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Refusal of colorectal cancer surgery in the United States: Predictors and associated cancer-specific mortality in a Surveillance, Epidemiology, and End Results (SEER) cohort

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ABSTRACT

Introduction: This study aims to understand patient factors associated with refusal of surgery for nonmetastatic colorectal cancer and the associated cancer-specific mortality.
Methods: Patients diagnosed with nonmetastatic colorectal cancer between 2004 and 2015 from the Surveillance, Epidemiology, and End Results Program were included.
Results: A total of 152,731 (99.4%) patients underwent surgery, and 983 (0.6%) refused surgery. Independent predictors of refusal included male sex, older age, minority race, single relationship status, being uninsured, more recent date of diagnosis, having an earlier stage of diagnosis, and rectal versus colon cancer. Refusing surgery for nonmetastatic colorectal cancer increased cancer-specific mortality (adjusted hazard ratio 5.10, 95% confidence interval 4.62–5.62).
Conclusion: Most patients diagnosed with nonmetastatic colorectal cancer undergo surgery in the United States. However, refusal of surgery is increasing and associated with higher cancer-specific mortality. A better understanding of surgical decision making in colorectal cancer is urgently needed.
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INTRODUCTION

Colorectal cancer is the fourth leading cause of cancer and cancer-related deaths in the United States [1]. Improved early detection and treatment have increased survival; contemporary 5-year estimates for nonmetastatic disease range between 60% and 90% [2]. Surgical resection is a key component of treatment, but it is also associated with morbidity and mortality and has a significant impact on patient quality of life. Whether or not to undergo surgery is a complex and personal decision. Even when surgery is recommended, some patients may not feel that it is in their best interest. Some may appropriately refuse to undergo curative surgery because of personal preferences, functional status, or ineffective shared decision making [3]. Prior studies have found significant variation in the utilization of cancer-directed surgery based on personal and disease characteristics, such as age, race and ethnicity, insurance status, and stage of disease [4–8]. Currently, there are no contemporary data on the predictors of refusal of surgery for nonmetastatic colorectal cancer in the United States. As such, this study aims to investigate predictors and effects of refusal of surgery for nonmetastatic colorectal cancer in the United States.

METHODS

Data Source. We conducted a retrospective cohort study using data from the Surveillance, Epidemiology, and End Results (SEER) Program. SEER collects cancer incidence data from population-based cancer registries covering approximately 35% of the US population [9]. The SEER registries collect data on patient demographics, primary tumor site, tumor morphology, stage at diagnosis, and initial course of treatment and follows patients longitudinally for vital status.

Study Population. Patients were included if they were 18 years or older at the time of first diagnosis of nonmetastatic primary colorectal adenocarcinoma. Patients who met any of the following criteria were excluded: metastatic disease at diagnosis, race/ethnicity unknown,

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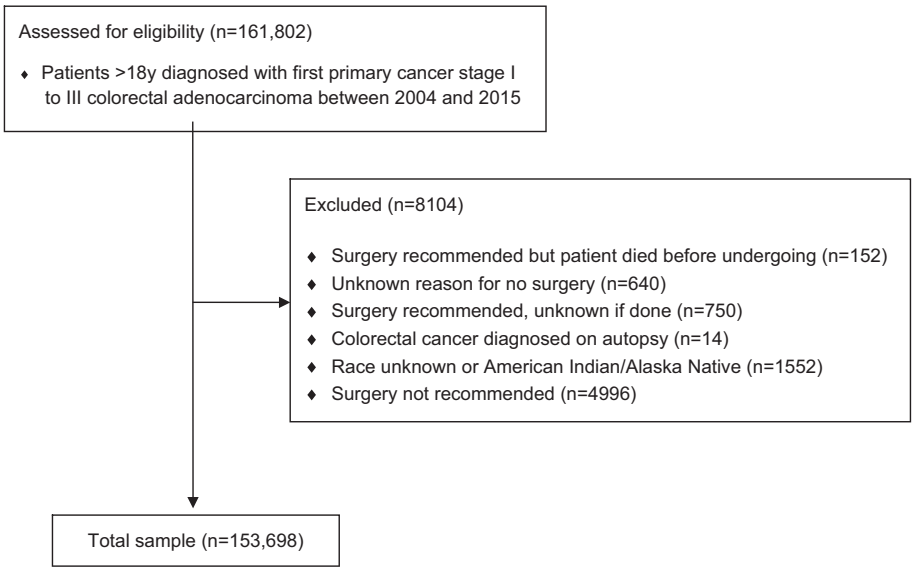

Fig 1. Flow diagram demonstrating selection of study population.

American Indians/Alaska Natives, colorectal cancer diagnosis at autopsy or death certificate, death prior to recommended surgery, unknown reason for no surgery, surgery was not recommended, or unknown if surgery was performed. Patients with metastatic disease were excluded because of the wide variation in management determined by the burden and location of metastases, which is information not available in SEER. Patients were excluded from the sample if their race/ethnicity was listed as other or American Indian/Alaska Native because of the small sample size.

Variable Definitions. Independent variables include sociodemographic and clinical characteristics. Sociodemographic characteristics include sex, age, race/ethnicity, marital status, urban versus rural living, and insurance status (available from 2007 onwards). Disease characteristics include year of diagnosis, the American Joint Committee on Cancer stage at diagnosis, and grade and location of primary tumor (colon versus rectal adenocarcinoma). Treatment characteristics include whether neoadjuvant or adjuvant chemotherapy or radiation was received.

The primary outcome was status of surgery. This was a binary variable where patients who were recommended surgery were classified as either refusing or undergoing surgery. The SEER coding manual defines patients as having refused surgery if surgery was exactly what was recommended by the physician and refused by the patient. For example, if 2 options were recommended by the physician and surgery was not chosen, then the patient was not listed as refusing surgery. Thus, it is likely that patients diagnosed with rectal cancer who were offered and opted for a watch-and-wait approach would not have been listed as refusing surgery. The secondary outcome was cancer-specific mortality.

Statistical Analysis. Bivariate analyses using χ^2 and Kruskal-Wallis tests were performed to compare baseline sociodemographic and clinical characteristics by refusal of surgery. A multivariable logistic regression was used to assess for significant predictors of refusal of surgery. Univariable and multivariable Cox proportional hazard regression was used to assess significant predictors of cancer-specific mortality. All multivariable regression analyses controlled for both sociodemographic and clinical characteristics in the same model. A sensitivity analysis adjusting for insurance status for patients diagnosed after 2007 and a subgroup analysis excluding patients diagnosed with stage I were conducted for the primary outcome only.

Complete case analysis was used to handle missing data. All statistical analyses were performed using STATA (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC).

RESULTS

A total of 153,698 patients were included in the study sample (Fig 1). Surgery was performed in 152,731 (99.4%) and recommended but refused in 967 (0.6%) patients. The proportion of patients that refused surgery increased over the study period (Fig 2).

Predictors of Refusal of Surgery: Bivariate Analyses. Sociodemographic factors significantly associated with refusal of surgery included older age, minority race/ethnicity, and single relationship status (Table 1). Clinical factors significantly associated with refusal of surgery included more recent date of diagnosis, earlier stage of diagnosis, unknown tumor grade, rectal versus colon cancer, and receiving chemotherapy. Among patients who were diagnosed with rectal cancer, patients who refused surgery were significantly more likely to undergo radiation ($n = 425$, 64.6% vs $n = 23{,}090$, 54.8%; $P < .01$).

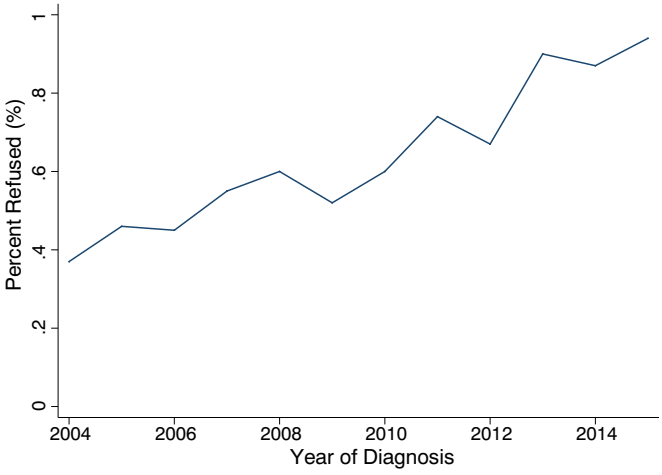

Fig 2. Increasing percent of patients refusing surgery between 2004 and 2015.

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Table 1
Baseline sociodemographic and clinical characteristics in patients in whom surgery was refused versus performed

	Total N *(%)*	*Surgery performed* n *(%)*	*Surgery refused* n *(%)*	P *value*
Sociodemographic characteristics				
Sex				.99
Female	74,416 (48.4)	73,948 (48.4)	468 (48.4)	
Male	79,282 (51.6)	78,783 (51.6)	499 (51.6)	
Age mean years ± standard deviation	67 ± 14	67 ± 14	75 ± 14	<.001
Age category				<.001
18–49	16,928 (11.0)	16,881 (11.1)	47 (4.9)	
50–64	48,399 (31.5)	48,218 (31.6)	181 (18.7)	
65–74	38,349 (25.0)	38,179 (25.0)	170 (17.6)	
≥75	50,022 (32.5)	49,453 (32.4)	569 (58.8)	
Race/ethnicity				<.001
White	107,909 (70.2)	107,296 (70.3)	613 (63.4)	
Black	16,564 (10.8)	16,415 (10.7)	149 (15.4)	
Hispanic	15,850 (10.3)	15,752 (10.3)	98 (10.1)	
Asian/Pacific Islander	13,375 (8.7)	13,268 (8.7)	107 (11.1)	
Marital status				<.001
Married	83,923 (54.6)	83,554 (54.7)	369 (38.2)	
Not married	63,305 (41.2)	62,772 (41.1)	533 (55.1)	
Unknown	6470 (4.2)	6405 (4.2)	65 (6.7)	
Urban versus rural living				.15
Rural	19,875 (12.9)	19,770 (12.9)	105 (10.9)	
Urban	133,812 (87.1)	132,950 (87.0)	862 (89.1)	
Unknown	11 (<1.0)	11 (<1.0)	0 (0)	
Insurance status				.73
Insured	106,435 (95.0)	105,688 (95.0)	747 (94.6)	
Uninsured	3559 (3.2)	3530 (3.2)	29 (3.7)	
Unknown	2018 (1.8)	2004 (1.8)	14 (1.8)	
Clinical characteristics				
Year of diagnosis				<.001
2004–2006	41,686 (27.1)	41,509 (27.2)	177 (18.3)	
2007–2009	39,384 (25.6)	39,164 (25.6)	220 (22.8)	
2010–2012	36,707 (23.9)	36,462 (23.9)	245 (25.3)	
2013–2015	35,921 (23.4)	35,596 (23.3)	325 (33.6)	
Stage				<.001
I	32,783 (21.3)	32,356 (21.2)	427 (44.2)	
II	59,155 (38.5)	58,881 (38.6)	274 (28.3)	
III	61,760 (40.2)	61,494 (40.3)	266 (27.5)	
Grade				<.001
Low	122,666 (79.8)	121,976 (79.9)	690 (71.4)	
High	26,448 (17.2)	26,363 (17.3)	85 (8.8)	
Unknown	4584 (3.0)	4392 (2.9)	192 (19.9)	
Location				<.001
Colon	110,922 (72.2)	110,613 (72.4)	309 (32.0)	
Rectal	42,776 (27.8)	42,118 (27.6)	658 (68.0)	
Chemotherapy				<.001
No/unknown	93,678 (60.9)	93,097 (61.0)	581 (60.1)	
Yes	60,020 (39.1)	59,634 (39.0)	386 (39.9)	

Predictors of Refusal of Surgery: Multivariable Analysis. Sociodemographic characteristics significantly associated with refusal of surgery included male sex (odds ratio [OR] 1.14, 95% confidence interval [CI] 0.99–1.31), older age (eg, ≥75 vs 18–49 years old; OR 7.03, 95% CI 5.18–9.53), minority race (eg, non-Hispanic black versus non-Hispanic white; OR 2.04, 95% CI 1.69–2.47), and being single versus married (OR 1.76, 95% CI 1.53–2.03; Table 2).

Clinical characteristics associated with significantly higher odds of refusing surgery included more recent date of diagnosis (eg, 2013–2015 vs 2004–2006; OR 2.51, 95% CI 2.08–3.03), earlier stage of diagnosis (eg, stage I vs III; OR 2.60, 95% CI 2.22–3.05), unknown tumor grade versus high-grade tumor (OR 7.22, 95% CI 5.52–9.43), and rectal versus colon cancer (OR 6.43, 95% CI 5.58–7.42; Table 2).

A subgroup analysis excluding patients with stage I disease demonstrated the association between sociodemographic and clinical characteristics and refusal of surgery persisted (Table 4). A sensitivity analysis controlling for insurance status in patients diagnosed after 2007 was conducted and demonstrated that patients without insurance were more likely to refuse surgery compared to those with insurance (OR 1.99, 95% CI 1.34–2.95; Table 2).

Predictors of Cancer-Specific Mortality. Patients who refused surgery had a higher cancer-specific mortality (hazard ratio [HR] 5.03, 95% CI 4.58–5.54; Table 3). This persisted after adjusting for sociodemographic and clinical characteristics (HR 4.77, 95% CI 4.33–5.26; Table 3) and across all included stages of disease (Fig 3).

DISCUSSION

Our study demonstrates that operative management for nonmetastatic colorectal cancer in the United States has remained persistently high between 2004 and 2015. Over the study period, surgery was significantly more likely to be refused in patients who were male, were older, belong to a minority race, were single, and were uninsured. Significant clinical characteristics associated with refusal of surgery included more recent date of diagnosis, an earlier stage of diagnosis, unknown tumor grade, and rectal versus colon cancer. Patients who refused surgery had a significantly higher cancer-specific mortality. Together, these findings may explain, in part, previously identified variations in colorectal cancer outcomes based on sociodemographic and clinical characteristics.

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Table 2
Multivariable logistic regression of predictors of refusal of surgery

	Main analysis		*Sensitivity analysis controlling for insurance status*	
	Odds of refusal OR (95% CI)	P *value*	*Odds of refusal OR (95% CI)*	P *value*
Sociodemographic characteristics				
Sex				
Female	Ref		Ref	
Male	1.14 (0.99–1.31)	.05	1.20 (1.03–1.39)	.02
Age category				
18–49	Ref		Ref	
50–64	1.38 (0.99–1.91)	.05	1.47 (1.02–2.10)	.04
65–74	2.08 (1.50–2.89)	<.01	2.36 (1.64–3.41)	<.01
≥75	7.03 (5.18–9.53)	<.01	8.29 (5.88–11.69)	<001
Race/ethnicity				
White	Ref		Ref	
Black	2.04 (1.69–2.47)	<.01	2.05 (1.67–2.52)	<.01
Hispanic	1.22 (0.98–1.52)	.07	1.18 (0.93–1.50)	.18
Asian/Pacific Islander	1.53 (1.24–1.90)	<.01	1.38 (1.09–1.76)	.01
Marital status				
Married	Ref		Ref	
Not married	1.76 (1.53–2.03)	<.01	1.67 (1.42–1.95)	<.01
Unknown	1.89 (1.44–2.48)	<.01	2.04 (1.52–2.73)	<.01
Urban versus rural living				
Rural	Ref		Ref	
Urban	1.11 (0.90–1.36)	.34	1.09 (0.86–1.37)	.49
Insurance status				
Insured	–		Ref	
Uninsured	–		1.99 (1.34–2.95)	<.01
Unknown	–		0.73 (0.42–1.28)	.28
Clinical characteristics				
Year of diagnosis				
2004–2006	Ref		–	
2007–2009	1.40 (1.14–1.71)	<.01	Ref	
2010–2012	1.77 (1.45–2.15)	<.01	1.26 (1.04–1.52)	.02
2013–2015	2.51 (2.08–3.03)	<.01	1.80 (1.51–2.15)	<.01
Stage				
I	2.60 (2.22–3.05)	<.01	2.53 (2.13–3.02)	<.01
II	1.08 (0.91–1.28)	.40	1.07 (0.89–1.30)	.45
III	Ref		Ref	
Grade				
Low	1.33 (1.06–1.68)	.14	1.26 (0.98–1.62)	.07
High	Ref		Ref	
Unknown	7.22 (5.52–9.43)	<.01	6.81 (5.07–9.13)	<.01
Location				
Colon	Ref		Ref	
Rectal	6.43 (5.58–7.42)	<.01	7.13 (6.08–8.36)	<.01

A patient's decision to decline recommended care is based on many complex and interrelated factors, including previous experiences and beliefs. Consistent with previous observational studies, we found that older patients were more likely to refuse cancer-directed surgery; this is often a decision that is made is after lengthy patient-physician discussions [10]. Several reports investigating the reasons for refusal in this population have demonstrated that older patients who are more likely to refuse surgical treatment desire more prognostic information [11]. Physicians may find it challenging to accurately counsel older patients regarding the gold standard age-appropriate treatment because the results of most clinical trials are not generalizable to this population. In addition, there is an ongoing debate as to what constitutes age-appropriate colorectal cancer care [12,13]. The proportion of older-aged patients being diagnosed with colorectal cancer will only continue to increase in the foreseeable future as the population ages. Thus, we must improve the quality and quantity of evidence available to help guide physicians in counseling this unique population [14].

Disparities in mortality from colorectal cancer have previously been identified in the United States based on race [15]. One potential pathway may be systematic differences in refusal of care. For example, Demissie et al found in a SEER cohort of patients diagnosed with colorectal cancer between 1988 and 1997 that a higher proportion of blacks refused surgery compared to whites [4]. Similarly, Baldwin et al found that, among patients diagnosed with stage III colon cancer between 1993 and 1996 in a SEER-Medicare cohort, blacks and whites were equally likely to see a medical oncologist, but blacks were significantly less likely to proceed to receive adjuvant chemotherapy [16]. Our results show that, in a contemporary SEER cohort, minority race is still a significant predictor of definitive management of colorectal cancer. The reasons for this are complex. Prior studies have demonstrated that blacks are less likely to trust the health care system and have cultural differences in attitudes toward medical illness and treatment making them more likely to refuse standard of care [17–20]. Patient-physician interactions may further exacerbate these factors because of differences in health literacy and lack of cultural proficiency, diversity, and implicit biases that exist within physicians and systems in the United States [21–24]. These factors are important causes of disparities in access to surgical care that may be intervenable with public health interventions [25,26].

Not only did we find sociodemographic factors to be associated with refusal of surgery, but we also found several clinical characteristics. For example, patients who had an earlier stage of diagnosis were more likely to refuse surgery compared to those with a more advanced stage. A proportion of patients with stage I disease may have undergone a complete polypectomy, where the benefits of more invasive surgery are difficult to measure against the risks and morbidity particularly in asymptomatic patients [27,28]. For these reasons, a subgroup analysis excluding patients with stage I disease was conducted and demonstrated that similar associations between refusal of surgery and sociodemographic and clinical characteristics persisted. Two clinical characteristics strongly associated

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Table 3
Cancer-specific survival analyses

	Unadjusted hazard ratio HR (95% CI)	P *value*	*Adjusted hazard ratio HR (95% CI)*	P *value*
Sociodemographic characteristics				
Sex				
Female	Ref		Ref	
Male	1.01 (0.99–1.03)	.43	1.20 (1.17–1.23)	<.01
Age category				
18–49	Ref		Ref	
50–64	1.01 (0.97–1.06)	.55	1.12 (1.07–1.18)	<.01
65–74	1.21 (1.16–1.27)	<.01	1.44 (1.37–1.51)	<.01
≥75	2.02 (1.94–2.12)	<.01	2.49 (2.37–2.60)	<.01
Race/ethnicity				
White	Ref		Ref	
Black	1.26 (1.22–1.31)	<.01	1.33 (1.28–1.38)	<.01
Hispanic	1.03 (0.99–1.07)	.14	1.09 (1.04–1.13)	<.01
Asian/Pacific Islander	0.89 (0.85–0.94)	<.01	0.90 (0.86–0.94)	<.01
Marital status				
Married	Ref		Ref	
Not married	1.49 (1.46–1.53)	<.01	1.37 (1.34–1.41)	<.01
Unknown	1.12 (1.05–1.20)	<.01	1.11 (1.04–1.19)	<.01
Urban versus rural living				
Rural	Ref		Ref	
Urban	0.95 (0.92–0.99)	.01	0.91 (0.88–0.95)	<.01
Clinical characteristics				
Year of diagnosis				
2004–2006	Ref		Ref	
2007–2009	0.96 (0.93–0.99)	.01	0.96 (0.93–0.99)	.01
2010–2012	0.93 (0.90–0.96)	<.01	0.92 (0.87–0.95)	<.01
2013–2015	0.92 (0.87–0.96)	<.01	0.90 (0.86–0.95)	<.01
Stage				
I	Ref		Ref	
II	2.05 (1.95–2.14)	<.01	2.0 (1.91–2.09)	<.01
III	4.16 (3.99–4.35)	<.01	4.34 (4.15–4.53)	<.01
Grade				
Low	0.58 (0.56–0.59)	<.01	0.69 (0.68–0.72)	<.01
High	Ref		Ref	
Unknown	0.61 (0.57–0.66)	<.01	0.75 (0.70–0.81)	<.01
Location				
Colon	Ref		Ref	
Rectal	1.02 (1.00–1.05)	.11	1.15 (1.12–1.18)	<.01
Surgery				
Not refused	Ref		Ref	
Refused	5.03 (4.58–5.54)	<.01	4.77 (4.33–5.26)	<.01

with refusal of surgery included rectal versus colon cancer and undergoing chemotherapy and radiation treatment. There are several possible explanations for this. Some patients with rectal cancer may have achieved a pathological complete response with neoadjuvant treatment and opted for a watch-and-wait approach [29]. However, if this treatment approach was offered as an alternative to surgery, it is unlikely that these patients would have been listed as refusing surgery in the SEER registry. Others may have wanted to avoid the morbidity associated with radical cancer surgery and opted for chemotherapy and radiation instead. Unfortunately, data on tumor distance from the anal verge and permanent colostomy are not available in the SEER registry but likely also represent important factors in the differential refusal between rectal and colon cancer. In the future, it will be important to understand why some patients refuse colorectal cancer surgery to determine if this represents patient-centered care or disparities in access.

It is concerning that the proportion of patients who refused surgery increased over the study period. For example, between 2004 and 2007, 0.4% of patients refused surgery compared to 0.9% between 2013 and 2015. Even after accounting for possible changes in patient and disease characteristics over time, more recent date of diagnosis remained a significant predictor of refusing surgery. A similar trend was seen in a SEER cohort of breast cancer patients diagnosed between 2004 and 2013 but not pancreatic or esophageal cancer [8]. It is unclear if these findings represent improved or worsening status of care. Because of the potential medicolegal implications of not recommending treatment, there is likely a very low threshold in borderline cases for the surgeon seeing the patient to allocate the responsibility of nontreatment in the record to the patient rather than saying that treatment was not recommended. In these cases, refusing surgery may have been in the patient's best interest. Given that refusing surgery increased the cancer-specific mortality by more than 5-fold, it is imperative that we develop a better

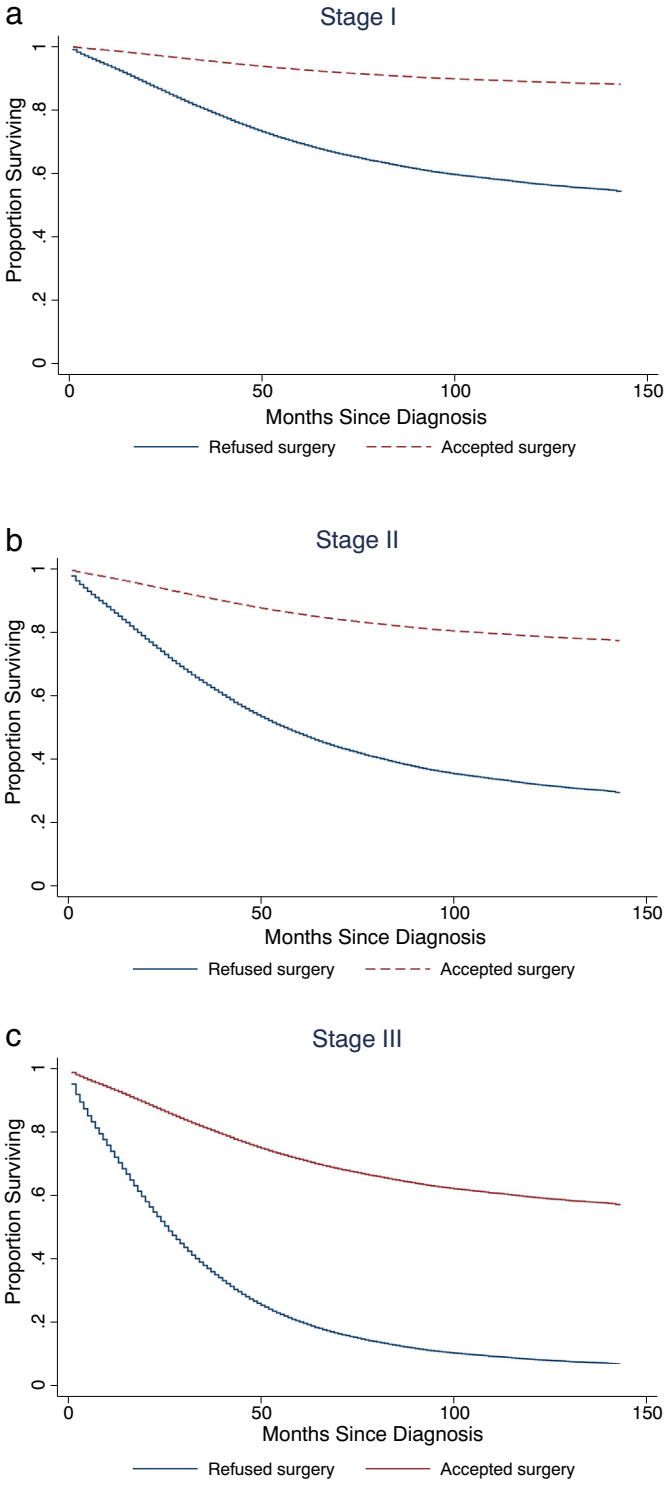

Fig 3. A, Adjusted cancer-specific mortality by stage and refusal of surgery. B, Adjusted cancer-specific mortality by stage and refusal of surgery. C, Adjusted cancer-specific mortality by stage and refusal of surgery.

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Table 4
Multivariable logistic regression of predictors of refusal of surgery subgroup analysis excluding patients with stage I

	Odds of refusal OR (95% CI)	P *value*
Sex		
Female	Ref	
Male	1.08 (0.90–1.29)	.40
Age category		
18–49	Ref	
50–64	1.44 (1.01–2.05)	.04
65–74	1.78 (1.23–2.58)	<.01
≥75	5.69 (4.04–8.01)	<.01
Race/ethnicity		
White	Ref	
Black	2.18 (1.71–2.79)	<.01
Hispanic	1.18 (0.89–1.57)	.24
Asian/Pacific Islander	1.27 (0.95–1.70)	.11
Marital status		
Married	Ref	
Not married	1.49 (1.24–1.80)	<.01
Unknown	1.69 (1.16–2.45)	.01
Urban versus rural living		
Rural	Ref	
Urban	1.38 (1.01–1.87)	.04
Year of diagnosis		
2004–2006	Ref	
2007–2009	1.41 (1.05–1.88)	.02
2010–2012	1.90 (1.44–2.50)	<.01
2013–2015	2.80 (2.15–3.64)	<.01
Stage		
II	Ref	
III	0.84 (0.71–1.00)	.06
Grade		
Low	1.20 (0.91–1.58)	.21
High	Ref	
Unknown	4.91 (3.51–6.88)	<.01
Location		
Colon	Ref	
Rectal	18.66 (14.65–23.78)	<.01

understanding of the reasons for this increasing trend in patient refusal and ensure that patients are optimally supported through this complex journey.

From a global perspective, the results of this study are encouraging. In our sample, 99.4% of patients underwent surgery. This is significantly more than the proportion of patients who underwent surgery for colorectal cancer in comparable high-income countries with universal health care (eg, 68.4% in England and 81.3% in Sweden) [30]. From a national perspective, the proportion of patients who were recommended and refused cancer-directed surgery in our study (0.6%) was similar to patients with breast cancer (0.6%) and less compared to patients with esophageal (5.7%), pancreatic (3.7%), and early-stage non–small cell lung cancer (1.5%) [7,8,31,32]. Sociodemographic predictors of refusal were similar across these cancer cohorts and included older age, minority race/ethnicity, lack of insurance, and single relationship status. Although none of the studies parsed out why refusal was higher in these groups, it is suggested that lack of social support and limited health literacy may reduce access to complex oncology care [33]. From a clinical perspective, the rates of refusal may have been higher in pancreatic and esophageal cancer compared to breast and colorectal cancer because of the fear of undergoing surgery associated with higher morbidity and mortality. Earlier stage at diagnosis was a predictor of refusal in esophageal and colorectal cancer, whereas more advanced stage was associated with increased refusal in pancreatic and breast cancer. One reason for the differing relationship with stage may be because some patients opt for noncurative local resection techniques to temporize symptoms in early-stage esophageal and colorectal cancer but this option is not available in early-stage breast and pancreatic cancer. Together, these findings demonstrate that although some factors driving refusal of care may be similar across cancer types, there exist some important differences that should be considered in future investigations.

The results of this study improve our understanding of contemporary sociodemographic and clinical characteristics associated with refusing colorectal cancer surgery. However, there is still a lot to be learned on the reasons behind these decisions. Decision making in surgery is potentially modifiable by tailoring discussions to individuals' needs. For example, studies have shown that patients who refuse cancer surgery are more likely to accept treatment if physicians acknowledge patient fears, provide hope, describe treatment possibilities and provide time to cope with the diagnosis prior to starting treatment [34]. Given the marked difference in survival between those undergoing resection and those who refuse surgery, a better understanding of how to best support diverse patients in their decision-making process is needed.

Limitations. The results of this study must be taken in the context of its limitations. The aim of this study was to assess variations in refusal of surgery based on sociodemographic and clinical characteristics and the associated cancer-specific mortality. The SEER Program does not record individual-level education, income, or employment status. This limited our ability to completely assess the relationship between socioeconomic status and refusal of surgery, which is important in an era where cost-sharing for cancer care is prevalent and may affect access [35]. Another limitation of this study is that we were unable to account for physician and hospital-level characteristics. Previous studies have shown that these factors can have important mediating effects on the decision to undergo surgery [36]. The proportion of patients refusing surgery was substantially smaller than the number undergoing surgery, resulting in a mismatch in size between comparator groups. This limited our ability to perform subgroup analyses, such as for colon versus rectal cancer. In addition, among patients with rectal cancer, information on tumor distance from the anal verge and response to neoadjuvant chemoradiation are not available in the SEER registry. This is important because the management varies greatly in terms of response to neoadjuvant chemoradiation and permanent ostomy formation, and these may be underlying mechanisms behind the differential decision conflict. In addition, details regarding which patients diagnosed with rectal cancer achieved a complete response after neoadjuvant chemoradiation and opted for a watch-and-wait are not available in the SEER registry. It is possible that some of these patients may have been classified as refusing surgery, although this is unlikely based on the definition of refusal of surgery used by the SEER registry. Finally, there may be heterogeneity in the performance status and comorbidities of patients, as these remain unmeasured confounders using SEER data. We assumed that patients who refused surgery did so on their own volition and would otherwise be fit enough for surgery. However, as previously mentioned, there may have been situations in which the surgeon recommended surgery and described the prohibitive operative risks to the patient. In these cases, the patient may not have been otherwise fit for surgery, but the decision was documented as refusal of surgery.

In conclusion, surgical management of nonmetastatic colorectal cancer is generally high in the United States, but the number of patients refusing surgery is increasing. We identified significant variations in rates of refusal based on sociodemographic and clinical factors. Refusing surgery was associated with a significantly higher, and potentially preventable, cancer-specific mortality. The results of this study not only provide much needed contemporary data regarding trends and outcomes of nonoperative management for colorectal cancer but, more importantly, also highlight how a deeper understanding of patient and physician motivations regarding surgical decision making is needed in colorectal cancer care.

Author Contributions

Megan Delisle: Conceptualization, Methodology, Formal analysis, Data curation, Writing - original draft, Visualization, Project

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administration. **Shubhi Singh:** Conceptualization, Methodology, Formal analysis, Writing - review & editing, Visualization. **Jeffrey Howard:** Conceptualization, Methodology, Formal analysis, Writing - review & editing, Visualization. **Nikhil Panda:** Conceptualization, Methodology, Formal analysis, Writing - review & editing, Visualization. **Alison Weppler:** Conceptualization, Methodology, Formal analysis, Writing - review & editing, Visualization. **Ying Wang:** Conceptualization, Methodology, Formal analysis, Writing - review & editing, Visualization, Supervision.

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Conflicts of Interest

The authors have no conflicts of interest to disclose.

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