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Original Article

Increased prevalence of colonic adenomas in patients with cystic fibrosis

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Abstract

Background: Cystic fibrosis (CF) is the most common lethal genetic illness in the Caucasian population. Studies have shown that CF patients are at an elevated risk of developing colon cancer. Colonic adenomas are the precursors of colon cancer. This study aims to determine the prevalence of adenomas in patients with cystic fibrosis.
Methods: All patients were recruited prospectively at The Ottawa Hospital Cystic Fibrosis Clinic from 2010 through 2015. Baseline demographic and cystic fibrosis disease characteristics were collected from the clinic's CF patient database. Upon presentation at the endoscopy unit, and after a brief history and physical exam, a colonoscopy was performed. Polyps were resected if detected and sent to the pathology department for characterization. Findings were compared with a control group (pairing each CF patient with 5 age and sex-matched controls) of near-average risk patients who underwent a colonoscopy at the same center.
Results: Of the 33 patients that provided informed consent to participate in the study, 30 patients underwent colonoscopy and 13/30 (43.3%) were found to have colonic adenomas compared to 7 (4.7%) of the 150 control patients. The relative risk ratio for adenoma detection in a CF patient as compared to a matched control patient was 9.29 (95% CI 4.04–21.31), $p < 0.01$.
Conclusions: Colonic adenomas are more prevalent in CF patients compared to the general population. This study suggests the need for additional research to support recently published screening guidelines for CF patients.

Keywords: Colonoscopy; Cystic fibrosis; Adenoma

1. Introduction

Colorectal cancer is the third most commonly diagnosed cancer in Canada with 25,100 new cases annually and 9300 deaths [1]. The risk of developing colon cancer is not considered significant in patients under the age of 50 without family history and screening is not recommended. Patients with cystic fibrosis (CF), however, have an elevated risk of developing colon cancer at a younger age [2], yet until recently; screening guidelines for this population had not been available.

CF is the most common life-threatening genetic illness in the Caucasian population [3]. The disorder is characterized by a defect in the chloride transporting channel known as CF transmembrane conductance regulator (CTFR) which disrupts epithelial fluid transport. This affects a number of organs including the airways, pancreatic ducts, bile ducts, and intestine [4]. Earlier diagnosis and advances in therapy have increased the

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life span of CF patients such that the condition is no longer considered paediatric, and the median survival age is over 40 years [5]. This improved lifespan has resulted in their developing other age-related conditions. In a study involving nearly 30,000 CF patients, an increased prevalence of digestive tract cancers was observed [2]. A more recent study involving 41,000 CF patients within the US CF Data Registry confirmed the increased risk of bowel cancer [6].

Although studies have identified elevated adenoma and colon cancer risk [6,7], there are no studies that have prospectively studied the prevalence of colonic adenomas (pre-cancerous lesions) in patients with cystic fibrosis in Canada compared to the general population. A relatively young patient with CF was diagnosed with colon cancer at our center and we wondered whether they may have benefited from earlier screening. Our study looks to evaluate the role of screening colonoscopy in a young CF population at our center. Our findings will be compared with those from age- and gender-matched near-average risk patients who have also undergone colonoscopy at our center.

2. Methods

All patients were recruited prospectively from The Ottawa Hospital Cystic Fibrosis Clinic from 2010 through 2015. This study was approved by the Ottawa Hospital Research Ethics Board. Baseline demographic and CF disease characteristics were collected from the center's patient database. Included in this database is information such as genotype, transplantation history, and the use of immunosuppressive drugs. All patients enrolled were 18 years of age or older, had confirmed diagnosis of CF (based on sweat chloride levels or 2 disease causing mutations), and were clinically stable (no recent acute pulmonary exacerbation). Patients were excluded if they had symptoms suggestive of a pulmonary exacerbation within the previous 4 weeks, were pregnant, had baseline FEV1 <25% predicted, inability to provide informed consent, or the colonoscopy was incomplete (no cecal intubation). Once patients were recruited, they underwent bowel preparation regimens as per standard preparation protocols which involved 4 L of polyethylene glycol 3350 (Colyte). In some cases, 2 L split prep dosing was used at the discretion of the endoscopist. Upon presentation at the endoscopy unit, a brief history and physical exam were performed, after which they underwent a colonoscopy. Bowel preparation was scored as good, fair or poor. Good bowel preparation was defined as when all residue was liquid and over 90% of the mucosal surface was visible, fair when there was some semisolid stool that could be suctioned or washed away and over 90% of the mucosa surface was visualized, and poor when semisolid stool could not be suctioned or washed away and <90% of the mucosal surface was visualized [8]. Resected polyps were sent to the pathology department for morphological and histological characterization. Data was then retrieved from the endoscopy and pathology reports from the patients' electronic medical records.

Frequency matching based on 5-year age intervals and sex was used for each CF patient who underwent colonoscopy, with a total of 5 control patients per CF patient. The control group was selected retrospectively and randomly from a database containing all colonoscopies performed at the Ottawa Hospital in 2011, with blinding to the colonoscopy results. A 2011 colonoscopy database was chosen because this year lies within the recruitment period for cystic fibrosis patients and the data was readily available. Using an entire year of data also allowed a greater number of possible control patients to be retrieved. Control group patients were only included if they underwent a colonoscopy for indications other than having a family history of colon cancer, positive fecal occult blood test, or other conditions (e.g. IBD) that are known to increase the risk of colon cancer.

3. Results

A total of 33 patients underwent colonoscopy; 1 was excluded as they had several previous colonoscopies and 2 others were excluded from the study due to incomplete colonoscopy resulting from poor bowel prep (including the only lung transplant patient in this study) (Fig. 1). The average age of the 30 study patients (63.3% male) was 39.6 (±12.7, range 22–70, median = 38) years at time of colonoscopy. Of these, adenomas were identified in 13 (43.3%), including one case (3.3%) of an advanced (villous) adenoma. The average age of patients in whom adenomas were detected was 45.0 years (range from 25 to 62). The average age of the 150 control patients was 40.1 (±12.3, range 22–70, median = 38) at time of colonoscopy. Of the 150 control patients, adenomas were detected in 7 (4.7%) (Table 1).

3.1. Statistics

A matched cohort relative risk ratio of 9.29 [95%: 4.04, 21.31] was calculated for adenoma detection in patients with cystic fibrosis as compared to the control groups (Table 2). A total of 18 different endoscopists performed colonoscopies in the control group. The weighted average adenoma detection rate for these colonoscopists is 27.3% based on their adenoma detection rate with respect to patients aged 50 to 75 with no family history and no positive fecal occult blood test. The CF group had their colonoscopies performed by one endoscopist, with an adenoma detection rate of 37.2% with respect to patients aged 50 to 75 with no family history and no positive fecal occult blood test. The adenoma detection rates were

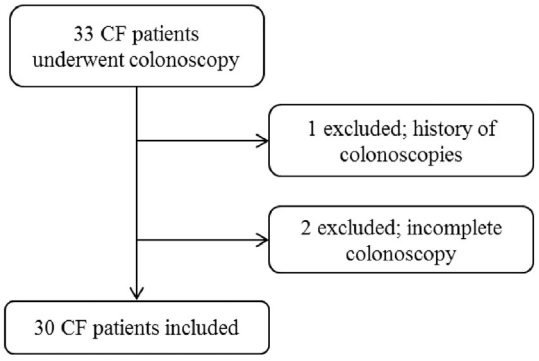

Fig. 1. Inclusion process for CF patient colonoscopies.

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