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Referral to Medical Oncology: A Crucial Step in the Treatment of Older Patients with Stage III Colon Cancer

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Abstract

Purpose— Adjuvant chemotherapy for stage III colon cancer produces a substantial survival benefit, but many older patients do not receive chemotherapy. This study examines factors associated with medical oncology consultation and evaluates the impact of such consultation on chemotherapy use.

Patients and Methods— We used the Surveillance Epidemiology and End Results–Medicare linked database and identified 7,569 patients, aged 66–99, with stage III colon cancer diagnosed from 1992–1999. Modified Poisson regression was used to assess the relative risk for seeing a medical oncologist and for receiving chemotherapy as a function of individual characteristics.

Results— 78.08% of patients saw a medical oncologist within 6 months of diagnosis. Patients who were female, white, married, had low comorbidity scores, were diagnosed in more recent years, or had four or more positive lymph nodes were more likely to see a medical oncologist. Patients seeing a medical oncologist were 10 times more likely to receive chemotherapy (odds ratio, 9.98; 95% confidence interval, 8.21–12.14), after controlling for demographic and tumor characteristics. Chemotherapy use increased over time, but was substantially lower among older, black, and unmarried patients.

Conclusions— Referral to medical oncology is one of the most important factors associated with receipt of chemotherapy among older patients with stage III colon cancer. Comorbidity decreases the likelihood of receiving chemotherapy, but its effect is the same for those who see a medical oncologist and all patients combined. Ensuring that high-risk patients are referred to medical oncology is a crucial step in quality care for patients with colon cancer.

Keywords

Medical oncologists; Consultation; Colon cancer; SEER-Medicare; Chemotherapy

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Disclosure of Potential Conflicts of Interest
The authors indicate no potential conflicts of interest.

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Learning Objectives

After completing this course, the reader will be able to:

1. Identify the predictors of seeing a medical oncologist for older colon cancer patients.
2. Discuss the association between seeing a medical oncologist and chemotherapy use in stage III colon cancer.
3. Outline the clinical implications for colon cancer care.

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Introduction

The incidence of colon cancer increases markedly with advancing age [1]. A number of studies have shown that older individuals with cancer are at risk for receiving less than optimal care [2–4]. In particular, several investigators have found that substantial percentages of older individuals with stage III (node-positive) colon cancer do not receive chemotherapy [5,6], and this is particularly marked among black elderly [5–7]. This is of great concern, because chemotherapy is associated with substantially better survival in stage III colon cancer [8–13], and the beneficial effects of chemotherapy are still apparent in older adults [8,14,15], at least up to age 80. For example, in randomized controlled trials, the 5-year survival rate for stage III colon cancer patients without chemotherapy was approximately 50%, whereas this rate was approximately 70% for those receiving chemotherapy [9–12,15,16].

In the U.S., chemotherapy is usually administered by medical oncologists. Colon cancer, as with many solid tumors, traditionally has been seen as a surgical disease; that is, the primary treatment is surgical. With the advent of effective chemotherapy, it became important that all patients also see a medical oncologist. However, shifts in practice patterns tend to occur slowly [17,18].

We hypothesized that a major reason why individuals with stage III colon cancer might not receive chemotherapy is that they were not referred to a medical oncologist. While there have been substantial numbers of studies of factors associated with less than definitive treatment of cancer [2–5,7], there have been few studies on factors associated with the appropriate evaluation of the newly diagnosed cancer patient. In this study we used the Surveillance Epidemiology and End Results (SEER)–Medicare linked database to examine factors associated with medical oncology consultation and the impact of such consultation on chemotherapy use.

Patients and Methods

Data Sources

Data for this study were obtained from three large databases, which were linked through collaborative projects and agreements involving the National Cancer Institute (NCI), the Centers for Medicare and Medicaid Services (CMS), and the American Medical Association (AMA) [19–21]. These databases contain: (a) population-based tumor registry data obtained from the SEER program, (b) Medicare enrollment information and claims submitted to CMS for services provided to Medicare beneficiaries, and (c) information collected by the AMA on all physicians in the U.S. (AMA Master file).

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Patients

Eligible patients for the study were male and female Medicare beneficiaries who were diagnosed with stage III colon cancer in 1992–1999, and who were 66–99 years of age at the time of diagnosis (n = 12,152). We evaluated each patient's enrollment status over the 6-month period from the month of diagnosis through the 5 months following the month of his/her cancer diagnosis. Patients were excluded who: (a) were not enrolled in both Medicare Parts A and B, (b) were health maintenance organization (HMO) members, or (c) died at any time during the 6-month period (n = 4,583). This resulted in a final sample size of 7,569 patients diagnosed with stage III colon cancer.

Identification of Patients Who Saw a Medical Oncologist

Patients who saw a medical oncologist were identified through information on either their Medicare physician claims (Carrier Claims file) or AMA Master file. The physician claims have a two-digit CMS provider specialty code (90 for medical oncologist, 83 for hematology oncologist) that represents the specialty reported to the carrier who processed the claim [21]. The physician claims also contain an encrypted UPIN number for the physician who provided the service. Through linkage with the AMA Master file, the primary and secondary specialty (medical oncologist, hematology oncologist) of a specific physician can be ascertained from residency training information and self-designated specialty [21].

In the physician claims for our eligible patients, there was 65% agreement between the two sources on whether or not the physician was a medical or hematology oncologist. Based on a review by Baldwin et al. [21] of the quality of physician characteristics in the claims, the general recommendation has been to search both sources for evidence of a particular physician specialty. This is the approach we used in our study. Hence, if a patient had a physician claim within the 6-month period from the month of diagnosis and the physician specialty (primary or secondary) was medical oncology or hematology based on either the AMA or CMS data, we defined the patient as "having seen a medical oncologist."

Measures

Tumor grade and nodal status were determined from the SEER data. We also used the SEER data to assign patients to different sociodemographic categories at the time of diagnosis according to race/ethnicity, marital status, and age. In addition, the socioeconomic characteristics of the patient's Census tract at the time of diagnos is were measured in terms of the percentage of residents living at or below the poverty level. Because the time period was from 1992 through 1999, these Census estimates were calculated as average values for the 1990 and 2000 Census years. The missing values in census data were categorized as "missing" in Table 1.

Each patient's preoperative comorbidity level was determined from claims data using the Charlson Comorbidity Index as adapted by Klabunde et al. [22,23]. The claims data were also used to define receipt of chemotherapy based on Medicare codes for chemotherapy administration as described in a previous publication [24]. Patients were identified as "receiving chemotherapy" if they had one or more of these codes on any claim within 6 months after their colon cancer diagnosis. These codes included the *International Classification of Diseases, Ninth Edition*, clinical modification (ICD-9-CM) procedure code of 99.25 for a hospital inpatient or outpatient facility claim of chemotherapy (injection or infusion of cancer chemotherapeutic substance); the common procedure terminology codes of 96400 to 96549, J9000 to J9999, and Q0083 to Q0085 for a physician or out-patient claim of chemotherapy administration; and the revenue center codes of 0331 (chemotherapy injected), 0332 (chemotherapy oral), and 0335 (chemotherapy i.v.) for an outpatient claim of chemotherapy.

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The ICD-9-CM V codes of V58.1, V66.2, or V67.2 for follow-up examination or care after chemotherapy were also used [24].

Statistical Analysis

Analyses were designed to: (a) identify factors related to seeing a medical oncologist and (b) examine the effect of seeing a medical oncologist on receipt of chemotherapy. The relationship between the different patient characteristics and "seeing a medical oncologist" was initially evaluated with likelihood ratio χ^2 test statistics.

Logistic regression for assessing the adjusted odds ratio is widely used when the event of a dichotomous outcome is rare [25,26]. However, logistic regression may overestimate risk association when the probability of outcome is high (in this case, seeing medical oncologists). Therefore, this study used the modified Poisson regression model, which allows for adjusting the odds ratio so that relative risk can more easily be approximated [27].

A series of modified Poisson regression models was then constructed to estimate the likelihood of being seen by a medical oncologist after successively including groups of variables representing: (a) sociodemographic characteristics, (b) tumor characteristics and SEER registry area, and (c) comorbidity and contextual factors. Modified Poisson regression models were also generated for the likelihood of receiving chemotherapy. All statistical analyses were performed with Statistical Analysis Software version 9.0 for Windows XP (SAS Institute, Inc, Cary, NC).

Results

Table 1 presents the characteristics of 7,569 patients with stage III colon cancer diagnosed between the years 1992 and 1999 who met eligibility criteria for the study. The average age of the cohort was 77.3 years, with a range of 66–99 years, and 58.07% were women. The majority of patients were non-Hispanic whites (83.33%). More than half (51.01%) were married. Most patients had zero comorbidity scores (67.76%). In addition, 78.08% of stage III patients saw a medical oncologist at least one time within 6 months after the date of diagnosis.

We next examined characteristics associated with seeing a medical oncologist. In bivariate analyses, younger patients, married patients, those with no or low comorbidity, and those with four or more positive lymph nodes were more likely to see a medical oncologist (Table 1). Also, those living in more affluent neighborhoods were more likely to see a medical oncologist. The percentage of patients seeing a medical oncologist also varied by SEER area. In addition, Table 1 illustrates an increase over time in the percent of stage III colon cancer patients seeing a medical oncologist, from 71.85% in 1992 to 82.32% in 1999.

In Table 2, we present a multivariate analysis of predictors of seeing a medical oncologist. The incidence of seeing a medical oncologist increased 2% annually. In addition, women, married individuals, and patients with four or more positive nodes were more likely to see a medical oncologist. Patients with high comorbidity scores (3+), black patients, and patients in some SEER registration areas were significantly less likely to see a medical oncologist.

Of the 7,569 patients diagnosed with stage III colon cancer, 58.51% received chemotherapy initiated within 6 months of diagnosis, which we thus categorized as adjuvant chemotherapy. There was a 2.2% annual increase in the likelihood of receiving chemotherapy. As expected, the receipt of chemotherapy was closely tied to seeing a medical oncologist: 73.32% of patients seeing a medical oncologist received chemotherapy, while 5.79% of patients who did not see a medical oncologist received chemotherapy. Conversely, 97.83% of those who received

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chemotherapy saw a medical oncologist, while only 50.22% of patients who did not receive chemotherapy saw a medical oncologist ($\chi^2 = 2{,}433.48$, $p < .0001$).

In a multivariate analysis of chemotherapy use among all patients with node-positive colon cancer (Table 3, model I), patients who saw a medical oncologist had a 10-fold higher chance of receiving chemotherapy. Increasing age and black ethnicity were associated with a lower chance of receiving chemotherapy. The model also shows significant variation by marital status. Finally, the analysis shows significant year-to-year increases in the chance of receiving chemotherapy throughout the 1990s.

Other investigators have reported that older age, African-American ethnicity, and presence of comorbidity are associated with a lower likelihood of receiving chemotherapy after a diagnosis of stage III colon cancer [5,7,28,29]. Because we found that these factors were also associated with a lower likelihood of seeing a medical oncologist, we next asked if disparities in referral to a medical oncologist were the explanation for the lower rates of chemotherapy in these patient groups (Table 3, model II). When multivariate analyses included only patients who saw a medical oncologist, there was no significant variation among SEER sites in receipt of chemotherapy. The lower likelihood of receiving chemotherapy associated with advancing age, black ethnicity, or being unmarried was somewhat smaller in magnitude but still present, while the effect of comorbidity on receipt of chemotherapy was similar for those who saw a medical oncologist and for all patients.

Discussion

In this population-based study of patients aged 66 years and older diagnosed with node-positive colon cancer, approximately 22% of patients did not see a medical oncologist within 6 months of diagnosis. As expected, seeing a medical oncologist was closely linked to receipt of chemotherapy. The chance of receiving adjuvant chemotherapy was 10 times higher for patients who saw a medical oncologist than for those who did not. Among patients who did not see a medical oncologist, only 6% received chemotherapy.

Adjuvant chemotherapy has a large survival benefit in this population of patients with stage III colon cancer. The number needed to treat to prevent one death at 5 years is approximately five, which is substantially better than for most other instances of use of adjuvant chemotherapy. Moreover, randomized trials and cohort studies have not found a lower efficacy in patients of advanced age [8,14]. Nevertheless, only 58.51% of the stage III colon cancer patients aged 66 and older received chemotherapy during this period, a finding made previously by other investigators [5,14,28,29]. Our findings suggest that lack of referral to medical oncology is one of the most important factors in the undertreatment of older patients with colon cancer.

Certain groups of patients were at particular risk for not seeing a medical oncologist. These included older patients, black patients, men, unmarried individuals, and those with three or more comorbidities. In addition, there was significant geographic variation in the likelihood of seeing a medical oncologist. These factors associated with seeing a medical oncologist are consistent with findings from studies in other cancers [30,31], and also in a study of colon cancer patients treated in a single HMO [32]. Our findings were encouraging in that there was a temporal trend of an increasing likelihood of seeing a medical oncologist throughout the 1990s.

Many of the patterns of chemotherapy use were explained by the patterns of referral to medical oncology. For instance, the increase in patients with node-positive colon cancer seeing a medical oncologist over the 1990s appeared to result in the increase in chemotherapy use over the same time period. However, some disparities persisted. While the results showed that older

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individuals, black patients, and unmarried patients were less likely to see a medical oncologist (Table 2), this only partly explained their lower likelihood of receiving chemotherapy (Table 3). Restricting the chemotherapy analyses to those patients who saw a medical oncologist had only a small effect on the receipt of chemotherapy for older patients, black patients, and the unmarried.

Even though adjuvant chemotherapy produces substantial improvements in survival for node-positive colon cancer, it is not clinically plausible that all such patients should receive chemotherapy. For example, very old patients or those with other severe complex disorders possess life expectancies that change the risk–benefit analysis [33]. In that regard, it is interesting that seeing a medical oncologist had little effect on the likelihood of those with multiple comorbidities receiving chemotherapy (Table 3). We also note that, while uncommon, chemotherapy can be administered by physicians other than medical oncologists. Siminoff et al. [30] reported that >10% of breast cancer patients were given chemotherapy by their surgeons before they saw a medical oncologist.

Our study has some limitations. First, the potential for inaccurate coding and missing values exists for any claims-based study, and clinical information available from billing data is not as detailed as that available from chart review [34]. Second, while the SEER–Medicare database is an excellent source to study older patients diagnosed with colon cancer, results are limited in their generalizability to younger populations across the U.S. In addition, the population in the SEER–Medicare database is somewhat more ethnically diverse, has a higher percentage of urban residents, is more highly educated, and has a higher income than the general older population [19,35]. Also, this study does not include information on factors such as physician and health system characteristics or patient preferences that might influence referral to a medical oncologist or receipt of chemotherapy, particularly if patients are not interested, willing, or able to receive chemotherapy. In order to design effective interventions, it is important to delineate the mechanisms producing less than optimal care. This involves describing the trajectory of care in increasing detail and examining the impact at each step in that trajectory of factors associated with less than optimal care [36]. Identifying the precise step(s) whereby certain patient characteristics are associated with less than optimal care should assist in the design of targeted, cost-effective interventions.

The current study represents a first step in that process, exploring whether a major block in receipt of chemotherapy is at the level of referral to a medical oncologist. As mentioned earlier, colon cancer, like virtually all solid tumors, has traditionally been viewed as a “surgical disease,” that is, the primary therapy for localized cancers is surgical resection. Thus all or almost all patients are seen by a surgeon early in the diagnostic pathway, and surgeons are regarded as the primary treating physician. With the advent of effective adjuvant chemotherapy for some localized cancers (e.g., breast and colon cancer), it has become important to involve medical oncologists in the evaluation and treatment of such patients. Such a process can be easily accomplished in the context of multidisciplinary cancer centers, but becomes more challenging in community practice [37]. Clearly, interventions to increase appropriate use of chemotherapy in stage III colon cancer should focus on increasing the percentage of such patients seen by a medical oncologist. It is reassuring that this percentage increased during the 1990s (Table 1), and that this increase was accompanied by an increase in the percentage of patients receiving chemotherapy. Nevertheless, even at the end of the study period substantial numbers of patients were not seeing a medical oncologist, suggesting that interventions to increase the participation of medical oncologists would result in higher percentages of stage III colon cancer patients receiving appropriate chemotherapy. However, our results also suggest that such interventions, while they may increase chemotherapy use among all demographic groups of patients with node-positive colon cancer (and thus will reduce the absolute disparities in receipt of chemotherapy), will not eliminate the relative disparities

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experienced by older patients, or those who are black or unmarried. Further work is required to explore the role of patient knowledge and attitudes, organizational factors, and factors involving access to chemotherapy services in maintaining those disparities.

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Table 1

Characteristics of 7,569 patients diagnosed with stage III colon cancer and percentage seeing a medical oncologist (5,910) within 6 months of diagnosis

Predictor	Group	*n*	% seeing an oncologist	*p*-value[a]
Age	66–69	1,255	90.68%	<.0001
	70–74	1,873	87.67%	
	75–79	1,885	82.12%	
	80–84	1,420	71.48%	
	85–99	1,136	49.91%	
Gender	Male	3,174	79.24%	.0388
	Female	4,395	77.25%	
Ethnicity	White	6,307	78.60%	.0392
	Black	580	77.76%	
	Asian	362	74.31%	
	Hispanic	260	73.85%	
	Other/unknown	60	68.33%	
Marital status	Married	3,861	83.61%	<.0001
	Unmarried	3,708	72.33%	
Comorbidity	0	5,129	78.85%	<.0001
	1	1,553	78.82%	
	2	557	75.76%	
	3+	330	66.67%	
Census tract poverty level %	0–5%	2,360	80.59%	0.005
	>5% to 9%	2,078	78.34%	
	>9%	3,035	76.14%	
	Missing	96	71.88%	
Year of diagnosis	1992	1,048	71.85%	<.0001
	1993	955	74.14%	
	1994	982	77.09%	
	1995	988	79.15%	
	1996	893	80.63%	
	1997	946	80.76%	
	1998	948	80.17%	
	1999	809	82.32%	
SEER area	Detroit	1,202	86.61%	<.0001
	Connecticut	1,141	78.53%	
	San Francisco	600	68.83%	
	Hawaii	201	73.63%	
	Iowa	1,277	77.53%	
	New Mexico	264	71.48%	
	Seattle	734	76.43%	
	Utah	294	72.45%	
	Atlanta	412	82.52%	
	San Jose–Monterey	318	73.90%	
	Los Angeles	1,106	78.66%	
Grade	Well-differentiated G1	384	75.52%	.5259
	Moderately differentiated G2	4,736	78.39%	
	Poorly/undifferentiated G3	2,155	78.10%	
	Unknown	292	76.37%	
Number of positive nodes	<3	5,202	76.78%	<.0001
	4–6	1,396	80.44%	
	7+	736	83.70%	
	Unknown	236	75.32%	

[a] *p*-values are not adjusted for multiple factors.

Abbreviation: SEER, Surveillance Epidemiology and End Results.

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Table 2

Characteristics associated with seeing a medical oncologist within 6 months of a diagnosis of stage III colon cancer

Predictor	Group	Relative risk (95% CI)[a] for medical oncology consultation
		***n* = 5,910/7,569**
Age	66–99 (each year increase)	0.976 (0.974–0.978)
Ethnicity[b]	White	1.00
	Black	0.934 (0.890–0.980)
	Asian	0.945 (0.877–1.017)
	Hispanic	0.948 (0.878–1.023)
Gender	Male	1.00
	Female	1.042 (1.018–1.068)
Marital status	Unmarried	1.00
	Married	1.078 (1.052–1.106)
Year of diagnosis	1992–1999 (each year increases)	1.020 (1.015–1.025)
SEER area	Detroit	1.00
	Connecticut	0.914 (0.881–0.948)
	San Francisco	0.842 (0.796–0.891)
	Hawaii	0.870 (0.786–0.964)
	Iowa	0.901 (0.868–0.936)
	New Mexico	0.817 (0.755–0.883)
	Seattle	0.882 (0.844–0.923)
	Utah	0.819 (0.764–0.878)
	Atlanta	0.955 (0.911–1.002)
	San Jose–Monterey	0.869 (0.813–0.929)
	Los Angeles	0.939 (0.904–0.976)
Grade[b]	Well differentiated	1.00
	Moderately differentiated	1.021 (0.966–1.080)
	Poorly/undifferentiated	1.022 (0.964–1.083)
Node[b]	<3 positive	1.00
	4–6 positive	1.045 (1.016–1.075)
	7+ positive	1.083 (1.046–1.121)
Comorbidity	0	1.00
	1	1.016 (0.988–1.044)
	2	1.003 (0.957–1.051)
	3	0.868 (0.808–0.933)
Poverty[a]	0–5%	1.00
	>5% to 9%	1.005 (0.975–1.035)
	>9%	0.992 (0.962–1.022)

[a] Estimates of relative risk are adjusted for multiple factors.

[b] Patients with unknown values (60 for ethnicity, 292 for tumor grade, 236 for node, 96 for poverty) were included as a separate category but not shown.

Abbreviations: CI, confidence interval; SEER, Surveillance Epidemiology and End Results.

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Table 3

Characteristics associated with receipt of adjuvant chemotherapy for all patients with stage III colon cancer (model I) and for patients with stage III colon cancer who saw a medical oncologist (model II)

Predictor	Group	Relative risk (95% CI)[a] for receipt of hemotherapy	
		Model I[b]	Model II[c]
Age	66–99 (each year increases)	0.961 (0.958–0.963)	0.960(0.958–0.963)
Ethnicity[d]	White	1.00	1.00
	Black	0.872 (0.812–0.937)	0.887 (0.826–0.952)
	Asian	0.985 (0.904–1.073)	0.982 (0.906–1.065)
	Hispanic	1.010 (0.929–1.097)	1.014 (0.935–1.099)
Gender	Male	1.00	1.00
	Female	0.980 (0.951–1.010)	0.983 (0.954–1.012)
Marital status	Unmarried	1.00	1.00
	Married	1.116 (1.079–1.154)	1.106 (1.070–1.142)
Year of diagnosis	1991–1999 (each year increases)	1.007 (1.001–1.014)	1.007 (1.000–1.013)
SEER area	Detroit	1.00	1.00
	Connecticut	1.005 (0.956–1.057)	1.011 (0.963–1.063)
	San Francisco	1.020 (0.952–1.094)	1.009 (0.943–1.080)
	Hawaii	0.986 (0.879–1.106)	1.005 (0.902–1.120)
	Iowa	1.003 (0.952–1.056)	1.004 (0.955–1.056)
	New Mexico	0.959(0.877–1.048)	0.975(0.894–1.062)
	Seattle	0.972(0.915–1.033)	0.983(0.927–1.044)
	Utah	0.960 (0.889–1.037)	0.987 (0.915–1.064)
	Atlanta	0.971 (0.902–1.046)	0.960 (0.893–1.033)
	San Jose–Monterey	0.941 (0.863–1.027)	0.961 (0.881–1.047)
	Los Angeles	1.044 (0.990–1.102)	1.043 (0.990–1.100)
Node[d]	<3 positive	1.00	1.00
	4–6 positive	1.064 (1.026–1.103)	1.056 (1.019–1.093)
	7+ positive	1.060 (1.015–1.108)	1.061 (1.016–1.108)
Poverty[d]	<5%	1.00	1.00
	>5% to 9%	1.012 (0.975–1.051)	1.013 (0.976–1.050)
	>9%	0.969 (0.932–1.008)	0.971 (0.934–1.008)
Comorbidity	0	1.00	1.00
	1	0.919 (0.884–0.955)	0.921 (0.887–0.957)
	2	0.864 (0.803–0.929)	0.854 (0.795–0.918)
	3	0.739 (0.655–0.835)	0.713 (0.632–0.804)
Seeing an oncologist	No	1.00	—
	Yes	9.983 (8.213–12.135)	—

[a] Estimates of relative risk are adjusted for multiple factors.

[b] For all 7,569 patients, 4,429 (58.51%) of whom received chemotherapy.

[c] For the 5,910 patients who saw a medical oncologist, 4,333 (73.32%) of whom received chemotherapy.

[d] Patients with unknown values (60 for ethnicity, 236 for node, 96 for poverty) were included as a separate category but not shown. Abbreviations: CI, confidence interval; SEER, Surveillance Epidemiology and End Results.