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Clinicopathological Features and Survival Outcomes of Colorectal Cancer in Young Versus Elderly

A Population-Based Cohort Study of SEER 9 Registries Data (1988–2011)

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Abstract: The incidence of colorectal cancer (CRC) in young adults is rising. We aimed to analyze the clinicopathological characteristics and survival outcomes of young versus elderly CRC patients. All patients diagnosed with CRC in the Surveillance, Epidemiology, and End Results program data (1988–2011) from the United States were evaluated. They were divided into 3 groups by age at diagnosis: group 1 (20–40 years old), group 2 (41–50 years old), and group 3 (>50 years old). The clinicopathological characteristics and CRC-specific survival (CRC-SS) were evaluated and compared among the 3 groups. A total of 279,623 CRC patients were included: 6700 (2.4%) in group 1, 19,385 (6.9%) in group 2, and 253,538 (90.7%) in group 3. Young CRC patients had more tumors located in rectum, fewer cases with multiple tumors, later stage, more mucinous carcinoma and signet ring-cell carcinoma, more poor differentiated tumors, and more lymph nodes (no. $\geq$12) examined. The 5-year CRC-SS rates of patients in groups 1, 2, and 3 were 65.1%, 67.1%, and 62.8%, respectively (group 1 vs group 2, $P = 0.001$; group 1 vs group 3, $P < 0.001$; group 2 vs group 3, $P < 0.001$). Multivariate analysis revealed older (>50 years old) age was an independent predictor of poor prognosis (hazard ratio, 1.545; 95% confidence interval, 1.456–1.639; $P < 0.001$). Young CRC patients had later stage presentation and more aggressive pathological features, but better survival. CRC patients aged 41 to 50 years had best CRC-SS in contrast to patients in another 2 age groups.

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Abbreviations: CI = confidence intervals, CRC = colorectal cancer, CRC-SS = colorectal cancer-specific survival, CSS = cancer-specific survival, HR = hazard ratios, SEER = Surveillance, Epidemiology, and End Results program.

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in the United States and a major health burden worldwide. The American Cancer Society estimated that 142,820 new CRC cases and 50,830 CRC deaths occurred in 2013.[1] In spite of these sobering epidemiological data, the annual report of 2010 cancer current status highlighted that CRC incidence rates in the United States had been dropping off.[2] This steady decline has largely been attributed to increases in the use of CRC screening in older population. It allows for the detection and removal of colorectal polyps before they progress to cancer. As a disease predominantly affecting older individuals, 90% of all CRC have been diagnosed in patients >50 years of age.[3] However, recent evidences suggest a constantly rising incidence of CRC in young individuals, a population not receiving routine screening.[4,5] The CRC incidence per 100,000 individuals for young individuals were 0.85 (ages 20–24 years) to 28.8 (ages 45–49 years) in the United States.[6] Consequently, the percentage of young patients in total CRC patients had been reported to range from 0.4% to as high as 35.6% in another literature review.[7]

The limited studies reveal a wide range of reported clinicopathological characteristics and prognosis for young CRC patients. Some studies have demonstrated that young CRC patients presented poor pathological features and advanced stage compared with older patients.[8,9] Nonetheless, others have found no difference when tumor stage and pathological features were compared with the older population.[3,10] As regards survival of young CRC patients, there is also a controversy.[11–13] These controversies are partly caused by no accepted clear definition of young CRC patient. Although most studies reported on young CRC patient as one 40 years old or less, some studies used the cutoff age of 50 years old. Furthermore, the biases associated with single-institution experiences or limit sample sizes may make the published data vary markedly.

In this study, we used population-based data from the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute in the United States to compare clinicopathological characteristics, prognostic factors, and overall survival among 3 age groups (20–40, 41–50, and >50 years) of CRC patients.

MATERIALS AND METHODS

Data Source

Data source was from the SEER 9 Registries program, a nationally representative collection of population-based registries of all incident cancers from Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah in the United States. The SEER registry is maintained by the National Cancer Institute, and provides

data on demographics (age at diagnosis, sex, and race/ethnicity), tumor location, cancer numbers, tumor size, the tumor, node, metastasis (TNM) stage, histology type, tumor grade, and number of lymph nodes evaluated. Overall and cancer-specific mortality are also reported but not recurrence. The SEER data released April 2014 is based on the November 2013 submission. We had got the permission to access the research data files with the reference number 10058-Nov2013. It did not include interaction with human subjects or use personal identifying information. The study did not require informed consent and was approved by the institutional review board of West China Hospital, China.

Patient Selection

Using the International Classification of Disease for Oncology, third edition (ICD-O-3) codes provided in SEER, we included patients with a diagnosis of primary colorectal cancer (age of diagnosis ≥20 years) from 1988 through 2011. The site codes used included the following: right colon (C18.0, C18.2–C18.4), left colon (C18.5–C18.7), large intestine NOS (C18.8–C18.9, C26.0), and rectum (C19.9 and C20.9). Patients were excluded if they had in situ or incomplete TNM stage.

Data Analysis

Data analysis was stratified by age at diagnosis: group 1 (20–40 years old), group 2 (41–50 years old), and group 3 (>50 years old). The clinicopathological characteristics and survival outcome were evaluated and compared among the 3 groups. Anatomic location analyses included the right colon (cecum, ascending colon, hepatic flexure, and transverse colon), the left colon (splenic flexure, descending colon, and sigmoid colon), and rectum (rectosigmoid junction and rectum). All TNM classification was restaged according to the criteria described in the 7th edition of American Joint Committee on Cancer (AJCC) Cancer Staging Manual. The histology type was divided into 3 classes according to SEER histology codes: adenocarcinoma (8010, 8140–8141, 8144–8145, 8210–8211, 8220–8221, 8230–8231, and 8260–8263), mucinous carcinoma (8480 and 8481), and signet ring-cell carcinoma (8490). Tumor grade was classified as: well differentiated (G1), moderately differentiated (G2), poorly differentiated (G3), and undifferentiated (G4). Deaths attributed to the CRC are treated as events, and deaths from other causes are treated as censored observation. Colorectal cancer-specific survival (CRC-SS) was calculated from the date of diagnosis to the date of cancer-specific death or the end of follow-up (cutoff date: December 2011).

Statistical Analysis

Continuous data were expressed as median and standard deviation and compared with the Kruskall–Wallis test among age groups. Categorical data were compared using the χ^2 test. Survival curves were generated using Kaplan–Meier estimates, and differences between the curves were analyzed by log-rank test. Univariate and multivariate Cox proportional hazard regression models were built for analysis of each characteristic on survival. The data were summarized with hazard ratio (HR) and their 95% confidence interval (CI). All reported P values were 2-sided. Throughout, P values <0.05 were judged as statistically significant. All statistical analyses were performed using R software system for statistical computing (Version 3.1.2, http://www.r-project.org/).

RESULTS

Demographic and Clinical Characteristics of Patients

We identified 279,623 patients (age of diagnosis ≥20 years) diagnosed with a primary CRC from 1988 through 2011 in the SEER data after excluding patients diagnosed with CRC in situ (n = 24,242) and those who had no information of TNM stage (n = 22,764). The characteristics of the patient cohort are shown in Table 1.

Demographical and Clinical Differences Among Age Groups

These 279,623 patients were divided into 3 groups for analysis. There were 6700 (2.4%) in group 1, 19,385 (6.9%) in group 2, and 253,538 (90.7%) in group 3. The details of demographical and clinical characteristics of patients according

TABLE 1. Demographic and Clinical Characteristics of CRC Patients

Characteristics	Category	CRC Patients N = 279,623 (%)
Age	Median (range, y)	71 (20–108)
	Mean ± SD, y	69.35 ± 13.15
	Group 1 (age 20–40 y)	6700 (2.4)
	Group 2 (age 41–50 y)	19,385 (6.9)
	Group 3 (age >50 y)	253,538 (90.7)
Sex	Female	137,817 (49.3)
	Male	141,806 (50.7)
Race	White	230,393 (82.6)
	Black	26,062 (9.3)
	Others	22,586 (8.1)
	Unknowns	582
Tumor location	Right colon	114,937 (42.1)
	Left colon	81,998 (30.0)
	Rectum	76,086 (27.9)
	Large intestine, NOS	6602
Cancer numbers	Single	192,001 (68.7)
	Multiple	87,602 (31.3)
	Unknowns	20
Tumor size	Median (range, cm)	4.2 (0–98.9)
	Mean ± SD, cm	4.656 ± 2.945
TNM stage	I	76,247 (27.3)
	II	80,222 (28.7)
	III	69,852 (25.0)
	IV	53,302 (19.0)
Histologic type	Adenocarcinoma	242,313 (89.2)
	Mucinous carcinoma	26,972 (9.9)
	signet ring-cell carcinoma	249 (0.9)
	Unknowns	7848
Tumor grade	Well	25,222 (10.3)
	Moderately	168,538 (68.9)
	Poorly	47,604 (19.5)
	Undifferentiated	327 (1.3)
	Unknowns	34,989
No. of lymph nodes examined	<12	160,606 (59.5)
	≥12	109,442 (40.5)

CRC = colorectal cancer, SD = standard deviation.

to age groups are shown in Table 2. The mean age of patients in 3 groups were 34.93 ± 4.60 years, 46.47 ± 2.80 years, and 72.03 ± 10.49 years, respectively. There were more males in group 1 (52.4%, $P = 0.001$) and group 2 (53.7%, $P < 0.001$) compared with group 3 (50.4%). No significant sex differences had been found between group 1 and group 2 ($P = 0.066$). The racial makeup of all age groups was predominantly white (72.0% in group 1, 74.6 % in group 2, and 83.5% in group 3) which had significant differences among 3 groups ($P < 0.001$).

Significant differences (all $P < 0.001$) among age groups had been observed concerning the clinical characteristics as follows: cancer numbers (fewer cases with multiple cancers in younger group), TNM stage (later stage in younger group), histologic type (more mucinous carcinoma or signet ring-cell carcinoma in younger group), tumor grade (higher grade in younger group), and number of lymph nodes examined (more lymph nodes examined in younger group). As regards to tumor location, the more tumors were located within the rectum in group 1 (39.3%, $P < 0.001$) and group 2 (39.3%, $P < 0.001$)

TABLE 2. Clinical and Pathological Characteristics of CRC Patients According to Age Groups

Characteristics	Age Groups (%)			*P*		
	Group 1 (Age 20–40 y)	Group 2 (Age 41–50 y)	Group 3 (Age >50 y)	Group 1 vs Group 2	Group 1 vs Group 3	Group 2 vs Group 3
	N = 6700	N = 19,385	N = 253,538			
Age (y, Mean ± SD)	34.93 ± 4.60	46.47 ± 2.80	72.03 ± 10.49	<0.001	<0.001	<0.001
Sex						
Female	3186 (47.6)	8966 (46.3)	125,665 (49.6)	0.066	0.001	<0.001
Male	3514 (52.4)	10,419 (53.7)	127,873 (50.4)			
Race						
White	4803 (72.0)	14,400 (74.6)	211,190 (83.5)	<0.001	<0.001	<0.001
Black	981 (14.7)	2763 (14.3)	22,318 (8.8)			
Others	890 (13.3)	2148 (11.1)	19,548 (7.7)			
Unknowns	26	74	482			
Tumor location*						
Right colon	1941 (29.8)	5346 (28.2)	107,650 (43.5)	0.011	<0.001	<0.001
Left colon	2010 (30.9)	6188 (32.6)	73,800 (29.8)			
Rectum	2555 (39.3)	7457 (39.3)	66,074 (26.7)			
Large intestine, NOS	194	394	6014			
Cancer numbers						
Single	5833 (87.1)	16,235 (83.8)	169,933 (67.0)	<0.001	<0.001	<0.001
Multiple	867 (12.9)	3149 (16.2)	83,586 (33.0)			
Unknowns	0	1	19			
Tumor size, cm						
≤5	3601 (68.4)	10,489 (68.3)	133,794 (67.5)	0.919	0.176	0.039
>5	1663 (31.6)	4861 (31.7)	64,351 (32.5)			
TNM stage†						
I	1392 (20.8)	4883 (25.2)	69,962 (27.6)	<0.001	<0.001	<0.001
II	1495 (22.3)	4324 (22.3)	74,403 (29.3)			
III	2175 (32.5)	5744 (29.6)	61,933 (24.4)			
IV	1638 (24.4)	44,34 (22.9)	47,230 (18.6)			
Histologic type						
Adenocarcinoma	5255 (84.2)	16,311 (88.9)	220,747 (89.3)	<0.001	<0.001	<0.001
Mucinous carcinoma	783 (12.5)	1773 (9.7)	24,416 (9.9)			
signet ring-cell carcinoma	202 (3.2)	255 (1.4)	2033 (0.8)			
Unknowns	460	1046	6342			
Tumor grade						
Well	468 (8.1)	1540 (9.1)	23,214 (10.5)	<0.001	<0.001	<0.001
Moderately	3679 (63.9)	11,651 (69.2)	153,208 (69.0)			
Poorly	1491 (25.9)	3415 (20.3)	42,698 (19.2)			
Undifferentiated	120 (2.1)	235 (1.4)	2915 (1.3)			
Unknowns	942	2544	31,503			
No. of lymph nodes examined						
<12	2894 (44.8)	9663 (51.4)	148,049 (60.5)	<0.001	<0.001	<0.001
≥12	3559 (55.2)	9147 (48.6)	96,736 (39.5)			

CRC = colorectal cancer, SD = standard deviation.
* Colon vs rectum: $P = 0.994$, $P < 0.001$, and $P < 0.001$ when group 1 vs group 2, group 1 vs group 3, group 2 vs group 3, respectively.
† Stage I + II vs III + IV: $P < 0.001$, $P < 0.001$, and $P < 0.001$ when group 1 vs group 2, group 1 vs group 3, group 2 vs group 3, respectively.

compared with group 3 (26.7%). But there was no significant difference between group 1 and group 2 ($P = 0.994$). In addition, the more tumors had small size (≤5 cm) in group 2 compared with group 3 ($P = 0.039$). However, no other significant differences had been observed between group 1 and group 2 ($P = 0.919$), or between group 1 and group 3 ($P = 0.176$) (Table 2).

Survival Differences Among Age Groups

The median follow-up period was 75 months (range, 0–467 months). The mean CRC-SS for patients in groups 1, 2, and 3 was 82, 80, and 63 months, respectively. Figure 1 shows the Kaplan–Meier survival curves for the different age groups. Overall, as shown in Figure 1, the CRC-SS of patients in group 3 were significantly worse than patients in group 1 and group 2 ($P < 0.001$). As shown in Table 3, the 3-year cumulative CRC-SS rates of patients in groups 1, 2, and 3 were 71.0%, 74.0%, and 69.4%, respectively (group 1 vs group 2, $P < 0.001$; group 1 vs group 3, $P < 0.001$; group 2 vs group 3, $P < 0.001$). The 5-year cumulative CRC-SS rates of patients in groups 1, 2, and 3 were 65.1%, 67.1%, and 62.8%, respectively (group 1 vs group 32, $P = 0.001$; group 1 vs group 3, $P < 0.001$; group 2 vs group 3, $P < 0.001$). Furthermore, the survival analyses were stratified by each stage in different age groups (stages I–IV, Figure 2A–D). It demonstrated that patients in group 3 had worse 3- and 5-year CRC-SS than those in group 1 ($P < 0.001$) and group 2 ($P < 0.001$) at stage I. The same trend of 3- and 5-year CRC-SS at stages II, III, and IV had been found (all $P < 0.001$). Compared with group 1, the patients in group 2 had better 3- and 5-year CRC-SS at stage I ($P < 0.001$, $P = 0.006$) and stage III ($P < 0.001$, 0.046), but not at stage II ($P = 0.572$ and 0.081) and stage IV ($P = 0.939$ and 0.740; Table 3).

Univariate Cox proportional hazard regression demonstrated the 41 to 50 years of age was better survival factor (HR 0.942, 95% CI 0.898–0.990, $P = 0.017$; Table 4). In addition to the older (>50 years) age (HR 1.165, 95% CI 1.117–1.215, $P < 0.001$; Table 4), factors associated with poor CRC-SS were black patients, tumor located right colon, single tumor number, later TNM stage, mucinous carcinoma or signet ring-cell carcinoma, poor differentiation, and less number of lymph nodes examined ($P < 0.001$, respectively; Table 4). In multivariate Cox proportional hazard regression, most of these factors remained independent prognostic factors, with the exception of mucinous carcinoma ($P = 0.428$). The older (>50 years) age remained an independent predictor of poor prognosis, with an HR of 1.545 (95% CI 1.456–1.639, $P < 0.001$; Table 4).

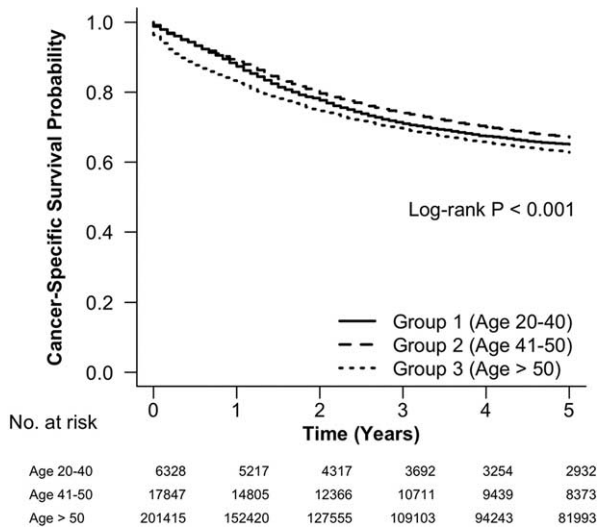

FIGURE 1. The overall cancer-specific survival for CRC patients in 3 age groups ($P < 0.001$). CRC = colorectal cancer.

DISCUSSION

At present, studies concerning CRC in young adults have some inconsistent findings including clinicopathological features and survival outcome. One problem leading to current controversial research results is lack of agreed definition of young CRC patient. Some researches on ''young'' include the patients aged <40 years old, whereas some use age 50 years as a cutoff point. A structured review of literatures up to 2003 revealed 37 out of 55 references defined ''young'' as patients <40 years old.[7] On the contrary, according to the Amsterdam Criteria, age 50 years is an important factor in the determination of patients with possible underlying hereditary predisposition to CRC such as Lynch syndrome. Furthermore, several guidelines recommend CRC screening to begin at age 50 years in average-risk individuals.[14] To date, the number of studies using 50 years as cutoff age progressively increases.[15] However, the frequency of CRC between 40 and 50 years of age is continuously rising, so there might be a confounding results of young-onset CRC entity and later-onset CRC in these studies. Some researchers indicated that young CRC patient maybe heterogenous group with spectrum of clinicopathological characteristics and survival outcomes.[16] To address this problem in the present study, we included 279,623 CRC patients from the national data of SEER program avoiding the biases associated with single-institution experiences or limit sample sizes. Furthermore, we divided CRC patients into 3 age groups: 20 to 40, 41 to 50, and >50 years for analysis.

In our study, we found the percentages of CRC patients aged 20 to 40, 41 to 50, and >50 years were 2.4%, 6.9%, and 90.7%, respectively. A recent comprehensive review described 11% of colon cancer and 18% of rectal cancer occurring in individuals <50 years.[6] Another review of 55 articles reported that the average percentage of young in the total CRC patients was 7% (range 0.4%–35.6%). Nevertheless, this review pretermitted patients aged 40 to 50 years.[7] The reporting of SEER (1995–1999) announced the similar age distribution (20–44 years [4.3%], 45–55 years [9%], and >55 years [86.7%]).[17] Compared with Western studies, the researches on Asian population showed the higher rates of young CRC patients which range from 3% to 9.2% in 20 to 40 years and 11.3% to 14.7% in 41 to 50 years.[16,18] In contrast to the overall decreasing trends, there is a rising incidence of CRC in young adults during the past decades. The analysis of age-related CRC incidence (1975–2010) starting at age 20 years revealed that overall age-adjusted CRC incidence rate decreased by 0.92 % over the time period examined, whereas the rate of patients aged 20 to 49 years old increased. In addition, the most significant increase in patient ages 20 to 34 years had been observed.[19] In line with the observation in the United States, the national data of Australia found that the incidence raised by 85% to 100% in patients aged 20 to 29 years, and by 35% in those aged 30 to 39 between 1990 and 2010.[20]

We herein found that there were more males in young patients (20–40 and 41–50 years) compared with those in patients aged >50 years. A literature review of 55 articles,

TABLE 3. The 3- and 5-Year Cancer-Specific Survival for CRC Patients With AJCC Stages I, II, III, and IV According to Age Groups

	Age Groups (% Standard Error)			*P*		
	Group 1 (Age 20–40 y)	Group 2 (Age 41–50 y)	Group 3 (Age >50 y)	Group 1 vs Group 2	Group 1 vs Group 3	Group 2 vs Group 3
3-y CRC-SS						
All stages	71.0 (0.006)	74.0 (0.003)	69.4 (0.001)	<0.001	<0.001	<0.001
I	96.0 (0.006)	97.8 (0.002)	93.3 (0.001)	<0.001	<0.001	<0.001
II	91.3 (0.009)	90.8 (0.005)	83.9 (0.002)	0.572	<0.001	<0.001
III	76.3 (0.010)	80.1 (0.006)	69.0 (0.002)	<0.001	<0.001	<0.001
IV	23.0 (0.012)	23.0 (0.007)	13.6 (0.002)	0.939	<0.001	<0.001
5-y CRC-SS						
All stages	65.1 (0.006)	67.1 (0.004)	62.8 (0.001)	0.001	<0.001	<0.001
I	93.8 (0.007)	95.7 (0.003)	89.9 (0.001)	0.006	<0.001	<0.001
II	87.2 (0.010)	85.0 (0.006)	77.4 (0.002)	0.081	<0.001	<0.001
III	68.1 (0.011)	69.7 (0.007)	58.5 (0.003)	0.046	<0.001	<0.001
IV	14.3 (0.010)	13.3 (0.006)	7.1 (0.002)	0.740	<0.001	<0.001

AJCC = American Joint Committee on Cancer, CRC = colorectal cancer, CRC-SS = Colorectal cancer-specific survival.

including 5051 CRC patients, showed that CRC affects both young adult males and females in a similar proportion. In this review, 514 % were men and 48.6 % were women.[7] The sexual-related hazard factors, including smoking and alcohol consumption and so on, need to be investigated in further epidemiological study. Our population-based cohort study reflected that tumors located on the right colon were seen less frequently in young patients (20–40 years [29.8%] and 41–50 years [28.2%]). Our result is consist with recent reviews and large cohort studies.[7,12,15] We further found that the patients aged 20 to 40 years had fewer cases with multiple cancers, more mucinous carcinoma or signet ring-cell carcinoma, higher grade, and later stage compared with CRC patients aged 41 to 50 years and >50 years. O'Connell et al[7] in their review suggested CRC in patients <40 years old located in the distal colorectum, had more aggressive pathological histology, such as poorer differentiation, more mucinous/signet ring carcinoma, and present with later stage comparing with older patients. Clinical studies attributed the later stage to lower rates of screening and delay in diagnosis in young CRC patients. There are doctor- and patient-related factors contributing to this delayed diagnosis in clinical. Some doctors may be inclined to attribute clinical presentation of changes in bowel habits or rectal bleeding to benign disease without further examination. On the contrary, some young patients neglect symptoms and refuse to seek medical attention or colonoscopy examination. So young patients with these symptoms should be evaluated for colorectal cancer to enable and achieve an earlier diagnosis. Some researchers suggested that average-risk screening begin at <50 years of age. However, the decision analysis has not identified momentous life-year gains for implementation of average-risk screening at young population. Furthermore, there are not yet robust evidences for both adenoma prevalence under age 50 and the duration of the adenoma–carcinoma sequence. Therefore, presently, the United States Preventive Services Task Force has deemed the current scientific evidence insufficient to justify this large-scale policy change.

O'Connell et al[7] reported that young CRC patients with early stage had better overall 5-year survival rates than older patients. In a recent SEER databases research excluded metastatic CRC, and obtained the similar results. In addition, they found that the overall 5-year CRC-SS rates of young and older patients were 78.6% and 75.3%, respectively. This significant difference only existed in patients with stages II and III.[12] Although some studies got the consistent finding of clinicopathological features in young CRC patients, the survival outcome was still inconsistent. Minardi et al[13] and Marble et al,[21] respectively, observed that CRC patients <40 years old had worse survival which had been attributed to these adverse prognostic histopathological factors and more aggressive disease. Moreover, our data showed that CRC patients aged 20 to 40 years had better 3- and 5-year CRC-SS rates than patients aged >50 years. The stratified analysis confirmed that CRC patients aged 20 to 40 years had this better prognosis in I to IV stage subgroups. In accordance with other large population-based analysis with SEER data, [22,23] our results had also been demonstrated in univariate and multivariate survival analysis. As an important reason, doctors preferred to apply comprehensive treatment including surgery and adjuvant therapy on young CRC patients. Young patients had less comorbidities, higher extensive lymphadenectomy rates, lower risk of postoperative complications, and better tolerate for side effect of chemoradiotherapy.[7] In this study, we found more patients received extensive lymphadenectomy (≥12 of lymph nodes examined) in young group than those in older group. As the National Comprehensive Cancer Network and American Society of Clinical Oncology guidelines recommending, it needs examination a minimum of 12 lymph nodes when staging CRC. Furthermore, our multivariate survival analysis showed examination >12 lymph nodes was associated with improved prognosis of CRC, which was in accord with previous reporting.[24]

As for CRC patients in group 2 (between 41 and 50 years of age), we found that their clinicopathological characteristics were between group 1 and group 3. Their characteristics similar to those in group 1 included sex, tumor location, and tumor size. There were more numbers of lymph nodes examined in group 2 than those in group 3; nevertheless, less than those in group 1. Interestingly, we found that the 3- and 5-year CRC-SS rates of CRC patients in group 2 were 74.0% and 67.1%, respectively. They had best CRC-SS in contrast to patients in other 2 age

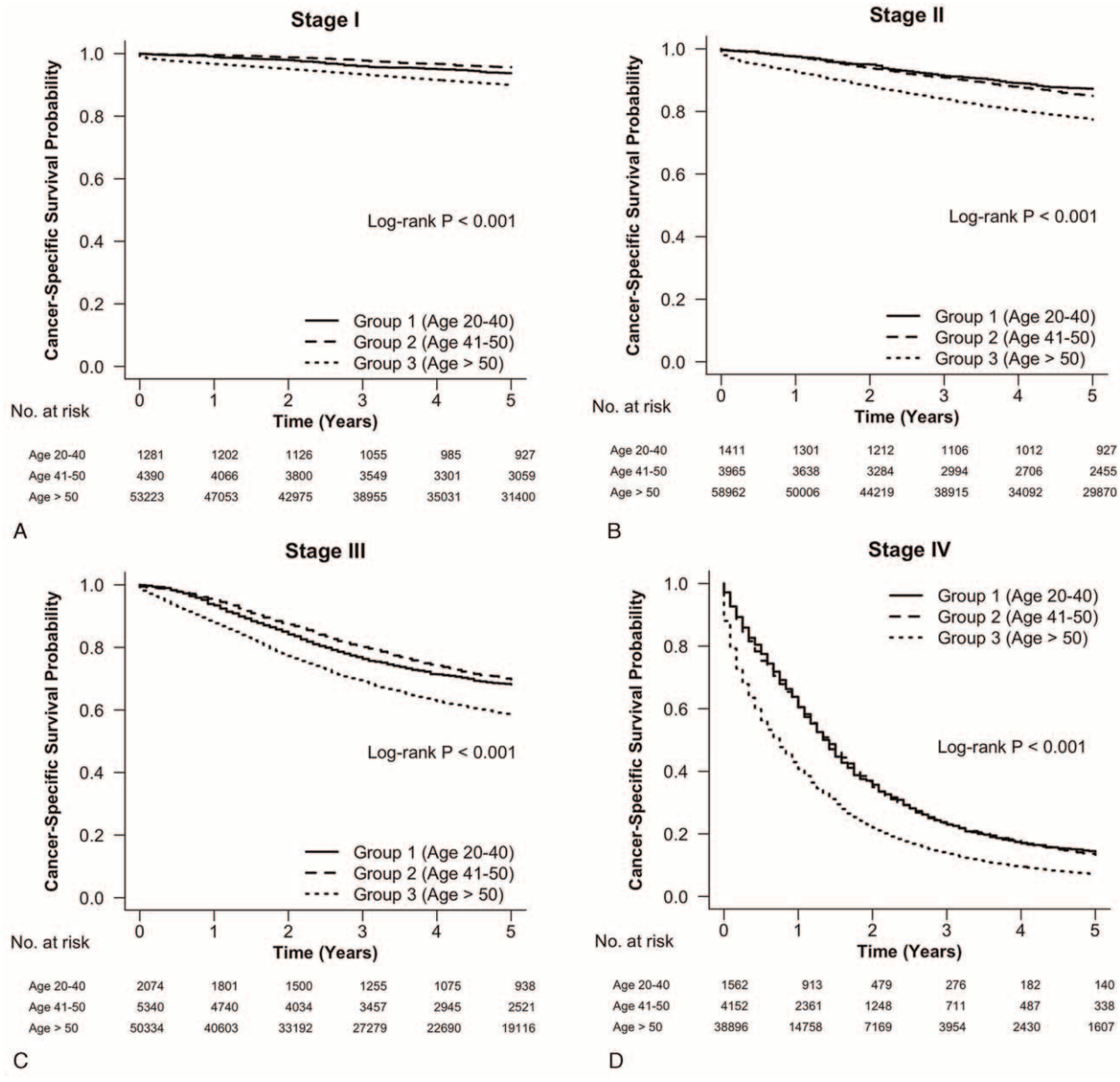

FIGURE 2. The survival analyses were stratified by each stage: (A) stage I ($P < 0.001$), (B) stage II ($P < 0.001$), (C) stage III ($P < 0.001$), and (D) stage IV ($P < 0.001$).

groups. A study of Asian population by Yeo et al[16] reported that CRC patients between 41 and 50 years of age had some unique features age group, though they had same survival. Focusing on different subgroup of young CRC patients, Taylor et al[25] showed that CRC patients between 40 and 50 years of age had early stage and better prognosis compared with patients <40 years of age, but had similar symptoms and duration. They further speculated that the poorer prognosis in patients <40 years of age is not because of late symptom reporting or delay in diagnosis, but to more aggressive disease. Our data suggested that CRC patients between 41 and 50 years of age, as a subgroup, had distinct clinicopathological characteristics and survival outcome compared with patients both >50 and 20 to 40 years of age.

In the present study, we used national population-based data to avoid the biases associated with single-institution experiences or limit sample sizes. Although the SEER data were considered as a cancer registry data meeting international standard, they were subject to a few of important limitations. The SEER registries used for this study were limited to small parts of the total US population. Furthermore, the data do not contain following important information: lymphatic/vascular invasion, cancer therapy (neoadjuvant, adjuvant, and quality of surgery) and local/distant recurrence status. Unfortunately, these prognostic factors of CRC patients could not be analyzed in our study. Because the AJCC stage was not available in the data until 1988, we did not include the CRC patients between 1973 and 1988 into our study. Finally, there is no information on the family history of

TABLE 4. Univariate and Multivariate Survival Analysis of Prognostic Factors in CRC Patients

	Univariate Survival Analysis			Multivariate Survival Analysis		
Variable	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Sex						
Female	1			1		
Male	1.004	0.990–1.017	0.601	1.033	1.013–1.053	0.621
Age, y						
20–40	1			1		
41–50	0.942	0.898–0.990	0.017	0.998	0.932–1.068	0.943
>50	1.165	1.117–1.215	<0.001	1.545	1.456–1.639	<0.001
Race						
White	1			1		
Black	1.275	1.247–1.303	<0.001	1.194	1.157–1.233	<0.001
Others	0.864	0.842–0.887	<0.001	0.874	0.843–0.906	<0.001
Location						
Right colon	1			1		
Left colon	0.841	0.827–0.856	<0.001	0.872	0.851–0.892	<0.001
Rectum	0.940	0.924–0.956	<0.001	0.930	0.908–0.954	<0.001
Cancer numbers						
Single	1			1		
Multiple	0.444	0.434–0.455	<0.001	0.605	0.586–0.624	<0.001
Tumor size, cm						
≤5	1			1		
>5	0.997	0.981–1.014	0.749	0.995	0.975–1.016	0.633
TNM stage						
I	1			1		
II	2.195	2.134–2.258	<0.001	2.256	2.159–2.358	<0.001
III	4.188	4.078–4.301	<0.001	3.620	3.413–3.839	<0.001
IV	22.411	21.832–23.005	<0.001	15.304	14.489–16.165	<0.001
Histologic type						
Adenocarcinoma	1			1		
Mucinous carcinoma	1.172	1.146–1.198	<0.001	1.013	0.982–1.045	0.428
signet ring-cell carcinoma	2.539	2.400–2.686	<0.001	1.237	1.135–1.349	<0.001
Tumor grade						
Well	1			1		
Moderately	1.487	1.444–1.532	<0.001	1.064	1.022–1.108	0.003
Poorly	2.727	2.643–2.815	<0.001	1.351	1.293–1.412	<0.001
Undifferentiated	3.271	3.073–3.482	<0.001	1.426	1.300–1.564	<0.001
No. of lymph nodes examined						
<12	1			1		
≥12	0.691	0.681–0.701	<0.001	0.840	0.823–0.857	<0.001

CI = confidence interval, CRC = colorectal cancer, HR = hazard ratio.

CRC; therefore, we are unable to evaluate the influence of familiar or hereditary CRC, particularly Lynch syndrome-associated CRC, if there is, on clinical characteristics and survival outcomes.

CONCLUSION

Analyzing 279,623 CRC patients from SEER data, we found that the patients aged 20 to 40 years had fewer cases with multiple cancers, more mucinous carcinoma or signet ring-cell carcinoma, higher grade, later stage, and more lymph nodes (no. ≥12) examined compared with CRC patients aged 41 to 50 years and >50 years. However, they have better survival outcome than older (>50 years old) patients. Multivariate analysis also revealed older (>50 years old) age was an independent predictor of poor prognosis. Furthermore, we found that CRC patients between 41 and 50 years of age had best CRC-SS in contrast to those in other 2 age groups. They might be a subgroup of young patients.

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