Original Article

An early report of a screening program for colorectal cancer in Guangzhou, China

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Background: We launched a screening program for colorectal cancer (CRC) in Yuexiu District, Guangzhou, China, in 2014. Here we aimed to report the early results of the program and evaluate the benefits of a screening questionnaire.

Methods: Residents aged between 50 and 74 were eligible for the screening. A questionnaire and two consecutive fecal immunological tests (FITs) were used as primary screening methods. Subjects who were positive for any of the two tests were referred for further examination with colonoscopy. Neoplasms were removed either colonoscopically or by colectomy. Atypical adenoma and CRC were defined as advanced neoplasms.

Results: A total of 6,971 residents in Dadong Street, Yuexiu District were screened with a questionnaire, and among them, 5,343 underwent at least one FIT. Four thousand and two hundred eleven (60.4%) were female, and 2,760 (39.6%) were male, with a median age of 62.0 years. Questionnaire and FITs identified 1,219 candidates for further examination with colonoscopy, among whom only 647 (53.1%) comply. As of this writing, 623 colonoscopy results were obtained, among which 270 (43.3%) had positive findings. The adenoma detection rate (ADR) was 43.3% (270/623). The ADR was 43.3% (270/623). Of the 270 patients, 10 (3.07%) had CRC, 81 (30.0%) had advanced adenoma, 178 had low-grade adenoma or other benign polyps, one had carcinoid. Except for three advanced CRC, all neoplasms detected were benign or in an early stage.

Conclusions: Our screening program help identified patients with colonic neoplasms at an early stage, precluding them from developing into the malignant disease. The addition of the questionnaire significantly increased the sensitivity of primary screening, while also decreasing the specificity. Long-term results should evaluate the social and economic benefits of this program.

Keywords: Polyps; colorectal cancer (CRC); early screening; fecal immunological test (FITs)

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Introduction

Colorectal cancer (CRC) is a significant threat to public health. In 2018, there is an estimate of 1.8 million new incidences and 0.81 million deaths globally. CRC ranks third in terms of incidence and second in mortality, accounting for one in ten cancer cases and deaths (1). In China, CRC has become the fifth most common cancers in men and the third most common cancers in women, with an estimate of 37.6 new cases per year (2). While the incidence of CRC is on the rise in both China and most other countries in the world, it has been declining in the past two decades in the United States (3). Between 2004 and 2013, both the incidence and mortality of CRC in the USA declined at an annual rate of about 3% (4). This trend is believed to result from the prevalence of CRC screening among high-risk adults (5).

Screening programs for the early detection of colorectal neoplasms have been launched in Haining (Zhejiang province), Tianjin, and Guangzhou (Guangdong province) to curb the upward trend of CRC incidence in China (6,7). For economic reasons, these programs use fecal occult blood test (FOBT) and a specially designed questionnaire as primary screening methods before visual inspection with colonoscopy examination. Although their long-term effect on CRC control is yet to be seen, early reports have shown promising results. Jiang *et al.* found that 20% of the subjects in Haining city undergoing colonoscopy had one or more neoplastic lesions, most of which were benign polyps. The similar detection rate was observed in another program in Tianjin city.

In 2015, we launched a screening program for CRC in Guangzhou in consort with local Disease Control Center. Up to date, we have screened 6,971 eligible population with questionnaire and FOBT and performed 652 colonoscopy examinations. Here, we reported the early results of this program and evaluated the usefulness of the questionnaire.

Methods

Screening protocol

We initiated a population screening program for colorectal neoplasms together with Guangzhou CDC in Yuexiu District, Guangzhou, Guangdong Province, China, in 2014. The eligible population included residents aged between 50 and 74 years. As of Dec 2018, 6,971 patients have been screened. To reduce the cost and increase detection rate, we adopted a two-step screening method: subjects were first evaluated for the risk of colorectal neoplasms using questionnaires and FOBT simultaneously; those who were positive in any of the tests were then referred for further evaluation with colonoscopy.

Primary screening

The primary screening included a questionnaire and two fecal immunological tests (FITs). We used the same questionnaire as was used in other screening programs in China. It included sex, age, persistent symptoms of the gastrointestinal tract, history of cancer, familial cancer history, diet habit, drinking, and smoking. Subjects were defined as high-risk if they had a history of polyps, any first-degree relatives with CRC cancer, or met ≥2 of the following conditions: chronic constipation or diarrhea, hematochezia, traumatic experience in the past 20 years, history of appendicitis, and history of cholecystitis.

FIT was used to detect occult blood in stools. Each subject was provided with two collection kits (supplied by ABON, China), and required to collect 10 to 50 mg stool twice in two consecutive weeks, following the manufacturer's recommendations. Samples were sent to local community health centers within 6 hours after collection. All subjects were required to undergo a second test regardless of the result of the first test.

Colonoscopy examination

Participants that were positive for primary screening were referred to Sun Yat-sen University Cancer Center or other medical centers for further examination with colonoscopy. Polyps of radius <0.5 cm were resected colonoscopically during the examination, if possible. Any neoplasm ≥0.5 cm was biopsied first and proceeded with polypectomy or colectomy depending on pathological report and feasibility of endoscopic surgery. Atypical adenomas, carcinoma *in situ*, and CRC were referred to as advanced neoplasms.

Statistics

Associations between categorical variables were assessed by Chi-square test, Fisher's exact test, or Wilcoxon's rank-sum test, as appropriate. A two-sided $P<0.05$ was considered statistically significant. All analyses were performed in R

Table 1 Basic information

Subsets	N (%)
Sex	
Female	4,211 (60.4)
Male	2,760 (39.6)
Age, years	
Median	62.0
≤60	2,861 (41.1)
>60	4,104 (58.9)
Education	
No education	35 (0.5)
Primary school	600 (8.6)
Middle school	5,169 (74.2)
Undergraduate	1,141 (16.4)
Graduate	26 (0.4)
Questionnaire result	
Positive	894 (12.8)
Negative	6,077 (87.2)
FITs results	
Positive	377 (8.3)
Negative	4,187 (91.7)
FITs & questionnaire	
Positive	1,219 (17.5)
Negative	5,752 (82.5)
Colonoscopy testing	
Yes	647 (53.1)
No	572 (46.9)
Colonoscopy results	
Hyperplastic polyp	16 (6.3)
Inflammatory polyp	57 (22.4)
Adenoma	170 (66.7)
Adenocarcinoma	11 (4.3)
Carcinoid	1 (0.4)
Pathology	
Advanced cancer	3 (0.5)
Early cancer	5 (0.8)
CRC of unknown stage	2 (0.3)
Advanced adenoma	81 (13.0)
Other polyps	178 (28.6)
Carcinoid	1 (0.2)
Negative	353 (56.7)

FIT, fecal immunological test; CRC, colorectal cancer.

(version 3.5.3).

Results

Completion rates

As shown in *Table 1*, a total of 6,971 residents from Dadong Street, Yuexiu District were screened by questionnaire, among whom 4,211 (60.4%) were female, and 2,760 (39.6%) were male. The median age was 62.0 years. 16.8% of the population screened had received higher education.

There were 894 (12.8%) subjects positive for the questionnaire, among whom 740 underwent FIT as required, 25 asked for direct colonoscopy examination, the other 129 were lost. Three hundred seventy-seven (8.3%) positive subjects were identified by FITs. The first and second FIT identified 253 and 232 of them, respectively. There were 76 subjects positive for both FITs. In total, Questionnaire and FITs identified 1,219 candidates for further examination with colonoscopy.

Colonoscopy examination

Among the 1,219 candidates for a colonoscopy, only 647 (53.1%) complied with the recommendation. Of them, 77.1% were positive for the questionnaire, and 36.8% were positive for FITs. Compliance rate was higher in patients >60 than in patients ≤60 (61.1% *vs.* 38.9%), although it was not statistically significant (P=0.092). The rate was not associated with sex (P=0.619) and education (P=0.261) (*Table 2*).

The results of the colonoscopy are listed in *Table 3*. As of this writing, 623 colonoscopy reports were obtained, among which 270 (43.3%) had positive findings. The adenoma detection rate (ADR) was 43.3% (270/623). Of the

Table 2 Comparisons between patients with and without colonoscopy follow-up

Name	Follow-up	No follow-up	P value
Sex			0.619
Female	388 (60.0)	351 (61.4)	
Male	259 (40.0)	221 (38.6)	
Age			0.092
≤60	252 (38.9)	250 (43.7)	
>60	395 (61.1)	322 (56.3)	
Questionnaire results			0.001
Positive	499 (77.1)	395 (69.1)	
Negative	148 (22.9)	177 (30.9)	
FIT results			0.093
Positive	161 (36.8)	216 (42.1)	
Negative	277 (63.2)	297 (57.9)	
Higher education			0.261
Yes	156 (24.1)	154 (26.9)	
No	491 (75.9)	418 (73.1)	

FIT, fecal immunological test.

270 patients, 10 (3.07%) had CRC, 81 (30.0%) had advanced adenoma, 178 had low-grade adenoma or other benign polyps, one had carcinoid. Except for three advanced CRC, all neoplasms detected were benign or in an early stage. Neoplasms were more likely to occur in male patients (56.9% *vs.* 34.9%, P<0.001), patients of >60 ages (49.6% *vs.* 35.1%, P<0.001), and patients with chronic constipation (46.0% *vs.* 34.9%, P=0.017).

Comparison of accuracies

Table 4 shows the predictive performance of the questionnaire and FIT. When the detection rate was concerned, the sensitivities of the questionnaire, FITs and their combination were 0.578, 0.475, and 0.919, respectively. The addition of the questionnaire to FITs improved sensitivity by more than 40%, but it also decreased the specificity to 0.088. We then looked into their positive predictive values (PPVs) for neoplasms, and found that PPVs of the questionnaire, FITs, and their combination were 0.397, 0.532, and 0.435, respectively.

Discussion

Population screening for early detection of polyps is thought to be the main reason for the decline in CRC incidence in the US (5,8). In this article, we presented preliminary results of a screening program for CRC in Yuexiu District, Guangzhou, China. We found that primary screening with questionnaire and FIT helped identify a considerable proportion of patients with benign polyps or CRC of early stage. Removing these neoplasms would hopefully help decrease CRC incidence in this area in the future.

Screening with colonoscopy is undoubtedly the most straightforward way to detect neoplasms on the colonic lumen. The problem is to whom we should recommend this test in order to make the best of resources. Take America as an example, to reach the goal of screening 80% of its eligible population with colonoscopy by 2024, 11 to 13 million colonoscopies would be needed annually in a colonoscopy-only program, but only 5.1 million would suffice when coupled with the FIT (9). In previous studies, FIT achieved a sensitivity of 0.8 and a specificity of 0.9. Commitment to an annual test with FIT yielded comparable outcome to that with colonoscopy every 5 years (10,11). In our study, two consecutive FITs yielded a detection rate of 8.3%, which was similar to that reported in the US (7–10%) and Tianjin (5.8%) programs (5,7). However, the sensitivity of FIT was only 47.5%, which meant among 242 colonoscopically confirmed positive patients only 115 were detected by FITs. Several factors may be responsible for this. First, according to an US study, although the accuracy of FIT was superior to that of traditional Hemoccult II testing, it varied between brands (12,13); also, methods of sample collection might have an impact on the result. Collins *et al.* found that specimens taken from spontaneously passed stools were better than those obtained by digital rectal examination (14). Participants in our study were not specifically guided in sample collection.

To further cut down the costs and improve sensitivity, we combined a high-risk screening questionnaire with the FIT as a primary screening regimen. In previous studies, this regimen showed better performance in detection rate and sensitivity than did FIT alone (6,15). In our study, the addition of questionnaire help increase sensitivity to as high as 0.919, and PPVs for neoplasms to 0.435, which were consistent with the results of Tianhe Guangzhou screening

Table 3 Comparisons between participants with positive and negative colonoscopic findings

Name	Positive	Negative	P value
Sex			<0.001
Female	134 (34.9)	250 (65.1)	
Male	136 (56.9)	103 (43.1)	
Age			<0.001
≤60	94 (35.1)	174 (64.9)	
>60	176 (49.6)	179 (50.4)	
Questionnaire results			0.016
Positive	156 (39.7)	237 (60.3)	
Negative	114 (49.6)	116 (50.4)	
FIT questionnaire			0.779
Positive	248 (43.5)	322 (56.5)	
Negative	22 (41.5)	31 (58.5)	
FIT results			<0.001
Negative	127 (37.9)	208 (62.1)	
Positive	115 (53.2)	101 (46.8)	
Chronic diarrhea			0.213
Yes	53 (38.7)	84 (61.3)	
No	217 (44.7)	269 (55.3)	
Chronic constipation			0.017
Yes	52 (34.9)	97 (65.1)	
No	218 (46.0)	256 (54.0)	
Familial colorectal cancer			0.954
Yes	48 (42.5)	65 (57.5)	
No	218 (43.6)	282 (56.4)	
Unknown	4 (40.0)	6 (60.0)	

FIT, fecal immunological test.

program. This questionnaire helped screen for patients with colonic neoplasms. However, it should be noted that the addition of the questionnaire also lead to a dramatic drop of specificity, meaning a considerable proportion of healthy subjects would be referred for unnecessary colonoscopy.

Moreover, when the questionnaire alone was evaluated, its sensitivity was 0.578, and its specificity only 0.393. Therefore, using a questionnaire to screening out ineligible subjects may seem economical, but it risks leaving out 40% of positive cases. Questionnaire alone was no substitute for the FIT, and its economic value should be reassessed.

In addition to screening cost, low adherence to screening protocol presents another challenge. As shown in *Table 1*, the compliance rate for one FIT was 76.6%, and only 65.5% had completed two FITs. The rate of colonoscopy follow-up was even lower, with only 51.3% of the high-risk participants undergoing the procedure. Although the same challenge is also facing screening programs in the US, with the rate ranging from 50% to 80%, the reasons for it may be different from ours. In the US, insurance bears a significant part of the responsibility, since it does not cover the cost of colonoscopy for those positive for FIT (5). In our study, we offered free colonoscopy tests for all eligible subjects; therefore, some other factors were responsible. We first assumed that education might be to blame, but compliance rates were not significantly different between subjects with Higher Education and those without (P=0.261). However, when we looked deeper into the data, we found that 77.1% of the participants undergoing colonoscopy were positive for the questionnaire, while the rate was only 36.8% for FITs, hinting that questionnaire, a self-evaluating tool had a stronger effect than laboratory-assessed FIT in persuading subjects of the necessity of colonoscopy. Thus, raising the public's awareness of the benefits and safety of colonoscopy may help improve compliance.

Several factors can be used as indicators of quality of colonoscopy, among which ADR, defined as the proportion of patients with adenoma or CRC among the population screened, is the most popular one. A target ADR is recommended to be ≥25%. Otherwise, there may be missing polyps (16,17). Our study yielded an ADR of 43.2% (270/625), significantly higher than recommended, suggesting an excellent quality of colonoscopy. The result was consistent with those of other screening programs conducted in the Chinese population, reflecting high operating skills of Chinese colonoscopists in these programs (6,7,15,18-21).

Conclusions

Our screening program help identified patients with colonic neoplasms at an early stage, precluding them from developing into the malignant disease. Long-term results should evaluate the social and economic benefits of this program.

Table 4 Sensitivities and specificities of questionnaire and FIT testing

Colonoscopy	Questionnaire results		FIT results		FIT & questionnaire	
	Positive	Negative	Positive	Negative	Positive	Negative
Positive	156	114	115	127	248	22
Negative	237	116	101	208	322	31
Sensitivities	0.578		0.475		0.919	
Specificities	0.329		0.673		0.088	
NPVs	0.504		0.621		0.585	
PPVs	0.397		0.532		0.435	

FIT, fecal immunological test; NPV, negative predictive value; PPV, positive predictive value.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The institutional review board of Sun Yat-sen University Cancer Center approved this study and written informed consent were obtained from all patients. The authenticity of this article has been validated by uploading the key raw data onto the Research Data Deposit public platform (www.researchdata.org.cn), with the approval RDD number as RDDA2019001156.

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