

Double iFOB Test and Single iFOB Test Positive for Colorectal Cancer Screening: An Experience in Songkhla Province, Thailand

Terachai Songkiatkawin, MD*

Jirat Jiratham-opas, MD*

Vallop Ditsuwan, Ph.D*,†

Thanittha Ditsuwan, Ph.D‡

Dusadee Rammasut, BNS*

Piyatida Suwanchot, BNS*

Supatcharapon Chat, Cert.*

*Hatyai Surgical Endoscopic Center, Hatyai Hospital, Songkhla

†Research and Development Institute, Thaksin University, Songkhla

‡Department of Disease Control 12, Songkhla

Abstract

Objective: This study was aimed to determine single and double immunochemical fecal occult blood test (iFOB) positive rate, prevalence of colorectal cancer (CRC) in average risk individuals (ARIs), burden colonoscopy, and identifying constraints for implementing CRC screening.

Methods: This study was a cross-sectional design. The targeted population was ARI aged between 50-70 years old. Two areas, in Songkhla province, were randomly selected. Fecal immunochemical test (FIT) and colonoscopy were used as screening and diagnostic tests. In Hat Yai, participant received one iFOB test and colonoscopy was indicated for those with a positive FIT. In Na Mom, 1-3 iFOB were provided to each individual and colonoscopy was indicated for the participant with double FIT positive. The study proposal was approved by the Hatyai Hospital Ethical Committee (ID 11 (25/03/2015)) and proper treatments were provided to all CRC suspected case.

Results: In Hat Yai, 883 participants were recruited and FIT positive was 274 (31.03%) whereas 94 (34.31%) received colonoscopy. We found that 8 (9.06%), 1 (1.13%), and 2 (2.27%) were small adenoma, advanced adenoma, and colon cancer. In Na Mom, 930 participants were enrolled. Only 13 (1.40%) participants were double FIT positive and 10 (76.92%) received colonoscopy. The results showed that 3 (30.00%), 2 (20.00%), and 2 (20.00%) were small adenoma, advanced adenoma, and colon cancer. CRC detection rate was 2.20/1,000 ARIs.

Conclusion: This study demonstrated superior colonoscopy participation rate for double FIT positive compared to single FIT positive. Double FIT positive screening strongly preferred over single FIT positive. It abruptly reduced colonoscopy invitee and similar CRC detection rate is reported.

Keywords: Colorectal cancer screening, immunochemical fecal occult blood, fecal immunochemical test, reducing burden of colonoscopy

Correspondence address: Vallop Ditsuwan, Ph.D, Research and Development Institute, Thaksin University, 140 Kanchanavanit Road, Moo 4, Tambon Khoa-Roob-Chang, Amphur Muang, Songkhla 90000, Thailand; Email: lop_di@yahoo.com

INTRODUCTION

Colorectal cancer (CRC) is one of the top five prevalence cancers in Thailand^{1,2}. From 2010-2012, approximately 70% of new CRC patients were diagnosed in late stage or metastasis³⁻⁵. World Health Organization (WHO) suggests that early detection in average risk individual (ARI) at age 50 years by screening of asymptomatic CRC or precursor lesions through population is important intervention resulting in reducing mortality, incidence, and costs of CRC⁶⁻⁸. Several CRC screening tests are available; including stool-based test, radiology, and endoscopic examinations of the colon⁹. Recent years have seen the development of stool-based tests (and for CRC screening being available which fall into three broad categories; 1) guaiac-based fecal occult blood test (gFOB); 2) immunochemical fecal occult blood test (iFOB) or fecal immunochemical test (FIT)¹⁰.

The effectiveness of fecal immunochemical test has been established¹¹⁻¹⁶. FIT is high sensitivity and specificity to CRC I-III and adenoma and non-invasive, low cost, and non-complicated intervention^{12-14, 16,17}. Population based screening programs for ARI, using FIT, are being considered in several countries including Thailand^{9,10,18,19}. However, the effectiveness of FIT (reducing CRC mortality) is highly dependent on participation rate, willingness to take part in colonoscopy, and accessibility to current treatment^{10, 11,18,20-24}. This is a cross-sectional study that was aimed to determine the results of single and double FIT test positive for screening CRC in ARI population and burden of colonoscopy, for diagnostic CRC, in Songkhla province, Thailand.

MATERIALS AND METHODS

Study design, population, and settings

Across-sectional study was conducted from 2015 to 2016. Two areas in Songkhla province (Hat Yai and Na Mom district) was selected, using simple random technique. The target population was average risk Thai individuals aged between 50-70 years old. All had no family history of CRC and was divided into two groups. The first group, in Hat Yai district, received one FIT test. The second group, in Na Mom district, 1-3 iFOB tests were completed for each individual.

Sample analysis

FITs (ABON[®], Inverness Medical Innovations Hong Kong Limited) was used for conducting CRC screening. Samples were collected (using providing fecal container), then transferred to and analyzed at Hatyai Hospital. FIT was considered positive if hemoglobin (Hb) concentration in either sample would exceed the test positivity threshold of 50 ngHb/g feces (100 ngHb/mL buffer).

Screening and diagnosis tests

FIT test was reported to target population within five weeks after sample was collected. In Hat Yai district, all single FIT test positive participants were invited to receive colonoscopy. In Na Mom district, only double FIT test positive (1st and 2nd round, or 1st and 3rd round) participants were invited to receive colonoscopy. Colonoscopy was conducted, by well-trained physicians, at Hatyai and Namom Hospitals.

Data collection and analysis

Data was analyzed using descriptive and inferential statistics (percentage, mean, and standard deviation, and Chi-square-test). Estimated burden of colonoscopy and yields related to CRC screening and diagnosis were calculated based on findings from our CRC screening in two districts. The extrapolation was made based on Songkhla population in 2015 available from the Official Statistics Registration System (OSRS), Department of Provincial Administration (DOPA), Ministry of Interior (MoI), Thailand²⁵.

Ethical approval

The Ethical Committee of Hatyai Hospital approved study protocol (ID 11 (25/03/2015). Proper treatments were provided for all CRC suspected cases. Recommendation to do repeated iFOB was provided for all FIT negative participants.

RESULTS

Socioeconomic characteristics

In this study, 1,816 participants were recruited. Most of participants in Hat Yai (66.82%) and Na Mom (67.20%) districts were female (Table 1). An average age was 59.64 (SD 5.76) years in Hat Yai and 58.48 (SD

Table 1 Demographic characteristics of participant involved CRC screening in Songkhla province

Demographic characteristics	Average risk (n=1,816)	
	Hat Yai (n=883) (%)	Na Mom (n=933) (%)
Gender*		
Female	530 (66.82)	627 (67.20)
Male	293 (33.18)	306 (32.80)
Age (year)*,†		
50-55	259 (29.33)	308 (33.01)
56-60	236 (26.57)	266 (28.51)
60-65	221 (25.03)	227 (24.33)
66-70	167 (18.91)	132 (14.15)
Occupational‡		
Housework	259 (29.33)	7 (0.75)
Labor	207 (23.44)	28 (3.00)
Trading	193 (21.86)	14 (1.50)
Civil service	58 (6.57)	16 (1.71)
Farming	44 (4.98)	869 (93.03)
Others/Not mentioned	122 (13.82)	0 (0.00)

Note *Chi test p -value > 0.05†Mean = 59.64 (SD 5.76) years and independent t-test, p -value > 0.05‡Chi test p -value < 0.05

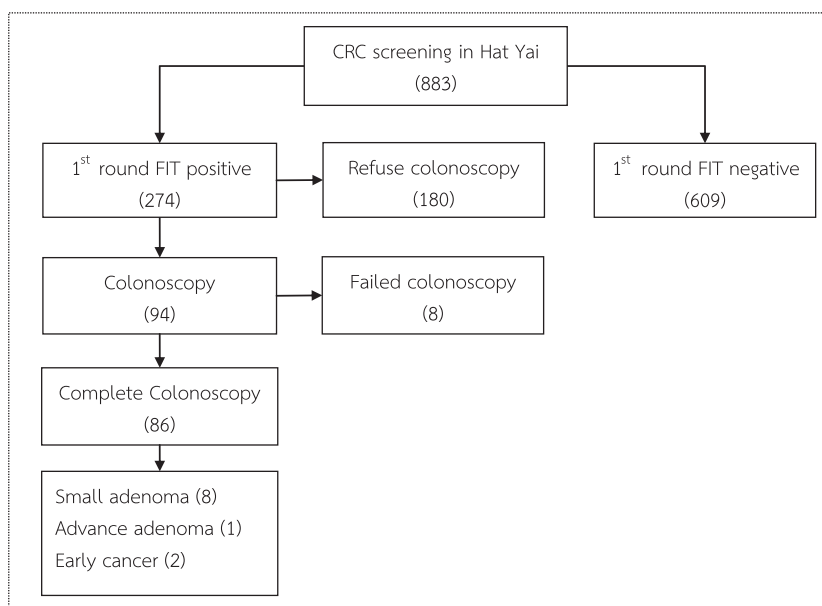
6.45) years in Na Mom. Most of participants in Na Mom were involved in agriculture, but half of participants in Hat Yai were housework or involved in trading. Occupation in rural (Na Mom) and urban area was significant different (Chi-square test, p -value < 0.05).

Yield of CRC screening

In Hat Yai district, 883 participants were recruited for CRC screening (Figure 1). The FIT test showed that 274 (31.03%) participants were positive. Results from colonoscopy showed that 8 (9.30%), 1 (1.16%), and 2 (2.33%) were small adenoma (<1 cm), advanced adenoma (tubulovillous), and colon cancer. Overall colonoscopy accepting rate was 86 (34.31%) whereas colonoscopy failure was 8 (8.51%).

In Na Mom district, 930 participants were involved. The 1st round CRC screening showed that 111 (11.94%) were FIT test positive (Figure 2). In the 2nd round, we found that 12 (10.81%) of 111, 1st FIT positive participants were FIT test positive. In the 3rd round, 1 (1.01%) of 99 2nd FIT negative participants were FIT positive. Finally, total ARIs double FIT test positive and eligible for colonoscopy were 13 (1.40%). The results from colonoscopy showed that 3 (30.00%), 2 (20.00%), and 2 (20.00%) were small adenoma (tubular adenoma < 1 cm), advanced adenoma (tubular adenoma ≥ 1 cm or 1 tubulovillous adenoma 1.5 cm), and colon cancer (1 early stage, 1 advanced stage) respectively. The overall colonoscopy participating rate was 10 (76.92%) while failure rate was zero.

In this study, no serious adverse event was reported during and/or after colonoscopy was performed. In Songkhla province, the prevalence of CRC (or CRC detection rate) in ARI screening, based on single or

**Figure 1** Schematic for and results from CRC screening in Hat Yai district

[†]Multiple counting (each ARI may have more than one result)

Table 3 Yields related to two CRC screening methods in Songkhla province, Thailand 2015*

Yields of CRC screening	Criteria for performing colonoscopy	
	Single FIT positive	Double FIT positive
1. FIT positive (Screening test)		
1 st FIT positive (FIT +)	84,746	32,457
2 nd FIT positive (FIT ++)	-	3,509 [†]
3 rd FIT positive (FIT +++)	-	292 [†]
2. Number of colonoscopy (Diagnostic test)		
Eligible colonoscopy	84,746	3,801
Accepted colonoscopy	29,073 [‡]	2,924 [‡]
3. CRC risk and other conditions		
Adenoma	2,474	877
Advance adenoma	309	585
Others conditions [§]	15,155	2,632
4. Number of CRC (Outputs)		
Early stage CRC	619	292
Advance stage CRC	0	292
Total CRC	619	584

Note *Based on 237,104 ARIs, age 50-70 years in Songkhla province in 2015

[†]Refusing 2nd and 3rd round FIT was low (zero refused rate)

[‡]Colonoscopy accepting or participatory rate (34.31% vs 76.92%) was significantly different (Chi square test, p -value < 0.05).

[§]Other conditions consisted of angiodysplasia, colitis, diverticulum, hemorrhoid, polyps and rectal ulcer.

Burden of colonoscopy and yields from CRC screening in Songkhla province

Extrapolations of total number of FIT positive, burden of colonoscopy, and yields related to single and double FIT positive criteria were investigated in this study. These were done using population in 2015 from the ORSR, DOPA, MoI, Thailand. We found 84,746 and 3,801 ARIs FIT positive and need colonoscopy if single FIT positive (Table 3). If double FIT or single FIT positive is adopted, both screening criteria would provide similar CRC cases in Songkhla province. Based on colonoscopy performing 8-12 cases/day/physician, it would take 8 years to perform and complete colonoscopy if single FIT is adopted. On the other hand, it would take only 292 days to execute colonoscopy if double FIT positive was adopted.

Constraints of implementing colorectal cancer

In this study, we found two issues that would distort CRC screening in Songkhla province. First

limitation is burden of physician and facilities for performing colonoscopy. This is major limitation that associates with proportion of FIT positive result. The second issue is fecal sample collection and FIT test procedure that was done in hospital laboratory. It may reduce feasibility and delay FIT positive report.

DISCUSSION

The overall 1st FIT test positive rate in AVI in Songkhla was 21.24% (385 cases). We found that urban and rural district, 11.94% in Na Mom vs 31.03% in Hat Yai, had dissimilarity in 1st FIT test positive rate (Chi-square test, p -value < 0.05). Chiang *et al.*²¹, investigated in the participant aged over 18 years old and reported that the patients who took FIT test (Hemoglobin less than 50 ng/mg in feces) being positive at 14.2%. On the other hand, comparison with the study in Lampang province¹⁸, which was investigated in the population from 50-65 years old, the participants who took FIT test (existing the hemoglobin less than 200 ng/ml in fecal) provided the positive result of 1.1%. Diversity in FIT positive rate was due to different test positivity threshold (50 ngvs 200 ngHb/g feces (100 ngHb/mL buffer). Another reason was demo-graphic characteristics. Study in Lampang and Songkhla provinces identified huge difference in FIT positive rate in urban and rural areas.

The colonoscopy refused rate was high in single FIT positive (65.69%), but was low in double FIT positive (23.08%). In addition, this study revealed that population in urban area (Hat Yai) tended to refuse colonoscopy more than the people in rural area (Na Mom). Individual health concern, CRC risk perception and living conditions may affect colonoscopy participation.

We found that refusing other screening was a common constraint when screening test was operated in urban area.

In this study, the prevalence of CRC was 2.20/1,000 average risk population. The prevalence of CRC based on single and double FIT test positive was 2.27/1,000 and 2.14/1,000 average risk population. Adenomas and CRC were detected in 50.00% and 20.00% in Na Mom, and 10.47% and 2.33% in Hat Yai, respectively, of those iFOBT positive individuals who had colonoscopy. A study in Lampang showed that there were 3.7% CRC and 30.6% adenomas¹⁸.

Number of FIT positive screenee is huge different comparing between single and double FIT positive. In Songkhla province, we found that colonoscopy delivery is major CRC screening burden. There are two strategies (increasing FIT cut-off, using double FIT positive) for reducing colonoscopic burden. Literature showed that it may reduce by increasing FIT cut-off point which was implemented in Lampang, however, it would increase false negative.

In this study, we anticipated that using double FIT positive would increase specificity of FIT test. To ensure that all the survey was conducted and suggestion based on well ethical consideration; all single FIT positive (+/-) received colonoscopy. The results showed that two subjects (3.23%) was risk of CRC (advanced adenoma).

CONCLUSION

Screening of CRC based on single/double FIT positive criterion in Songkhla province provides a similar CRC detection rate in ARIs. It demonstrated superior colonoscopy participation rate for double FIT positive compared to single FIT positive. We suggested that double FIT positive screening should strongly be preferred over the single FIT positive. We revealed that it reduces huge number of colonoscopy invitee while similar CRC detection rate was reported.

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บทคัดย่อ ประสิทธิภาพการตรวจคัดกรองมะเร็งลำไส้ใหญ่และทวารหนักในกลุ่มเสี่ยงปานกลางจังหวัดสงขลาโดยการตรวจหาเลือดในอุจจาระ ด้วยวิธีเคมีอิมมูโน เปรียบเทียบผลการทดสอบเป็นบวกหนึ่งและสองครั้ง

ธีระชัย ทรงเกียรติคุณ, (พบ, วว. ศัลยศาสตร์)*, จิรัชย์ จิระธรรมโอภาส, (พบ, วว. ศัลยศาสตร์)*, วันลด ดิษสุวรรณ, (ปร.ด. เศรษฐศาสตร์สุขภาพ)*†, ธนิษฐา ดิษสุวรรณ, (ปร.ด. ระบาดวิทยา)*‡, ดุษฎี งามสุด (ศม. การศึกษาเพื่อพัฒนาชุมชน)*, ปิยธิดา สุวรรณโชติ (พย.บ.)*, สุพัชรพล ชชาติ (ปวส.เทคโนโลยีสารสนเทศ)*

วัตถุประสงค์: เพื่อศึกษาผลการตรวจหาเลือดในอุจจาระ ความชุกภาระงานและปัญหาในการตรวจคัดกรองมะเร็งลำไส้ใหญ่และทวารหนักในกลุ่มเสี่ยงปานกลางด้วยวิธีการส่องกล้องทางทวารหนัก

วิธีการศึกษา: การศึกษาเชิงสำรวจในกลุ่มเป้าหมายอายุ 50-70 ปี ที่มีความเสี่ยงต่อการเป็นมะเร็งลำไส้ใหญ่และทวารหนักระดับปานกลาง โดยสุ่มกลุ่มตัวอย่างจาก 2 อำเภอในจังหวัดสงขลา ทำการคัดกรองมะเร็งลำไส้ใหญ่และทวารหนักด้วยชุดทดสอบหาเลือดในอุจจาระด้วยวิธีเคมีอิมมูโน กลุ่มตัวอย่างในอำเภอหาดใหญ่ จะทำการส่องกล้องทางทวารหนักหากมีผลการตรวจพบเลือดในอุจจาระเป็นบวก 1 ครั้ง ส่วนกลุ่มตัวอย่างในอำเภอนาหม่อมจะทำการส่องกล้องทางทวารหนักหากมีผลการตรวจพบเลือดในอุจจาระเป็นบวก 2 ใน 3 ครั้ง

เริ่มศึกษาหลังจากโครงการวิจัยได้รับการพิจารณาอนุมัติจากคณะกรรมการจริยธรรม โรงพยาบาลหาดใหญ่ (ลำดับที่ 11 (25/03/2015))

ผลการศึกษา: อำเภอหาดใหญ่มีผู้เข้าร่วม 883 คน โดย 274 คน (31.03%) ตรวจพบเลือดในอุจจาระและ 94 คน (34.31%) ยินยอมเข้ารับการส่องกล้องทางทวารหนักพบว่า 8 คน (9.06%), 1 คน (1.13%) และ 2 คน (2.27%) เป็น Small adenoma, Advance adenoma และ Colon cancer ตามลำดับ

อำเภอนาหม่อมมีผู้เข้าร่วม 930 คน โดย 13 คน (1.40%) ตรวจพบเลือดในอุจจาระ 2/3 ครั้ง และ 10 คน (76.92%) ยินยอมเข้ารับการส่องกล้องทางทวารหนัก พบว่า 3 คน (30.00%), 2 คน (20.00%) และ 2 คน (20.00%) เป็น Small adenoma, Advance adenoma และ Colon cancer ตามลำดับ

ความชุกของมะเร็งลำไส้ใหญ่และทวารหนักในกลุ่มเสี่ยงปานกลาง จังหวัดสงขลาเป็น 2.20 คน/1,000 ประชากร

สรุปและอภิปรายผล: ผลการศึกษาแสดงให้เห็นอย่างเด่นชัดว่าการตรวจหาเลือดในอุจจาระ โดยใช้ผลการทดสอบเป็นบวก 2 ใน 3 ครั้ง ให้ผลดีกว่าการใช้ผลการทดสอบเป็นบวกครั้งเดียวสำหรับการตรวจคัดกรองมะเร็งลำไส้ใหญ่และทวารหนักในกลุ่มเสี่ยงปานกลาง เนื่องจากสามารถลดภาระงานในการส่องกล้องทางทวารหนักได้จำนวนมาก โดยความสามารถในการค้นหาผู้ป่วยมะเร็งลำไส้ใหญ่และทวารหนักรายใหม่ไม่แตกต่างกัน