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DIVERTICULOSIS IS ASSOCIATED WITH INTERNAL HEMORRHOIDS ON COLONOSCOPY: POSSIBLE CLUES TO ETIOLOGY

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Hemorrhoids are a common but poorly understood gastrointestinal condition¹. Bowel habits and fiber consumption are frequently cited as risk factors for hemorrhoids, but research has been inconclusive². Recent genome-wide association studies (GWAS) have suggested an association between diverticular disease and hemorrhoids³. We sought to investigate the association between colonic diverticulosis and internal hemorrhoids to validate the prediction from the GWAS.

We performed a case-control study of patients who underwent screening colonoscopy between 2013 and 2015. Inclusion and exclusion criteria are detailed in the supplemental methods. Patients completed a detailed questionnaire including diet and bowel habits before the procedure. Per protocol, endoscopists evaluated the colon for diverticulosis and internal hemorrhoids. A research assistant was present during the entire procedure. The number, location, size, and depth of diverticula were recorded. Upon retroflexion in the rectum, internal hemorrhoids were noted as not present or present. If present, they were graded as “small”, “medium”, or “large”. The hemorrhoid size estimates were subjective. Multivariate analyses were performed with logistic regression to estimate odds ratios and 95% confidence intervals. Additional methods are described in the supplement.

Our analysis included 616 participants. Among participants, 58% (355) had internal hemorrhoids and 41% (261) had no hemorrhoids. Of the 355 participants with hemorrhoids,

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Data will not be available to other researchers

55% had hemorrhoids described as medium or large size and 45% had small hemorrhoids. Participants with hemorrhoids were more likely to be older, male, and Black than those without hemorrhoids (Supplemental materials Table 1). There was no difference between cases and controls in body mass index, total daily fiber intake, physical activity, regular laxative use, or average number of bowel movements per week (Supplemental materials Table 1).

In our cohort, 42% of participants had diverticulosis on colonoscopy. After adjusting for confounding variables, colonic diverticulosis was associated with internal hemorrhoids of any size compared to no diverticulosis (OR 1.64, 95% CI: 1.10–2.46) (Table 1). When limited to medium or large internal hemorrhoids, the association with diverticulosis was stronger (OR 2.21, 95% CI 1.37–3.58). Among participants with diverticulosis, 23% had 1–3 diverticula, 41% had 4–10 diverticula, and 34% had more than 10 diverticula. The association between diverticulosis and internal hemorrhoids increased with the number of diverticula (Supplemental Table 2). Participants with the most diverticula (>10) had the highest odds of internal hemorrhoids (OR 3.33, 95% CI 1.70–6.55).

Because hemorrhoids are classically associated with a low fiber diet and constipation, we also looked at associations with bowel habits and diet. Compared to patients who reported having one bowel movement daily, there was no association between patients who had less than one bowel movement daily and hemorrhoids (OR 0.74, 95% CI 0.44–1.25) or greater than one bowel movement daily and hemorrhoids (OR 0.89, 95% CI 0.55–1.43) (Table 1). Compared to patients with normal stool consistency defined as Bristol stool types 3–5, there was no association between hard stool (Bristol stool types 1–2) (OR 0.68, 95% CI 0.34–1.34) or loose stool (Bristol stool type 6–7) (OR 0.82, 95% CI 0.38–1.76) and hemorrhoids. We looked at the association between bowel habits and hemorrhoids when participants were off laxatives and found no change in our estimates.

There was no association between participants in highest quartile of dietary fiber intake compared to those in the lowest quartile and hemorrhoids (OR 1.02, 95% CI 0.60–1.74). There was no association between hemorrhoids and rare laxative use (OR 1.31, 95% CI .76–2.26), occasional laxative use (OR 1.15, 95% CI .48–2.79), or regular laxative use (OR 1.17, 95% CI .60–2.29).

In this case-control study of patients undergoing screening colonoscopy, we demonstrated that diverticulosis is associated with an increased risk of hemorrhoids after adjusting for confounding variables. Notably, the association was greater when limited to medium and large hemorrhoids. There was a stepwise increase in risk of hemorrhoids with increasing number of diverticula. In fact, patients with the most diverticula (>10) had the greatest odds of hemorrhoids compared to patients without diverticulosis. We found no association between hemorrhoids and bowel movement frequency, stool consistency, or laxative use.

Our study was inspired by a recent GWAS meta-analysis study which revealed a significant association between hemorrhoids and diverticular disease.³ The meta-analysis found 102 novel hemorrhoidal risk loci associated with smooth muscle, epithelial, and connective tissue dysfunction. Genes associated with extracellular matrix and connective

tissue were identified, including the elastin protein previously implicated in diverticulosis pathogenesis.⁴ Using a linkage disequilibrium score regression with existing GWAS studies, they found genetic correlations between hemorrhoids and diverticular disease ($r_g=0.23$, $P_{FDR}=6.68\times 10^{-9}$). These genetic correlations reveal the proportion of variance that two conditions share secondary to genetic causes.

In contrast, our study included participants who had a screening colonoscopy with a standard exam and deliberate protocol to grade diverticulosis and hemorrhoids. Our analysis looked at the association between the specific finding of diverticulosis and hemorrhoids, not the heterogeneous grouping of diverticular disease, which includes diverticulitis and related complications based on diagnostic codes. Since we had data on the number and depth of diverticulosis and size of the hemorrhoids, we were able to also look at these associations.

Our study has limitations. We did not distinguish between patients with symptomatic and asymptomatic hemorrhoids. We did not ask participants if they strained or experienced incomplete evacuation with defecation. Inter-observer error or day-to-day reproducibility for grading hemorrhoids was not evaluated. Additionally, our study did not consider external hemorrhoids and internal hemorrhoid categorization was subjective (none, small, medium, large) and vulnerable to variability based on endoscopist.

In conclusion, our study suggests that among patients undergoing screening colonoscopy, internal hemorrhoids are associated with diverticulosis. There was a dose response relationship with greater risk for hemorrhoids among patients with a greater number of diverticula. We found no association between hemorrhoids and bowel movement frequency, Bristol stool category, or laxative use. We hypothesize that neuromuscular or connective tissue dysfunction plays a larger role in hemorrhoid pathogenesis than traditionally associated risk factors such as constipation or dietary fiber intake.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Colonic diverticulosis, dietary fiber intake, bowel habits and association with internal hemorrhoids on colonoscopy

Table 1.

	All cases (hemorrhoids) (n=355)		Controls (n=261)		Adjusted odds ratio [/]	95% CI
	No.	(%)	No.	(%)		
Diverticulosis						
None	184	52	179	69	REF	--
Any	173	49	82	31	1.64	1.10–2.46
Dietary fiber intake						
1 st quartile	65	18	51	20	REF	
2 nd quartile	59	17	48	18	1.07	0.62–1.85
3 rd quartile	71	20	41	16	1.43	0.82–2.48
4 th quartile	62	17	52	20	1.02	0.60–1.74
Bowel movement frequency						
<1 bowel movement daily	45	13	43	16	0.74	0.44–1.25
1 bowel movement daily	153	43	107	41	REF	--
>1 bowel movement daily	61	17	45	17	0.89	0.55–1.43
Bristol Stool Scale						
Types 1 & 2	21	6	22	8	0.68	0.34–1.34
Types 3,4,5	186	52	131	5	REF	--
Types 6 & 7	16	5	15	6	0.82	0.38–1.76
Laxative use						
Never	175	49	137	52	REF	--
Rarely (<1/month)	43	12	29	11	1.31	0.76–2.26
Occasionally (1 day or more/month)	16	5	10	4	1.15	0.48–2.79
Regularly (3 days or more/week)	26	7	19	7	1.17	0.60–2.29
Irritable bowel syndrome						
No	236	66	162	62	REF	--
Yes	22	6	30	11	0.51	0.28–0.95

[/] Adjusted for age, sex, dietary fiber consumption