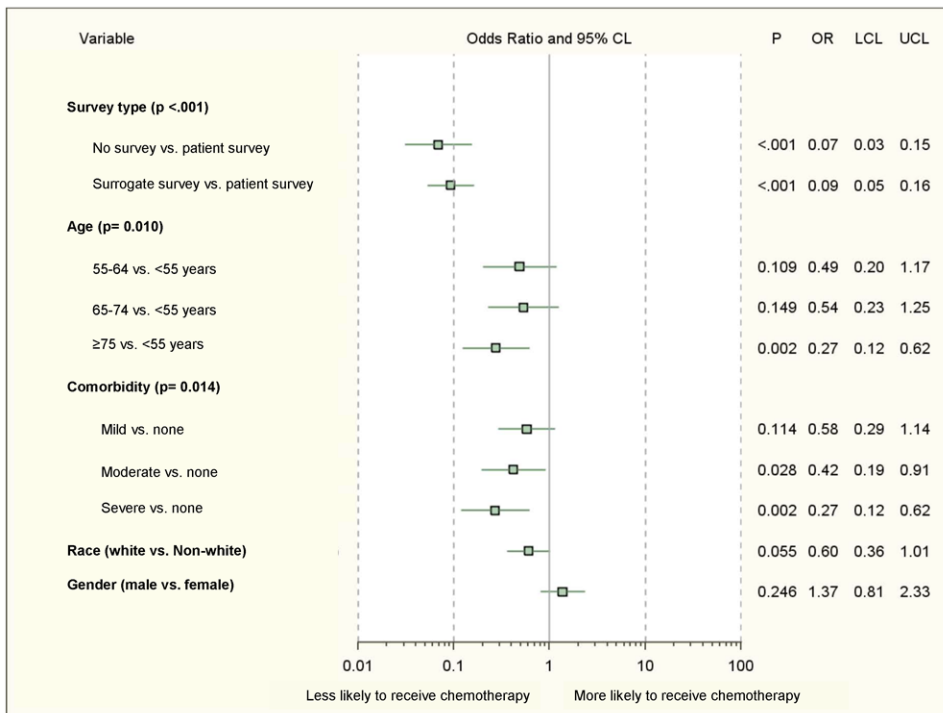
Figure 4.
Factors associated with receipt of chemotherapy (n=635; 4 insurance and 1 race values with insufficient data).
CL, confidence limit; OR, adjusted odds ratio; LCL, lower confidence limit; UCL, upper confidence limit
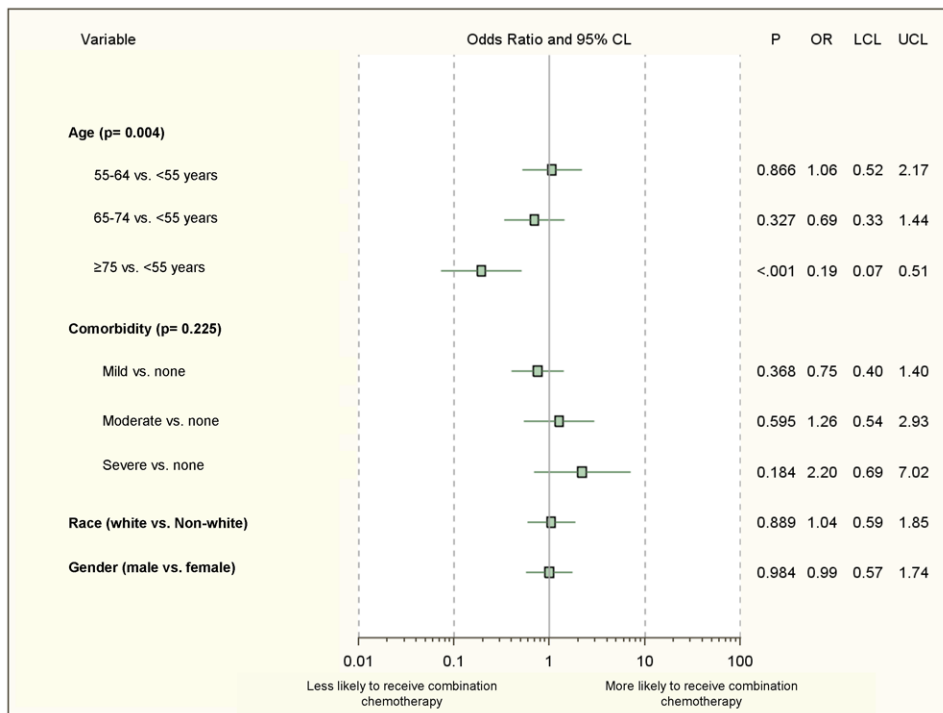
Figure 5.
Factors associated with receipt of combination chemotherapy vs. single-agent first-line therapy (n=271; 116 with insufficient data regarding chemotherapy regimens).
CL, confidence limit; OR, adjusted odds ratio; LCL, lower confidence limit; UCL, upper confidence limit

Table 1

Patient characteristics (n=702).

Characteristic	n	%*
Age in years		
<55	170	24
55-64	168	24
65-74	178	25
75	186	27
ACE-27 Comorbidity Index (score)		
None (0)	221	32
Mild (1)	265	38
Moderate (2)	126	18
Severe (3)	90	13
Race		
Unknown	1	<1
Non-white	274	39
White	427	61
Gender		
Female	268	38
Male	434	62
Insurance		
Missing	38	5
Public	103	15
Medicare + Supplemental	209	30
Veterans Administration	117	17
Private	235	34
Geographic region		
West/Midwest	421	60
South	146	21
Atlantic	135	19
Health system		
Fee-for-Service	420	60
Integrated health system	282	40
Survey respondent		
Survey completed by patient	441	63
Survey completed by patient surrogate	200	29
Survey not completed	61	9
Primary tumor site		
Missing	7	1
Colon	528	75

Characteristic	n	%[*]
Rectum	142	20
Colorectal	25	4

[*] Percents might not sum to 100 due to rounding.

Table 2

Role of patient preferences and beliefs in receipt of chemotherapy (n=409 [*]).

	Total	No chemotherapy		Received chemotherapy		p-value [^]
	n	n	%	n	%	
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?						<0.001
Relieve pain or discomfort as much as possible	164	17	10	147	90	
Extend life as much as possible	204	2	1	202	99	
Declined to answer/ Don't know	39	1	3	38	97	
Missing response	2	2	100	0	0	
If you had to make a choice now, would you prefer treatment that extends life as much as possible, even if it means using up all of your financial resources, or would you want treatment that costs you less, even if it means not living as long?						0.103
Prefer treatment that costs less	110	8	7	102	93	
Prefer treatment to extend life at the risk of using all financial resources	245	8	3	237	97	
Declined to answer/ Don't know	52	4	8	48	92	
Missing response	2	2	100	0	0	
After talking with your doctors about chemotherapy, how likely did you think it was that chemotherapy would help you live longer						0.008
Not likely/ A little likely	29	3	10	26	90	
Somewhat likely/Very likely	337	3	1	334	99	
Not applicable/Don't know	20	1	5	19	95	
Missing response	23	15	65	8	35	
After talking with your doctors about chemotherapy, how likely did you think it was that chemotherapy would help you with problems you were having because of your [cancer]?						<0.001
Not likely/A little likely	38	4	11	34	89	
Somewhat likely/Very likely	261	0	0	261	100	
Not applicable/Don't know	87	3	3	84	97	
Missing response	23	15	65	8	35	

[*] Limited to survey responses from full patient survey or full surrogate survey for living patients, since items of interest were only asked in these survey versions.

[^] Two-sided Fisher's exact test excluding missing responses, "not applicable," or "Don't know."