RESEARCH ARTICLE

Distribution Characteristics of 3,369 Chinese Colorectal Cancer Patients for Gender, Age, Location and Tumor Size During Colonoscopy

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Abstract

__Background__: Studies have shown the existence of gender- and age-related differences in the incidence and anatomic distribution of colorectal cancers. The purposes of this study were to analyze the distribution characteristics of colorectal cancer patients regarding gender, age, location and tumor size in the course of colonoscopy. __Materials and Methods__: All colorectal cancer patients who underwent colonoscopy in the First Affiliated Hospital of Guangxi Medical University from 2003 to 2012 were included in our retrospective study. Demographic information (age and gender) and colonoscopy report information (tumor size and location) were collected and analyzed. To compare the gender differences in tumor location and tumor size, as well as the size differences in tumor location, the chi-square test was used. __Results__: A total of 3,369 colorectal cancer patients (2,007 men *vs* 1,362 women) were included in our study. Statistical analysis showed there was no gender difference in the anatomic distribution of the tumors ($p>0.05$). However, there was a gender difference in tumor size ($p<0.05$). In addition, our study found there was a significant difference in tumor size between rectal and colon tumors ($p<0.001$). __Conclusions__: There was no gender difference in the anatomic distribution of colorectal tumors. In addition, tumors observed in men were larger than in women.

Keywords: Colorectal cancer - gender - age - location - size - China

Introduction

Colorectal cancer (CRC) is the third most common cancer and the third leading cause of cancer death in the United States. According to the data provided by the American National Center for Health Statistics, in 2014, an estimated 136,830 individuals will be diagnosed with CRC and 50,310 will die of the disease (Siegel et al., 2014a). Studies showed that there was gender- and age- related differences in the incidence of CRC. Male gender had a higher CRC incidence than female, and CRC incidence increased with advancing age. Moreover, both gender and age may affect the incidence of CRC in different anatomic locations of colorectal. It was reported that compared with men, women have a higher percentage of proximal colon tumors and a lower percentage of rectal tumors. In addition, there was a notable increase in proximal colon tumors and decrease in rectal tumors with advancing age (Siegel et al., 2014b). The anatomic site itself is an effect factor in CRC incidence. Some statistical reports demonstrated that the most common tumor location is the proximal colon, followed by the rectum. And in different parts of colorectal, the histological characteristics of colorectal cancers also exhibit differences (Nawa et al., 2008).

A colonoscopy can be proposed to persons complaining of intestinal symptoms such as abdominal pain, bloating, discomfort or occult blood in the stools, as well as to asymptomatic persons. It has been widely accepted and recommended that colonoscopy can serve as the most effective method of screening colorectal tumors in patients over 50 years old. In the course of colonoscopy, related information about tumor location and tumor size can been collected. Further combining demographic information, we can analyze the distribution characteristics of colorectal cancer patients on gender, age, location and tumor size from the perspective of colonoscopy.

Materials and Methods

Patients and methods

We retrospectively reviewed all the patients, who underwent colonoscopy in the First Affiliated Hospital of Guangxi Medical University (Guangxi, China) from

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Bin Cai et al

January 2003 to December 2012. Of these, patients diagnosed with colorectal cancer were recruited in our study. All the endoscopists in our study had a rich colonoscopy operational experience. All patients accepted sufficient bowel preparations. All removed specimen were examined in pathology.

Data collected from the colonoscopy and pathology reports included demographic information (age and gender), tumor location, tumor size and pathological type. Patients were grouped according to gender (men and women), age (<30, 30~39, 40~49, 50~59, 60~69, 70~79, ≥80 years old), tumor location (proximal colon, distal colon and rectum), tumer size (tumor accounts for ≤1/2 or >1/2 the circumference of the intestine). Proximal colon included ileocecal, ascending colon, liver flexure and transverse colon. Distal colon included splenic flexure, descending colon and sigmoid colon. When calculating the number of tumors in different locations, if a patient's tumor appeared in more than one anatomical location simultaneously, then the primary anatomical location was determined by comparing the tumor size. Exclusion criteria included: a history of colorectal surgery; a history of anticancer treatment; or any previous history of malignant tumors. All data were collected by LZX and WMY together, and reviewed by CB.

Statistical analysis

Patient characteristics were described with frequencies and percentages for categorical variables. To compare the gender differences in tumor locations and tumor sizes, as well as the size differences in tumor locations, the chi-square test was used. A two-tailed P value less than 0.05 was considered statistically significant. All analyses were performed using SPSS 17.0 (Chicago, IL, USA).

Results

A total of 3, 369 individual patients (2, 007 men *vs* 1, 362 women) diagnosed with CRC were included in our study according to the inclusion criteria. Of these, 97.60% of the cancers (3, 288/3, 369) were adenocarcinoma. 23.9% (804/3, 369) of the tumors were located in the proximal (25.3%, 855/3, 369) of the tumors were located in the distal colon and 50.8% (1, 710/3, 369) of the tumor were located in the rectum. Patients varied in age from 16 years old to 94 years old in this study. The average age was 61.84 years, with a standard deviation of 6.95 years. 88.21% of colorectal cancer cases occurred in patients over 50 years.

Table 1 showed the gender distribution in each age group. The proportion of male patients was higher than that of female ones in most age groups, apart from a relatively lower proportion of men in the <30 years group. The ratio of male to female tumor cases in age groups varied from 0.9:1 to 2:1. Analysis of the number of cases per decade showed the highest value appeared in 50~59 years group. In addition, we found the peak in men was in 60~69 years group; however, in women it happened in 50~59 years group Figure 1.

Table 2 showed the anatomic distribution of tumors in age and gender groups. Among the 3, 369 cases of CRC, 1, 710 cases (1, 004 men *vs* 706 women) were located in the rectum, 804 cases (490 men *vs* 314 women) were in the proximal colon and 855 cases (513 men *vs* 342 women) were in distal colon. The most common tumor location is the rectum (50.8%), followed by distal colon (25.3%). Chi-square test showed there was no gender difference in the location distribution of tumors from the perspective of the whole life span (*p*>0.05). However, in the 30~39 age group, there was a gender difference in the location distribution of tumors (*p*=0.02). Men were more prone to proximal colon cancer than women in the 30~39 age group. Figure 2a showed the trends in the proportion of each tumor location with the growth of age. Interestingly, in patients over 50 years old, the major population of cancers, a turning point in change trend appeared at the
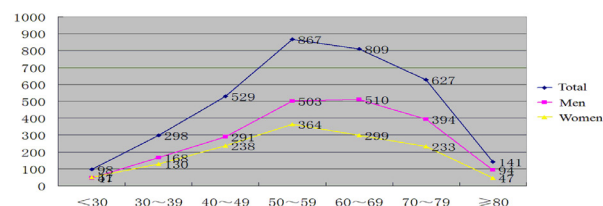

Figure 1. Male and Female Colorectal Cancer Incidence Trends in All Age Groups
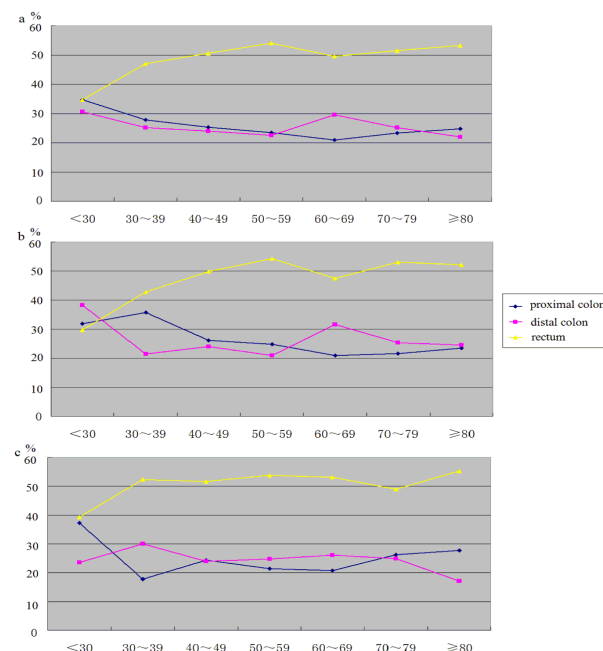

Figure 2. Proportion Trends of Each Tumor Location in All Age Groups. A: the total trends in the proportion of each tumor location with advancing age; B: the trends in men group; C: the trends in women group

Table 1. Gender Distribution in Each Age Group

	n	men	women	ratio of men to women
<30	98	47 (48.0%)	51 (52.0%)	0.9:1
30~39	298	168 (56.4%)	130 (43.6%)	1.3:1
40~49	529	291 (55.0%)	238 (45.0%)	1.2:1
50~59	867	503 (58.0%)	364 (42.0%)	1.4:1
60~69	809	510 (63.0%)	299 (37.0%)	1.7:1
70~79	627	394 (62.8%)	233 (37.2%)	1.7:1
≥80	141	94 (66.7%)	47 (33.3%)	2:01
total	3,369	2,007 (59.6%)	1,362 (40.4%)	1.5:1

Table 2. Anatomic Distribution of Tumors in Age and Gender Groups

	Proximal colon			Distal colon			Rectum			p value
	n	Men	Women	n	Men	Women	n	Men	Women	
<30	34	15	19	30	18	12	34	14	20	>0.05
30~39	83	60	23	75	36	39	140	72	68	0.02
40~49	134	76	58	127	70	57	268	145	123	>0.05
50~59	203	125	78	195	105	90	469	273	196	>0.05
60~69	169	107	62	239	161	78	401	242	159	>0.05
70~79	146	85	61	158	100	58	323	209	114	>0.05
≥80	35	22	13	31	23	8	75	49	26	>0.05
Total	804	490	314	855	513	342	1,710	1,004	706	>0.05

Table 3. Tumor size Distribution in Gender and Location Groups

	Tumor size (*vs* the circumference of the intestine)		
	≤1/2	>1/2	*P* value
men	728	1, 279	0.04
women	561	801	
proximal colon	261	543	>0.05
distal colon	264	591	
colon	525	1, 134	<0.001
rectum	764	946	

age of 60. Between 50~60 years old, the proportion of rectal and distal colon tumors appeared a downward trend, and the proportion of proximal colon tumors appeared an upward trend. However, after the age of 60 years, the proportion of rectal and distal colon tumors appeared an upward trend, and the proportion of proximal colon tumors appeared a downward trend. Then we analyzed this change in men and women group respectively. Figure 2b showed this change was evident in men group. However, in women group it was not evident Figure 2c.

In addition, among 2, 007 male cases, 63.7% (1, 279/2,007) of the tumors accounted for more than half the circumference of the intestine, and 36.3% (728 /2, 007) accounted for less than or equal to half. While in women, 58.8% (801/1, 362) of the tumors accounted for more than half the circumference of the intestine, and 41.2% (561/1, 362) accounted for less than or equal to half. Chi-square test showed there was a gender difference in tumor size (*p*=0.04). In the course of colonoscopy, tumors observed in men were larger than in women. We also compared the relationship between tumor size and tumor location Table 3. Chi-square test showed there was a significant difference in tumor size between rectal and colon tumors (*p*<0.001). Colon tumors were observed larger than rectal tumors in the course of colonoscopy. However, there was no difference in tumor size between proximal and distal colon tumors (*p*>0.05).

Discussion

Increasing age is the strongest non-modifiable risk factor for colorectal cancer incidence and mortality (Morrison et al., 2011). In our study, 88.25% of colorectal cancer cases occurred in people over 40 years. This result was consistent with a study from Malaysia that more than 90% of colorectal cancer cases occurred after the age of 40 (Shah et al., 2014). In addition, our study found the proportion of male colorectal cancer patients was greater than female ones in most age groups. And the ratio of male to female tumor cases had an increasing tendency with advancing age. The latest colorectal cancer report from American Cancer Society demonstrated that the lifetime probability of a colorectal cancer diagnosis is 4.7% in women and 5.0% in men. Incidence and mortality rates are 30% to 40% higher in men than in women overall. And the male to female incidence rate ratio (IRR) varies by age. For example, the IRR is 1.1 from birth to 49 years, 1.4 for those aged 50 to 79 years, and 1.2 for those over 80 years old (Siegel et al., 2014b). A retrospective study from Thailand also demonstrated that both benign colorectal tumors and CRC were more commonly found in males (63%) than females (37%) (Kotepui et al., 2013).

The reason for higher rates in men is not entirely clear. A potential reason is that men have a higher exposure to risk factors, including physical inactivity, excess body weight, high intake of red meat, high alcohol intake, and cigarette smoking (Giovannucci, 2002; Larsson and Wolk, 2006). In addition, exposure to endogenous or exogenous estrogen may also contribute to a lower incidence in women. Observational studies have demonstrated a reduced risk of colorectal cancer among women taking postmenopausal hormones (Grodstein et al., 1999). And in the Women's Health Initiative (WHI) clinical trial, estrogen plus progestin therapy reduced the risk of developing CRC (Chlebowski et al., 2004). However, the role of oestrogen signalling in CRC is not completely understood. It has been discovered that the oestrogen receptor β (ERβ) was abundantly expressed in the normal colonic epithelium (Papaxoinis et al., 2010). ERβ has a crucial role in colonic-cell homeostasis, including modulation of proliferation and organised cell death (Kennelly et al., 2008). Some previous studies have showed that loss of ERβ expression in CRC is associated with poorer differentiation of tumors and more advanced cancer stages (Jassam et al., 2005; Elbanna et al., 2012). And a previous study demonstrated that ERβ-positive colorectal tumors were associated with a better overall survival (Fang et al., 2010). In addition, male gender is more likely to undergo a screening colonoscopy. The difference in screening behavior between male and female gender may also lead to a higher male proportion in all detected colorectal cancers (Chong, 2012). It's worth noting that the Asian Americans showed lower rates in receiving CRC screening than whites and African Americans. Within Asian subgroups, there are large disparities; Korean Americans reported to undergo the lowest CRC screening, while higher screening rates were

found among Japanese Americans (Hwang, 2013).

Comparing the number of cases in all age groups, we found the highest value was in 50~59 years group. Such a result can reasonably support most national guidelines, which recommend that screening programs for CRC start by age 50 years for both men and women of average risk (Levin et al., 2008). However, some studies demonstrated that CRC incidence and mortality were higher in men than in women, and women mainly reached equivalent levels when 4 to 8 years older (Brenner et al., 2007; Rundle et al., 2008). It has been proposed that the age for starting screening colonoscopy should be sex specific. Sung et al (Sung et al., 2008) suggested in the Asia Pacific consensus recommendations for colorectal cancer screening that women may start screening at later ages because of the relatively low incidence of CRC at ages 50 to 55 years. But in our study, we found that the numbers of tumor cases in women and men group were both close to the peak in 50~59 years group. For this reason, we suggest that the recommended age for women should be the same as men.

American colorectal cancer statistics report showed the most common tumor location was the proximal colon (42%), followed by the rectum (28%). And the location distribution varied by sex. Compared with men, women had a higher percentage of proximal tumors (46% *vs* 38%) and a lower percentage of rectal tumors (24% *vs* 31%) (Siegel et al., 2014b). However, a multi-center survey, including 31, 246 chinese colorectal cancer patients, showed 62.68% of the tumors were located in the rectum, followed by 19.59% of the tumors in the proximal colon. In our study, 50.8% (1710/3369) of the tumors were located in the rectum, 23.9% (804/3369) of the tumors were in the proximal colon and 25.3% (855/3369) of the tumors were in the distal colon. Our findings were consistent with the above Chinese survey report that in the Chinese population the most common colorectal cancer location is the rectum. Ethnic differences may be one important reason for the different colorectal cancer predilection sites between American and Chinese patients. In addition, some articles from western countries demonstrated the proportion of distal colon and rectal tumors was considerably lower among women than among men (Bonithon-Kopp and Benhamiche, 1999; McCashland et al., 2001). However, our study did not find any significant gender difference in the anatomic distribution of tumors. A latest study from Malaysia, reviewing 1, 212 colorectal cancer patients undergoing treatment between January 2001 and December 2010, showed that significant ethnic differences in age and site distribution (Magaji et al., 2014). Therefore, we suggested that when making references to the statistics of colorectal cancer, the ethnic factor must be taken into account.

In our study, there were also some differences in anatomic distribution by age; for example, 53.2% of colorectal cancers in patients aged 80 years and older were in the rectum, compared with 34.7% in those aged younger than 30 years. 38.1% of colorectal cancers in men aged younger than 30 years were in the distal colon, compared with 24.5% in those aged 80 years and older.

A retrospective 15-year study, evaluating the anatomical distribution of colorectal carcinoma in Iran, reported that there was no statistical difference between the age at diagnosis in the right and left sided cancers. In addition, there were modest differences in anatomical distribution between the sexes with a slightly higher proportion of females diagnosed with left sided colon cancers (Omranipour et al., 2012). In addition, we found an interesting phenomenon that between 50~60 years old, the proportion of rectal and distal colon tumors appeared a downward trend, and the proportion of proximal colon tumors appeared an upward trend. However, after the age of 60 years, the proportion of rectal and distal colon tumors appeared an upward trend, and the proportion of proximal colon tumors appeared a downward trend. This change was evident in men group, but not evident in women group. We do not know whether the phenomenon is one of coincidence, and there are no similar reports currently.

Regarding tumor size, we found tumors observed in men were larger than in women. This may be due to gender differences in the exposure of risk factors and estrogen. In addition, we found there was a significant difference in tumor size between rectal and colon tumors. Colon tumors were observed larger than rectal tumors in the course of colonoscopy. However, there was no difference in tumor size between proximal and distal colon tumors. These results were only observed in the course of colonoscopy; therefore, they could not fully represent the exact tumor size. A recent study analyzed the tumor size by measuring the maximum diameter. They found the average size determined for all locations was 5.05cm, with a median located at 4.82 and a standard deviation of 1.99. Depending on location, average size ranged from 5.43cm in the right colon, 4.89cm in the transverse colon, 3.54cm in the left colon and 3.97cm in the rectum (Mogoanta et al., 2014). It has been reported that tumor size could be an independent prognostic parameter for patients with colorectal cancer, especially in the colon cancers (Kornprat et al., 2011). The reasons of the tumor size differences in various parts of the colorectal are unclear. It has been reported that, fundamentally, the colon develops from 2 different embryonic areas of the primitive gut: the midgut, which gives rise to the small intestine through to the proximal two thirds of transverse colon, and the hindgut, which gives rise to the distal third of the transverse colon through the upper anal canal (Jacobs et al., 2007). In addition, a latest study demonstrated that the underlying carcinogenic pathway or molecular backgrounds differ according to the cancer locations among CRC patients. They found the MLH1-PEN was prominent in proximal colon cancer, MSH6-PEN in distal colon and rectal cancer, and APC-PEN in distal colon respectively (Effendi et al., 2013). Some studies reported right-sided colon cancer was more likely to be detected at an advanced stage with severe symptoms. And Polypoid-type early cancer was dominant in the left colon (Nawa et al., 2008). The popularity of sigmoidoscopy screening may also contribute to discovering distal tumors at the early stage.

We must acknowledge that there are some limitations in our study. First, it was completed in a single academic center. This may make our results only represent a regional situation. Second, although the majority of tumors were

adenocarcinomas, our studies also included other types of tumors that may have an effect on the distribution of tumor size and location. Third, some of our findings were differed from other previous reports; therefore, it is still necessary to conduct larger size and better design studies to confirm our results. Despite these limitations, our study has several strengths. All data included in our study were rigorously reviewed. Our study included a large sample of 3, 369 individual patients, so that each group contained a sufficient number of samples for comparison. In conclusion, through this retrospective study of 3, 369 Chinese colorectal cancer patients, we found 88.25% of colorectal cancer cases occurred in patients over 40 years old. And the proportion of male patients was greater than that of female ones (1.5:1). The most common tumor location is the rectum (50.8%), followed by distal colon (25.3%). And there was no gender difference in the location distribution of tumors. In addition, our study found, in the course of colonoscopy, tumors observed in men were larger than in women. And there was a significant difference in tumor size between rectal and colon tumors. However, there was no difference in tumor size between proximal and distal colon tumors.

Acknowledgements

References

Bonithon-Kopp C, Benhamiche AM (1999). Are there several colorectal cancers? Epidemiological data. *Eur J Cancer Prev*, **8**, 3-12.

Brenner H, Hoffmeister M, Arndt V, et al (2007). Gender differences in colorectal cancer: implications for age at initiation of screening. *Br J Cancer*, **96**, 828-31.

Chlebowski RT, Wactawski-Wende J, Ritenbaugh C, et al (2004). Estrogen plus progestin and colorectal cancer in postmenopausal women. *N Engl J Med*, **350**, 991-1004.

Chong VH (2012). Gender preference and implications for screening colonoscopy: impact of endoscopy nurses. *World J Gastroenterol*, **18**, 3590-4.

Effendi YSR, Zain LH, Siregar GA, et al (2013). Adenomatous Polyposis Coli, mismatch repair, and microsatellite instability in colorectal cancer based on different locations. *Acta Med Indones*, **45**, 275-83.

Elbanna HG, Ebrahim MA, Abbas AM, et al (2012). Potential value of estrogen receptor beta expression in colorectal carcinoma: interaction with apoptotic index. *J Gastrointest Cancer*, **43**, 56-62.

Fang YJ, Lu ZH, Wang F, et al (2010). Prognostic impact of ERbeta and MMP7 expression on overall survival in colon cancer. *Tumour Biol*, **31**, 651-8.

Giovannucci E (2002). Modifiable risk factors for colon cancer. *Gastroenterol Clin North Am*, **31**, 925-43.

Grodstein F, Newcomb PA, Stampfer MJ (1999). Postmenopausal hormone therapy and the risk of colorectal cancer: a review and meta-analysis. *Am J Med*, **106**, 574-82.

Hwang H (2013). Colorectal cancer screening among Asian Americans. *Asian Pac J Cancer Prev*, **14**, 4025-32.

Jacobs ET, Thompson PA, Martinez ME (2007). Diet, gender, and colorectal neoplasia. *J Clin Gastroenterol*, **41**, 731-46.

Jassam N, Bell SM, Speirs V, et al (2005). Loss of expression of oestrogen receptor beta in colon cancer and its association with Dukes' staging. *Oncol Rep*, **14**, 17-21.

Kennelly R, Kavanagh DO, Hogan AM, et al (2008). Oestrogen and the colon: potential mechanisms for cancer prevention. *Lancet Oncol*, **9**, 385-91.

Kornprat P, Pollheimer MJ, Lindtner RA, et al (2011). Value of tumor size as a prognostic variable in colorectal cancer: a critical reappraisal. *Am J Clin Oncol*, **34**, 43-9.

Kotepui M, Piwkham D, Songsri A, et al (2013). Histopathology analysis of benign colorectal diseases and colorectal cancer in Hatyai Hospital, Songkhla, Thailand. *Asian Pac J Cancer Prev*, **14**, 2667-71.

Larsson SC, Wolk A (2006). Meat consumption and risk of colorectal cancer: a meta-analysis of prospective studies. *Int J Cancer*, **119**, 2657-64.

Levin B, Lieberman DA, McFarland B, et al (2008). Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *Gastroenterology*, **134**, 1570-95.

Magaji BA, Moy FM, Roslani AC, et al (2014). Descriptive epidemiology of colorectal cancer in University Malaya Medical Centre, 2001 to 2010. *Asian Pac J Cancer Prev*, **15**, 6059-64.

McCashland TM, Brand R, Lyden E, et al (2001). Gender differences in colorectal polyps and tumors. *Am J Gastroenterol*, **96**, 882-6.

Mogoanta SS, Vasile I, Totolici B, et al (2014). Colorectal cancer - clinical and morphological aspects. *Rom J Morphol Embryol*, **55**, 103-10.

Morrison DS, Batty GD, Kivimaki M, et al (2011). Risk factors for colonic and rectal cancer mortality: evidence from 40 years' follow-up in the Whitehall I study. *J Epidemiol Community Health*, **65**, 1053-8.

Nawa T, Kato J, Kawamoto H, et al (2008). Differences between right- and left-sided colon cancer in patient characteristics, cancer morphology and histology. *J Gastroenterol Hepatol*, **23**, 418-23.

Omranipour R, Doroudian R, Mahmoodzadeh H (2012). Anatomical distribution of colorectal carcinoma in Iran: a retrospective 15-yr study to evaluate rightward shift. *Asian Pac J Cancer Prev*, **13**, 279-82.

Papaxoinis K, Triantafyllou K, Sasco AJ, et al (2010). Subsite-specific differences of estrogen receptor beta expression in the normal colonic epithelium: implications for carcinogenesis and colorectal cancer epidemiology. *Eur J Gastroenterol Hepatol*, **22**, 614-9.

Rundle AG, Lebwohl B, Vogel R, et al (2008). Colonoscopic screening in average-risk individuals ages 40 to 49 *vs* 50 to 59 years. *Gastroenterology*, **134**, 1311-5.

Shah SA, Neoh HM, Rahim SS, et al (2014). Spatial analysis of colorectal cancer cases in Kuala Lumpur. *Asian Pac J Cancer Prev*, **15**, 1149-54.

Siegel R, Ma J, Zou Z, et al (2014a). Cancer statistics, 2014. *CA Cancer J Clin*, **64**, 9-29.

Siegel R, Desantis C, Jemal A (2014b). Colorectal cancer statistics, 2014. *CA Cancer J Clin*, **64**, 104-17.

Sung JJ, Lau JY, Young GP, et al (2008). Asia Pacific consensus recommendations for colorectal cancer screening. *Gut*, **57**, 1166-76.