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

Ming Li, Jin Gu

Ming Li, Jin Gu, Department of Surgery, Beijing Cancer Hospital, Peking University School of Oncology, Beijing Institute for Cancer Research, Beijing 100036, China
Correspondence to: Dr. Jin Gu, Department of Surgery, No. 52 Fucheng Road, Beijing Cancer Hospital, Beijing 100036, China. zljgu@bjmu.edu.cn
Telephone: +86-10-88141032 Fax: +86-10-88122437
Received: 2004-07-09 Accepted: 2004-11-17

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.

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 χ² 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 (%) | P     |
| Total number of CRCs       | 3,420     | 6,781     |       |
| Male                       | 2,053 (60.0) | 3,780 (55.74) |       |
| Female                     | 1,367 (39.9) | 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 (%) | P     |
| Rectum                      | 2,484 (72.6) | 4,539 (66.9) | <0.001 |
| Colon                       | 936 (27.4) | 2,242 (33.1) | <0.001 |
| 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) |       |
| Transverse colon            | 87 (2.5) | 275 (4.1) | <0.001 |
| Ascending colon             | 266 (8.4) | 757 (11.2) | <0.001 |
| Total proximal CRCs         | 373 (10.9) | 1,032 (15.2) | <0.001 |
| Total number of CRCs        | 3,420     | 6,781     |       |

**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 3 Dukes’ staging |
|------------------------|
| Stage                  | 1980s (%) | 1990s (%) | P     |
| 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                  | 2,053     | 3,772     |       |

**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[9,10], 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. Some suggested that hormonal replacement therapy may decrease the incidence of CRC in females. 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.

In low-risk countries, rectal cancer accounts for the largest proportion of all colorectal cancers. 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. 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. 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, and varying etiologic factors.

In the past 40 years, since the first description on CRC shift toward the proximal colon by Axtell and Chiaze, many investigators confirmed it from various countries. 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 segments have different embryologic origins, morphology, physiology, and function. 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. 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. 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. Also Gervaz showed that distal colon cancer were more likely to express a nonfunctional p53 protein and a p53 gene mutation than proximal tumors. 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 sigmoidoscopy has been proven as an effective tool for screening against colorectal cancer 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. 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 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., 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 consequently 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.

REFERENCES
1. Pisani P, Parkin DM, Bray F, Ferlay J. Erratum: Estimates of the worldwide mortality from 25 cancers in 1990. Int J Cancer 1999; 83: 18-29
2. Bourt RW, DiSario JA, Cannon-Albright L. Genetics of colon cancer: impact of inheritance on colon cancer risk. Annu Rev Med 1995; 46: 371-379
3. Greenlee RT, Hill-Harmon MB, Murray T, Thun M. Cancer statistics 2001. CA Cancer J Clin 2001; 51: 15-36
4. Zheng S. Recent study on colorectal cancer in China: early detection and novel related gene. Chin Med J 1997; 110: 309-310
5. Statistic bulletin on the development of Chinese health service 2001. The information center on health statistics of Ministry of Health P.R China. 2002, 4 Beijing
6 Lev R. The National Cancer Data Base report on colorectal cancer. Cancer 1995; 76: 538-539
7 Coleman MP, Esteve J, Damiecki P, Arslan A, Renard H. Trends in cancer incidence and mortality. IARC Sci Publ 1993; 121: 1-806
8 Parkin DM, Muir CS. Cancer incidence in the Five Continents. Comparability and quality of data. IARC Sci Publ 1992; 120: 45-173
9 Lands WE, Hamazaki T, Yamazaki K, Okuyama H, Sakai K, Goto Y, Hubbard VS. Changing dietary patterns. Am J Clin Nutr 1990; 51: 991-993
10 Kotake K, Koyama Y, Nasu J, Fukutomi T, Yamaguchi N. Relation of family history of cancer and environmental factors to the risk of colorectal cancer: a case-control study. Jpn J Clin Oncol 1995; 25: 195-202
11 Levin KE, Dozois RR. Epidemiology of large bowel cancer. World J Surg 1991; 15: 562-567
12 Wilkink AB. Overview of the epidemiology of colorectal cancer. Dis Colon Rectum 1997; 40: 483-493
13 Trends in colorectal cancer incidence-United States, 1973-1986. MMWR 1989; 38: 728
14 Gonzalez EC, Roetzelheim RG, Ferrante JM, Campbell R. Predictors of proximal vs. distal colorectal cancers. Dis Colon Rectum 2001; 44: 251-258
15 Hebert-Croteau N. A meta-analysis of hormone replacement therapy and colon cancer in women. Cancer Epidemiol Biomarkers Prev 1998; 7: 653-659
16 Paganini-Hill A. Estrogen replacement therapy and colorectal cancer risk in elderly women. Dis Colon Rectum 1999; 42: 1300-1305
17 Fleshner P, Slater G, Aufsies AH Jr. Age and sex distribution of patients with colorectal cancer. Dis Colon Rectum 1989; 32: 107-111
18 Waterhouse JAA, Muir CS, Shanmugaratnam K, Powell J. IARC Scientific Publication No42. International Agency for Research on Cancer: Lyon, 1982
19 Devesa SS, Chow WH. Variation in colorectal cancer incidence in the United States by subsite of origin. Cancer 1993; 71: 3819-3826
20 Koyama Y, Kotake K. Overview of colorectal cancer in Japan: report from the Registry of the Japanese Society for Cancer of the Colon and Rectum. Dis Colon Rectum 1997; 40 (10 Suppl): S2-9
21 Levi F, Randimbison L, La Vecchia C. Trends in subsite distribution of colorectal cancers and polyps from the Vaud Cancer Registry. Cancer 1993; 72: 46-50
22 Dubrow R, Bernstein J, Holford TR. Age-period-cohort modeling of large-bowel-cancer incidence by anatomic subsite and sex in Connecticut. Int J Cancer 1993; 53: 907-913
23 Kee F, Wilson RH, Gilliland R, Sloan JM, Rowlands BJ, Moorehead RJ. Changing site distribution of colorectal cancer. BMJ 1992; 305: 158
24 Jass JR. Subsite distribution and incidence of colorectal cancer in New Zealand, 1974-1983. Dis Colon Rectum 1991; 34: 56-59
25 Axtell LM, Chiazea J Jr. Changing relative frequency of cancers of the colon and rectum in the United States. Cancer 1966; 19: 750-754
26 Rhodes JB, Holmes FF, Clark GM. Changing distribution of primary cancers in the large bowel. JAMA 1977; 238: 1641-1643
27 Mamazza J, Gordon PH. The changing distribution of large intestinal cancer. Dis Colon Rectum 1982; 25: 558-562
28 Beart RW, Melton LJ 3rd, Maruta M, Dockerty MB, Frydenberg HB, O’Fallon WM. Trends in right and left sided colon cancer. Dis Colon Rectum 1983; 26: 393-398
29 Schub R, Steinheber FU. Rightward shift of colon cancer. A feature of the aging gut. J Clin Gastroenterol 1986; 8: 630-634
30 Demers RY, Severson RK, Schottenfeld D, Lazar I. Incidence of colorectal adenocarcinoma by anatomic subsite. An epidemiologic study of time trends and racial differences in the Detroit, Michigan area. Cancer 1997; 79: 441-447
31 Gervaz P, Bouzourene H, Cerottini JP, Chaubert P, B, Benhattar J, Secic M, Wexner S, Givel JC, Belin B. Dukes B colorectal cancer: distinct genetic categories and clinical outcome based on proximal or distal tumor location. Dis Colon Rectum 2001; 44: 364-372
32 Cucino C, Buchner AM, Sonenberg A. Continued rightward shift of colorectal cancer. Dis Colon Rectum 2002; 45: 1035-1040
33 Mensink PB, Kolkman JJ, Van Baaren JV, Kleibeuker JH. Change in anatomic distribution and incidence of colorectal carcinoma over a period of 15 years. Dis Colon Rectum 2002; 45: 1393-1396
34 Takada H, Ohsawa T, Iwamoto S, Yoshida R, Nakano M, I, Okuno M, Masuya Y, Hasegawa K, Kamano N, Hioki K, Muto T, Koyama Y. Changing site distribution of colorectal cancer in Japan. Dis Colon Rectum 2002; 45: 1249-1254
35 Buflia J. Colorectal cancer: evidence for distinct genetic categories based on proximal or distal tumor location. Ann Intern Med 1990; 113: 779-788
36 Distler P, Holt PR. Are right- and left- sided neoplasms distinct tumors? Dig Dis 1997; 15: 302-311
37 Kim H, Jen J, Vogelstein B, Hamilton SR. Clinical and pathological characteristics of sporadic colorectal carcinomas with DNA replication errors in microsatellite sequences. Am J Pathol 1994; 145: 148-156
38 Thibodeau SN, French AJ, Cunningham JM, Tester D, Burgart LJ, Roche PC, McDonnell SK, Schaid DJ, Vockley CW, Michels VV, Farr GH Jr, O’Connell MJ. Microsatellite instability in colorectal cancer: different mutator phenotypes and the principal involvement of hMLH1. Cancer Res 1998; 58: 1713-1718
39 Newcomb PA, Norfleet RG, Storer BE, Surawicz TS, Marcus PM. Screening sigmoidoscopy and colorectal cancer mortality. J Natl Cancer Inst 1992; 84: 1572-1575
40 Selby JV, Friedman GD, Quesenberry CP Jr, Weiss NS. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. N Engl J Med 1992; 326: 653-657
41 Painter J, Saunders DB, Bell GD, Williams CB, Pitt R, Bladen J. Depth of insertion at flexible sigmoidoscopy: implications for colorectal cancer screening and instrument design. Endoscopy 1999; 31: 227-231
42 West DW, Slattery ML, Robison LM, Schuman KL, Ford MH, Mahoney AW, Lyon J, Sorensen AW. Dietary intake and colon cancer: sex- and anatomic site-specific associations. Am J Epidemiol 1989; 130: 885-894

Science Editor: Wang XL and Guo SY  Language Editor: Elsevier HK