Original Article

Features of colorectal cancer in China stratified by anatomic sites: A hospital-based study conducted in university-affiliated hospitals from 2014 to 2018

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Abstract

Objective: The clinical and biological characteristics of colorectal cancer have been found to differ depending on the anatomic site of the cancer. However, for Chinese patients, there is limited information on the proportion of cases at each site and the related features. In this study, we explored the location, distribution and other features of colorectal cancers at each anatomic site in Chinese patients.

Methods: We conducted a hospital-based study using hospitalization summary reports from 10 Peking University-affiliated hospitals from 2014 to 2018; the reports covered a total of 2,097,347 hospitalizations. Incident cases were chosen as the study population, and their epidemiological features were further analyzed.

Results: A total of 20,739 colorectal cancer patients were identified. Rectum was the most common location (48.3%) of the cancer, whereas the proportions of patients with distal and proximal colon cancer were 24.5% and 18.6%, respectively. Patients with rectal cancer were predominantly male and were the youngest for all anatomical sites (each P<0.001). The highest proportion of emergency admissions, the longest hospital stays and the highest hospitalization costs were found in patients with proximal colon cancer (each P<0.001). The proximal colon cancer subgroup included the highest proportions of patients with medical histories of cholecystectomy, cholecystolithiasis and/or gallbladder polyps and appendectomy (P=0.009, P<0.001 and P<0.001, respectively). The distal colon cancer subgroup included the highest proportions of patients with medical histories of diabetes and hypertension (P<0.001, respectively).

Conclusions: The patterns of colorectal cancer observed in this study differ from those reported for Western patients and show a significantly higher proportion of patients with rectal cancer. Different epidemiological features were also found based on anatomic sites. Further studies based on tumor location should be conducted to facilitate more accurate screening and treatment.

Keywords: Anatomic site; colorectal cancer; database; hospitalization

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Introduction

With modern changes in lifestyle, colorectal cancer (CRC) has become the most common malignant tumor of the digestive system in the past 20 years (1). According to the latest statistics released by the American Cancer Society, CRC was predicted to have the third highest morbidity and mortality rates in 2020, with 147,950 newly diagnosed cases and more than 50,000 deaths (2). Although the incidence of CRC is approximately 4-fold higher in developed countries than in developing countries, there is no obvious difference in mortality rates (3). Many epidemiological studies have also found that the average age of patients with CRC is decreasing: a nationwide study in the United States revealed that the number of newly diagnosed cases and deaths in patients under the age of 50 years old will reach 17,930 and 3,640, respectively, in 2020; this represents a significant upward trend compared with previous years (4). A number of large population-based studies conducted in recent years in other developed countries also showed significant upward trends in the proportion of newly diagnosed CRC patients younger than 50 years (5,6). Changes in diet and lifestyle could explain this phenomenon. More importantly, the high morbidity and mortality and the trend toward a younger age at onset make this disease increasingly intractable (7,8).

The colorectum can be separated into the proximal colon, the distal colon and the rectum, each of which originates from a different embryological structure (9), and CRCs at these sites have been found to have different clinical and pathophysiological features (10). Morbidity associated with tumors at different locations was found to differ with sex and age, with higher risks of proximal colon cancer in women and of distal colon cancer in men and a lower risk of rectal cancer in the elderly population (11). Later stage at diagnosis and worse prognosis were also found in proximal colon cancer patients compared to those with distal colon or rectal cancer (12). CRCs at different locations were also reported to be related to diverse risk factors and to have different etiologies (13). Additionally, molecular heterogeneity was found among CRCs located at different anatomic sites. Higher risks of microsatellite instability and CpG island methylator phenotype and higher incidences of genetic mutations, including mutations in *KRAS*, *PIK3CA* and *BRAF*, were found in proximal colon cancers, while mutations in *TP53* were found to be more common in patients with distal colon and rectal cancer and to possibly affect prognosis (14,15).

The availability of more detailed information on the features of CRC, especially the incidence of CRC at each location and the associated hospitalization costs, could help investigators determine the regional clinical and basic features of CRC, identify potential regional risk factors, rationally allocate healthcare resources and create policies that alleviate the medical burdens on both individuals and society (16). Although a number of comprehensive studies have identified the characteristics of CRC in many developed countries (4,5), the detailed epidemiological features of CRC in developing countries such as China have been poorly studied. There are no statistics on the proportion of cases of colorectal tumors at various sites based on analyses of large-scale, high-quality population datasets in China. Therefore, in this study, we aimed to summarize the epidemiological features of CRC patients in China stratified by anatomic site; the features studied included the proportions, basic characteristics, associated risk factors and other trends based on 5-year hospitalization summary reports (HSRs) provided by university-affiliated comprehensive hospitals.

Materials and methods

Data source

Data were acquired from the HSR database of Peking University-affiliated hospitals. This is a patient-level database containing information on patients hospitalized in 10 comprehensive and/or tertiary hospitals affiliated with Peking University; the patients come from across the nation, and the database includes reports on a total of 2,097,347 hospitalizations. HSRs are submitted by hospitals annually, with strict adherence to the requirements of the National Health Commission of the People's Republic of China (17). A system was developed to handle data integration, storage, management, and analysis and to display the results, with safety and quality control measured embedded in each layer. The general and clinical information on each patient, including demographic characteristics (age, sex and other parameters), hospitalization information (admission route, length of hospital stay, costs and other factors), diagnosis, type of operation and the corresponding International Classification of Databases 10 (ICD-10) codes, was collected from the system. Ethics approval was obtained from the Ethics Committee of

Peking University Third Hospital (IRB00006761-M2019387).

Study population

Data for the 5-year period from January 1, 2014, to December 31, 2018 were analyzed according to their availability. Individuals who 1) were pathologically diagnosed with primary CRC between 2014 and 2018, 2) were hospitalized in one or more of the involved hospitals for treatment, and 3) had at least one complete hospitalization record were included. Individuals with 1) no definite diagnosis or 2) carcinoma of the colorectum that had metastasized from other organs were excluded. Personal data were anonymized to protect patient privacy.

CRC identification

CRC was identified using ICD-10 codes C18.0–18.9, C19.9 and C20.0, as in previous studies; medical terms used to describe Chinese patients included colorectal/colon/rectal/proximal colon/distal colon/cecum/ascending colon/hepatic flexure/transverse/splenic flexure/descending colon/sigmoid colon/rectosigmoid junction cancer (4,18). Due to their distinct embryonic and/or postnatal development, different anatomical factors and biological characteristics are present in the proximal and distal colon and in the rectum; therefore, cancers that arose in these three regions were separated into individual groups for analysis (9). For patients in whom the anatomic site was identifiable, tumors originating from the cecum, ascending colon, hepatic flexure and transverse colon were classified as being in the proximal colon (ICD-10 codes: C18.0, C18.2–C18.4, C18.802). Tumors originating from the splenic flexure or the descending or sigmoid colon were classified as being in the distal colon (ICD-10 codes: C18.5–C18.7, C18.801). Those originating from the rectum and the rectosigmoid junction were classified as being in the rectum (ICD-10 codes: C19.9, C20). Patients with multiple primary colorectal tumors were allocated to a separate subgroup, and other CRC patients were identified as not otherwise specified (ICD-10 codes: C18.1, C18.9) according to previous related reports (19,20). A fuzzy string matching algorithm in which the database was searched using Chinese medical terms was constructed and used to extract potential CRC patients from the database to avoid omission of patients, as previously reported (16). The keywords were the Chinese diagnostic terms used in different patterns. A total of 1,000 CRC patients were randomly chosen from the selected target population, and the diagnoses were independently manually reviewed by two gastroenterologists to determine the actual target patients. We continued to refine our classification strategy using R software (Version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria) by validation until the consistency was determined to be greater than 99%.

Statistical analysis

The selected individuals were classified by inputting various keywords related to diagnostic, surgical and pathological information using R software. Incident cases were chosen as the study population in this study using diagnostic information from surgery or endoscopy as a standard. Patients who had multiple visits to any of the included hospitals were identified using their health care card numbers, and only their first visits were included. The proportions of cancers at each anatomic site were calculated. Age, sex, hospitalization costs, stay, mode of treatment and disease-related risk factors were analyzed in each subgroup. Because most guidelines recommend endoscopy for individuals over 50 years old, and patients were stratified into age groups of ≤49 years, 50–74 years and ≥75 years, as previously reported (5).

Continuous data are described using means and standard deviations, and categorical variables are presented as frequencies and proportions. Student's *t* tests were used to compare continuous variables, and Chi-squared tests were used to compare categorical variables. IBM SPSS Statistics (Version 26.0; IBM Corp., New York, USA) was used for all statistical analyses, and a two-sided test with $P<0.05$ was considered to indicate statistically significant.

Results

Basic information

Data from 10 Peking University-affiliated hospitals met the quality control criteria and were included in further analyses. Patients came from across the country but were mainly from northern China. In total, we obtained data on 2,097,347 hospitalizations that occurred between January 1st, 2014 and December 31st, 2018 (289,561, 309,776, 462,175, 490,020 and 545,815 cases in 2014, 2015, 2016, 2017 and 2018, respectively). In the final analysis, 20,739 individual CRC patients were included (3,540, 3,261,

4,634, 4,881 and 4,423 patients in 2014, 2015, 2016, 2017 and 2018, respectively); 59.6% of these patients were male, and 40.4% were female. The average age of the included patients was 61.5 years. The mean hospital stay was 14.19 d, and the mean hospitalization cost was 62,114.24 CNY.

Characteristics of study population based on anatomic sites and annual trends from 2014 to 2018

Patients were subsequently classified according to the anatomic site of the cancer; there were 4,220 proximal colon cancer patients, 5,559 distal colon cancer patients, 10,960 rectal cancer patients, 234 patients with multiple tumor locations, and 1,711 patients with unclassified tumor sites. The locations at which patients with cancers at each of these anatomic sites resided were summarized and visualized; Beijing, Tianjin and Inner Mongolia were the three major places of residence of patients with CRC and of patients with cancer at each anatomical subsite. Rectal cancer accounted for the largest proportion (48.3%) of the cancers; it had a mean age at diagnosis of 60.44 years and a male-to-female ratio of 1.65, and distal colon cancer ranked second at 24.5%, with a mean age at diagnosis of 63.03 years and a male-to-female ratio of 1.50. Proximal colon cancer accounted for 18.6% of the cases and had a mean age at diagnosis of 61.63 years and a male-to-female ratio of 1.08; 1.0% of the patients appeared to have multiple tumor sites, and the detailed tumor location of 7.5% of the patients was not clearly recorded (*Figure 1*). The changes in the proportions of cancers at each of these sites between 2014 and 2018 were analyzed. A decrease in rectal cancer (from 54.7% in 2014 to 51.8% in 2018) and an increase in distal colon cancer (from 25.5% in 2014 to 27.8% in 2018) were found, and changes in proportions over the course of five years were significant (*Figure 2*, P<0.001).

General patient information classified by anatomic sites

The general patient information is shown in *Table 1*. The mean age of the included patients was 61.29 years. Proximal colon cancer patients (63.03 years) were the oldest, and rectal cancer patients (60.44 years) were the youngest, with a significant difference among the groups (P<0.001) and between each group (*Figure 3A*). There were more male patients than female patients in each anatomic site subgroup, and the rectal cancer subgroup contained a higher proportion of male patients than the proximal and distal colon cancer subgroups (P<0.001). A longer hospital

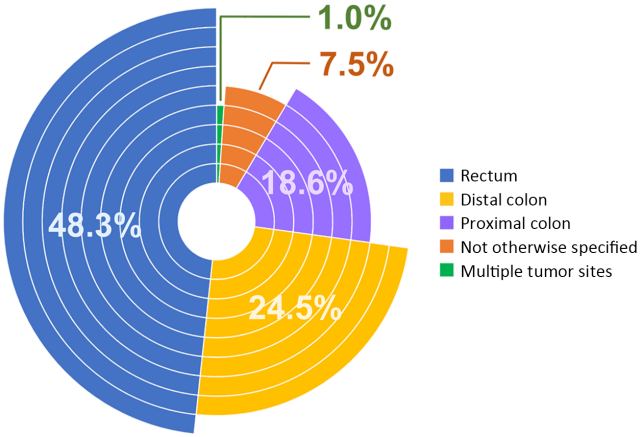

Figure 1 Proportion of cancers at each anatomic site.

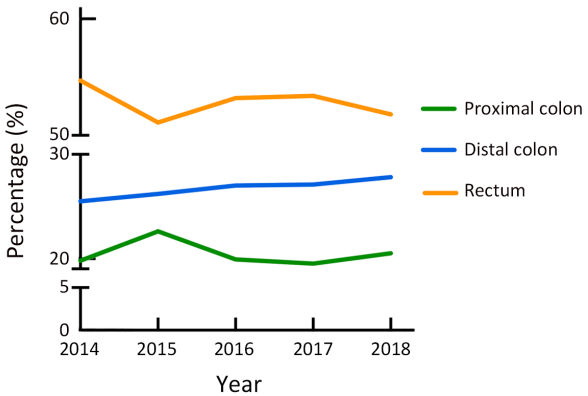

Figure 2 Changes in proportions of patients with proximal colon cancer, distal colon cancer, and rectal cancer from 2014 to 2018 (P<0.001).

stay, higher hospitalization cost, a higher proportion of patients who required emergency surgery and a higher proportion of patients with bowel obstruction (*Figure 3B*) were found in the subgroup of proximal colon cancer patients than in other subgroups (each P<0.001).

Patients were divided into three age groups (≤49, 50–74 and ≥75 years; *Table 1*). The proximal colon cancer subgroup contained the highest proportion of patients older than 75 years. The rectal cancer subgroup contained the highest proportion of patients in the ≤49-year-old age group. A significant difference in age was found after stratification by anatomic sites (P<0.001).

Distribution of risk factors across different anatomic sites

CRC was previously reported to be related to various risk factors, including cholecystectomy, cholecystolithiasis, gallbladder polyps, appendectomy, hypertension and

Table 1 General information on colorectal cancer patients and age distributions across anatomic site subgroups

Variables	n (%)			P
	Proximal colon cancer (N=4,220)	Distal colon cancer (N=5,559)	Rectal cancer (N=10,960)	
Age (year)				<0.001
≤49	667 (15.8)	889 (16.0)	1,885 (17.2)	
50–74	2,612 (61.9)	3,719 (66.9)	7,683 (70.1)	
≥75	941 (22.3)	951 (17.1)	1,392 (12.7)	
Mean ($\bar{x}\pm s$)	63.03±13.46	61.63±12.65	60.44±11.95	
Gender				<0.001
Male	2,190 (51.9)	3,336 (60.0)	6,828 (62.3)	
Female	2,030 (48.1)	2,223 (40.0)	4,132 (37.7)	
Admission				<0.001
Emergency	218 (5.2)	243 (4.4)	277 (2.5)	
Outpatient	3,018 (71.5)	4,057 (73.0)	8,030 (73.3)	
Others	984 (23.3)	1,259 (22.6)	2,653 (24.2)	
Bowel obstruction				<0.001
No	3,692 (87.5)	4,964 (89.3)	10,538 (96.1)	
Yes	528 (12.5)	595 (10.7)	422 (3.9)	
Hospitalization stay (d) ($\bar{x}\pm s$)	15.94±11.81	14.63±30.04	13.29±14.84	<0.001
Hospitalization costs (CNY) ($\bar{x}\pm s$)	69,330±49,451	64,807±50,634	57,978±48,099	<0.001

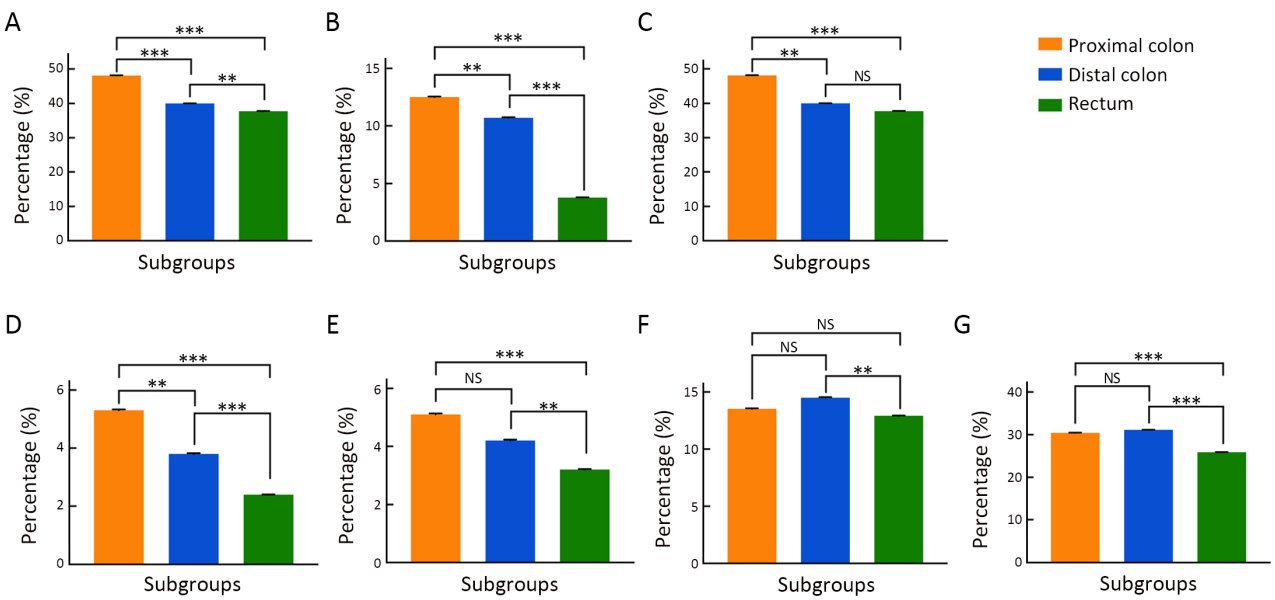

Figure 3 Comparisons of general information and associated risk factors among all anatomical site subgroups and between each pair of anatomical site subgroups. (A) Sex (male); (B) bowel obstruction; (C) cholecystomy history; (D) gallstone/gallbladder polyp history; (E) appendectomy history; (F) diabetes mellitus; (G) hypertension. **, P<0.01; ***, P<0.001; NS, no significance.

diabetes. Therefore, the proportions of patients with the abovementioned risk factors in each anatomic site subgroup were further analyzed, and P values were calculated for the comparisons among the three groups and between each pair of anatomical site subgroups for each risk factor (*Table 2*, *Figure 3C–G*). The proximal colon cancer subgroup

Table 2 Proportion of colorectal cancer-related risk factors in each anatomic site subgroup

Variables	n (%)			P
	Proximal colon cancer (N=4,220)	Distal colon cancer (N=5,559)	Rectal cancer (N=10,960)	
Cholecystectomy history				0.009
No	4,087 (96.8)	5,422 (97.5)	10,710 (97.7)	
Yes	133 (3.2)	137 (2.5)	250 (2.3)	
Gallstone/gallbladder polyp				<0.001
No	3,998 (94.7)	5,350 (96.2)	10,695 (97.6)	
Yes	222 (5.3)	209 (3.8)	265 (2.4)	
Appendectomy history				<0.001
No	4,007 (94.9)	5,325 (95.8)	10,613 (96.8)	
Yes	213 (5.1)	234 (4.2)	347 (3.2)	
Diabetes mellitus				<0.001
No	3,648 (86.5)	4,754 (85.5)	9,548 (87.1)	
Yes	572 (13.5)	805 (14.5)	1,412 (12.9)	
Hypertension				<0.001
No	2,938 (69.6)	3,828 (68.9)	8,116 (74.1)	
Yes	1,282 (30.4)	1,731 (31.1)	2,844 (25.9)	

contained the highest proportion of patients with histories of cholecystectomy, cholecystolithiasis and/or gallbladder polyps and appendectomy (P=0.009, P<0.001 and P<0.001, respectively). Diabetes and hypertension were both more common in distal colon cancer patients (P<0.001 for both).

Discussion

Compared with its global incidence, the incidence of CRC in China is moderate to high, and the mortality rate due to CRC in China is higher than the worldwide average (21). China currently has the largest number of cases of CRC worldwide, accounting for 28.20% of total cases, and the largest number of deaths caused by CRC, accounting for 28.11% of the total global deaths due to CRC (22). However, the detailed epidemiological characteristics of CRC in China, in particular for cancers stratified by anatomic site, have remained unclear. Due to differences in the embryological origins of the proximal colon, distal colon and rectum, the microbiota, histological appearance and genetic/molecular features of CRCs at different anatomic sites differ significantly, leading to differences in cancer prognosis according to anatomic sites (23,24). Therefore, this study aimed to estimate the proportion of cases of CRC at different anatomic sites and to summarize differences in the epidemiological features among proximal colon cancer, distal colon cancer and rectal cancer. This study is the largest sample size till now to evaluate the proportion of cases of CRC that occur at each of these anatomic sites in Chinese individuals.

A significantly higher proportion of rectal cancer cases, accounting for nearly half of the cases, were found in this study compared to cases of CRC at other anatomical sites. Distal and proximal colon cancers were both less common than rectal cancer, and the proportion of patients with proximal colon cancer was 18.6%. The proportion of patients with rectal cancer in our study was much higher than proportions previously reported for European countries (20) and North America (4), which ranged from 18% to 29%, and was similar to proportions reported for other Asian countries, including Japan (25) and Korea (26), in which the proportion was approximately 48%. A lower proportion of patients with proximal colon cancer than distal colon cancer was previously reported for Asian countries, and a similar finding was made in this study, whereas a different pattern had been observed in Western countries; in the United States, for example, the proportion of patients with proximal colon cancer was reported to be double that of patients with distal colon cancer (4). There may be several underlying reasons for these disparities. First, differences in dietary patterns and lifestyles among the various regions might be one of the main causes of this

phenomenon (27). Second, genetic differences among people of different ethnicities should also be taken into account because different gene expression patterns are found in people of different ethnicities and at different anatomic sites (28). For example, a number of genes, including *L1TD1*, *EFCAB2*, *PPP1R21*, *SLCO2A1* and *HLA-G*, were found to have distinctive prognostic value in CRC in East Asians (29), and loss of HLA-G expression was found to be closely related to the progression of rectal cancer (30). Third, patients with rectal cancer often exhibit clearly recognizable symptoms, including bloody stool and changes in bowel evacuation habits, while colon cancer, especially proximal colon cancer, is often asymptomatic. Many of the lesions present in asymptomatic patients with CRC can be found through CRC screening examinations. The existence of the CRC screening program established in 1992 in Japan (31), the nationwide health check-up program for CRC established in 1999 in Korea (32), the CRC screening program in the United States and its high participation rate of 65% (33) and the large number of national CRC screening programs in Europe established after 2010 (34) might contribute to the relatively higher proportions of patients diagnosed with proximal colon cancer in these regions. In contrast, although a population-based cancer screening program was established in urban China in 2012 (35), the overall participation rate among the high-risk population with regard to screening colonoscopies has been relatively low (14.0%), resulting in a relatively high proportion of patients diagnosed with rectal cancer; this might be expected to decrease in subsequent years with the increasing popularity of screening interventions (36).

Consistent with the tendency observed in recent decades in some Asian countries (25,37), our study reported a downward trend in the proportion of patients with rectal cancer in China; this proportion was reported to be 71.2% in the 1980s, 66.7% in the 1990s and 48.3% in this study. At the same time, compared to previous reports on Chinese patients, our results further confirmed the "rightward shift" of tumor location in CRC patients (38); the proportion of colon cancer patients, especially those with proximal colon cancer, increased significantly from 10.9% in the 1980s to 15.2% in the 1990s and finally to 18.6% in this study (39). Colon cancer has been found to be positively related to Western dietary habits and body mass index (BMI), as shown in studies that evaluated the complex epigenetic interactions among dietary intake, obesity and malignant colon tumor occurrence (40), and to be negatively related to physical activity, which is not related to the incidence of rectal cancer (13,41). Such alterations are likely to reflect lifestyle factors and dietary trends, including the enhanced intake of animal protein, especially red meat and/or processed meat, and high-sugar foods, the prevalence of sedentary lifestyles with decreased physical activity, and the consequent outcome of excess body weight (42). Furthermore, an epidemiological study of CRC in China between 1990 and 2009 showed that the increase in the detection rate of CRC in the proximal colorectum was higher than the increase in the detection rate of CRC located in the distal colon and rectum (43). It can reasonably be predicted that with the increased adoption of Western lifestyles and physical inactivity by the Chinese population, especially by young Chinese individuals, such a trend will become increasingly obvious. Additionally, a decrease in the proportion of patients with colon cancer was found in some European countries, and this is believed to be related to advocacy for healthy habits and diets (5,44). Since primary prevention has been proven to be a vital strategy for diminishing the burden imposed by CRC, wide-ranging changes that encourage healthier lifestyle choices should be advocated for and implemented, as they have been shown to be effective in a number of high-income countries (45).

In our results, a significant predominance of males was observed in patients with CRC, especially rectal cancer, consistent with previous global data (4). Drinking and smoking, which are more common in males, are risk factors for CRC, especially rectal cancer (46,47); thus, the predominance of males among rectal cancer patients may result from differences in lifestyles, dietary habits and work environments between males and females in urban areas of China. Furthermore, recent studies have found a causal relationship between androgens and CRC, and it is likely that the presence of androgens leads to a higher incidence of CRC in males (48). In addition, our results showed that the average age of rectal cancer patients was significantly lower than the average age of colon cancer patients in this study. Globally, CRC tends to be diagnosed at a relatively young age, and a rapid increase in the incidence of rectal cancer in young people has been observed (5). A study conducted in the United States (49) analyzed the incidence of colon and rectal cancers over a 20-year period and found that although the age at onset decreased for both types of cancer, the trend toward a younger age at onset was more

pronounced in rectal cancer patients. Studies have also found that the incidence of rectal cancer in patients less than 40 years of age in the United States has quadrupled since 1980 (50). The colon and rectal cancer incidence rates were projected to increase by 90.0% and 124.2%, respectively, among people 20–34 years of age by 2030 (51). However, the exact reasons for this are still largely unknown. Multiple genetic, lifestyle, and environmental risk factors can contribute to the development of rectal cancer in young populations. Since studies have proven that young-onset CRC displays more malignant histological features than CRC that occurs later in life (52), youth with a relevant syndrome or a family history of CRC or related diseases, including familial polyposis, hereditary nonpolyposis CRC and ulcerative colitis, should receive additional attention (53).

To further explore the epidemiological characteristics of CRC in China, we analyzed the general and hospitalization information and compared the associations of risk factors among different tumor locations. Interestingly, the subgroup of patients with proximal colon cancer included a significantly higher proportion of patients with emergency admissions. The current insufficient screening for CRC in China might explain this finding. Because it is located in a less accessible anatomic site, proximal colon cancer typically has fewer perceptible symptoms than CRC at other anatomic sites, leading to an increase in the percentage of proximal cancers diagnosed at later stages or with acute severity, especially if no screening has been performed (54). This is further supported by the significantly higher bowel obstruction rate and higher emergency admission rate found in this subgroup in this study. The significantly higher hospitalization cost and length of stay found in proximal colon cancer patients in this study could also result from the higher rate of emergencies among these patients, for these patients often suffer from bowel obstruction, which requires conservative treatment before surgery in many cases. Longer time for preoperative preparation to ensure safety, and a longer period postoperative recovery and is usually linked to a worse prognosis and higher financial and emotional burdens. Therefore, more affordable and less invasive techniques should be developed and adopted to support the implementation of screening to minimize the financial burden and prevent the need for invasive procedures (55), and population-based screening, especially in rural areas, is recommended in China to support the development of relevant policies.

The associations of gallstones, gallbladder polyps, cholecystectomy and appendectomy with enhanced risk of CRC were previously reported (56), especially for cancers located in the proximal colon (57). Our data showed that the proximal colon subgroup included a significantly higher proportion of patients who had undergone cholecystectomy than did either of the other two anatomical site subgroups. Interestingly, similar trends were also found when case histories of cholecystolithiasis, gallbladder polyps or appendectomy were included as risk factors. Enhanced exposure followed by a change in the metabolism of bile acids due to these risk factors might be the potential underlying mechanism. Cholecystectomy, cholecystolithiasis and the presence of gallbladder polyps could disturb the periodic release of bile acids and thereby enhance the dehydroxylation and dehydrogenation of primary bile acids. This, in turn, would lead to the formation of more secondary and keto bile acids, disturb general metabolic pathways and increase the risk of CRC (58). As the first site of arrival of bile acids, the proximal colon is the region that is most exposed to bile acid and its metabolites, whereas the rectum is the least exposed. This may be related to the influence of bile acid metabolism and is consistent with the results of this study. An imbalance in the intestinal microbiota, increased colonic epithelial permeability, increased bacterial translocation, and changes in transmembrane and intracellular cascade mechanisms that affect resistance to apoptosis are also important possible causes (59). Over the course of a 5- to 15-year follow-up period after appendectomy, Song *et al.* (60) identified appendectomy as a risk factor for the development of proximal colon cancer. The loss of immune function may be an important factor that affects the pathogenesis of CRC after appendectomy, a procedure that may eliminate the "safe room" role played by the appendix (61). In addition, we found higher proportions of patients with histories of hypertension and diabetes in the distal colon cancer subgroup; these were also reported to be risk factors for CRC and are therefore also worthy of further investigation (62).

This study investigated a large sample population treated at hospitals affiliated with Peking University and therefore yielded good estimates of the proportion of patients in each anatomic site subgroup and the associations of specific CRC locations with risk factors. This study not only revealed the pattern of CRC in the largest dataset in China

to date but also explored differences between cases of CRC at each anatomic site that are related to general patient characteristics and risk factors. However, this study has several limitations. First, as a hospital-based study, the database included medical centers rather than an entire region or province. However, as Peking University-affiliated hospitals represent the largest network of university-affiliated hospitals in China, the patient population examined in this study is to some extent representative of the national population, especially the population of northern China. Second, detailed anatomic information for some cases was not retrievable from the HSRs; therefore, we classified these cases as "others" in the analysis. Third, case ascertainment was limited because HSRs did not provide information about laboratory test results, imaging findings, or prognostic information. Detailed information about treatment methods and TNM stage was missing from the HSRs in this database due to their finite quality. Contacting with patients to gather additional information was also not possible due to the requirement for anonymity.

Conclusions

Rectal cancer accounts for a higher proportion of CRC cases in China (especially northern China), with a significant decreasing tendency and a male predominance. The subgroup of patients with proximal colon cancer had higher incidences of bowel obstruction and emergency admission, higher hospitalization costs and longer lengths of stay, differences that could be linked to the lack of implementation of a large-scale screening program. Different age and sex distributions, hospitalization-related conditions and medical histories were found in subgroups with cancers at different anatomic sites; this indicates that targeted medical treatment, additional studies and relevant policies that are based on colorectal tumor location are needed. The regional risk factors for CRC in Chinese patients based on anatomic sites need to be further investigated.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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