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The comparison of fecal occult blood test screening and flexible sigmoidoscopy in reducing mortality risk in colorectal cancer patients: Systematic review and meta-analysis

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Introduction: Colorectal cancer is a malignancy originating from the colon and is the second most common new case in women. Most patients come for treatment at an advanced stage so they have a low life expectancy. Screening in colorectal cancer patients is expected to be used for early detection so as to speed up the management of colorectal cancer patients. Fecal occult blood test (FOBT) and flexible sigmoidoscopy (FS) are colorectal cancer screening that has been applied. However, the effectiveness of the two is still contradictory, so a systematic review and meta-analysis is needed to evaluate their effectiveness.
Objective: To explore the use of FOBT and FS in colorectal cancer screening.
Methods: A literature search was performed on Pubmed, Google scholars, and Cochrane, CINAHL. Selection of titles and abstracts based on inclusion and exclusion criteria, double filter, journal read in full. This study was assessed for its validity.
Result: There are 10 journals analyzed. The use of FS is more effective than FOBT in reducing colorectal cancer mortality. The use of FOBT has an effect on colorectal cancer mortality 0.86 (95% CI 0.79, 0.94 p = 0.001). The use of FS had a significant effect on colorectal cancer 0.82 (95% CI 0.88, 0.98 p = 0.03). Both of these screenings cannot reduce the incidence of colorectal cancer.
Conclusion: FS more effective to reducing mortality than FOBT on colorectal cancer.

Keywords: fecal occult blood test, flexible sigmoidoscopy, colorectal cancer

INTRODUCTION

Colorectal cancer is a malignancy originating from the large intestine, consisting of the colon and/or rectum. According to a Globocan study (2020), colorectal cancer is the second most common new case in women after breast cancer, and the third most common cancer in men after lung and prostate cancer.[1] In Asia itself, there has been a significant increase in both the incidence and mortality of colorectal cancer, and there are data that the incidence (51.8%) and mortality (52.4%) per 100,000 population are the highest in the world.[2] The prevalence of colorectal cancer based on research at Referral Hospitals in Indonesia showed 73.7% of all gastrointestinal malignancies in 2002-2011.[3] The prevalence of colorectal cancer is estimated to increase by 2.38% annually. Colon cancer increased 9.24% in adolescents and decreased prevalence of rectal cancer. The increase in the prevalence of right-sided colorectal cancer also increased by 6.52% in all populations and 6.57 in elderly patients and left-sided colorectal cancer did not experience an increase.[4]

The incidence of colorectal cancer is mostly found in individuals over 60 years of age. This new case finding is also influenced by the increasing ability of the early diagnosis of colorectal cancer. Most patients come for treatment at an advanced stage so they have a low life expectancy.[5] Screening in colorectal cancer patients is needed for early detection thereby accelerating the management of colorectal cancer patients.

An ideal screening for colorectal cancer should have high sensitivity and sensitivity, be safe, and be inexpensive.[6] Fecal Occult Blood Testing (FOBT) is a screening modality for colorectal cancer in patients with suspected gastrointestinal cancer. FOBT can be used to detect heme or globin resulting from gastrointestinal bleeding.[7] This method is often used because it is non-invasive. This method is used in several countries such as France, Finland and United Kingdom.[6]

In addition to non-invasive methods, several invasive methods are also often used, such as flexible sigmoidoscopy (FS) and colonoscopy. This method can directly visualize and detect colonic polyps and advanced malignancy. This method is used in several developed countries such as America, Germany, Poland, Austria and Italy.[6] Research on the comparison of these two methods is still controversial. Therefore, a systematic review is needed to discuss the effectiveness of these two screening methods for colorectal cancer.

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The aim of this study was to identify a randomized control trial on FOBT or FS as a screening modality in the asymptomatic population and to differentiate the effectiveness of colorectal cancer mortality using sigmoideoscopy and FOBT methods.

METHOD

Research Design

The article included in this study was a randomized controlled trial with the topic of colorectal cancer which reported mortality from colorectal cancer that had been screened by sigmoidoscopy, FOBT or without screening. The FOBT examination included in this study was the FOBT examination.

Data Collection

The literature search was completed on December 17, 2022 from 3 databases, namely Pubmed, Google Scholars, and Cocraine. The keywords used were "FOBT", "fecal occult blood test", "Flexible Sigmoidoscopy", "mortality", and "risk factor" and their combinations. The inclusion criteria were research journals and English. The exclusion criteria are journals that are not free to download, review articles, and systematic reviews. The results of the three databases. The journals are screened for titles and abstracts according to the inclusion and exclusion criteria, filtered for multiple journals and can be accessed freely. After reading the article, a critical appraisal was carried out.

The population in this study was over 18 years old as a volunteer or a population taken from medical records. The intervention in this study was the use of FOTB using a guaic test whether using rehydration or not and using an immunological test. Sigmoidoscopy examination using an endoscope. The outcome of this study was the mortality of the patients who were screened. In addition, an analysis of the incidence of colorectal cancer after screening was carried out.

Bias Analysis

Assessment of method quality was performed by reviewers according to the Cochrane collaboration bias determination tool.

Data Analysis

The relative risk results of each study will be analyzed using Review Manager 5.0. Results are considered significant if $p < 0.05$. Heterogeneity was assessed using the Higgins I^2, which evaluates the percentage of total variation across studies that is attributable to heterogeneity. If $I^2 > 50\%$, which is considered to reflect substantial heterogeneity, a random effect model is used. If $I^2 \leq 50\%$, which is considered not to reflect heterogeneity, the fixed effect model is used.

RESULT

The literature search on systematic reviews uses the PRISMA method as follows.

The figure above describes the selection of journals for this systematic review and meta-analysis. Journal searches used Pubmed, Google Scholars, and Cochrane databases. From the three databases, 833 journals were obtained whose titles were relevant to the topic, which were then checked for duplication and read. The last number of journals used were 10 randomized control trial journals, the bias analysis of all of these journals was shown in Table 1.

Bias analysis from 9 randomized control trial showed that majority of research have good quality,[8-16] except got Lindholm with moderate quality.[17]

The results of the literature search are in Table 2 and Table 3. Based on these results it is known that there are 10 journals that examine mortality and 6 studies on colorectal cancer incidence. The highest number of subjects and the longest follow-up were in the study of Scholefield et al., 2012. In the journals that examined mortality, there were 5 journals each that examined FOBT and FS screening. In the journals that researched incidence, there were 4 journals that researched using FS and 2 journals that researched using FOBT.

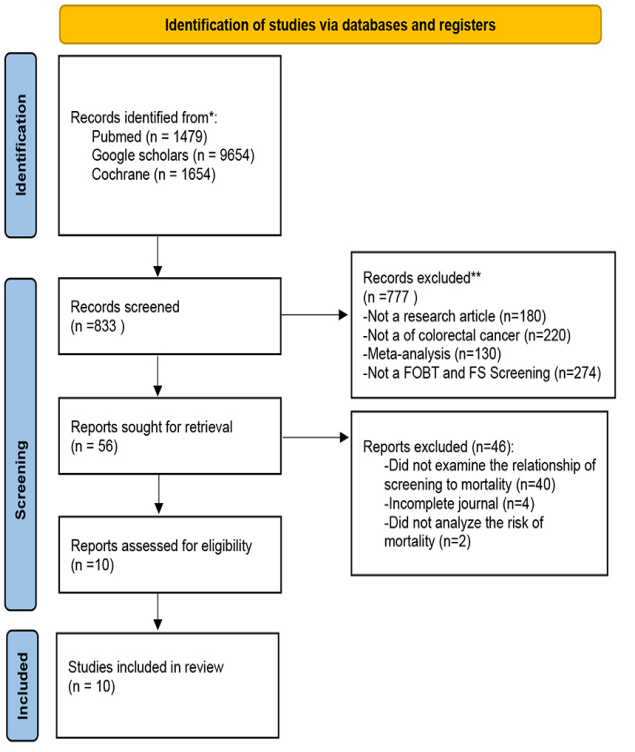

Figure 1. Journal Selection Flow

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Table 1. Bias Analysis

Author	Randomization (Selection Bias)	Allocation concealment (Selection Bias)	Blinding (Performance Bias)	Incomplete outcome data (Attrition bias)	Selective reporting (Reporting bias)	Quality
Atkin 2002[8]	+	+	+	+	+	Good
Atkin 2010[9]	+	+	+	+	+	Good
Hoff 2009[10]	+	+	+	+	+	Good
Holme et al., 2014[11]	+	+	+	+	+	Good
Jorgensen 2002[12]	+	+	+	+	+	Good
Schoen 2012[13]	+	+	+	+	+	Good
Scholefield 2012[14]	+	+	+	+	+	Good
Scholefield 2002[15]	+	+	+	+	+	Good
Segnan 2011[16]	+	+	+	+	+	Good
Lindholm 2008[17]	-	+	+	+	+	Moderate

Table 2. Review of Mortality Journal of Colorectal Cancer Patients After Screening

Author	Population		Screening	Follow up (years)	Risk Relative	Hazard Ratio
	Control	Intervention				
Atkin *et al.*, 2010[9]	112939	57099	FS	11	-	0.97 (0.94–1.00)
Hoff *et al.*, 2009[10]	13823	41913	FS	7	-	0.73 (0.47-1.13)
Holme *et al.*, 2014[11]	78220	10283	FS	13	-	0.73 (0.55-1.1)
Jorgensen *et al.*, 2002[12]	351670	352343	FOBT	13	0.82 (0.69-0.97)	-
Lindholm *et al.*, 2008[17]	34164	34144	FOBT	9	0.84 (0.71-0.99)	-
Schoen *et al.*, 2012[13]	77455	77455	FS	5	0.84 (0.67-1.06)	-
Scholefield *et al.*, 2002[15]	843463	844419	FOBT	10	0.87 (0.78-0.97)	-
Scholefield *et al.*, 2012[14]	1286877	1286526	FOBT	20	0.91 (0.78-0.97)	-
Segnan *et al.*, 2011[16]	17136	9911	FS	10	0.78 (0.58-1.08	-

Figures 2 and 3 show an analysis of the use of screening on mortality in colorectal cancer patients. The results of the analysis showed that the use of FOBT had an effect on colorectal cancer mortality 0.86 (95% CI 0.79, 0.94 p = 0.001). The use of FS had a significant effect on colorectal cancer 0.82 (95% CI 0.88, 0.98 p = 0.03).

Figures 4 and 5 show an analysis of the use of screening on the incidence of colorectal cancer patients. The results of the analysis showed that the use of FOBT and FS had no effect on the incidence of colorectal cancer.

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Table 3. Journal of Incidence of Colorectal Cancer Patients After Screening

Author	Population		Screening	Follow up (years)	Risk Relative	Hazard Ratio
	Control	Intervention				
Atkin *et al.*, 2002[8]	113178	40674	FS	15	1.7 (1.6–1.7)	-
Atkin *et al.*, 2010[9]	112939	57099	FS	11	-	0.77 (0.70–0.84)
Schoen *et al.*, 2012[13]	77455	77455	FS	5	0.79 (0.72-0.85)	-
Scholefield *et al.*, 2002[15]	843463	844419	FOBT	10	0.99 (0.91-1.07)	-
Scholefield *et al.*, 2012[14]	1286877	1286526	FOBT	20	0.97 (0.91-1.03)	-
Segnan *et al.*, 2011[16]	17136	9911	FS	10	0.82 (0.69-0.96)	-

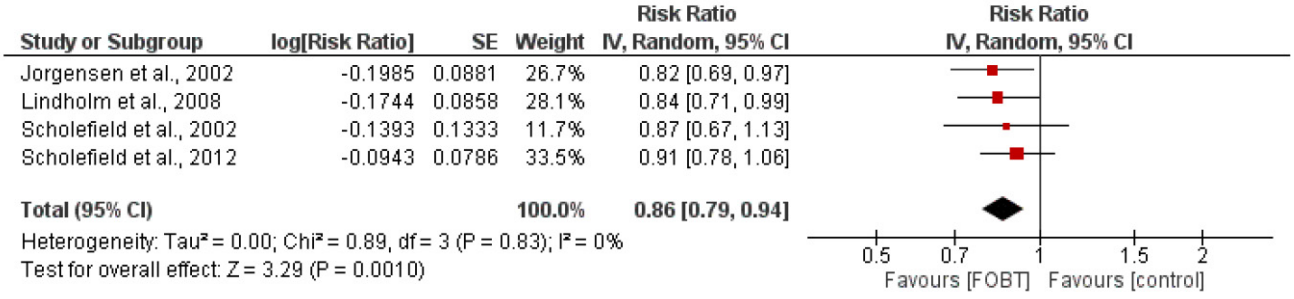

Figure 2. FOBT Analysis of Colorectal Cancer Patient Mortality

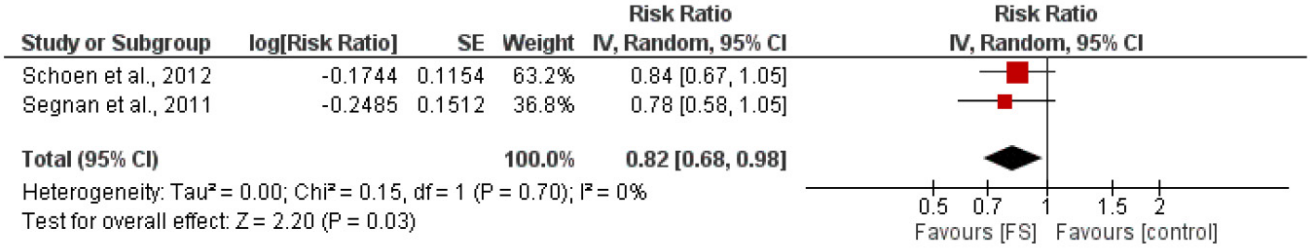

Figure 3. FS Analysis of Colorectal Cancer Patient Mortality

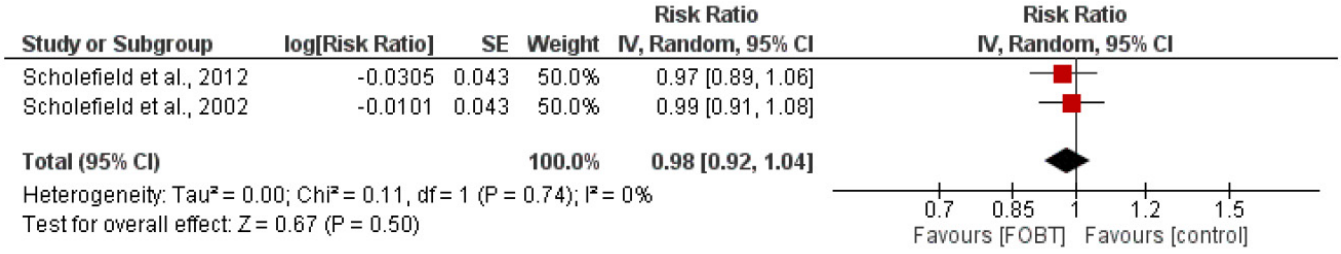

Figure 4. FOBT Analysis of the Incidence of Colorectal Cancer Patients

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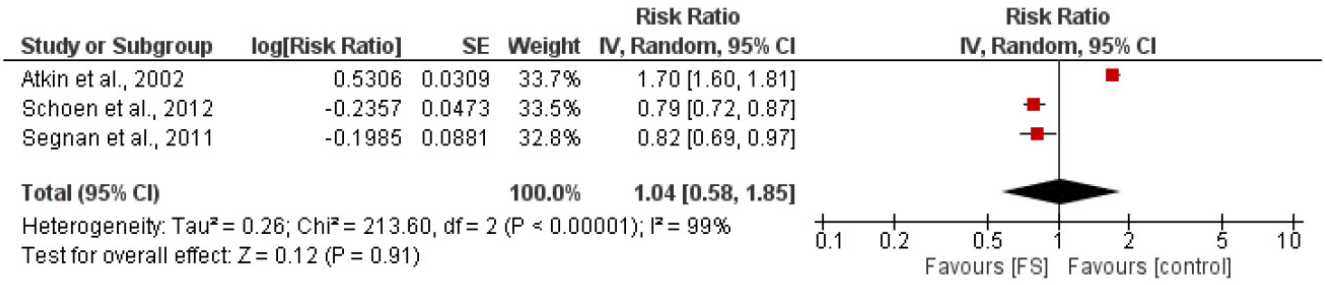

Figure 5. FS Analysis of the Incidence of Colorectal Cancer Patients

DISCUSSION

FOBT is a screening procedure that is commonly used to evaluate the blood content in stool. This study shows that FOBT is associated with mortality of colorectal cancer patients. However, FOBT is not associated with colorectal cancer incidence.

Several studies have shown that the use of FOBT can increase the incidence due to sensitive and specific early detection. Research in Denmark by Jorgensen et al., (2002) showed that there was a decrease in the mortality of patients who underwent FOBT screening.[12] The results of this study were also supported by the study of Lindholm et al (2008) which showed that screening in Sweden could reduce the mortality rate of CRC patients.[17] These results was also supported by research by Scholefield et al., (2002) and Scholefield et al., (2012).[14,15]

FOBT is not assosiated to the incidence of colorectal cancer. It shows that FOBT cannot predict the incidence of colorectal cancer. This result is different from previous research. Research by Ramdzan et al (2019) showed that FOBT is a screening method with a sensitivity level of 31% (95% CI: 25.38%) and a specificity of 87% (95% CI: 86.89%).[7] This difference in results is thought to be caused by differences in the number of studies used.

The use of FS to detect advanced colorectal neoplasms is already used for colorectal cancer screening in Germany. This method has a sensitivity value of 92% for detecting colorectal cancer.[18] The results of this study indicate that the FS method significantly reduces mortality in colorectal cancer. Three previous studies also showed that there was a decrease in the hazard ratio in patients who were screened for FS compared to controls.[9-11]

The results of this study indicate that the use of the FS method for screening didn't associated with the incidence of colorectal cancer. This result is different from previous research. In another study conducted in America, it was found that screening using FOBT showed a significant reduction in the number of new cases of colorectal cancer. patients had performed FOBT.[19]

Mortality in colorectal cancer patients can be caused by cancer and non-cancer. Patients after a diagnosis of colorectal cancer have a higher risk of communicable diseases, such as septicemia within the first year, regardless of age. In addition, deaths from suicide and self-inflicted injury significantly increase over the age of 50 compared to the general population.[20]

The most common non-cancer deaths are cardiovascular disease, especially heart disease and cerebrovascular disease. The high risk of heart disease in colorectal cancer patients may be due to cardiac side effects of systemic chemotherapy. Acute cardiotoxicity is a potentially high side effect of 5-FU and capecitabine treatment.[21]

This study shows that FOBT and FS can reduce the mortality of colorectal cancer patients. However, this study did not evaluate the side effects of the two methods and the costs used.

This study has several limitations that should be considered when interpreting the results. The quality of the primary studies included in the meta-analysis varies, and some studies may have limitations in their design or reporting that could affect the overall results. Additionally, some studies may not provide long-term follow-up data, limiting the ability to assess the long-term effectiveness of fecal occult blood test screening and flexible sigmoidoscopy. Differences in the intervals at which the screening tests were administered across studies may affect the outcomes and limit the generalizability of the findings. Furthermore, the included studies may originate from different countries with varying healthcare systems, and demographic differences among study populations could impact the applicability of the results to other settings. Incomplete reporting of adverse effects or complications associated with the screening methods is another limitation, as this information is crucial for a comprehensive assessment of the benefits and risks. Finally, if the review only includes studies published in English, it may exclude relevant research published in other languages, potentially introducing language bias.

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CONCLUSION

Colorectal cancer screening using the FS method is more effective in reducing patient mortality than FOBT. Neither of these screenings can reduce the incidence of colorectal cancer.

Further research is needed to evaluate the side effects and costs involved. This aims to consider the application of the screening widely.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

ETHICAL STATEMENT

Ethical approval was not required due to the nature of this study which use online registry databases.

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AUTHORS' CONTRIBUTIONS

The study was conducted and the manuscript was written solely by the author.

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