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Original Article

Association Between Time to Colonoscopy After Abnormal Fecal Immunochemical Test and Risk of Adenoma, Advanced Colorectal Neoplasia and Colorectal Cancer Incidence

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ABSTRACT

Objective: Colorectal cancer (CRC) is a significant health concern in Thailand, with high incidence and late-stage diagnosis rates. This study investigates the timing of colonoscopy following a positive fecal immunochemical test (FIT) and identifies risk factors for colorectal neoplasms.

Material and Methods: A retrospective analysis included Thai patients aged 50-75 with a positive FIT who underwent colonoscopy. Exclusions were made for prior colonoscopy, colorectal surgery history, hereditary syndromes, inflammatory bowel disease, and incomplete pathology reports. Data from January 2018 to December 2021 were assessed for demographics, colonoscopy findings, and pathology outcomes.

Results: The study encompassed 2,717 participants with balanced age and gender distributions. Preliminary risk factors associated with the development of adenoma and advanced colorectal neoplasia (ACRN) included age [odds ratio (OR): 1.03, 95% confidence interval (CI): 1.02-1.05, p-value<0.001], gender (OR for males: 1.60 for adenoma, 1.69 for ACRN, p-value<0.001), and smoking (OR: 1.92, p-value=0.001). The timing of colonoscopy within one-year post-FIT did not exhibit statistically significant associations with adenoma, ACRN, or CRC.

Conclusion: This study provides valuable insights into CRC screening in Thailand. It suggests that timing within a year of colonoscopy might not be the sole determinant of improved outcomes post-FIT. Preliminary risk factors encompassed age, gender, and smoking. Future studies should focus on larger cohorts to investigate adverse outcomes, such as late-stage CRC and CRC-related mortality.

Keywords: colonoscopy, colorectal cancer, colorectal neoplasms, fecal immunochemical test, screening interval

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INTRODUCTION

Colorectal cancer (CRC) is a significant health concern in Thailand, emerging as the predominant malignancy in males and the third most common in females[1-2]. Unfortunately, over 70% of CRC cases in Thailand are diagnosed at advanced stages, typically stages 3 and 4, where treatment options are limited, and complete recovery is often elusive[1-2]. This underscores the critical importance of effective CRC screening, which remains the primary tool for reducing mortality rates and enhancing patient outcomes.

Current national guidelines recommend CRC screening for individuals aged 50 to 75, offering two key methods: the fecal immunochemical test (FIT), to be taken every 1–2 years, and colonoscopy, to be performed every 5–10 years[3-4]. However, colonoscopy, being an invasive procedure requiring specialized gastroenterologists, poses practical challenges for widespread use.

In response to these challenges, the Ministry of Public Health of Thailand has implemented a two-step screening approach, starting with FIT for at-risk individuals and subsequently followed by colonoscopy in case of a positive FIT result. Nevertheless, ensuring timely colonoscopy within six months of a positive FIT result, as recommended by international studies, continues to be a matter of concern. This is particularly true in the context of the ongoing COVID-19 pandemic and the substantial volume of patients actively participating in this comprehensive screening program[5-7].

This study aims to fill critical knowledge gaps by examining the optimal timing of colonoscopy following a positive FIT result and identifying preliminary risk factors for polyps and CRC in the Thai population. These findings can significantly contribute to the improvement of CRC screening programs in Thailand, ultimately ensuring more timely detection and treatment for those at risk.

MATERIAL AND METHODS

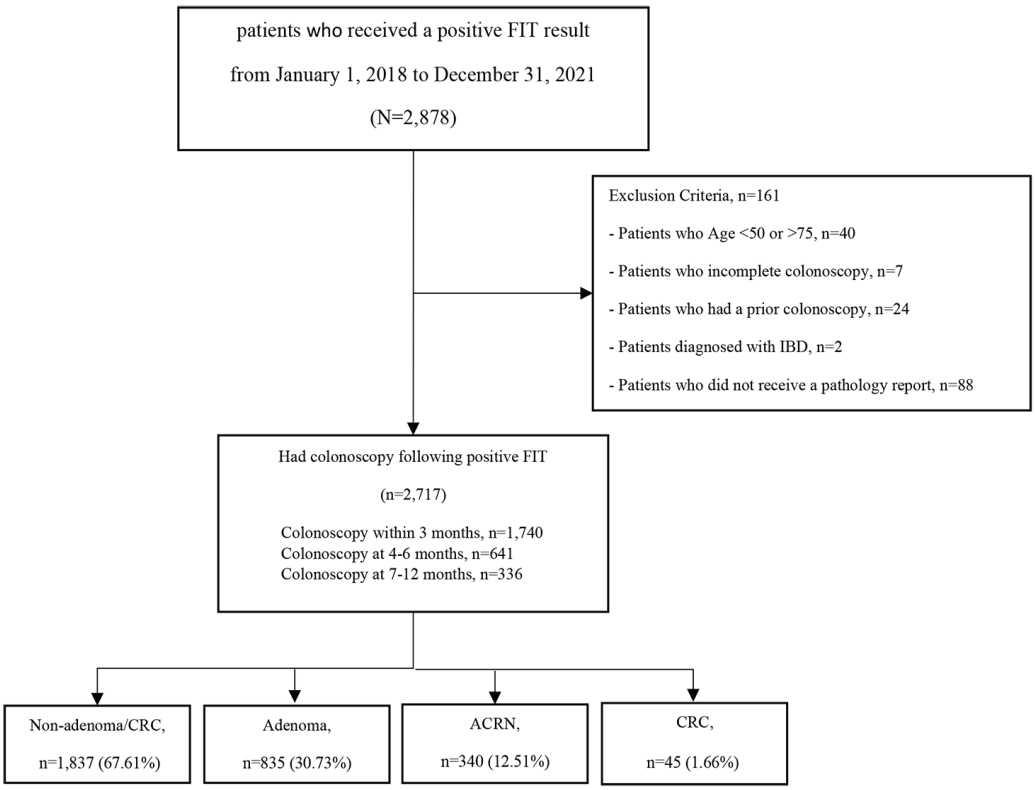
Study population and data collection

We conducted a retrospective analysis targeting Thai patients between the ages of 50 and 75, aligning them with specific inclusion and exclusion criteria. Patients with the following characteristics will be included: (1) Thai nationals aged between 50 and 75 years. (2) Individuals who received a positive FIT result (Weakly positive or Positive). (3) Those who underwent a complete colonoscopy. Excluded from the study are: (1) Individuals who undertook a colonoscopy prior to the detection of fecal occult blood. (2) History of colorectal surgical procedures. (3) Family history of colorectal cancer or genetic syndromes such as Familial Adenomatous Polyposis or Lynch syndrome. (4) Diagnosis of Inflammatory Bowel Disease (IBD). (5) Individuals who, post-colonoscopy and biopsy/polypectomy, did not receive a pathology report.

During the study period, spanning from January 1, 2018, to December 31, 2021, data collection will be conducted at the Inpatient and Outpatient Departments of the Endoscopy Center at Chiangrai Prachanukroh Hospital. The eligible patient cohort will undergo comprehensive data gathering, including demographic details, FIT results, colonoscopy findings, and pathology reports. Subsequently, the acquired data will be stratified into three distinct intervals: 0–3 months, 4–6 months, and 7–12 months following the identification of fecal occult blood, thereby facilitating subsequent statistical analyses. Detailed of study flow is presented in Figure 1.

Outcomes and statistical analysis

The primary objectives of this study encompass examining the correlation between the time interval from a positive FIT result to colonoscopy and the incidence of adenoma, advanced colorectal neoplasia (ACRN) and CRC. Moreover, the study seeks to identify preliminary risk factors associated with these outcomes.



FIT=fecal immunochemical test; FAP=familial adenomatous polyposis; IBD=inflammatory bowel disease; CRC=colorectal cancer; ACRN=advanced colorectal neoplasm

Figure 1 Patient flow diagram

ACRN is defined as a colonic polyp larger than 10 mm in size, exhibiting tubulovillous or villous architecture, or displaying high-grade dysplasia. CRC is pathologically defined as adenocarcinoma.

We used descriptive statistics to describe patient demographic and laboratory factors. To assess the relationship between the time interval and outcomes while controlling for confounding factors, multivariate logistic regression analysis will be performed. These confounding factors include age, gender, body mass index (BMI), smoking history, and anemia status. Statistical significance will be set at p-value<0.05. The data analysis will be executed using Stata 16 software.

RESULTS

Demographic and clinical characteristics of the study population

In our 2,717 participants, the mean age of the entire study population was 60.18 years (±5.53). Gender distribution was balanced, consisting of 44.83% males and 55.17% females. The mean body mass index (BMI) was 23.69 kg/m2 (±6.73), with participants categorized into underweight (6.50%), normal weight (39.28%), overweight (22.78%), and obese (31.16%) groups. A small proportion of participants reported being current smokers (4.42%). Concerning hemoglobin concentration, the mean value was 12.9 mg/dL (±1.57), with 69.78% within the normal

range, 26.46% having mild anemia, and 3.75% having moderate to severe anemia. Detailed distributions of these demographics and clinical characteristics are presented in Table 1.

Comparison between adenoma groups

Table 2 presents demographic and clinical characteristics across different colorectal conditions. Among participants without adenoma/CRC (67.61%), the mean age was 59.84 years (±5.47) and a gender distribution of 40.66% males and 59.34% females. For those with adenomas (30.73%), the mean age slightly rose to 60.86 years (±5.59) and a gender distribution of 54.01% males. The ACRN group (12.51%) had a mean age of 60.18 years (±5.53) and 56.76% males. Finally, participants diagnosed with CRC (1.66%) were older, with a mean age of 61.02 years (±5.53) and 46.67% being male. BMI, smoking status, and hemoglobin level also varied across these groups.

Table 1 Demographic and clinical characteristics of study population

Patient characteristic	Total (n=2,717)
Age, year (mean±S.D.)	60.18±5.53
Sex, n (%)	
Male	1,218 (44.83)
Female	1,499 (55.17)
BMI, kg/m^2 (mean±S.D.)	23.69±6.73
BMI categorical, n (%)	
Underweight	176 (6.50)
Normal	1,064 (39.28)
Overweight	617 (22.78)
Obese	844 (31.16)
Current smoker, n (%)	120 (4.42)
Hemoglobin, mg/dl (mean±S.D.)	12.9±1.57
Normal (13 in male, 12 in female), n (%)	1,896 (69.78)
Mild anemia (10 – lower limit of normal), n (%)	719 (26.46)
Moderate to severe anemia (less than 10), n (%)	102 (3.75)

BMI=body mass index; S.D.=standard deviation

Table 2 Demographic and clinical characteristics of study population with adenoma (categorical)

Patient characteristic, n (%)	Non-adenoma/CRC, 1,837 (67.61)	Adenoma, 835 (30.73)	ACRN, 340 (12.51)	CRC, 45 (1.66)
Age, year (mean±S.D.)	59.84±5.47	60.86±5.59	60.18±5.53	61.02±5.53
Sex, n (%)				
Male	747 (40.66)	451 (54.01)	193 (56.76)	21 (46.67)
Female	1,090 (59.34)	384 (45.99)	147 (43.24)	24 (53.33)
BMI, kg/m^2 (mean±S.D.)	23.69±7.78	23.68±3.77	23.61±3.62	23.65±2.93
BMI categorical, n (%)				
Underweight	120 (6.60)	54 (6.50)	19 (5.60)	1 (2.22)
Normal	714 (38.95)	332 (39.95)	140 (41.30)	19 (42.22)
Overweight	434 (23.68)	173 (20.82)	72 (21.24)	11 (24.44)
Obese	557 (30.39)	271 (32.61)	107 (31.56)	14 (31.11)
Current smoker, n (%)	61 (3.32)	59 (7.07)	18 (5.29)	0 (0)
Hemoglobin, mg/dl (mean±S.D.)	12.82±1.55	13.11±1.58	13.14±1.57	12.48±1.67
Normal (13 in male, 12 in female)	1,248 (67.94)	618 (74.01)	248 (72.94)	30 (66.67)
Mild anemia (10 – lower limit of normal)	517 (28.14)	189 (22.63)	82 (24.12)	13 (28.89)
Moderate to severe anemia (less than 10)	72 (3.92)	28 (3.35)	10 (2.94)	2 (4.44)

ACRN=advanced colorectal neoplasia; CRC=colorectal cancer; S.D.=standard deviation; BMI=body mass index

Association between time to colonoscopy and risk of adenoma, ACRN, and CRC

Table 3 demonstrates the association between the duration from an abnormal FIT to a colonoscopy and the risk of adenoma, ACRN, and CRC incidence. For those undergoing colonoscopy within 1–3 months post–FIT, they served as the reference group. However, when the wait was extended to 4–6 months, there was a slight increase in the odds for adenoma at an unadjusted OR of 1.22 (95% CI: 1.01–1.49, p–value=0.04) and an adjusted OR of 1.21 (95% CI: 0.99–1.47, p–value=0.06), although no significant associations were observed for ACRN (adjusted OR: 0.95, 95% CI: 0.72–1.25, p–value=0.73) and CRC (adjusted OR: 0.56, 95% CI: 0.24–1.28, p–value=0.17). For those waiting 7–12 months, the odds ratios suggested no increased risk for adenoma (adjusted OR: 0.93, 95% CI: 0.72–1.21, p–value=0.61), ACRN (adjusted OR: 0.77, 95% CI: 0.53–1.12, p–value=0.18), or CRC (adjusted OR: 0.60, 95% CI: 0.21–1.71, p–value=0.34) compared to the reference group.

Table 3 Association between time to colonoscopy after abnormal FIT and risk of adenoma, ACRN and CRC incidence

Time to colonoscopy after abnormal FIT, months	Total	Adenoma	ACRN	CRC	Incidence Adenoma unadjusted OR (95% CI)	Incidence Adenoma adjusted OR (95% CI)	Incidence ACRN unadjusted OR (95% CI)	Incidence ACRN adjusted OR (95% CI)	Incidence CRC unadjusted OR (95% CI)	Incidence CRC adjusted OR (95% CI)
1–3	1,740	512	223	33	REF	REF	REF	REF	REF	REF
4–6	641	219	80	7	1.22 (1.01–1.49)	1.21 (0.99–1.47)	0.96 (0.73–1.27)	0.95 (0.72–1.25)	0.55 (0.24–1.26)	0.56 (0.24–1.28)
7–12	336	97	36	4	0.98 (0.76–1.27)	0.93 (0.72–1.21)	0.81 (0.56–1.18)	0.77 (0.53–1.12)	0.60 (0.21–1.71)	0.60 (0.21–1.71)

FIT=fecal immunochemical test; ACRN=advanced colorectal neoplasia; CRC=colorectal cancer; OR=odds ratio; CI=confidence interval; REF=reference

Preliminary risk factors

Table 4 presents preliminary risk factors associated with the development of adenoma, ACRN, and CRC. Statistically significant odds ratios (ORs) indicate factors that influence the risk of adenoma and ACRN. Age displayed a significant association with both adenoma (OR: 1.03, 95% CI: 1.02–1.05, p–value<0.001) and ACRN (OR: 1.03, 95% CI: 1.01–1.05, p–value=0.005), with each yearly increase in age associated with higher odds of these conditions. Being male significantly increased the risk of adenoma (OR: 1.60, 95% CI: 1.35–1.89, p–value<0.001) and ACRN (OR: 1.69, 95% CI: 1.34–2.15, p–value<0.001), whereas their odds for CRC were not statistically significant. Current smokers had a significantly elevated risk of adenoma (OR: 1.92, 95% CI: 1.31–2.80, p–value=0.001) but showed no significant association with ACRN. Obese individuals showed a non–significant trend towards higher odds for adenoma. Interestingly, having anemia (below the normal limit) was associated with reduced odds of adenoma (p–value: 0.001) but did not significantly impact ACRN or CRC odds.

These statistically significant findings underscore the importance of age, gender, and smoking status as influential factors in the development of adenomas and advanced colorectal neoplasia within our study population.

DISCUSSION

Optimal timing of colonoscopy

Our research explored the correlation between the interval from a positive FIT to a subsequent colonoscopy within one year and the occurrence of adenoma, advanced

Table 4 Preliminary risk factore

Patient characteristic	Odds ratio for Adenoma (95% CI)	p-value	Odds ratio for ACRN (95% CI)	p-value	Odds ratio for CRC (95% CI)	p-value
Age, Year	1.03 (1.02–1.05)	<0.001	1.03 (1.01–1.05)	0.005	1.03 (0.97–1.08)	0.32
Sex, Male	1.60 (1.35–1.89)	<0.001	1.69 (1.34–2.15)	<0.001	1.15 (0.63–2.08)	0.64
Current smoker	1.92 (1.31–2.80)	0.001	1.01 (0.59–1.71)	0.97	omitted	
BMI categorical; Obese	1.17 (0.98–1.40)	0.085	1.05 (0.81–1.34)	0.72	0.98 (0.51–1.88)	0.96
Anemia	0.72 (0.60–0.88)	0.001	0.80 (0.62–1.04)	0.09	1.08 (0.57–2.05)	0.81

ACRN=advanced colorectal neoplasia; CRC=colorectal cancer; BMI=body mass index

colorectal neoplasia ACRN, and colorectal cancer CRC in the Thai population. The study revealed that the timing of colonoscopy within one year following a positive FIT result did not show statistically significant associations with the risk of these outcomes. This finding suggests that the timeframe within which colonoscopy is conducted may not be a critical determinant of the incidence of adenoma, ACRN, or CRC in this specific population. Our results align with previous studies that have reported mixed findings regarding the impact of time to colonoscopy on colorectal neoplasm risk[3,5].

The study by Gellad et al[3]. found no significant association between the time interval from a positive fecal occult blood test to colonoscopy and the risk of advanced colorectal neoplasia. In contrast, Corley et al[4]. reported that a delay in colonoscopy after a positive fecal test result was associated with an increased risk of colorectal cancer and higher cancer stage at diagnosis. However, it's important to note that these studies were conducted in different populations, and variations in healthcare systems and patient demographics may contribute to the differences in results.

Our findings may provide reassurance to healthcare systems facing challenges in providing prompt colonoscopy services, particularly during the ongoing COVID-19 pandemic. While timely access to colonoscopy remains a crucial component of colorectal cancer screening.

Preliminary risk factors

Our study identified several preliminary risk factors associated with the development of adenoma and ACRN. Age exhibited a significant association with both adenoma and ACRN, with each yearly increase in age associated with higher odds of these conditions. This finding is consistent with previous research demonstrating that advancing age is a well-established risk factor for colorectal neoplasms[4,5].

Being male was found to significantly increase the risk of adenoma and ACRN, highlighting the gender-related differences in susceptibility to these conditions. Previous studies have also reported a higher incidence of colorectal neoplasms in males[4,5].

Current smoking emerged as a notable risk factor, with current smokers having a significantly elevated risk of adenoma. This finding is in line with existing evidence linking smoking to an increased risk of colorectal neoplasms[4,5].

We found that individuals with anemia below the normal limit had significantly reduced odds of adenoma. However, this association did not significantly affect the odds of ACRN or CRC. Given that our study was conducted in Northern Thailand, where there is a high prevalence of thalassemia patients, this may have acted as a confounder in our analysis.

Our study suggests that other factors, such as age, gender, and smoking status, may play more substantial roles in the development of colorectal neoplasms in the

Thai population. These results underscore the complexity of colorectal cancer risk factors and the need for a multifaceted approach to screening and prevention.

Practical Implications

Our study contributes valuable insights into CRC screening programs in Thailand. The absence of a statistically significant association between the timing of colonoscopy after a positive FIT result and the risk of adenoma, ACRN, or CRC suggests that timely access to colonoscopy may not be the sole determinant of improved outcomes. This finding may provide reassurance to healthcare systems facing challenges in providing prompt colonoscopy services, particularly during the ongoing COVID-19 pandemic. However, it is essential to consider that our study focused on a specific population, and further research is warranted to validate these findings in broader contexts.

Limitation

Several limitations of this study should be acknowledged. First, the retrospective nature of the study introduces potential bias and limits our ability to establish causation. Second, the study population was confined to a specific age group and may not be representative of the entire Thai population. Third, we relied on clinical data, which may have limitations in accuracy and completeness. Finally, the study did not explore other potential risk factors that could contribute to the development of colorectal neoplasms.

CONCLUSION

In conclusion, our study provides insights into the association between the timing of colonoscopy after a positive FIT result and the risk of adenoma, ACRN, and CRC in the Thai population. We found that the timing of colonoscopy did not show statistically significant associations with these outcomes, suggesting that other factors may play a more significant role in the development of colorectal neoplasms. Age, gender, and smoking status were identified as preliminary risk factors, emphasizing the need for a multifaceted approach to colorectal neoplasm prevention and screening.

These findings can inform healthcare strategies in Thailand and contribute to the refinement of CRC screening programs. However, further research is required to validate these findings and explore additional risk factors that may influence colorectal neoplasm development in diverse populations. Our study underscores the importance of continued efforts to enhance early detection and prevention of colorectal neoplasms, ultimately improving patient outcomes and reducing the burden of CRC in Thailand.

CONFLICT OF INTEREST

The author declares no conflict of interests.

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