

• COLORECTAL CANCER •

Changing patterns of colorectal cancer in China over a period of 20 years

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Abstract

AIM: To determine whether any changes have occurred on the patterns of colorectal cancer in China.

METHODS: Data from 21 Chinese articles published from 1980 to 1999, were used to analyze the time trend of colorectal cancer according to the patients' age at diagnosis, sex, the site of the tumor, stage, and the pathology.

RESULTS: From 1980s to 1990s, the mean age of the colorectal cancer patients has increased. The percentage of the female patients rose. The distribution of colorectal carcinoma shows a predominance of rectal cancer. However, the proportion of proximal colon cancer (including transverse and ascending colon) increased significantly accompanied by a decline in the percentage of rectal cancer. Similarity in the percentage of distal colon cancer between two decades was revealed. In the 1990s, statistically more Stage B patients were found than those in 1980s. In addition, databases show a significant decrease in the Stage D cases. The proportion of adenocarcinoma increased, but the mucinous adenocarcinoma decreased during two decades.

CONCLUSION: These findings indicate that the pattern of colorectal cancer in China has been changing. Especially, a proximal shift due to the increasing proportion of ascending and transverse colon cancer has occurred in China.

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Key words: Colorectal carcinoma; Time trends; Age; Sex; Subsite; Pathology

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INTRODUCTION

Colorectal carcinoma (CRC) is one of the most common

tumor types in the world, with approximately 400 000 deaths annually^[1]. It is a frequent cause of cancer death in the developed world^[2]. For example, in the USA, despite a slight decrease in its incidence and mortality during the past two decades, CRC has remained the third most common cancer, affecting approximately 140 000 people and causing approximately 50 000 cancer-related deaths per year^[3]. In China, the incidence rate was initially low, but in recent years, due to the changes of life style and nutritional habits, the rate is increasing. The most impressive increase in the incidence rates of CRC was observed from 1972-1974 to 1987-1989, being 85% in males and 79% in females. The average rate of increase in incidence is 4.2% per year^[4]. According to the report of the Ministry of Health PR China in 2002, the incidence rate of CRC has ranked third in 1990s, from the sixth most common cancer in 1970s, and the death rate of CRC has increased to 10.25/10⁵ annually, which is the fifth leading cause of cancer mortality^[5].

Recent epidemiologic studies have suggested that the anatomic distribution of colorectal cancer may have undergone a distal to proximal shift over several decades. Lev^[6] has reported that during 1986 to 1992, cecal and ascending colon tumors increased in incidence from 33.9% to 36%, tumors of the transverse colon increased from 15.8% to 17.2%, and tumors of the sigmoid colon decreased from 36.0% to 33.4%.

So besides the increasing incidence rate and mortality rate, we still want to know whether there are some changes on patterns of CRC in China. But because a National Colorectal Cancer Registry system has not been established yet in China, so we compiled all the Chinese articles on CRC in order to compare the changing patterns between 1980s and 1990s. These articles were published on the journals included by the Chinese S&T Journal Citation Reports (CJCR). It is difficult to collect only articles in SCI, because in 1980s, few Chinese journals were included by SCI.

MATERIALS AND METHODS

Data were obtained from 21 Chinese articles published from 1980 to 1999 in CJCR. The articles involved 25 hospitals and 11 geographic areas of China. The study was based on the records of 10 201 patients reported during 20 years. According to the time of falling ill, they were divided into two groups, 1980s and 1990s. The former included 3 420 patients, and the latter had 6 781. These cases were recorded under sex, age, the subsites distribution of the CRC, Dukes' classification and the pathologic data. The distribution of the CRC was categorized into five segments: rectum (excluding

anal canal cancer), sigmoid, descending colon, transverse colon, and ascending colon (including cecum cancer but excluding appendicular neoplasm). On the other hand, we classified as proximal colon (ascending and transverse colon), distal colon (descending and sigmoid colon) and rectum. The patients without these detailed data were excluded.

Statistical analysis

Statistical analysis was performed using the SPSS 10.0 program. Independent samples' *t* test was used to compare the difference of age between two groups. Other data was examined by χ^2 test and statistical significance was accepted at $P < 0.05$.

RESULTS

Incidence and patient characteristics

In the 1980s group, 3 420 patients were reported, including 2 053 men and 1 367 women. The ratio was 1.50:1. But in the 1990s group, 6 781 patients were registered, among them there were 3 780 men and 3 001 women, and the ratio was 1.26:1. There is a significant difference between the two groups on the gender constituent ratio ($P < 0.05$). The mean age of 1980s group was 56.83, which was lower than 59.66 in 1990s (Table 1).

Table 1 Epidemiologic results

	1980s (%)	1990s (%)	<i>P</i>
Total number of CRCs	3 420	6 781	
Male	2 053 (60.03)	3 780 (55.74)	
Female	1 367 (39.97)	3 001 (44.26)	
Male/female ratio	1.50:1	1.26:1	0.02
Mean age (yr)	56.83	59.66	

Distribution of CRC

The CRC localization changed in the two decades. The distribution of CRC shows a predominance of rectal cancer. However, the proportion of rectal cancer in CRC has decreased significantly from 71.2% in 1980s to 66.7% in 1990s ($P < 0.001$). The proportion of transverse colon and ascending colon individually increased significantly ($P < 0.001$). Meanwhile, the percentage of patients with proximal colon cancer among those with colorectal cancer certainly increased significantly (10.9% *vs* 15.2% $P < 0.001$). But the data revealed similarity in the percentage of distal colon cancer between two groups ($P > 0.05$, Table 2).

Table 2 Distribution of CRC

Localization	1980s (%)	1990s (%)	<i>P</i>
Rectum	2 484 (72.6)	4 539 (66.9)	<0.001
Colon	936 (27.4)	2 242 (33.1)	<0.001
Distal			
Sigmoid	337 (9.9)	844 (12.4)	<0.001
Descending colon	226 (6.6)	366 (5.4)	0.02
Total distal CRCs	563 (16.5)	1 210 (17.85)	
Proximal			
Transverse colon	87 (2.5)	275 (4.1)	<0.001
Ascending colon	286 (8.4)	757 (11.2)	<0.001
Total proximal CRCs	373 (10.9)	1 032 (15.2)	<0.001
Others			
Total number of CRCs	3 420	6 781	

Dukes' classification

Of all CRCs, complete tumor staging is available in 2 300 and 3 772 patients in 1980s and 1990s respectively. Distributions among different categories of the Dukes' classification are shown in Table 3. In 1990s statistically more Stage B CRCs were found than in 1980s ($P < 0.001$) and databases show a statistically significant decrease in the Stage D cases.

Table 3 Dukes' staging

Stage	1980s (%)	1990s (%)	<i>P</i>
A	306 (13.3)	416 (11.0)	0.01
B	679 (29.5)	1 399 (37.1)	<0.001
C	823 (35.8)	1 379 (36.6)	
D	492 (21.4)	578 (15.3)	<0.001
Total	2 300	3 772	

Pathologic classification

The pathologic data of the CRCs were classified into adenocarcinoma, mucinous adenocarcinoma and others which mean carcinoid, adenosquamous carcinoma, and so on. We can see in Table 4, that recent pathologic classification in CRC in China has significantly changed. The proportion of adenocarcinoma increased but the mucinous adenocarcinoma decreased ($P < 0.001$).

Table 4 Pathologic classification

Pathologic classification	1980s (%)	1990s (%)	<i>P</i>
Adenocarcinoma	1 251 (82.1)	3 838 (85.6)	<0.001
Mucinous adenocarcinoma	231 (15.2)	465 (10.4)	<0.001
Others	42 (2.8)	180 (4.0)	
Total	1 524	4 483	

DISCUSSION

Rates of CRC vary considerably with geography. The disease is common in USA, Australia, Western Europe, and Scandinavia and is relatively uncommon in Asia, Africa, and South America^[7,8]. In recent years, there were some changes on the pattern of CRC, such as increasing incidence rate in Japan and Eastern Europe^[9-11], continued rightward shift of CRC^[11-13] and so on. Compared with Western countries, the incidence of CRC in China is low, but the dietary habits and lifestyle of Chinese have changed greatly, and the incidence is increasing rapidly. Thus, it is worthwhile to study the time trends for the changing patterns on CRC in China. This study collected 10 201 cases to investigate the age, male/female ratio, subsite distribution and pathologic changes on CRC in China over a period of 20 years.

CRC is primarily a cancer of the older population and risk for it increases with age^[7,8]. The increase of mean age may contribute to the population aging during 20 years in China. But we failed to show that there is a significance between the two decades.

It is clearly shown that the proportion of the female patients on CRC in China increased significantly from 1.50:1 in 1980s to 1.26:1 in 1990s. One possible explanation for the role of

gender may be the effect of female hormones^[14]. Some suggested that hormonal replacement therapy may decrease the incidence of CRC in females^[15,16]. Female sex hormones are known to affect cholesterol metabolism, which in turn affects bile acid production, a pathway linked to the development of colorectal cancer^[17].

In low-risk countries, rectal cancer accounts for the largest proportion of all colorectal cancers^[18]. The proportion of rectal cancer among all colorectal cancers is generally less than 40% in Europe and North America, in contrast to the 50% or more in Asia^[19]. In our study, rectal cancer is the main part of the colorectal cancer in China, no matter what was in 1980s or 1990s. However, the ratio of patients with colon cancer to all CRC cases has increased greatly in both sexes. In 1980s, the proportion of the colon cancer is 27.4%, but 33.1% in 1990s. Correspondingly, the percentage of rectal cancer decreased obviously. Likewise, several recent studies reported consistent results^[19-24]. The reason for this is not clear. It may be continued anatomic rightward shift of CRC, which were mentioned as follows, improved diagnostic accuracy for lesions in colon^[19], and varying etiologic factors^[21,23,24].

In the past 40 years, since the first description on CRC shift toward the proximal colon by Axtell and Chiazze^[25], many investigators confirmed it from various countries^[14,24,26-34]. The present study indicates the distribution of colon cancer in China changed greatly in 20 years, a significant increase in proximal colon cancer including transverse and ascending colon. The ratio of proximal colon cancer to all CRCs increased about 4.3%. Nevertheless the proportion of total distal colon cancer (sigmoid and descending) remains static. To exclude the possible question that the rightward shift may be due to the decreasing proportion of rectal cancer among all CRC, we limited our further analysis to data for the colon alone. It also concluded that there was an actual increase in right-sided cancer. So the proximal shift may be a reason for the increased ratio of colon cancer to rectal cancer as mentioned before.

There may be several potential causes for the rightward shift in CRC. The proximal and distal colon has different embryologic origins, morphology, physiology, and function^[35]. Cecum, ascending colon, and proximal two-thirds of the transverse colon derives from the midgut, whereas the segment comprising the splenic flexure to the upper anal canal derives from the hindgut. The distinct embryologic origins of each segment are reflected in the dual blood supply of the normal colon. The proximal colon is primarily involved with water absorption and solidification of fecal contents, but the distal colon functions primarily for storage^[19]. The metabolic pathways such as that of glucose, butyrate, and polyamines are also different. It has therefore been hypothesized that proximal and distal colons are two different organs^[36]. It may mean differences in differential sensitivities and exposures to carcinogens for the proximal and distal sections of colon and rectum.

The colon cancer is associated with genetic factors. Some studies reported that high-frequency microsatellite instability was significantly associated with tumors occurring in the proximal colon^[37,38]. Also Gervaz showed that distal colon cancer were more likely to express a nonfunctional p53

protein and a p53 gene mutation than proximal tumors^[31]. In the future, such genetic variations by cancer site may provide more clues to understanding the reasons of rightward shift of CRC.

The fecal occult blood test, digital examination of rectum, rigid and flexible sigmoidoscopy, barium enema X-ray as well as colonoscopy are particularly geared toward the diagnosis and screening of colorectal cancer. In 1980s, the colonoscopy was not popular in China especially in the suburban. So the rectal and sigmoid cancers are inclined to be found and diagnosed. Following the increased use of colonoscopy, more and more was the detection of proximal lesions with the observed time trends in 1990s. Although sigmoidoscope has been proven as an effective tool for screening against colorectal cancer^[39,40] and detects almost 80% CRC in China, it has the limitation that it would miss the proximal cancer for 20%. Accompanying the continuing rightward shift, the miss rate (meaning the ratio of miss out diagnosis cases to all CRC patients) may rise, especially on symptomatic patients. The miss rate may even be higher when one takes into account that approximately 25% of all patients who underwent sigmoidoscopy, the entire sigmoid is not adequately visualized^[41]. So the use of barium enema X-rays and total colonoscopy appears more appropriate for symptomatic patients, especially elderly people and women.

There are some other theories to explain the rightward shift of CRC. Gonzalez^[14] considered that five co-morbid conditions were associated with a greater likelihood of proximal lesions: congestive heart failure, cerebrovascular disease, chronic pulmonary disease, ulcer disease, and diabetes mellitus. West *et al.*^[42] demonstrated that a high-fat diet increased the risk for proximal colon cancer, whereas a high-protein diet increases the risk for distal neoplasm.

Screening seems attractive because of the difference in prognosis between early and late stage of CRC. During 20 years, China has developed the screening system. So the Dukes' D stage CRC has shrunk significantly and Dukes' B has been the main part of all cases.

Finally, our data indicated that the proportion of adenocarcinoma increased, correspondingly, mucinous adenocarcinoma decreased. The reasons for it needs further study.

Future studies should examine the subsites of CRC to clarify further analytical epidemiological findings, carcinogenic mechanisms, various risk factors, and prognosis to reduce the mortality.

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