

## GASTROENTEROLOGY

## Distributions of colorectal cancer in two Chinese cities with contrasting colorectal cancer epidemiology

Q1 Wai K Leung<sup>1,\*</sup>, Wei-Qing Deng<sup>2,†</sup>, Li Li<sup>2,†</sup>, Dan Li<sup>2,†</sup> and W L Li<sup>3,§</sup>

Q2 Department of <sup>1</sup>Medicine and <sup>2</sup>Surgery, University of Hong Kong, Queen Mary Hospital, Hong Kong, <sup>†</sup>Department of Gastroenterology, Second Affiliated Hospital, Chongqing Medical University, and <sup>§</sup>Department of Gastroenterology, The First People Hospital of Neijiang City, Sichuan Province, China

### Key words

colonoscopy, epidemiology, proximal colonic cancer, rectal cancer.

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### Correspondence

Wai K Leung, MD, 4/F, Professorial Block, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong, China. Email: waikleung@hku.hk

### Conflict of interest

None to declare

### Abstract

**Background and Aim:** The incidence of colorectal cancer (CRC) is rising rapidly in Chinese. We studied the anatomic distributions and characteristics of CRC in Hong Kong (HK) and Chongqing (CQ) with different CRC epidemiology.

**Methods:** It was a retrospective study conducted in three large regional hospitals of the two cities. We identified all patients newly diagnosed with CRC between 2003 and 2012. The distribution and characteristics of CRC of the two cities were compared.

**Results:** Of CRC, 3664 new cases were diagnosed within the study period. CRC was more common in men (>56%) in both cities. The mean age at diagnosis was significantly younger in CQ, the lower prevalence area, than in HK (62.1 vs 70.4 years;  $P < 0.001$ ). Rectal cancer was the predominant (61.3%) cancer in CQ, but only 18% of cancers in HK were rectal cancer ( $P = 0.0001$ ). Right-sided colonic cancer, however, was more common in HK than CQ (27.2% vs 17.4%;  $P < 0.001$ ). Women had more right-sided colonic cancer than men in both cities ( $P < 0.002$ ), and there was an age-related increase in right-sided colonic cancer in HK but not in CQ. Multivariate analysis showed that older age, female, and living in HK were independent risk factors associated with right-sided colonic cancer.

**Conclusions:** There are significant differences in the distribution of CRC between HK and CQ. The discrepancy may be partly accounted by older population and an increase in proximal colonic cancer, particularly in women, in HK.

### Introduction

Colorectal cancer (CRC) is the third most common cancer in men and the second commonest cancer in women globally.<sup>1</sup> Although the incidence of CRC is generally considered to be lower in China than in western countries, there are emerging data to show that CRC incidence is also rising rapidly in Chinese population.<sup>1,2</sup> In 2011, there were more than 310 000 new cases of CRC diagnosed in China, which accounted for 9% of all new cancer cases.<sup>3</sup> In Hong Kong, CRC has now emerged as the second commonest cancer.<sup>4</sup> The age-standardized rate of CRC in Hong Kong is 37 per 100 000, which is at least two times higher than the corresponding figure in Mainland China.<sup>3,4</sup> Because China covers a wide geographic area, there are large variations in CRC incidences, and the actual age-standardized rate is found to be much lower in rural than in urban area.<sup>5</sup>

With the rapid economic development in China, the incidence and characteristics of CRC are also evolving quickly.<sup>6,7</sup> In a recent epidemiological study from Southern China that studied the trend of CRC epidemiology over the past 20 years,<sup>8</sup> several characteristics were observed including the rising age of CRC patients and the decrease in the proportion of young CRC patients. There was also a significant reduction in the proportion of rectal cancers with time.

To further characterize the trend of CRC in Chinese, we compared the distribution and characteristics of CRC in Hong Kong and Chongqing, which have very different CRC epidemiology. Hong Kong is a very modernized city in Southern China with the highest CRC incidence among all Chinese cities,<sup>9</sup> whereas Chongqing is a rapidly developing city in Western China with much lower CRC incidence. Both cities are densely populated with majority of people of ethnic Han origin. The total population in Hong Kong and Chongqing is 7 and 29 million, respectively. The results will provide new insights into the changing pattern of CRC epidemiology in Chinese.

### Methods

**Study design and cases.** It was a retrospective cohort study conducted in three large regional hospitals in Hong Kong (Queen Mary Hospital) and Chongqing (the Second Affiliated Hospital of the Chongqing Medical University and the First People Hospital of Neijiang City, Sichuan Province). The former two hospitals are university teaching hospitals, whereas the latter is a large regional hospital of Sichuan Province. All hospitals are regional hospitals serving mainly local residents.

We included all CRC newly diagnosed by colonoscopy in the endoscopy centers of the three participating hospitals between 1 January 2003 and 31 December 2012. The number of colonoscopy performed in the Queen Mary Hospital of Hong Kong was 4864 in 2012. The corresponding number of colonoscopy performed in the two hospitals in Chongqing was 4967 and 2640 in the same year. All three hospitals had their individual central computer database for colonoscopy reports. Standard definition colonoscopy systems were used in all three hospitals during the study period including the Olympus CF-240 system and Fujinon 2200 system. Electronic endoscopy records of all colonoscopy performed in these hospitals within the study period was retrieved. All cases of CRC were verified histologically to be adenocarcinoma. Patients' baseline demographic characteristics (age and gender) and the location of colorectal tumor were recorded. The location of tumor as noted on colonoscopy was further confirmed by surgical record if operation was contemplated. We excluded patients with family history of familial adenomatous polyposis or hereditary non-polyposis CRC syndrome. Patients who had previous CRC, colonic resection, or synchronous cancers were also excluded. This study was approved by the institutional review board of the Hospital Authority Hong Kong West Cluster and University of Hong Kong. Because of the retrospective nature of the study, patient's consent could not be obtained. All patients' identity were kept anonymous and replaced by a unique study code during data storage and analysis.

**Definition.** Because of the variations in defining the exact length of rectum and the difficulties in correctly differentiating upper rectal cancer from rectosigmoid cancer,<sup>10,11</sup> we have chosen to include rectosigmoid cancer as rectal cancer in all analyses. Colon cancer included all cancer proximal to the rectosigmoid region. Right-sided colonic cancer included cancer proximal to the hepatic flexure.

**Statistical analysis.** The primary outcome was the difference in the distribution of right-sided colonic and rectal cancers between the two cities. Data of the two Chongqing hospitals were pooled together for subsequent analysis. Categorical data were expressed as percentage and compared by chi-squared test or Fisher's exact test where appropriate. Continuous variables were expressed as mean with SD. Student *t*-test was used for comparison of numerical data. Multivariate analysis was performed to identify for risk factors associated with rectal and right-sided colonic cancers, respectively. Patient's age, year of diagnosis (first 5 years vs second 5 years), gender, and cities where patients lived (Hong Kong vs Chongqing) were entered into backward logistic regression. Risk was expressed as adjusted odds ratio (OR) with 95% confidence intervals (CI). Statistical analysis was performed by SPSS statistical software (version 20, IBM Inc., USA).

**Results**

**Patients' characteristics.** A total of 3667 new cases of CRC (1347 in Hong Kong and 2320 in Chongqing) were diagnosed during the 10-year study period in the three participating hospitals (Table 1). CRC was more common in men than women in both cities with a male to female (M:F) ratio of 1.30 and 1.34 in Hong Kong and Chongqing, respectively. The mean age at diagnosis was significantly older in Hong Kong than in Chongqing

**Table 1** Characteristics of colon and rectal cancer in two cities

	Hong Kong	Chongqing	<i>P</i>
Number of cases	1347	2320	NA
Mean age in years (SD)	70.4 (12.3)	62.1 (13.5)	<0.0001
Men (%)	762 (56.6)	1330 (57.3%)	0.68
Male : female ratio	1.30	1.34	—
Cancer distribution:			
Rectal cancer	256 (19.0%)	1422 (61.3%)	<0.001
Right-sided cancer	367 (27.2%)	404 (17.4%)	<0.001

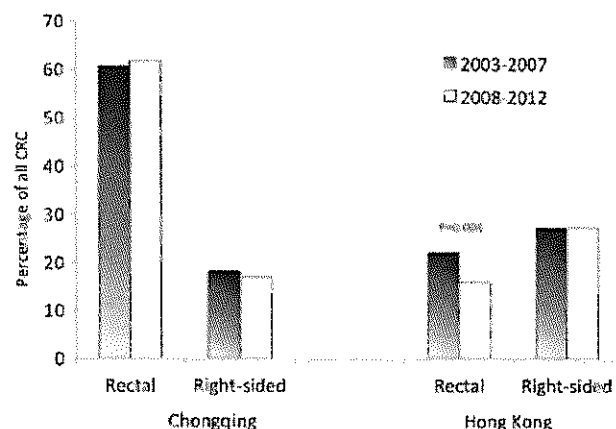
NA, non-applicable.

(70.4 vs 62.1 years; *P* < 0.0001). In Hong Kong, there were significantly more patients who were aged ≥70 years (59.5% vs 31.9%; *P* = 0.0001) and a smaller proportion of young (<40 years) CRC patients (1.3% vs 6.7%; *P* = 0.0001). For patients with known tumor staging, there was no significant difference in the cancer staging between the two cities.

**Distribution of colon and rectal cancers.** Rectal cancer was the predominant cancer in Chongqing that accounted for 61.3% of all cancers. In contrast, only 19% of all CRC in Hong Kong were rectal cancer (*P* < 0.001). Accordingly, right-sided colonic cancer accounted for 27.2% of all cancers in Hong Kong, which were significantly higher than the corresponding proportion in Chongqing (17.4%; *P* < 0.001; Table 1). During the 10-year study period, the proportions of rectal cancer decreased in Hong Kong (from 23.1% in the first 5 years to 16% in the second 5 years; *P* = 0.004; Fig. 1), whereas the proportions of right-sided colon cancer remained stable. There was no significant change in the distribution of cancers during the 10-year study period in Chongqing.

**Patient's characteristics and cancer distribution.**

We further characterized the association between age and gender on CRC distribution. The proportions of right-sided colonic cancer were significantly higher in women in both cities (*P* ≤ 0.002; Table 2). In contrast, rectal cancer was more common in Hong Kong men than women (*P* = 0.008).



**Figure 1** Changes in the proportion of cancer distribution during the 10-year study period in Hong Kong and Chongqing. CRC, colorectal cancer.

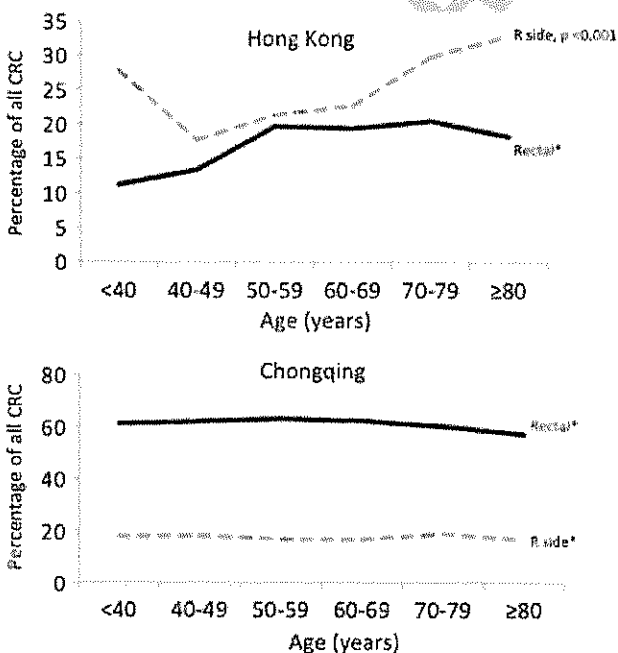
**Table 2** Proportion of rectal, proximal, and right-sided colon cancer in two cities

	Male	Female	P
Chongqing	N = 1330	N = 990	—
Rectal cancer	828 (62.3%)	594 (60%)	0.28
Right-sided colonic cancer	204 (15.3%)	200 (20.2%)	0.002
Hong Kong	N = 762	N = 585	—
Rectal cancer	164 (21.5%)	92 (15.7%)	0.008
Right-sided colonic cancer	178 (23.4%)	189 (32.3%)	<0.001

In Hong Kong, there was an overall age-related increase in the proportions of right-sided colonic cancer ( $P < 0.001$ ; Fig. 2). When the age-related changes were further stratified by gender, the age-related increase in right-sided colonic cancers was only observed in women ( $P = 0.001$ ; Fig. 3a) but not in men.

A very different age-related and gender-related distribution pattern was noted in Chongqing. Age-related increase in right-sided colonic cancers was only noted in female patients ( $P = 0.002$ ; Fig. 3b). Correspondingly, there was a significant drop in the proportion of rectal cancer with ages in women ( $P = 0.003$ ). In Chongqing men, the proportion of right-sided colon cancer decreased with age ( $P = 0.011$ ), and the proportion of rectal cancer remained static.

**Risk factors for rectal and right-sided colonic cancers.** Multivariate analysis showed that male gender (OR, 1.19; 95% CI, 1.03–1.37) and living in Chongqing (OR, 6.67; 95% CI, 5.88–7.69) were the two significant risk factors associated with



**Figure 2** Changes in the proportions of rectal, proximal, and right-sided colonic cancers with ages in Hong Kong and Chongqing. \* $P =$  not significant. CRC, colorectal cancer.

rectal cancer (Table 3). There was no significant association between rectal cancer and age. For right-sided colonic cancer, female gender (OR, 1.47; 95% CI, 1.27–1.72), patient's age in years (OR, 1.01; 95% CI, 1.00–1.01), and living in Hong Kong (OR, 1.67; 95% CI, 1.41–1.97) were found to be independent risk factors (Table 4).

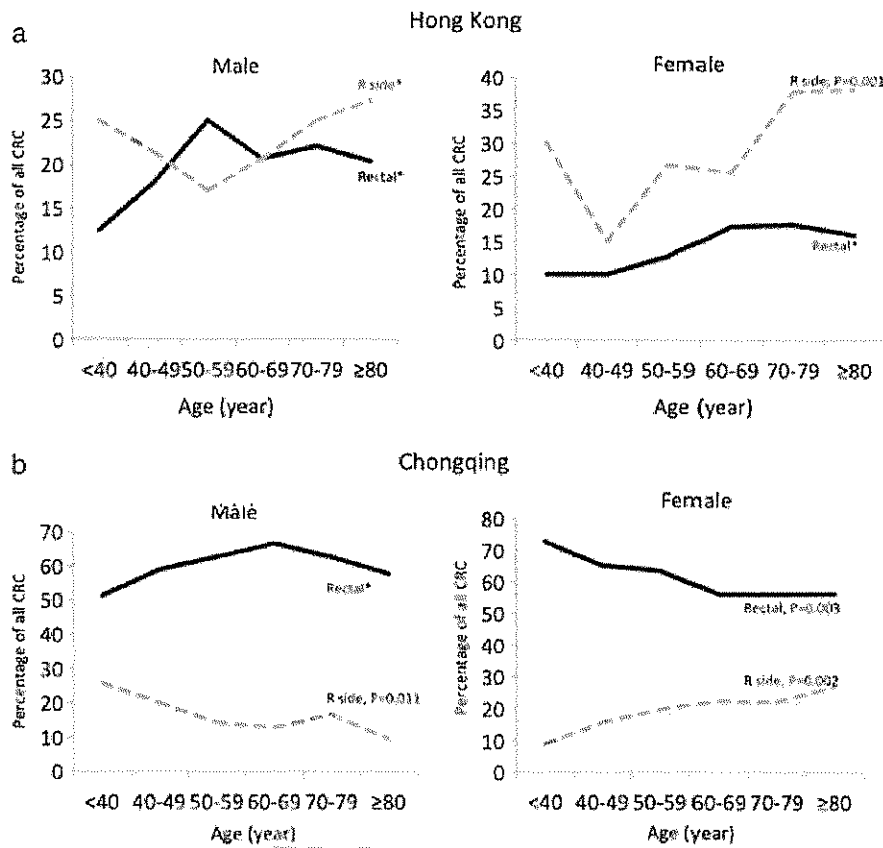
**Discussion**

This is the first study that directly compared the distribution of CRC in two Chinese cities with different backgrounds of CRC incidences over a 10-year period. Unlike previous studies that looked at the evolving changes of CRC epidemiology in a single region over time,<sup>6–9</sup> we reported the dynamic changes of cancer distribution between two places over one decade. In this study, many novel observations were made that would contribute to our understanding of CRC development in a population with rapidly rising CRC incidence.

When compared with Chongqing, the mean age of cancer patients was significantly older in Hong Kong. This is most likely related to the aging population in Hong Kong. In fact, people living in Hong Kong have one of the highest life expectancy in the world with a mean of 83.5 years in 2012.<sup>12</sup> The corresponding life expectancy in China is 75.2 years,<sup>13</sup> which is about 8 years younger. While CRC can be considered to be an age-related cancer, the larger proportion of aging population may account for the higher background cancer incidence and older age at diagnosis in Hong Kong. On the other hand, there are larger proportions of young (<40 years) CRC in Chongqing. While most young onset CRC are hereditary in nature and the actual incidence of young CRC should be relatively stable among Chinese, the apparent higher proportion of young CRC in Chongqing could be attributed to the overall lower cancer incidence.

Rectal cancer is the predominant cancer in Chongqing as reported previously in other reports from different parts of China.<sup>6–8</sup> However, colon cancer is the dominating cancer in Hong Kong, and rectal cancer accounts for less than 20% of all CRC. In this cohort study that covered a period of 10 years, we could also demonstrate a further reduction in the proportion of rectal cancer in the second 5-year interval in Hong Kong. In contrast, right-sided colonic cancer accounts for 27% of all CRC in Hong Kong but only 17% of cancer in Chongqing. Proximal shift of cancer distribution has been previously reported in many western countries<sup>14,15</sup> and some parts of Asia including Japan.<sup>16</sup> The proximal shifting of colon cancer has been shown to be related to increasing age in an Italian population.<sup>17</sup> Based on our observations, the proximal shift of colonic cancer may not have started yet in area with lower cancer incidence in China. This is further supported by our multivariate analysis that living in Hong Kong is a risk factor associated with development of right-sided colonic cancer. A close monitoring of the changes in cancer distribution in regions with lower cancer incidence may help to understand the changing CRC epidemiology.

Colorectal cancer is usually more common in men. In this study, both cities showed a slight male predominance with a male to female ratio of  $\geq 1 : 3$ . However, right-sided colonic cancer was more common in women in both cities. There is also an age-related increase in right-sided colonic cancer in women in both cities. It



**Figure 3** Age-related changes in the proportions of rectal, proximal, and right-sided colonic cancers in male and female patients in (a) Hong Kong and (b) Chongqing \**P* = not significant. CRC, colorectal cancer.

**Table 3** Risk factors for rectal cancer: multivariate analysis

	Rectal cancer (N = 1678)	Non-rectal cancer (N = 1989)	OR	95% CI	P
Age (years)	63.2	66.9	1.0	0.99–1.0	0.31
Male	992	1100	1.19	1.03–1.37	0.019
Female	686	889	1	—	—
Hong Kong	256	1091	1	—	—
Chongqing	1422	898	6.67	5.88–7.69	<0.001
Year of diagnosis:					
First 5 years	662	856	1.09	0.94–1.26	0.27
Second 5 years	1016	1133	1	—	—

CI, confidence intervals; OR, odds ratio.

**Table 4** Risk factors for right-sided colonic cancer: multivariate analysis

	Right-sided cancer (N = 771)	Non right-sided cancer (N = 2896)	OR	95% CI	P
Age (years)	67.1	64.7	1.01	1.00–1.01	0.012
Male	382	1710	1	—	—
Female	389	1186	1.47	1.27–1.72	<0.001
Hong Kong	367	980	1.67	1.41–1.97	<0.001
Chongqing	404	1916	1	—	—
Year of diagnosis:					
First 5 years	336	1182	1.05	0.89–1.24	0.54
Second 5 years	435	1714	1	—	—

CI, confidence intervals; OR, odds ratio.

was associated with a further drop in rectal cancer with ages among Chongqing women. The age-related increase in proximal cancer, however, could not be demonstrated in men from both cities. Similar observation was also made by a previous Japanese study, which showed that proximal shift of colon cancer with increasing age was only seen among women.<sup>18</sup> Paradoxically, there was an age-related decline in the proportion of right-sided colonic cancer in male patients from Chongqing. These data suggest that some unknown factors, other than environmental factors, which should be equally exposed in both genders, contribute to the development of proximal colonic cancer in women. It remains to be determined whether sex hormones or other lifestyle factors such as smoking and alcohol play a role on the differential locations of CRC between women and men.<sup>19,20</sup>

Our findings may have implications on screening of CRC in China, a geographic diverse country. For regions with lower CRC incidence, sigmoidoscopy may still be a valid screening option particularly in male subjects as majority of cancers are still located in the rectum and distal colon. However, for areas with increasing CRC incidence, total colonoscopy is a better option. Colonoscopy is particularly favored over sigmoidoscopy in identifying right-sided colonic cancer, particularly in women and elderly subjects.

This study has several limitations. It was a retrospective study that might be subjected to selection biases. There are also considerable differences in the socioeconomic development and healthcare system of the two cities that could not be adjusted in our analysis. However, there was no cancer registry in Chongqing City or even for the whole Sichuan province. In order to make a fair comparison between two cities, we compared all newly diagnosed CRC by endoscopy in the university-affiliated hospitals in both cities. As this study was based on colonoscopy reports of CRC, some baseline clinical information of the patients, like metabolic syndrome and diabetes,<sup>21</sup> which would increase the risk of right-sided colonic cancer, was also lacking. Other lifestyle risk factors for cancer development such as smoking and alcohol use of the patients were also not available in the analysis. Further studies may be needed to characterize the importance of other risk factors in contributing to the difference in cancer epidemiology between the two places.

To conclude, we found a significant difference in cancer distribution between Hong Kong and Chongqing. While rectal cancer is the dominant cancer in Chongqing, right-sided colonic cancer is far more prevalent than rectal cancer in Hong Kong. There was also a contrasting age-related change of cancer distributions in both genders between the two cities. Development of right-sided cancer is associated with female gender, older age, and living in area with high CRC incidence. These findings may help to understand the changing epidemiology of CRC in Chinese, which would guide our future screening strategy for CRC.

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