

## Colonic diverticulosis as an isolated colonoscopy finding for iFOBT-positive patients

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### ABSTRACT

Colonic diverticular disease is a common medical condition throughout the world. It is one of the most common findings during the endoscopic evaluation of the colon, such as colonoscopy. A retrospective cohort single-center study was carried out for all patients referred for colonoscopy with a positive immunochemical fecal occult blood test (iFOBT) results in 2016–2018, mostly within the National Bowel Cancer Screening Program in QLD, Australia. The cohort of 319 patients was isolated from all iFOBT-positive individuals with such finding as diverticular disease. Colonic diverticulosis affected the patients above 43 years old with positive iFOBT, more males than females in this study. In most cases, colonoscopy consisted of benign findings, and diverticular disease was revealed in 47.7% of the patients with such indication for colonoscopy as positive iFOBT. About 28.8% of the patients were diagnosed with colonic diverticulosis only. The sigmoid colon was affected by diverticulosis in 96.2% of the cases. Overall, colorectal cancer (CRC) diagnosis rate of 2.7% for the patients in the positive FOBT cohort (Group A) is comparable with other studies. However, the diverticulosis group's CRC rate of 1.6% (Group B) was lower than in available published data.

**Key words:** *Bowel cancer, Colonic diverticulosis, Colonoscopy*

The National Bowel Cancer Screening Program (NBCSP) in Australia started in 2006, aiming to reduce morbidity and mortality from bowel cancer. Initially, it was restricted to 55–65-year-old patients and extended to 50 years old in 2008. The latest guidelines in 2020 recommend biennial screening that covers a population from 50 up to 74 years. The current participation is around 41% of the targeted population, and reduced mortality is down to 15% among targeted program participants due to early diagnosis of bowel cancer during colonoscopy (as per data in 2019) [1].

NBCSP test kit consists of two immunochemical fecal occult blood tests (iFOBTs) that need to be done consecutively in 2 days (if possible) and returned to the pathology provider by the participants. iFOBT sensitivity is around 83% and specificity 93%, according to the Australian Institute of Health and Welfare [2]. Further, follow-up with a general practitioner includes a potential referral to the hospital for colonoscopy as a category 1 (review in 30 days by the Surgical or Gastroenterology team). NBCSP is expected to prevent 92,200 bowel cancer cases and 59,000 deaths from 2015–2040 with <10% overall colonoscopy demand [3].

There are multiple potential reasons for possible positive iFOBT results – diverticular disease, hemorrhoids, inflammatory bowel disease, angiodysplasia, colorectal cancer (CRC), adenoma, and many other medical conditions including not only the colon but also upper gastrointestinal tract as well. Bevan *et al.* show 15.5% frequency for diverticular disease and 5.8% for hemorrhoids as non-neoplastic findings during colonoscopy within the English BCSP. CRC was found in 8.9% of the colonoscopy cases [4].

Colonic diverticular disease is a common medical condition throughout the world. The theory that diverticulosis affects only the population in developed countries is less and less supported in the surgical community [5]. Colonic diverticulosis is one of the most common findings during the endoscopic evaluation of the colon, such as colonoscopy [6]. Predisposing factors for this condition are a low-fiber diet and physical inactivity, which are widespread issues in the population of Australia [7].

This study aimed to analyze colonoscopy findings for asymptomatic iFOBT-positive patients within one of the most disadvantaged areas in Australia – Caboolture area in Queensland state with an index of relative socioeconomic disadvantage score equal to 1 [8].

#### Access this article online

Received - 24 December 2022  
Initial Review - 26 December 2022  
Accepted - 30 December 2022

#### Quick Response code



DOI: 10.32677/ejms.v8i1.3756

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## METHODOLOGY

A retrospective cohort single-center study was carried out for all patients referred for colonoscopy with iFOBT-positive results to Caboolture Hospital (QLD, Australia) in 2016–2018. Ethics committee approval was obtained for this study. Data were collected from the patient's medical records/charts, endoscopy services information system solution, operating room management information system, and AUSLAB/AUSCARE (Pathology systems) databases.

We recorded such data as age, sex, and additional indications for colonoscopy apart from positive iFOBT (iron deficiency anemia (IDA), diarrhea, weight loss, altered bowel habits, rectal bleeding), colonoscopy findings for iFOBT-positive patients, presence (or absence) of diverticular disease including the part of the affected colon, a new diagnosis of CRC based on biopsy during colonoscopy, hemorrhoids with or without banding, and angiodysplasia.

Data from all individuals with iFOBT-positive results who underwent colonoscopy were considered (Group A). We included the patients within NBCSP and all other patients outside the screening age of 50–74 years. All endoscopy reports with complete colonoscopy were singularly reviewed.

Group A patients were narrowed down to the positive iFOBT patients with colonic diverticulosis and classified as Group B patients. Exclusion criteria were iFOBT-positive patients with an additional indication (IDA and other) for colonoscopy.

The data analysis was performed using Stata version 17.0 (StataCorp LP, College Station, TX).

## RESULTS

We analyzed data from 7270 colonoscopies performed by 16 surgical and gastroenterology consultants from January 2016 to December 2018. As a result, 669 (9.2% of total) colonoscopies were identified with positive iFOBT as an indication (Group A).

The patients' age varied from 17 to 92 years (354 males and 315 females, 52.9% and 47.1%, respectively, median=67, IQR 57–73 with acceptable data distribution for age and gender). Most patients (n=465, 69.5%) were within NBCSP screening age and older (n=135, 20.2%). Young patients below 50 years of age represented only 10.3% (n=69).

The cohort of 319 (47.7% of Group A) patients was isolated with such finding as a diverticular disease (Group B). The patients' age with colonic diverticulosis was between 43 and 92 years (177 males and 142 females, 55.5% and 44.5%, respectively, median=71, IQR 65–76). Gender had no statistical difference for diverticulosis versus non-diverticulosis patients in Group A (p=0.203 for males and p=0.203 for females) (Fig. 1).

Colonic diverticulosis involved the entire colon in 10.7% of the cases (n=34) or a combination of the different parts of the colon (as per colonoscopy reports) – ascending colon involved in 20.7% (n=66), transverse colon – 15.4% (n=49), descending colon – 40.1% (n=128), and sigmoid colon in 96.2% (n=307). Diverticulosis of the sigmoid colon alone was found in 53.6% of the patients (n=171) (Fig. 2).

Thirty-two patients (10.0%, Group B) were on dual antiplatelet therapy (DAPT – Aspirin with Clopidogrel), non-vitamin K antagonist oral anticoagulants (NOACs – Apixaban, Rivaroxaban, and Dabigatran), or Warfarin for different medical reasons. Therefore, those medications were appropriately withheld before the procedure as per protocol at Caboolture Hospital.

Different types of polyps were identified and removed for 197 patients (61.8%, Group B). In addition, 73 patients (22.9%, Group B) were diagnosed with grade I to III non-bleeding hemorrhoids, and 11 were banded. Angioectasia and angiodysplastic lesions were found in five patients (1.6%, Group B) during colonoscopy and two patients (0.6%, Group B) had healing anal fissures. CRC was identified in five patients (1.6%, Group B). Some of them had a combination of the abovementioned findings. The remaining patients (n=92, 28.8%, Group B) were diagnosed with only one isolated colonoscopy finding, such as diverticulosis, and no specimens were collected (Fig. 3).

According to colonoscopy and histopathology results, 18.7% of patients (n=125, Group A) were discharged from the hospital with a recommendation to repeat colonoscopy within the next 1 or 3 years as per National Health and Medical Research Council guidelines. Only 12.0% of patients (n=80, Group A) returned for repeat colonoscopy as advised. About 10.9% of the patients (n=73, Group A) are required to repeat colonoscopy in 5 or 10 years, but the time frame to follow that up would be only in 2021–2028 and is outside of the goals of the current study. Furthermore, there

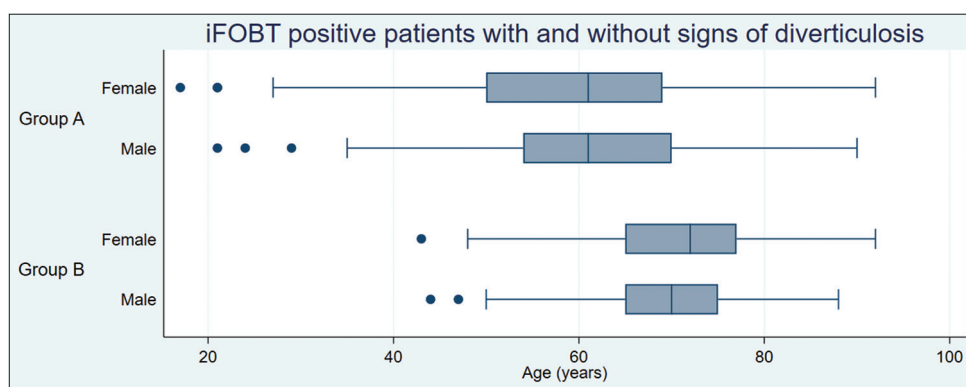


Figure 1: All positive iFOBT patients (n=669) and iFOBT-positive patients with diverticulosis (n=319)

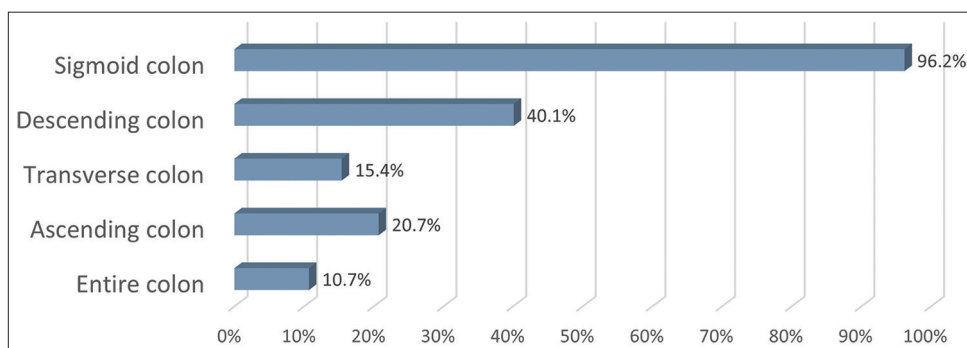


Figure 2: Location of identified colonic diverticulosis during colonoscopy

	Group A (all iFOBT-positive patients, n=669)	%	Group B (iFOBT-positive patients with diverticulosis, n=319)	%
Diverticulosis	319	47.7%	319	100%
Polypectomy			197	61.8%
Isolated diverticulosis			92	28.8%
Haemorrhoids			73	22.9%
Banding of haemorrhoids			11	3.4%
CRC	18	2.7%	5	1.6%
Angioectasia/angiodysplastic lesions			5	1.6%
Anal fissure			2	0.6%

Figure 3: Colonoscopy findings for Group B

were no referrals for a second colonoscopy for positive iFOBT patients diagnosed with only colonic diverticulosis.

Overall, 2.7% of patients diagnosed with CRC were referred for colonoscopy (n=18, Group A and n=5, Group B, p=0.274) due to positive iFOBT. Furthermore, there were no registered significant post-colonoscopy complications (bowel perforation, etc.) for Group A patients.

**DISCUSSION**

In general, iFOBT can be positive for any gastrointestinal occult or obvious bleeding starting from the oral cavity and to the level of the rectum. van der Vlugt *et al.* reported that only 0.14% of individuals with positive iFOBT were diagnosed with esophageal or gastric cancer among a cohort of 16,165 screening participants [9]. Jung *et al.* reported that 0.68% of patients were diagnosed with proximal upper gastrointestinal cancer within 1 year after a negative colonoscopy for positive iFOBT [10]. Some studies concluded that recommending a routine esophagogastroduodenoscopy (OGD) is questionable due to low iFOBT-positive predictive value for proximal upper gastrointestinal cancer [11].

Colonic diverticulosis is a common source of the lower gastrointestinal bleeding, which is hard to prove if it is occult [12]. Diverticular bleeding ceases spontaneously in 90% of the cases. Predisposing factors can be hypertension, diabetes mellitus, ischemic heart disease, and anticoagulation. A 25% recurrence rate of such bleeding in 4 years is a well-known surgical problem [13]. Given the incidence of diverticular bleeding, we can hypothesize about diverticulosis as the sole cause of positive iFOBT.

The incidence of CRC confirmed histologically after

colonoscopy for positive iFOBT varies from 3.2% [10] and up to 8.9% [4]. Diverticular disease was identified in 15.5% and 36.5% of the same cohort of patients, as per Bevan *et al.* and Morini *et al.*, respectively [4,14]. However, it is important to note that the prevalence of diverticulosis can vary widely depending on the specific population being studied, and other factors such as the specific FOBT test used, and the methods used to detect diverticulosis.

Diverticulosis is not associated with an increased risk of advanced CRC in the general population that underwent a colonoscopy for other indications besides positive FOBT [15,16]. Centers for Disease Control and Prevention in the United States does not even include diverticulosis as a risk factor for CRC. The location of CRC does not correlate with the affected part of the large bowel by diverticular disease either. However, Cooper *et al.* reported an association between diverticulosis and increased risk of interval CRC within 6 months after a negative colonoscopy [17]. Ma *et al.* provided the cohort study results with a linkage of diverticular disease with a risk of overall incident CRC [18]. Nakahara *et al.* state that there is no statistical difference in the relationship between colon neoplasms and colonic diverticulosis within the screening program for positive FOBT patients [19]. However, the early CRC is strongly associated with diverticular disease. Otherwise, diverticulosis correlates with a higher risk of polyps and adenomas [16]. Despite the large samples of patients, the studies mentioned above give us the controversial impression of a direct association between colonic diverticulosis and CRC risk.

The current limitation of such studies is an absence of clear recommendations for the patients to have both OGD and colonoscopy if the indication is only positive FOBT. Nowadays, colonoscopy alone is the gold standard investigation for these patients.

Furthermore, an inability to suspect diverticulosis as the only cause for iFOBT-positive result limits the significance of such a finding unless the patient was thoroughly investigated endoscopically, including capsule endoscopy to exclude small bowel pathology.

**CONCLUSION**

Colonic diverticulosis is a prevalent medical condition at screening colonoscopy for positive iFOBT. It affected the patients above

43 years old with positive iFOBT, more males than females in this study. In most cases, colonoscopy consisted of benign findings, and diverticular disease was revealed in 47.7% of the patients with such indication for colonoscopy as positive iFOBT. About 28.8% of the patients were diagnosed with colonic diverticulosis only. The sigmoid colon was affected by diverticulosis in 96.2% of the cases.

Overall, the CRC diagnosis rate of 2.7% for the patients in the positive FOBT cohort (Group A) is comparable with other studies. However, the diverticulosis group's CRC rate of 1.6% (Group B) was lower than in available published data.

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*Funding: None; Nil; Conflict of Interest: None Stated.*

**How to cite this article:** Hordiychuk A, Ratnayake S. Colonic diverticulosis as an isolated colonoscopy finding for iFOBT-positive patients. *Eastern J Med Sci*. 2023;8(1):7-10.