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Association between Diverticular Disease and Pre-Neoplastic Colorectal Lesions in an Urban African-American Population

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Abstract

Background—It is unclear whether there is a shared pathway in the development of diverticular disease (DD) and potentially neoplastic colorectal lesions since both diseases are found in similar age groups and populations.

Aim—To determine the association between DD and colorectal pre-neoplastic lesions in an African-American urban population.

Methods—Data from 1986 patients who underwent colonoscopy at the Howard University Hospital from January 2012 through December 2012 were analyzed for this study. The presence of diverticula and polyps was recorded using colonoscopy reports. Polyps were further classified into adenoma or hyperplastic polyp based on histopathology reports. Multiple logistic regression was done to analyze the association between DD and colonic lesions.

Results—Of the 1986 study subjects, 1,119 (56%) were females, 35% had DD and 56% had at least one polyp. There was a higher prevalence of polyps (70 vs. 49%; OR = 2.3; 95% CI: 1.9–2.8) and adenoma (43 vs. 25%; OR = 2.0; 95% CI: 1.7–2.5) in the diverticular vs. non-diverticular patients. Among patients who underwent screening colonoscopy, the presence of diverticulosis was associated with increased odds of associated polyps (OR = 9.9; 95% CI: 5.4–16.8) and adenoma (OR = 5.1; 95% CI: 3.4–7.8).

Conclusion—Patients with DD are more likely to harbor colorectal lesions. These findings call for more vigilance on the part of endoscopists during colonoscopy in patients known to harbor colonic diverticula.

Keywords

Adenoma; Hyperplastic polyp; Colorectal cancer; Diverticular disease

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Introduction

Diverticular disease (DD), a condition associated with the bulging of pouches from the colon surface, is thought to result from increased intraluminal pressure. It was found incidentally during colorectal cancer screening. In the United States, the prevalence of DD has increased from 5–10% in 1920 to 35–50% in 1960s [1]. DD affects 20–30% of patients who are younger than 50 years, around 50% who are older than 70 years and more than 65% who are older than 80 years. Diverticulosis and colorectal adenoma or carcinoma is rare among the Africans and people of the other developing countries. Studies suggest an increasing incidence of DD due to westernization of dietary habits and lifestyle [2, 3].

In recent years, there has been an increase in the prevalence of DD and colorectal carcinoma [2, 4–6], both of which seem to share a common etio-pathology related to low fiber diet and increasing age. Colon cancer is found in 17% of patients thought to have complicated DD. Studies have suggested that factors like advancing age, low fiber diet [2, 3], low physical activity [7], and obesity [8] had a link to both DD and colorectal neoplasia [9–13]. However, previous studies that have evaluated the association between DD and colorectal neoplasia have shown inconsistent results with some showing a positive association [10, 11] and some not showing [14]. In this study, we evaluated the association between diverticulosis and pre-neoplastic colonic lesions among an urban African-American population in Washington, D.C.

Methods

Patients and Study Design

Medical records of patients who underwent colonoscopy at the Howard University Hospital, Washington, D.C. from January 2012 through December 2012 were reviewed. This study was approved by the institutional review board. Indications for colonoscopy included screening or diagnosis for symptoms like altered bowel habits, constipation, abdominal distension, hematochezia, weight loss, and anemia. Polyethylene glycol-based lavage solution was recommended for pre-procedural bowel preparation. The bowel preparation was classified as excellent, good, and fair, or classified poor based on the degree of visibility of colonic mucosa devoid of stool. Colonoscopy was rescheduled if the bowel preparation was poor.

During the procedure, the patients were sedated with intravenous midazolam and fentanyl with or without diphenhydramine. Complete colonoscopy was defined as cecal intubation followed by identification of appendiceal orifice, ileo-cecal valve, and cecal strap. We defined cecum, ascending colon and transverse colon including splenic flexure as proximal colon and descending colon, sigmoid, recto-sigmoid and sigmoid colon as distal colon. Diverticulosis was defined as the presence of endoscopically diagnosed diverticula in any part of the colon. Polyp was defined as any localized projection above the surrounding colonic mucosa detected during colonoscopy. The number, size, and location of polyps were recorded at the time of colonoscopy, which was performed by certified endoscopists (A.S., R.B., and A.L.) using standard or high definition, adult or pediatric colonoscopes with white light or narrow band imaging (NBI). Polypectomies were performed for polyps and biopsies

for any suspicious colonic lesion. Gastrointestinal pathologists (E.L.L. and B.S.) confirmed the histopathology of removed polyps. In our analysis, adenoma includes tubular adenoma, tubulovillous, villous, and sessile adenomas. Hyperplastic polyps (HPP) include pre-adenomatous lesions without pronounced dysplasia. Our outcomes of interest were the prevalence of polyps, adenoma, and HPP among patients with and without diverticulosis.

Statistical Analysis

We used t-test and Chi-square test to compare the characteristics (age, sex, clinical symptoms) of patients by the presence or absence of diverticulosis. Logistic regression models were used to evaluate the association of diverticulosis with the prevalence of polyps, HPP, and adenoma. Separate logistic regression models of analysis based on colonoscopy indication were performed in two groups. In each logistic regression analysis, we adjusted the effect of DD for age, gender, and the effect of ruling out polyp in the diagnostic colonoscopy subgroup. We also compared the outcomes for screening procedures as compared with diagnostic procedures. We calculated odds ratios (OR) and 95% confidence intervals. STATA 12.0 (Stata-Corp., College Station, Tex., USA) was used for all analysis.

Results

Patients' Characteristics

Of the 1986 African-American patients enrolled, 702 (38%) had DD. Eight hundred and sixty seven (44%) were male, the median age of patients was 57 years (range 18–92 years), and 762 (35%) were older than 60 years. Patients with DD were older. The frequency of polyps, adenomas, and HPP in all patients was 56, 31, and 24%, respectively.

Five hundred and fifty (28%) colonoscopies were performed for screening purposes. Non-screening indications (72%) included abdominal pain, upper or lower gastro-intestinal bleeding, anemia, weight loss, rule out polyp (asymptomatic screening), unintentional weight loss, family history of colon cancer, and high risk conditions including history of polyp and/or IBD, family history of genetic syndromes and/or colorectal cancer. Fewer patients in the DD group underwent screening colonoscopy (19 vs. 32%, $p < 0.001$). There was no difference between the two groups of patients in terms of other indications and sex distribution (table 1).

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The prevalence of adenoma in the DD group was almost twice that in the non-DD group and the difference was statistically significant (43 vs. 25%, $p < 0.001$). In both genders, the frequency of polyps and adenomas was higher in patients with DD (data are not shown). The prevalence of HPP was higher as well. In logistic regression, the odds of diagnosing a polyp, or an adenoma in the DD group were more than double and these differences were statistically significant (table 2, $p < 0.001$).

Relationship between DD and Adenoma Characteristics

We expanded our analysis further to explore any relationship between the adenomas' characteristics (size and number of adenoma) to DD status. In 618 patients who had

adenoma, the median number of adenomas was 1 (range 1–6) and the median size of adenoma was 0.6 cm (range 0.1–3.5 cm). The number of adenoma and size were not different between the two groups of patients.

Screening versus Diagnostic Colonoscopies

We further performed a subgroup analysis in 550 (28%) screening colonoscopy patients and 1,436 (72%) non-screening colonoscopy patients to assess the relationship between DD and colon lesions in each subgroup. The frequencies of patients diagnosed with DD, polyp, and HPP were relatively higher in the non-screening group (table 3). Nevertheless, on logistic regression, the presence of DD increased the odds of polyp to 9.9, adenoma to 5.1, and HPP to 3.6 after adjusting for age and gender in patients with screening colonoscopy ($p < 0.001$ for all; table 4a). In contrast, the odd of diagnosing a polyp and an adenoma in the non-screening colonoscopies was less significant (i.e. OR = 1.5 for polyp and 1.5 for adenoma; table 4b). There was no additional risk of detecting an HPP in non-screening colonoscopy. We noted that DD was associated with a higher risk of polyp and adenoma among those with diverticulosis particularly during screening colonoscopies.

Discussion

According to the American Cancer Society (Cancer Facts and Figures, 2008; <http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2008/index>), colorectal cancer is the third most common cancer in men and women and the fourth most common cancer overall, representing about 12% of all cancers in the United States [15]. Overall, it is the second leading cause of cancer-related deaths next only to lung cancer. It has the highest incidence and mortality in African-American men and women. Colorectal adenoma directly predisposes individuals to invasive adenocarcinoma [16]. There have been conflicting reports on the potential association between DD and colorectal neoplasm [10, 11, 14, 17–20]. This study to our knowledge is the first to assess any association between DD and precancerous colorectal lesions in an urban African-American population. Our study suggests that the presence of DD in patients undergoing screening colonoscopy should prompt the endoscopists to be extra vigilant with colonic mucosa inspection. This is of particular importance since stools sometimes get stuck in the colon as a result of the diverticula's presence and might prevent detailed examination of the adjacent colonic mucosa. Our findings are comparable to some previous studies. First, Gohil et al. in their retrospective review of 300 patients reported that 36% of them had DD and 47.3% had adenoma [17, 18]. Our findings that that adenoma was detected in 43% are similar to Gohil et al.'s findings [17, 18].

The patients diagnosed with DD were older than the patients without DD, which is consistent with the widely known association of increasing prevalence of DD with age [3, 21]. There was no gender-based difference in terms of the frequency of polyp or adenoma in both groups contrary to the report by Morini et al. that patients with diverticulosis were at 3.5 times higher risk of developing colon adenoma and this difference was only significant for male patients in a case-control study of 150 individuals in Italy [10, 11]. Such an association with male patients was not encountered in our population.

We found that patients with DD were at higher risk of experiencing a polyp and/or adenoma (age and gender adjusted OR = 2.3 and 2.0 for polyp and adenoma, respectively). Rondagh et al. found in a large retrospective cohort study (n = 2,310) that patients younger than 60 years with diverticulosis have higher risk of synchronous adenomas, serrated polyps, and advanced adenoma [18], thereby suggesting age as an independent predictor for increased risk of colorectal adenoma in patients with DD. Another study by Morini et al. [10, 11] has also asserted higher risk of harboring adenomas, advanced adenomas in sigmoid colon of patients with DD. Gohil et al. reported in a retrospective cohort study an increased adenoma detection rate in patients with diverticulosis, undergoing colonoscopy [17]. Findings of all of the above studies are consistent with our results.

There were reports of DD-associated polyps that include inverted diverticula or polypoid prolapsing mucosal folds [22, 23]. It can be assumed that the presence of diverticula during colonoscopy should make the endoscopists more vigilant for polyps' exploration. Indeed, the presence of DD was not only a persistent risk for pre-neoplastic colon lesions for diagnostic colonoscopies, but also for screening colonoscopies where DD was associated with higher risk of polyps and adenomas. Most importantly, these risks remained significant even after adjusting for age and sex. Our findings matched those of Gohil et al. who also reported more than two times increased risk of diagnosing colorectal adenoma in first time colonoscopy screening patients. However, the increased susceptibility of African Americans as indicated by the OR of 9.9 that is many times higher than that in non-screening patients reflects an important issue of relevance to health disparity. Indeed, diverticula might be used as an internal marker for heightened risk of colorectal lesions in this population at high risk for colon cancer. Different methods of colonoscopy were applied for the patients regardless of the presence or absence of DD and we believe the heterogeneity of colonoscopy instruments will have minimal effect on results.

Redundant mucosal folds occur in a large majority (90 to 100%) of patients with advanced sigmoid DD, although only a minority develop grossly polypoid lesions or frank prolapse-like histologic alterations of the mucosa [22, 24]. Thickening of the taenia coli, which leads to the shortening of the sigmoid, is believed to be the initiating pathogenic event in the development of these lesions. Although historically HPP are considered potentially nonneoplastic, recent recognition of the serrated carcinogenic pathway point to the contrary.

The diagnosis of DD, polyp, and adenoma in non-screening colonoscopies indicates that these patients might be at higher risk of developing colorectal neoplasms. Hence, this might be associated with the manifestation of the symptoms. More importantly, the risk of diagnosing polyps or adenomas was much higher in screening colonoscopies. This finding supports colorectal cancer screening recommendation of African Americans at early age, for instance 45, and shortening the followups periods to less than 5 years if DD of any degree is detected. We recommend considering DD to be one of the high-risk factors in the same category as personal history of polyp or family history of familial syndromes for colorectal screening guidelines.

We are not aware of any previous study that has evaluated the association between DD and colorectal pre-neoplastic lesions in urban African Americans for a direct comparison with

our study. However, we have a large sample size that gives the study enough statistical power. Our study has, however, some limitations. Since this is a cross-sectional study, the causal relationship between DD and colorectal pre-neoplasia cannot be assessed. Additionally, our patients were from a single center that might not be representative of the entire African-American population in the United States. Because of the retrospective nature of this study, data on confounding factors such as lifestyle, dietary habits, fiber intake and physical activity were not available. In conclusion, the findings of DDs during colonoscopy should prompt an extra vigilance of the part of the endoscopists, as these patients may present a higher risk of harboring or developing potentially neoplastic colorectal lesions.

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Table 1

Demographic and clinical characteristics of patients based on DD status

	Patient without DD (n = 1,284)	Patient with DD (n = 702)	p value
Age, years, median (IQR)	56 (51–62)	60 (54–68)	<0.001
Gender, male, n (%)	568 (44)	299 (43)	0.5
Colonoscopy indications, n (%)			
Screening colonoscopy	414 (32)	136 (19)	<0.001
Diagnostic colonoscopy	870 (68)	566 (81)	
Family history of cancer	29 (2)	15 (2)	0.9
High risk for polyp	24 (2)	20 (3)	0.16
Abdominal pain	121 (9)	66 (9)	0.9
Anemia	70 (5)	43 (6)	0.5
GI bleeding	237 (18)	127 (18)	0.8
Rule out polyp	183 (14)	145 (21)	<0.001
Weight loss	44 (3)	32 (5)	0.2

Table 2

Association of diverticular disease with prevalent colorectal polyps

Diverticular diseases	Any polyp		Adenomas		Hyperplastic polyps	
	n (%)	adjusted OR (95% CI)*	n (%)	adjusted OR (95% CI)*	n (%)	adjusted OR (95% CI)*
No (n = 1,284)	623 (49)	Reference	318 (25)	Reference	268 (21)	Reference
Yes (n = 702)	491 (70)	2.3 (1.9–2.8)	300 (43)	2.0 (1.7–2.5)	211 (30)	1.6 (1.3–2.0)

* Adjusted for age and gender.

Table 3

Demographic and clinical characteristics of patients by colonoscopy indications

	Patients with non- screening colonoscopy (n = 1,436)	Patients with screening colonoscopy (n = 550)	p
Age, median (IQR)	57 (51–65)	56 (52–63)	0.019
Gender, male, n (%)	630 (44)	237 (43)	0.8
Colonoscopy indication, %			
Family history of cancer	39 (3)	5 (1)	0.014
High risk	44 (3)	0	<0.001
Colonoscopy findings, %			
DD	566 (39)	136 (25)	<0.001
Polyp	838 (58)	276 (50)	<0.001
Histology finding, %			
Adenoma	452 (31)	166 (30)	0.6
HPP	366 (25)	113 (21)	0.021

Table 4

Association of diverticular disease with prevalent colorectal polyps

a Screening colonoscopy (n = 550)						
Diverticular diseases	Any polyp		Adenomas		Hyperplastic polyps	
	n (%)	OR (95% CI)*	n (%)	OR (95% CI)*	n (%)	OR (95% CI)*
No (n = 414)	160 (39)	Reference	87 (21)	Reference	63 (15)	Reference
Yes (n = 136)	116 (85)	9.9 (5.4–16.8) ¹	79 (58)	5.1 (3.4–7.8) ¹	50 (37)	3.6 (2.3–5.6) ¹

b Diagnostic colonoscopy (n = 1,436)						
Diverticular diseases	Any polyp		Adenomas		Hyperplastic polyps	
	n (%)	OR (95% CI)*	n (%)	OR (95% CI)*	n (%)	OR (95% CI)*
No (n = 870)	463 (53)	Reference	231 (27)	Reference	205 (24)	Reference
Yes (n = 566)	375 (66)	1.5 (1.2–2.0) ¹	221 (39)	1.5 (1.2–1.9) ²	161 (28)	1.24 (0.97–1.60) ³

* Adjusted for age and gender.

** Adjusted for age, gender, and polyp rule out.

¹ p value <0.001.² p value = 0.001.³ p value = 0.09.