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Differential Effects of Race, Socioeconomic Status, and Insurance on Disease-Specific Survival in Rectal Cancer

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Abstract

BACKGROUND: National Comprehensive Cancer Network guideline adherence improves cancer outcomes. In rectal cancer, guideline adherence is distributed differently by race/ethnicity, socioeconomic status, and insurance.

OBJECTIVE: This study aimed to determine the independent effects of race/ethnicity, socioeconomic status, and insurance status on rectal cancer survival after accounting for differences in guideline adherence.

DESIGN: This was a retrospective study.

SETTINGS: The study was conducted using the California Cancer Registry.

PATIENTS: This study included patients aged 18 to 79 years diagnosed with rectal adenocarcinoma between January 1, 2004, and December 31, 2017, with follow-up through November 30, 2018. Investigators determined whether patients received guideline-adherent care.

MAIN OUTCOME MEASURES: ORs and 95% CIs were used for logistic regression to analyze patients receiving guideline-adherent care. Disease-specific survival analysis was calculated using Cox regression models.

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RESULTS: A total of 30,118 patients were examined. Factors associated with higher odds of guideline adherence included Asian and Hispanic race/ethnicity, managed care insurance, and high socioeconomic status. Asians (HR, 0.80; 95% CI, 0.72–0.88; $p < 0.001$) and Hispanics (HR, 0.91; 95% CI, 0.83–0.99; $p = 0.0279$) had better disease-specific survival in the nonadherent group. Race/ethnicity were not factors associated with disease-specific survival in the guideline adherent group. Medicaid disease-specific survival was worse in both the nonadherent group (HR, 1.56; 95% CI, 1.40–1.73; $p < 0.0001$) and the guideline-adherent group (HR, 1.18; 95% CI, 1.08–1.30; $p = 0.0005$). Disease-specific survival of the lowest socioeconomic status was worse in both the nonadherent group (HR, 1.42; 95% CI, 1.27–1.59) and the guideline-adherent group (HR, 1.20; 95% CI, 1.08–1.34).

LIMITATIONS: Limitations included unmeasured confounders and the retrospective nature of the review.

CONCLUSIONS: Race, socioeconomic status, and insurance are associated with guideline adherence in rectal cancer. Race/ethnicity was not associated with differences in disease-specific survival in the guideline-adherent group. Medicaid and lowest socioeconomic status had worse disease-specific survival in both the guideline nonadherent group and the guideline-adherent group. See **Video Abstract** at <http://links.lww.com/DCR/B954>.

Abstract

El cumplimiento de las guías de la National Comprehensive Cancer Network mejora los resultados del cáncer. En el cáncer de recto, el cumplimiento de las guías se distribuye de manera diferente según la raza/origen étnico, nivel socioeconómico y el cobertura médica.

Determinar los efectos independientes de la raza/origen étnico, el nivel socioeconómico y el estado de cobertura médica en la supervivencia del cáncer de recto después de tener en cuenta las diferencias en el cumplimiento de las guías.

Este fue un estudio retrospectivo.

El estudio se realizó utilizando el Registro de Cáncer de California.

Pacientes de 18 a 79 años diagnosticados con adenocarcinoma rectal entre el 1 de enero de 2004 y el 31 de diciembre de 2017 con seguimiento hasta el 30 de noviembre de 2018. Los investigadores determinaron si los pacientes recibieron atención siguiendo las guías.

Se utilizaron razones de probabilidad e intervalos de confianza del 95% para la regresión logística para analizar a los pacientes que recibían atención con adherencia a las guías. El análisis de supervivencia específico de la enfermedad se calculó utilizando modelos de regresión de Cox.

Se analizaron un total de 30.118 pacientes. Los factores asociados con mayores probabilidades de cumplimiento de las guías incluyeron raza/etnicidad asiática e hispana, seguro de atención administrada y nivel socioeconómico alto. Los asiáticos e hispanos tuvieron una mejor supervivencia específica de la enfermedad en el grupo no adherente HR 0,80 (95 % CI 0,72 – 0,88, $p < 0,001$) y HR 0,91 (95 % CI 0,83 – 0,99, $p = 0,0279$). La raza o el origen étnico no fueron factores asociados con la supervivencia específica de la enfermedad en el grupo que cumplió con las guías. La supervivencia específica de la enfermedad de Medicaid fue peor tanto en el grupo no adherente HR 1,56 (IC del 95 % 1,40 – 1,73, $p < 0,0001$) como en el grupo adherente a las guías HR 1,18 (IC del 95 % 1,08 – 1,30, $p = 0,0005$). La supervivencia específica de la enfermedad del

nivel socioeconómico más bajo fue peor tanto en el grupo no adherente HR 1,42 (IC del 95 %: 1,27 a 1,59) como en el grupo adherente a las guías HR 1,20 (IC del 95 %: 1,08 a 1,34).

Las limitaciones incluyeron factores de confusión no medidos y la naturaleza retrospectiva de la revisión.

La raza, el nivel socioeconómico y cobertura médica están asociados con la adherencia a las guías en el cáncer de recto. La raza/etnicidad no se asoció con diferencias en la supervivencia específica de la enfermedad en el grupo que cumplió con las guías. Medicaid y el nivel socioeconómico más bajo tuvieron peor supervivencia específica de la enfermedad tanto en el grupo que no cumplió con las guías como en los grupos que cumplieron. Consulte **Video Resumen** en <http://links.lww.com/DCR/B954>. (Traducción— Dr. Francisco M. Abarca-Rendon)

Keywords

Health care disparities; National Comprehensive Cancer Network guideline adherence; Rectal cancer

Approximately 43,340 people in the United States develop rectal cancer annually.¹ Adenocarcinomas constitute a substantial portion of these cases. Treating rectal adenocarcinomas depends on the characteristics of cancer such as size, location, extent of disease, nodal involvement, and distant metastasis. Rectal cancer management is complex, necessitating a coordinated, multispecialty approach involving expertise from Gastroenterology, Radiology, Pathology, Colorectal Surgery, Radiation Oncology, and Medical Oncology. The surgery required (total mesorectal excision–based lower anterior resection or abdominal perineal resection) is technically complex, requiring surgical expertise and often referral to large volume centers.² Temporary or permanent ostomy procedures complicate the timing of radiation and/or chemotherapy treatments, and even after reanastomosis, patients experience major quality-of-life issues (low anterior resection syndrome) related to bowel function. Over the past 30 years, treatment for locoregional stage rectal cancer has shifted from surgery followed by chemoradiation (1990s) to upfront (neoadjuvant) chemoradiation followed by surgery, and adjuvant (ie, postoperative) chemotherapy (2000s) to current National Comprehensive Cancer Network (NCCN) guideline-directed total neoadjuvant therapy (where chemoradiation and chemotherapy for a total of 6 mo are given before surgical resection), short-course neoadjuvant chemoradiation, and emerging strategies for watchful waiting after total neoadjuvant therapy (ie, nonsurgical management of rectal cancer). Given the complex nature of treatment for rectal cancer, adherence to NCCN guidelines has added importance to guideline treatment. Additionally, factors related to access to care such as race/ethnicity, SES, and insurance status may have substantial effects on outcomes.

Significant deviation from ideal cancer care was first described in the late 1990s.³ These deviations can best be described as a complex mix of tumor biology, treatment-related, and patient-level factors.^{4,5} As a result, NCCN first published clinical practice guidelines in November 1996 to standardize care, including care for rectal cancer.⁶ Since then, several

studies have shown that poor compliance with NCCN guidelines leads to worse overall survival.^{7–11}

We previously reported that nonadherence to NCCN guideline care had shown worse survival in rectal cancer, among other cancers.¹² Furthermore, in rectal cancer, we found differences in the distribution of guideline adherent care by race/ethnicity, SES, and type of primary insurance. However, how these factors impact survival in rectal cancer is unknown. Therefore, we designed this study to analyze disease-specific survival (DSS) of patients with rectal cancer based on NCCN guideline adherence accounting for the influence of differences in race/ethnicity, socioeconomic status (SES), and insurance status.

MATERIALS AND METHODS

We used the California Cancer Registry (CCR) to obtain data on patients diagnosed with rectal cancer between 2004 and 2017 and with follow-up until November 30, 2018. The CCR is a statewide population-based cancer surveillance system in California that has collected information about tumor characteristics, patient characteristics, tumor diagnosis, and treatment for all cancers diagnosed in California since 1988. The CCR rectal cancer data included age at diagnosis, year of diagnosis, race/ethnicity, sex, insurance status, SES, marital status, tumor stage, and tumor grade of differentiation. The Yost score was used to stratify SES into quintiles for patients diagnosed before 2006, and the Yang index was used to stratify SES into quintiles for patients diagnosed after 2006. The Yost score and Yang index are composite indices of SES contained in the CCR that are based on principal component analysis of block group-level census variables such as education, income, and occupation.^{13–15} We identified the cases using the primary site codes (C199 and C209) from the Surveillance, Epidemiology, and Results (SEER) program.

We included 35,722 cases of patients aged 18 to 79 years diagnosed with first or only rectal cancer. We excluded patients with rectal cancer identified from autopsy or death certificates only (n = 99) and those who had missing clinical information or treatment information (n = 5505). The cause of death was recorded with the International Classification of Diseases criteria. A total of 30,118 patients with rectal cancer were identified for this study.

The institutional review board of the University of California, Irvine (HS#2018–4735), and the State of California Health and Human Services Agency Committee for the Protection of Human Subjects (19–03-0044) approved this study.

As per NCCN guidelines for rectal cancer, we created indicators for adherence to surgery, chemotherapy, and radiation treatment and defined NCCN guideline–adherent treatment (Table 1). Descriptive statistics of the sample population and bivariate analysis of adherent status and insurance, sociodemographic variables, and clinical variables are presented in Table 2. We developed a multivariate logistic regression model to assess the effect of each variable on the likelihood of receiving NCCN guideline–adherent care. Other than race/ethnicity, primary payer status, and SES, the multivariate model controls for age at diagnosis, year of diagnosis, marital status, tumor stage, and tumor grade. We conducted survival analyses using DSS as the outcome. For DSS, we defined cancer-specific mortality

as death caused by colorectal cancer. We censored patients who died from other causes or who were alive until the end of follow-up on November 30, 2018. Univariate DSS analyses were performed using the Kaplan-Meier estimates of survival probability and the log-rank test. After verifying the proportional hazards assumption, we performed a multivariate DSS analysis using the Cox proportional hazards model stratified on NCCN guideline adherence status (adherent, nonadherent) and controlling for patients' sociodemographic characteristics and tumor characteristics (as stated in the above model). We generated adjusted HRs and 95% CIs. The data analysis for this article was generated using SAS software, version 9.4 (SAS Institute Cary, NC). We set statistical significance at $p < 0.05$, using 2-tailed tests.

RESULTS

The final analytic cohort included 30,118 patients diagnosed with rectal adenocarcinoma (Table 2). Patients aged 65 years or older (37.9% or 11,413 patients) comprised the largest proportion. More patients (60.1% or 18,092 patients) were diagnosed in the latter half of the study (ie, after the year 2010). We found most patients were male, non-Hispanic white, married, and had managed care insurance. SES was evenly distributed among the patients.

In regard to tumor stage, 31.7% had stage I, 18.8% had stage II, 26.8% had stage III, and 22.7% had stage IV. The grade of tumor differentiation was primarily grade II or moderately well differentiated (60.9%).

Overall, 13,676 patients (45.4%) received NCCN guideline-adherent care (Table 3). Among patients aged 18 to 44 years (2764), a majority (56.5%) received guideline-adherent care, whereas among patients 65 years or older (11,413), a majority (62.2%) did not. Asians, Hispanics, and those of other/unknown ethnicity had higher odds of receiving guideline-adherent care (OR, 1.15; 95% CI, 1.07–1.23; $p = 0.0001$) as compared to non-Hispanic whites (OR, 1.55; 95% CI, 1.31–1.85; $p < 0.0001$). As compared to those with the highest SES, patients with the lowest SES had lower odds of receiving guideline-adherent care (OR, 0.79; 95% CI, 0.72–0.86; $p < 0.0001$). Also compared to the highest SES, lower-middle SES (OR, 0.79; 95% CI, 0.73–0.85; $p < 0.0001$) and middle SES had lower odds of receiving guideline-adherent care (OR, 0.88; 95% CI, 0.81–0.94; $p = 0.0005$). Higher-middle SES guideline-adherent care was not statistically significant (OR, 0.97; 95% CI, 0.91–1.05; $p = 0.4817$). As compared to patients with managed care, uninsured patients had the lowest odds of receiving guideline-adherent care (OR, 0.84; 95% CI, 0.75–0.95; $p = 0.0047$).

DSS was worse for patients with rectal cancer who did not receive NCCN guideline-adherent care (HR, 1.86; 95% CI, 1.77–1.95; $p < 0.0001$).

Compared to non-Hispanic whites as a referent group, Asians (in aggregate) had better DSS in the nonadherent group with an adjusted HR of 0.80 (95% CI, 0.72–0.88; $p < 0.001$; Table 4). Also, compared to non-Hispanic whites, Hispanics had better DSS in the nonadherent group (HR, 0.91; 95% CI, 0.83–0.99; $p = 0.0279$; Table 4). Of note, DSS was not statistically significant in all race/ethnic groups in the guideline-adherent group.

Compared to patients with the highest SES as a referent group, lower SES quintile was associated with increased disease-specific mortality in both the adherent and nonadherent

groups. DSS was slightly better in the guideline-adherent group compared to the guideline nonadherent groups in all SES quintiles (Table 4). Compared to the highest SES, patients with the lowest SES were observed to have increased disease-specific mortality in the nonadherent group (HR, 1.42; 95% CI, 1.27–1.59) and the adherent group (HR, 1.20; 95% CI, 1.08–1.34). Similar findings were observed in the lower-middle, middle SES, and higher-middle SES quintiles (Table 4).

Compared to managed care insured patients, uninsured patients were observed to have worse disease-specific mortality in the nonadherent group (adjusted HR, 1.44; 95% CI, 1.25–1.65; $p < 0.0001$). Patients with Medicaid had worse DSS in both the nonadherent group (HR, 1.56; 95% CI, 1.40–1.73) and the adherent group (HR, 1.18; 95% CI, 1.08–1.30; $p = 0.0005$). Interestingly, compared to managed care insured patients, patients with other insurance had better DSS in the nonadherent group (HR, 0.88; 95% CI, 0.78–0.99; $p = 0.0334$) and the adherent group (HR, 0.87; 95% CI, 0.79–0.96; $p = 0.0043$).

DISCUSSION

Using a large, statewide registry for California, we observed disparities in receiving NCCN guideline-adherent care by race/ethnicity, SES, and insurance. In addition, NCCN guideline adherence was strongly associated with improved DSS in adjusted analysis, accounting for other major clinical and demographic factors. In the adherent and nonadherent groups, DSS was associated with Asians, Medicaid patients, and patients with the lowest, lower-middle, and middle SES.

Race/ethnicity played a significant role in guideline adherence. Among the nonadherent group, race was prognostic for survival. However, in the adherent group, race was not statistically significant for DSS. Several studies described non-white race with worse DSS in patients with rectal cancer.^{16,17} In contrast, we found that non-white race, in particular Asians and Hispanics, had better DSS in the guideline nonadherent group. A study in California had similar findings, which strengthen our results.¹⁸ Of note, the proportions of the patients with cancer in our study loosely represent the population of California.¹⁹ We reported that all race/ethnic cohorts in the guideline-adherent group had no statistically significant findings in DSS.

Interestingly, in both the nonadherent and adherent groups, we found no statistically significant difference in DSS for non-Hispanic blacks. This contrasts with several other studies demonstrating decreased survival in black patients with rectal cancer.^{20–25} Our findings provide further evidence that previously observed rectal cancer survival differences by race/ethnicity may be explained by other factors not routinely taken into account in registry data (such as SEER).

Lower SES correlated with decreased guideline adherence. Both in the adherent and nonadherent groups, low SES was associated with lower DSS for patients with rectal cancer in California. High SES was associated with improved DSS in both the adherent and nonadherent groups. This finding contrasts with a Swedish study that demonstrated no difference in survival in terms of SES for rectal cancer.²⁶ However, unlike the United States,

Sweden offers universal health care to its citizens, so SES is not linked to health care access in the way these factors are linked in the United States. In our study, SES is the main driver of both adherence and survival, as opposed to other studies that claimed increasing age, comorbidities, and insurance status as the main proponents of guideline adherence.^{25,27,28}

We demonstrated an association between primary payer status and guideline adherence. Differences were observed in payer status in the adherent group and nonadherent group. As compared to managed care, patients with Medicaid had worse DSS in both the adherent and nonadherent groups. In opposition, a National Cancer Database study found no significant association with primary payer status and guideline adherence.²⁹ The differences in hospital volumes and geographic regions of California played a role. Similar to our findings, a SEER-based study and CCR study found better survival for patients with other insurance than those with Medicaid or no insurance.^{30–32} We reported that patients without insurance had a 44% increased risk in disease-specific mortality. Without insurance, access to care is compromised, which correlates to the increased risk of disease-specific mortality we found.³⁰

As reported previously, we observed a large (86%) increased disease-specific mortality risk for NCCN guideline nonadherence in colon and rectal cancer after adjustment for factors.^{12,25} Of note, this is the strongest predictor of disease-specific mortality other than tumor stage and grade (data not shown). In a univariate analysis stratified by stage, NCCN guideline adherence was associated with statistically significant, modest improvements in DSS and overall survival among patients with stage I and III rectal cancer, which is consistent with reported literature.^{27,28,32} Among patients with stage IV rectal cancer, NCCN guideline adherence was associated with major improvements in DSS (Figs. 1 and 2).

Limitations

Our study contained several limitations. First, we did not know the type or amount of chemotherapy and radiation given to the patients. Also, CCR lacks detailed reasons for deviations from guidelines. Such deviations may include performance status, patient preference for treatment, and clinical gestalt. Decision-making and preferences by a surgeon at the time of surgery impact the type of procedure performed.³³ We also could not disaggregate between different Asian ethnic groups, thus masking potentially lower survival that has been shown in other cancers.³⁴ SES was determined via the Yost score and Yang index. The Yost score and Yang index are useful and accurate in the analysis of large homogeneous areas. However, this may not apply to many urban Californian counties that include a mix of high and low SES neighborhoods. Treatment setting was not available for the analysis. In addition, there is heterogeneity in categorizing health insurance as many types of insurance differ across the spectrum. Our findings related to insurance status are intriguing (ie, Medicaid patients having poor DSS in both adherent and nonadherent groups) and raise questions about access to care, quality of care, and other socioeconomic factors not fully taken into account in our analysis. As such, these results must be interpreted with caution as the categorical breakdown is crude, including heterogeneous groups. Additional limitations are there in adherent and nonadherent populations that we statistically cannot

account. Despite these limitations, we found nonadherence to guidelines was associated with lower DSS at the population level.

CONCLUSION

NCCN rectal cancer guideline adherence is associated with improved DSS among patients with rectal cancer. Race/ethnicity were not factors for DSS in the guideline-adherent group. Lower SES was associated with increased disease-specific mortality in both the guideline-adherent and nonadherent groups. Medicaid was associated with lower DSS in both the guideline-adherent and nonadherent groups, whereas other insurance (fee for service, Tricare, Veterans' Affairs, or not otherwise specified) were associated with improved DSS in both the guideline-nonadherent and -adherent groups. As a result, focusing on guideline adherence specifically by race/ethnicity, SES, and type of insurance can improve rectal cancer care in California.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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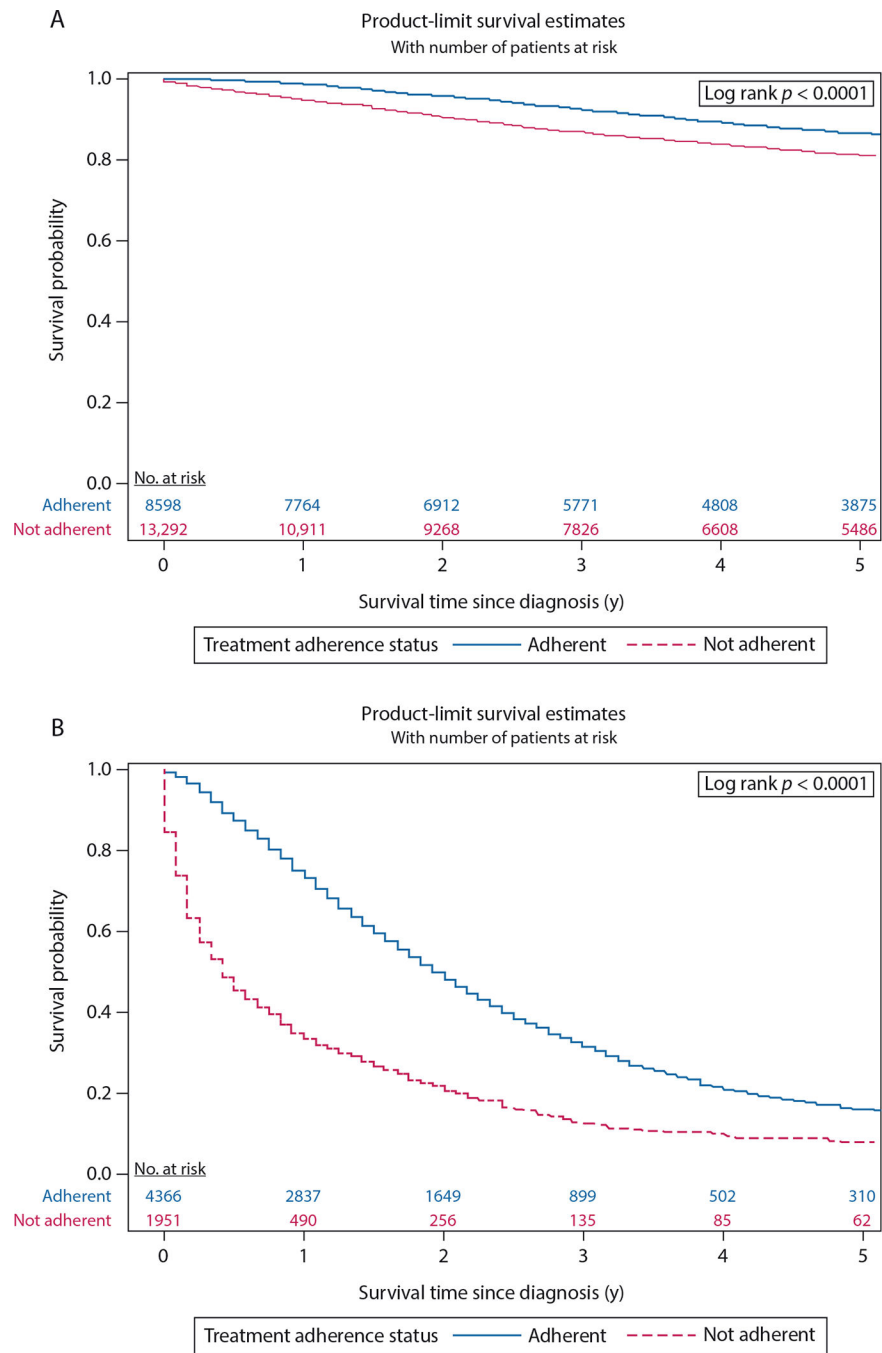


FIGURE 1. Kaplan-Meier colorectal cancer-specific survival graph by treatment adherence status. Event of disease-specific survival includes death from rectal and colon cancer. A, Tumor stage I to III. B, Tumor stage IV.

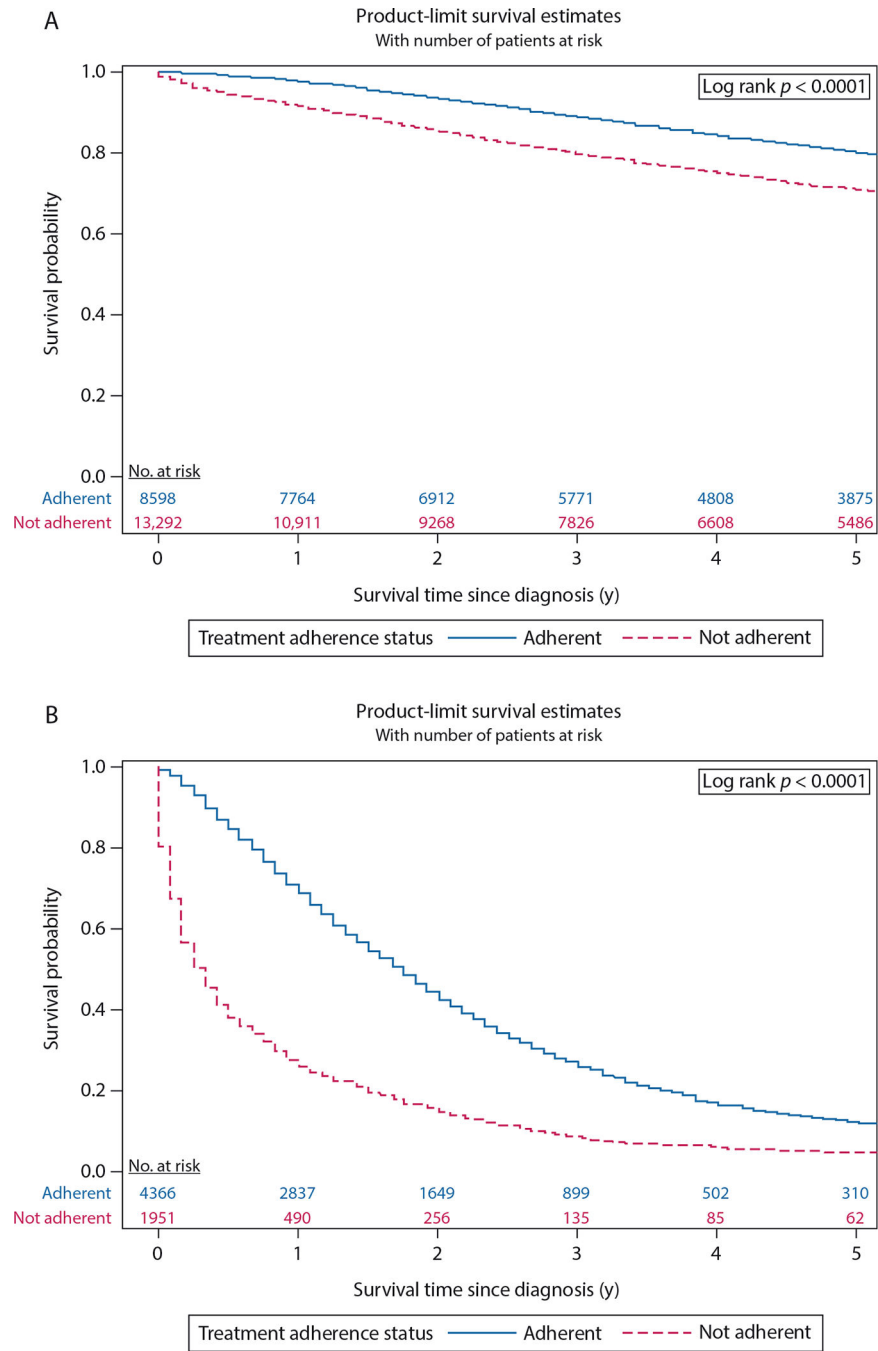


FIGURE 2. Kaplan-Meier disease-specific survival graph by treatment adherence status. A, Tumor stage I to III. B, Tumor stage IV.

TABLE 1.

Definition for NCCN guideline–adherent care

Stage of rectal cancer ^a	Adherent treatment		
	Surgery	Chemotherapy	Radiation therapy
Stage I	Transanal excision/transabdominal resection	No	No
Stage II and III	Transabdominoperineal resection/low anterior resection/ total mesorectal excision	Yes	Yes
Stage IV		Yes	Yes/no

NCCN = National Comprehensive Cancer Network.

^aIf neoadjuvant chemotherapy was administered, clinical stage was used. If not, stage was clinical stage and/or pathological stage.

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TABLE 2.

Patient characteristics by treatment adherence status

Clinical variables	Total			Nonadherent care			Adherent care			p ^a
	n	%		n	%		n	%		
Total	30,118	100.0		16,442	54.6		13,676	45.4		<0.0001
Age at diagnosis, y										
18–44	2763	9.2		1201	43.5		1562	56.5		
45–54	7095	23.6		3460	48.8		3635	51.2		
55–64	8847	29.4		4677	52.9		4170	47.1		
65	11,413	37.9		7104	62.2		4309	37.8		<0.0001
Year of diagnosis										
2004–2009	12,026	39.9		6831	56.8		5195	43.2		
2010	18,092	60.1		9611	53.1		8481	46.9		
Race/ethnicity										<0.0001
Non-Hispanic white	16,349	54.3		9141	55.9		7208	44.1		
Non-Hispanic black	1723	5.7		964	55.9		759	44.1		
Hispanic	6788	22.5		3618	53.3		3170	46.7		
Asian	4662	15.5		2446	52.5		2216	47.5		
Other/unknown	596	2.0		273	45.8		323	54.2		<0.0001
Sex										
Male	17,584	58.4		9399	53.5		8185	46.5		
Female	12,525	41.6		7037	56.2		5488	43.8		
Insurance										<0.0001
Managed care	13,920	46.2		7451	53.5		6469	46.5		
Medicare	6927	23.0		4247	61.3		2680	38.7		
Medicaid	3260	10.8		1635	50.2		1625	49.8		
Other insurance (FFS, Tricare, VA, or NOS)	4649	15.4		2375	51.1		2274	48.9		
Not insured or unknown	1362	4.5		734	53.9		628	46.1		<0.0001
SES										
Lowest SES	5162	17.1		2893	56.0		2269	44.0		
Lower-middle SES	6036	20.0		3461	57.3		2575	42.7		

Clinical variables	Total			Nonadherent care			Adherent care			p ^a
	n	%		n	%		n	%		
Middle SES	6257	20.8		3441	55.0		2816	45.0		
Higher-middle SES	6388	21.2		3362	52.6		3026	47.4		
Highest SES	6275	20.8		3285	52.4		2990	47.6		
Marital status									<0.0001	
Single, separated, divorced, widowed, unmarried, or unknown	12,855	42.7		7258	56.5		5597	43.5		
Married	17,263	57.3		9184	53.2		8079	46.8		
Tumor stage									<0.0001	
I	9533	31.7		5857	61.4		3676	38.6		
II	5676	18.8		3672	64.7		2004	35.3		
III	8080	26.8		4801	59.4		3279	40.6		
IV	6829	22.7		2112	30.9		4717	69.1%		
Grade or differentiation of the tumor									<0.0001	
Grade I or well differentiated	3472	11.5		1605	46.2		1867	53.8		
Grade II or moderately well differentiated	18,353	60.9		10,769	58.7		7584	41.3		
Grade III or poorly differentiated	3667	12.2		1930	52.6		1737	47.4		
Grade IV or undifferentiated/anaplastic	316	1.0		181	57.3		135	42.7		
Grade and differentiation not stated	4310	14.3		1957	45.4		2353	54.6		

FFS = fee for service; NOS = not otherwise specified; SES = socioeconomic status; VA = Veteran's Affairs.

^aThe X² test for the difference between nonadherent group and adherent group.

TABLE 3.

ORs from logistic regression on receiving NCCN guideline-adherent care

Clinical variables	OR	95% CI		p
Age at diagnosis	0.98	0.98	0.98	<0.0001
Year of diagnosis	0.99	0.98	0.99	0.0002
Sex				
Male		Ref		
Female	0.94	0.90	0.99	0.0187
Race/ethnicity				
Non-Hispanic white		Ref		
Non-Hispanic black	0.98	0.88	1.09	0.6614
Hispanic	1.09	1.02	1.17	0.0073
Asian	1.15	1.07	1.23	0.0001
Others/unknown	1.55	1.31	1.85	<0.0001
Insurance				
Managed care		Ref		
Medicare	0.92	0.86	0.98	0.0128
Medicaid	0.91	0.83	0.99	0.0221
Other insurance (FFS, Tricare, VA, or NOS)	1.00	0.93	1.07	0.9725
Not insured or unknown	0.84	0.75	0.95	0.0047
SES				
Lowest SES	0.79	0.72	0.86	<0.0001
Lower-middle SES	0.79	0.73	0.85	<0.0001
Middle SES	0.88	0.81	0.94	0.0005
Higher-middle SES	0.97	0.91	1.05	0.4817
Highest SES		Ref		
Marital status				
Single, separated, divorced, widowed, unmarried or unknown		Ref		
Married	1.17	1.12	1.23	<0.0001
Tumor stage				
I		Ref		
II	1.02	0.95	1.10	0.5856
III	1.23	1.15	1.31	<0.0001
IV	4.12	3.84	4.42	<0.0001
Grade or differentiation of the tumor				
Grade I or well differentiated		Ref		
Grade II or moderately well differentiated	0.52	0.48	0.56	<0.0001
Grade III or poorly differentiated	0.54	0.49	0.60	<0.0001
Grade IV or undifferentiated/ anaplastic	0.42	0.33	0.54	<0.0001
Grade and differentiation not stated	0.73	0.66	0.80	<0.0001

FFS = fee for service; NCCN = National Comprehensive Cancer Network; NOS = not otherwise specified; Ref = reference; SES = socioeconomic status; VA = Veteran's Affairs.

TABLE 4. Adjusted HRs for colorectal cancer–specific survival using a Cox model stratified by adherence status

Clinical variables	Nonadherence (n = 16,442)			Adherence (n = 13,676)				
	Adjusted HR	95% CI	p	Adjusted HR	95% CI	p		
Age at diagnosis	1.024	1.020	1.027	<0.0001	1.009	1.006	1.012	<0.0001
Year of diagnosis	1.01	1.00	1.02	0.0342	0.99	0.98	1.00	0.2729
Female	0.88	0.83	0.94	0.0002	0.91	0.85	0.97	0.003
Race/ethnicity								
Non-Hispanic white		Ref			Ref			
Non-Hispanic black	1.05	0.93	1.19	0.4208	1.06	0.93	1.22	0.3888
Hispanic	0.91	0.83	0.99	0.0276	0.99	0.91	1.07	0.7599
Asian	0.80	0.72	0.88	<0.0001	0.92	0.84	1.01	0.076
Other/unknown	1.04	0.80	1.37	0.7596	0.89	0.69	1.13	0.3296
Insurance								
Managed care		Ref			Ref			
Medicare	1.15	1.06	1.25	0.0008	1.04	0.95	1.13	0.4216
Medicaid	1.56	1.40	1.73	<0.0001	1.18	1.08	1.30	0.0005
Other insurance (FFS, Tricare, VA, or NOS)	0.88	0.78	0.99	0.0334	0.87	0.79	0.96	0.0043
Not insured or unknown	1.44	1.25	1.65	<0.0001	1.08	0.94	1.24	0.2968
SES								
Lowest SES	1.42	1.27	1.59	<0.0001	1.20	1.08	1.34	0.0012
Lower-middle SES	1.36	1.22	1.51	<0.0001	1.20	1.08	1.33	0.0004
Middle SES	1.20	1.07	1.34	0.0013	1.24	1.13	1.37	<0.0001
Higher-middle SES	1.21	1.08	1.36	0.0009	1.07	0.97	1.18	0.1714
Highest SES		Ref			Ref			
Marital status								
Single, separated, divorced, widowed, unmarried or unknown		Ref			Ref			
Married	0.78	0.73	0.84	<0.0001	0.83	0.78	0.89	<0.0001
Tumor stage								
I	2.40	2.13	2.70	<0.0001	3.09	2.52	3.78	<0.0001
II		Ref			Ref			

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Clinical variables	Nonadherence (n = 16,442)			Adherence (n = 13,676)		
	Adjusted HR	95% CI	P	Adjusted HR	95% CI	P
III	3.44	3.08	<0.0001	4.16	3.45	<0.0001
IV	26.20	23.45	<0.0001	32.66	27.39	<0.0001
Grade or differentiation of the tumor						
Grade I or well differentiated		Ref			Ref	
Grade II or moderately well differentiated	1.13	0.99	0.0726	1.26	1.09	0.0025
Grade III or poorly differentiated	1.74	1.50	<0.0001	2.01	1.71	<0.0001
Grade IV or undifferentiated/anaplastic	2.24	1.67	<0.0001	2.01	1.51	<0.0001
Grade and differentiation not stated	1.86	1.60	<0.0001	1.58	1.34	<0.0001

FFS = fee for service; NOS = not otherwise specified; Ref = reference; SES = socioeconomic status; VA = Veteran's Affairs.