Sequential screening in the early diagnosis of colorectal cancer in the community

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Abstract

Background Colorectal cancer (CRC) is the third most prevalent type of cancer in the world. Its prognosis is closely related to the disease stage at the time of diagnosis. Early detection of symptomless CRC or precursor lesions through population screening could reduce CRC mortality. However, screening programs are only effective if enough people are willing to participate. The incidence of CRC has a significantly increasing trend in China.

Objective Evaluation of the necessity of screening colonoscopy for community fecal occult blood-positive patients and exploration of the differences in the epidemiology of colorectal adenomas (CRA) and CRC of community screening patients and patients with different symptoms.

Methods We selected the 40–79 years age group of healthy people in the community of the Fengxian District of Shanghai who had two consecutive fecal occult blood and screening colonoscopies completed in our hospital between June 1, 2014 and October 31, 2014 as the screening group. Patients in the same age group with different symptoms (such as abdominal pain, bloody stool, diarrhea, change in bowel habits, weight loss, anemia, etc.) who had completed colonoscopy in our hospital during the same period comprised up the control group. Differences in the detection rates of colorectal polyps and CRC in the two groups and differences in the detection rates of CRA and early CRC between the two groups were compared.

Results There were 2251 patients in the colonoscopy screening group and 1836 patients in the control group. The colorectal polyps detection rates of the two groups were 19.46% (438/2251) and 21.95% (403/1836), respectively, and the difference was not statistically significant ($p = 0.052$). The CRC detection rates of the two groups were 0.8% (18/2251) and 2.02% (37/1836), respectively, the difference of which was statistically significant ($p = 0.001$). The detection rates of CRA were 17.73% (399/2251) and 19.88% (365/1836), respectively, which was not statistically significantly different ($p = 0.083$). Finally, the detection rates of early CRC were 0.36% (8/2251) and 0.44% (8/1836), respectively, which was not statistically significantly different in the two groups ($p = 0.803$).

Conclusion The detection rates of CRA among community screening patients and patients with different symptoms were not different. However, the detection rate of CRC in community screening patients was lower than that of the patients with different symptoms. Therefore community colonoscopy screening of fecal occult blood-positive asymptomatic healthy people is necessary, as it can help with the early detection and treatment of CRA.

Keywords Colorectal cancer · Colonoscopy · Fecal occult blood · Screening

Introduction

Worldwide, colorectal cancer (CRC) is an important health concern. It is the third most common cancer in men and the second most common in women. It is also the fourth most common cause of cancer mortality (Siegel et al. 2015; Zavoral et al. 2014). It is the most common malignant tumor in China, and, with China's social and economic development, people's lives, diet, environmental, and other changes, the

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incidence of CRC has a significantly increasing trend in China (Chen et al. 2016).

Early detection of CRC is one of the best approaches to reduce related deaths. Screening remains the basis for CRC prevention. As with most cancers, early detection vastly improves prognosis. The five-year survival is nearly 90% for localized lesions and 70% for regional ones, but plummets to 13% with distant metastasis (Nelson and Thorson 2009). Many patients are diagnosed in an advanced stage, thus resulting in poor survival. Early detection of symptomless CRC or its precursor lesions by population screening could reduce CRC mortality, since removal of these precursors during colonoscopy reduces the incidence of CRC (Winawer et al. 1993). Depending on mortality, the mortality benefit of CRC screening is somewhere between 25 and 50% of deaths prevented (Brenner et al. 2014). A broad spectrum of choices is available for CRC screening, including fecal occult blood testing (FOBT) and colonoscopy. FOBT is a non-invasive, widespread screening method that can reduce CRC-related mortality. Colonoscopy is the best choice for screening high-risk populations, as it allows the simultaneous detection and removal of preneoplastic lesions.

Colorectal adenomas (CRA) are the main preneoplastic lesions, so the early and timely detection and removal of preneoplastic lesions is key to the prevention of CRC. As commonly known, the majority of early CRC populations have no obvious symptoms. Early detection of preneoplastic lesions and CRC is very important, but this requires screening a large number of asymptomatic populations, so selecting convenient, effective, and economic screening methods is very important. FOBT, high-risk factors questionnaire, and digital rectal examination can be used for the initial screening to discover high-risk populations that should undergo further colonoscopy screening.

Therefore, ascertaining high-risk populations by initial screening and then screening colonoscopy and biopsy remains the most effective and convenient method of screening of CRC and preneoplastic lesions. The usefulness is confirmed by the growing evidence that colonoscopy-based screening programs are able to reduce CRC incidence and mortality. We report on a controlled study of CRC sequential screening in the community.

Materials and methods

Study population, FOBT, bowel preparation, and colonoscopy requirements

The Research and Ethics Committee approved our study protocol. The asymptomatic population screening group selected for this study was aged 40–79 years from the community in Fengxian District, Shanghai (Southbridge Town, Light Town,

Green Village Town, Qixian Town). All patients were tested twice by FOBT (double antibody sandwich immunoassay chromatography), with an interval of one week between tests. Two consecutive positive fecal occult blood and screening colonoscopies were completed at Shanghai Jiao Tong University Affiliated Sixth People's Hospital South Campus from June 1, 2014 to October 31, 2014. Patients with different symptoms (such as abdominal pain, bloody stool, diarrhea, change in bowel habits, weight loss, anemia, etc.) who had completed colonoscopy at the same institution, during the same period, and originating from the same age group made up the control group.

All patients underwent polyethylene glycol electrolyte powder bowel preparation, and were then asked to discharge watery stool deemed to meet the requirements. In case the patient did not meet the requirements, then additional polyethylene glycol electrolyte powder was ingested.

All participants underwent colonoscopy at Shanghai Jiao Tong University Affiliated Sixth People's Hospital South Campus. Colonoscopies were performed in a standardized fashion by experienced gastroenterologists who had more than 5 years of experience in endoscopic operations and it required more than 5 min when exiting the colonoscopy. The location and size of all polypoid lesions were recorded and the tumor specimens were pathologically classified as previously described.

Definition of detection rates

- (1) Polyp detection rate (PDR). The proportion of patients who had at least one colorectal polyp during the colonoscopy period.
- (2) Colorectal adenoma rate (CRAR). At least one patient with histopathologically confirmed adenomas was found to account for the proportion of colonoscopy subjects.
- (3) Colorectal cancer rate (CRCR). At least one patient with histopathologically confirmed CRC accounted for the proportion of colonoscopy subjects in that period of time.
- (4) Advanced adenoma (AA). A tubular adenoma with diameter ≥ 1 cm, adenoma containing a villous component ($> 25\%$), or a high-grade intraepithelial neoplasia.
- (5) Early colorectal cancer (ECC). Refers to any size of colorectal epithelial tumor that is confined to the mucosa and submucosa, with or without lymph node metastasis.

Statistical analyses

Baseline clinical characteristics were compared using chi-squared tests. All statistical analyses were performed with SPSS 19.0 for Windows and statistical charts were drawn using GraphPad Prism 7. All tests of statistical significance

were two-sided and a p -value of less than 0.05 was considered statistically significant.

Results

Demographic and baseline patient clinical characteristics

In total, 2251 (996 males and 1255 females) and 1836 (919 males and 917 females) individuals underwent colonoscopy in the screening and control groups, respectively.

Table 1 shows that the detection rates of colorectal polyps during colonoscopy for the screening and control groups were 19.46% and 21.95%, respectively. Comparison between the two groups showed no significant difference ($p = 0.052$). The detection rates of CRC during colonoscopy for the screening and control groups were 0.80% and 2.02%, respectively. Comparison between the two groups showed a significant difference ($p = 0.001$).

Primary site and pathological type of colorectal polyps in the two patient groups

The results show that the detection rate of colorectal polyps for men was significantly higher than for women in the screening and control groups ($p = 0.032$). There were no significant differences in the distribution of types of pathology in the screening and control groups (Table 2). Figure 1a shows that the 60–69 years age group had the highest incidence of colorectal polyps among the two groups, and Fig. 1b indicated that colorectal polyps were mainly distributed in the rectum and

sigmoid. There was no significant difference in the detection rates of adenomatous polyps between the two groups (Fig. 1c). Comparison between the two groups showed a significant difference in the LGIN type (Fig. 1d).

Primary site and TNM stage of CRC in the two groups

This study shows that the detection rate of CRC was significantly higher for women than men in the screening group. However, in the control group, the result was the opposite (Table 3). Figure 2a shows that the 60–69 years age group had the highest incidence of CRC in the two groups. Figure 2b shows that there was no significant difference in the detection rate of early CRC in the two groups. Figure 2c shows that cases of CRC were mainly distributed in the rectum and sigmoid in the two groups.

Discussion

CRC is one of the most common malignant tumors in world. It has a good prognosis following early diagnosis and treatment. However, the majority of early CRC patients has seldom obvious clinical symptoms and signs. Therefore, screening for the early diagnosis of CRC is necessary for a large number of asymptomatic people. Initial screening can find high-risk populations and screening colonoscopy and biopsy remains the most effective and convenient method of screening for CRC and preneoplastic lesions. The usefulness is confirmed by the growing evidence that colonoscopy-based screening programs are able to reduce CRC incidence and mortality. Two studies (Siegel et al. 2012; Jacob et al. 2012) reported that an

Table 1 Demographic and clinical characteristics of the patients in the two groups

Characteristic	Screening group, n (%)	Control group, n (%)	χ^2	p -Value
Total cases	2251	1836		
Sex				
Male	996 (44.25)	919 (50.05)	13.70	0.000
Female	1255 (55.75)	917 (49.95)		
Age (years)				
40–49	55 (2.44)	436 (23.75)	434.18	0.000
50–59	813 (36.12)	610 (33.22)	3.73	0.056
60–69	1135 (50.42)	603 (32.84)	127.85	0.000
70–79	248 (11.02)	187 (10.19)	0.74	0.415
Colonoscopy results				
Normal	1370 (60.86)	1049 (57.14)	5.81	0.016
Colorectal polyps	438 (19.46)	403 (21.95)	3.84	0.052
Colorectal cancer	18 (0.80)	37 (2.02)	11.26	0.001
Colorectal submucosal tumor	11 (0.48)	7 (0.38)	0.27	0.644
Colorectal inflammation	99 (4.40)	104 (5.66)	3.44	0.070
Ulcerative colitis	2 (0.09)	15 (0.82)	12.94	0.000
Hemorrhoids	313 (13.90)	221 (12.04)	3.11	0.084

Table 2 Pathological characteristics of colorectal polyps in the two groups

Characteristic	Screening group, <i>n</i> (%)	Control group, <i>n</i> (%)	χ^2	<i>p</i> -Value
Total cases	438	403		
Sex				
Male	263 (60.05)	271 (67.25)	4.69	0.032
Female	175 (39.95)	132 (32.75)		
Pathological type				
Tubular adenoma	275 (62.92)	255 (63.28)	0.02	0.887
Tubular villous adenoma	114 (26.03)	107 (26.55)	0.03	0.876
Villous adenoma	10 (2.28)	3 (0.74)	3.27	0.093
Inflammatory polyps	24 (5.48)	18 (4.47)	0.45	0.530
Hyperplastic polyps	15 (3.42)	20 (4.96)	1.25	0.302
Pathological grade				
LGIN	345 (78.77)	232 (57.57)	43.80	0.000
HGIN	9 (2.05)	9 (2.23)	0.03	1.000

increased use of lower gastrointestinal endoscopy led to a reduction in the incidence and mortality due to CRC in an average-risk population in the USA. A large population-based cohort study (Pezzoli et al. 2007) showed that a 5-year colonoscopy-based screening for CRC in asymptomatic subjects achieved decreases of 48% in CRC incidence and 81% in mortality in Italy.

In our study, we found that the detection rates of colorectal polyps during colonoscopy for the screening and control groups were 19.46% (438/2251) and 21.95% (403/1836), respectively. Comparison between the two groups showed no significant difference ($p = 0.052$). The colorectal polyps detection rate amongst males was 26.41% (263/996) in the screening group and 13.94% (175/1255) amongst females. In the control group, it was 29.49% (271/919) for males and 14.39% (132/917) for females. The difference between the males and females

in the two groups was statistically significant ($p = 0.000$). It was found that the detection rates of CRC during colonoscopy for the screening and control groups were 0.80% and 2.02%, respectively. Comparison between the two groups showed a significant difference ($p = 0.001$). The CRC detection rate amongst males in the screening group was 0.60% (6/996), whilst that amongst females was 0.96% (12/1255). In the control group, it was 2.50% (23/919) for males and 1.53% (14/917) for females. The difference between males and females in the two groups was not statistically significant ($p > 0.05$). In Asia, a multinational multicenter study showed that the colorectal polyps detection rate for colonoscopy screening in asymptomatic populations was 18.5%. The CRC detection rate was 1% higher for males compared to females (Byeon et al. 2007).

We found that there was no significant difference between the 50–59 years and 70–79 years age groups when comparing the age distribution of the two colorectal polyps groups ($p > 0.05$). However, there were significant differences among the other age groups ($p < 0.05$). There were no statistically significant differences in the distributions of colorectal polyps and pathological type among the two groups. We found that the rectum and sigmoid colon were the most common sites of colorectal polyps in the two groups. In the screening group, the rectum and sigmoid colon polyps accounted for 75.80% (332/438) of the detection of colorectal polyps, while it was 75.19% (303/403) in the control group. Colorectal adenomas accounted for 91.10% (399/438) in the screening group and 90.57% (365/403) in the control group, with no statistically significant difference between the two groups.

There was no significant difference between the two groups in terms of gender, age, location, or distribution of CRC, but there was a significant difference in the detection rate of CRC in the 60–69 years age group compared to the other age groups. Rectum and sigmoid colon cancer

Fig. 1 Comparison of the age, area, polyps type, and pathological type in the two groups of colorectal polyps patients

Table 3 TNM stage of CRC in the two groups

Characteristic	Screening group, <i>n</i> (%)	Control group, <i>n</i> (%)	χ^2	<i>p</i> -Value
Total cases	18	37		
Sex				
Male	6 (33.33)	23 (62.16)	4.04	0.083
Female	12 (66.67)	14 (37.84)		
TNM stage ^a				
Tis ^b	5 (27.78)	5 (13.51)	1.66	0.268
T1	3 (16.67)	3 (8.11)	0.91	0.381
T2	5 (27.78)	6 (16.22)	2.08	0.177
T3	5 (27.78)	20 (54.05)	3.37	0.087
T4	0 (0)	3 (8.11)	1.54	0.543
N0	6 (33.33)	8 (21.62)	0.88	0.510
N1	8 (44.44)	10 (27.03)	1.67	0.231
N2	4 (22.22)	19 (51.35)	4.22	0.047
M0	15 (83.33)	16 (43.24)	7.91	0.008
M1	3 (16.67)	21 (56.76)		

^a Based on the TNM staging system (American Joint Committee on Cancer, AJCC, 2010)

^b Invasive tumor confined to mucosa, including intramucosal

accounted for 72.22% (13/18) of the detections of CRC in the screening group, while it was 70.27% (26/37) in the control group. The rectum and sigmoid were the most common sites for CRC in the two groups, which was consistent with colorectal polyps predilection sites. We speculate that this may be related to the function and microenvironment of the rectum and sigmoid. Stool in the rectum and sigmoid stay for longer, which could easily lead to changes of the intestinal bacteria and microenvironment. However, the detailed mechanism for this needs further study.

Fig. 2 Comparison of the age, cancer stage, and area in the two groups of colorectal cancer patients

Our study had some limitations. If the results of colonoscopy was normal in patients who were tested positive twice with FOBT, whether endoscopy should be performed to exclude upper gastrointestinal diseases needs further study. In addition, we did not compare the colonoscopy results in patients with a negative result for FOBT in the community. These shortcomings can provide us with experience in subsequent screening studies.

In summary, the detection rate of colorectal polyps showed no significant difference between community screening patients and patients with different symptoms. Men had a higher prevalence than women and there was no difference in the site or histological type distribution. The rectum and sigmoid were the most common sites for colorectal polyps, primarily colorectal adenomas. The rectum and sigmoid were the most common sites for CRC. Comparing the detection rates of CRC, the patients with different symptoms had a higher rate than patients undergoing community screening. These results show that colonoscopy among asymptomatic fecal occult blood-positive healthy populations in the community are necessary for the early detection and treatment of colorectal adenomas. We believe that the incidence rate of CRC will decrease in the future in China following screening in the community.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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