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Diarrhea-Predominant Irritable Bowel Syndrome Is Associated With Diverticular Disease: A Population-Based Study

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Abstract

OBJECTIVES—A subset of patients with colonic diverticular disease have chronic gastrointestinal symptoms, and some have a clinical diagnosis of irritable bowel syndrome (IBS), but whether IBS and diverticular disease are linked is uncertain. We aimed to evaluate this association in the community.

METHODS—A population-based, cross-sectional survey was conducted by mailing a valid symptom questionnaire to the eligible residents of Olmsted County, MN, aged 30–95 years. Colonic diverticular disease (diverticulosis and diverticulitis) was ascertained through a review of the complete medical history of all responders. Subjects with at least one relevant test (colonoscopy, computed tomography (CT) scan, CT colonography, or barium enema) were included. IBS was defined using Rome II criteria.

RESULTS—Among 2,267 eligible respondents, there were 1,712 subjects who had undergone colon testing (76%): 919 women (54%); mean ($\pm$ s.d.) age 65 ($\pm$ 11 years). Colonic diverticular disease was identified in 44.4% (95% confidence interval (CI) 42.1–46.8) of the subject. IBS was reported by 8.8% (95% CI 6.9–11.0) of men and 17.0% (95% CI 14.6–19.6) of women. After adjusting for age and gender, the presence of IBS was associated with an increased odds for diverticulosis (odds ratio (OR) = 1.8, 95% CI 1.3–2.4) but not diverticulitis (OR = 1.7, 95% CI 0.9–3.2). In those 65 years of age or older, the presence of IBS was associated with a ninefold higher odds for diverticulosis (OR = 9.4, 95% CI 5.8–15.1). Relative to the non-IBS subgroup, diarrhea-predominant IBS and mixed IBS were significantly associated with an increased odds for diverticular disease (OR = 1.9, 95% CI 1.1–3.2; OR = 2.6, 95% CI 1.0–6.4, respectively).

CONCLUSIONS—There is a significantly increased odds for colonic diverticulosis in subjects with IBS (relative to those without IBS). These results suggest that IBS and colonic diverticular disease may be connected.

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Potential competing interests: Talley and Mayo Clinic have licensed the Talley Bowel Disease Questionnaire.

INTRODUCTION

Colonic diverticular disease is the fifth most important gastrointestinal (GI) disease in terms of health-care costs in Western countries (1). A subset of patients with diverticulosis have chronic GI symptoms and some have typical symptoms of the irritable bowel syndrome (IBS) (2). However, any overlap of IBS and diverticular disease in the general population is poorly documented, and whether any association is due to chance because both conditions are prevalent remains controversial (2).

A fiber-depleted diet has been suggested as a major etiologic factor in the development of colonic diverticular disease (3) and in a subset of IBS patients with constipation (4). The physiological effects of insoluble fiber, include increasing bulk inducing voluminous stools, resulting in a wider-bore colon and thus preventing hypersegmentation and high intraluminal pressures (3,5). In patients with IBS, fiber supplements can improve constipation symptoms, which has been shown to correlate with reduced rectosigmoid pressures (6,7). Fiber deficiency may also be linked to alterations in colonic flora that precede full-blown acute diverticulitis (8). It has been demonstrated experimentally in humans that wheat bran alters the anaerobic/aerobic bacterial ratios (9). Altering flora may in turn change the immune response of the host (10). The link between acute gastroenteritis and the subsequent development of IBS is well established (11,12), and immune activation and low-grade inflammation may conceivably contribute to the expression of the syndrome (13).

The etiological role of altered colonic motility in colonic diverticular disease has been explored, with the demonstration of higher resting, postprandial, and neostigmine-stimulated pressures in patients with diverticulosis compared with controls (14). Visceral sensation may also be altered in patients with colonic diverticular disease; a heightened perception to mechanical distension in the diverticula bearing sigmoid and in the unaffected rectum was noted in patients with symptomatic, uncomplicated diverticular disease (15). Similar pathophysiological findings have been reported in IBS (16).

We hypothesized that, in the community, IBS is associated with the presence of colonic diverticular disease because these conditions share a common etiopathogenesis. We used the resources of the Rochester Epidemiology Project (REP), the Olmsted County population, and validated symptom surveys with detailed chart reviews to investigate this hypothesis; the present study has provided a unique opportunity to describe the epidemiology of colonic diverticular disease, including symptomatic diverticular disease, in the community.

METHODS

This study is a cross-sectional study performed as part of a prospective, population-based cohort study (17–19). This research was approved by the Mayo Foundation Institutional Review Board.

Subjects and survey method

The Olmsted County population comprises approximately 124,000 persons, of whom 89% are white; socio-demographically, the community is similar to the United States white population (20). Residents of Olmsted County receive their medical care almost exclusively from two group practices: Mayo Medical Center and Olmsted Medical Center. The Mayo Clinic has maintained a common medical record system with its two affiliated hospitals (Saint Marys and Rochester Methodist) for over 100 years. Recorded diagnoses and surgical procedures are indexed, including the diagnoses made for outpatients seen in office or clinic consultations, emergency room visits or nursing home care, as well as the diagnoses recorded for hospital inpatients, at autopsy examination or on death certificates. This system

was further developed by the REP, which created similar indices for the records of other providers of medical care to local residents, most notably the Olmsted Medical Group and its affiliated Olmsted Community Hospital (Olmsted Medical Center). Thus, details of the medical care provided to the residents of the County are available for study. Annually, over 80 % of the entire population is attended by one or both of these two practices, and 96 % are seen at least once during any given 4-year period. Therefore, the REP medical records linkage system also provides what is essentially an enumeration of the population, from which samples can be drawn.

We used this system to draw a series of random samples, stratified by age and gender, of the residents of Olmsted County between 1988 and 1993. The cohorts were mailed validated GI symptom questionnaires. The results of these studies have been reported previously (21). In 2003, a new study questionnaire and an explanatory letter were mailed to the subjects who had been randomly sampled for prior surveys. Subjects who had died ($n = 40$), moved from Olmsted County ($n = 86$) or denied research authorization (as required by Minnesota law) ($n = 25$), and those who had responded to ($n = 659$) or explicitly refused ($n = 185$) an earlier follow-up survey were excluded from this mailing. The Talley Bowel Disease Questionnaire (BDQ) (22) was mailed to subjects 30–95 years of age. Reminder letters were mailed at 2, 4, and 7 weeks. Subjects who indicated at any point that they did not wish to complete the survey were not contacted further. Otherwise, non-responders were contacted by telephone at 10 weeks to request their participation and verify their residence within the county. A total of 4,194 eligible subjects were mailed a survey.

Questionnaires

The original Talley BDQ was designed as a self-report instrument to measure the symptoms experienced over the previous year and to collect past medical history data.

Previous testing has shown the BDQ to be reliable, with a median κ statistic for symptom items of 0.78 (range, 0.52–1.00). In the outpatient setting, it has also been shown to have adequate content, and predictive and construct validity (22).

For the follow-up mailing, a modification of the original BDQ was developed to be more visually appealing and easier to follow. The modified BDQ contained 56 gastrointestinal symptom-related items; 19 items that measured past illness, health-care use, and socio-demographic variables; and a valid measure of non-gastrointestinal somatic complaints, the SSC (23).

Risk factors—Information regarding the *a priori* risk factors was as follows:

1. Demographics: age and gender.
2. Body mass index (BMI): based on self-reported recording of height and current weight.
3. SSC: this is a measure of somatization based on 17 common symptoms, including headache, insomnia, fatigue, and nervousness. The SSC requests that the subject rate (on a scale of 0 to 4) how often each symptom occurs and how bothersome they are. The ratings are summed to give a total score (potential range, 0 – 136). Individual items were also evaluated.
4. Abdominal pain: we collected quantitative information on the following: (1) pain severity based on a five-point scale (from “none at all” to “very severe”); (2) pain frequency based on a five-point scale (from “less than once a month” to “daily”); (3) pain duration based on a four-point scale (from “less than 30 min” to “more

than 6 h”); (4) pain location based on a four-point scale (none, above umbilicus, below umbilicus, and both above and below umbilicus).

5. IBS: Subjects were classified as having IBS based on the symptoms recorded in the questionnaire. IBS and the subtype of IBS was defined using modified Rome II criteria (24). The definition applied required recurrent abdominal pain or discomfort more than 6 times per year that had to have at least two of the following: (1) relief with defecation, (2) onset associated with a change in frequency of stool, and (3) onset associated with a change in form (appearance) of stool. IBS was sub-typed as (a) diarrhea-predominant (D-IBS): IBS with loose or watery stools for at least 25% and hard or lumpy stool for <25% of the bowel movements; (b) constipation-predominant (C-IBS): IBS with hard or lumpy stool for at least 25 % and loose or watery stools for <25% of the bowel movements; (c) mixed IBS (M-IBS): meeting the criteria for both D-IBS and C-IBS; (d) un-subtyped IBS (U-IBS): IBS not meeting the criteria for the other three categories (24).
6. Functional constipation: this was defined as having at least two of the following: (1) straining during in at least 25% of the defecations, (2) lumpy or hard stools in at least 25% of the defecations, (3) sensation of incomplete evacuation for at least 25% of the defecations, (4) fewer than 3 defecations per day. There had to be insufficient criteria for IBS (25).
7. Functional diarrhea: this was defined as having at least two of the following: (1) loose (mushy) or watery stools in more than 25% of the defecations, (2) stool urgency in more than 25% of the defecations, (3) more than 3 defecations per week, and (4) reporting diarrhea as the usual bowel pattern. There had to be insufficient criteria for IBS (24).
8. Chronic constipation was defined as having any one symptom of constipation applied to define C-IBS or functional constipation.
9. Chronic diarrhea was defined as having any one symptom of diarrhea applied to define D-IBS or functional diarrhea.
10. Socioeconomic factors: marital status (married or not) and educational level (professional training, high school or college, or less than high school).
11. Use of cigarettes and alcohol: We checked the medical records for the use of cigarettes (yes/no) and alcohol (yes for current use of more than 7 times per week, no for never or no current use).

Diagnostic ascertainment of colonic diverticular disease

The presence of colonic diverticular disease was ascertained through a medical record abstraction of all responders. All information pertaining to diagnosis was then recorded in a specifically designed clinical data form. Each clinical record was reviewed by well-trained abstractors. We excluded those with active intra-abdominal and pelvic malignancy, ulcerative colitis, Crohn’s disease, microscopic colitis, and other organic GI disorders from 2 years prior through 2 years after the date of the survey.

The diagnosis of diverticular disease was established by using any positive colon test among colonoscopy, flexible sigmoidoscopy, abdomen computed tomography (CT) scan and/or CT colonography, or barium enema. Colonic diverticular disease covers the whole spectrum of diverticulosis, mild or subclinical diverticulitis, and overt diverticulitis. Diverticulosis indicated the presence of one diverticulum or multiple diverticula (25). Diverticulitis was defined using two diagnostic categories: (1) definite diverticulitis: clinical diagnosis and the

evidence of active inflammation on an abdominal CT scan or any surgical intervention, and pathological evidence of active inflammation on diverticulum, and (2) probable diverticulitis: clinical diagnosis and antibiotic treatment for presumed diverticulitis. The abdominal CT findings of active inflammation included thickening of the bowel wall >5 mm, paracolic fat streaking, intraluminal air bubbles, abscesses, sinus tracts, or extraluminal air (26). We excluded cases in the diverticulitis group for which imaging studies showed no evidence of diverticulosis ($n = 7$).

To assess the reliability of data abstraction, one experienced gastroenterologist (H.J.) re-reviewed in a blind manner the medical records of 255 subjects (15 %) who were randomly selected from the study subjects. This validation work was performed using the same method as that used by experienced data abstractors.

To evaluate the reliability of colonic testing for the diagnosis of diverticular disease, we assessed the agreement of colonoscopy vs. CT colonography or CT scan or barium enema in subjects who underwent at least two different colon tests.

Statistical analysis

Percent observed agreement and κ values, along with 95% confidence intervals, were calculated to assess the reliability of data abstraction. A κ value of 0 indicates agreement completely accounted for by chance. A κ value of 0.0–0.2 indicates slight agreement, 0.2–0.4 indicates fair agreement, 0.4–0.6 indicates moderate agreement, 0.6–0.8 indicates substantial agreement, and 0.8–1.0 indicates near perfect agreement (27).

The analysis dataset consisted of the 1,712 eligible subjects who had undergone at least one colon test assessment. Based on the responses to specific symptom items from the returned surveys, we estimated the proportion of subjects who met the Rome II criteria for IBS. Among the eligible subjects, 1,695 (99%) provided questionnaire data for identifying IBS, of whom 223 subjects (13 % of eligible sample) reported IBS, and this provided approximately 80 % power to detect an association corresponding to a difference of 10% in the rate of colonic diverticular disease in subjects reporting IBS compared with those without IBS (e.g., 40 % vs. 50 %).

The univariate associations of socio-demographic and clinical characteristics with the presence of colonic diverticular disease were evaluated using the chi square test. Potential predictors of colonic diverticular disease vs. the reference group (those without colonic diverticular disease) were assessed using logistic regression analyses, adjusting for age and gender. The odds ratios (OR) and 95% CI (confidence interval) were computed from the estimated coefficients (and their s.e.) in the regression models. A similar logistic regression approach was used to identify characteristics, including IBS, that predicted diverticulosis, and diverticulitis.

RESULTS

A total of 2,298 subjects responded to the questionnaires, giving a 55 % response rate. Overall 53 % of the responders were female, with the mean ($\pm$ s.d.) age of responders being 62 ($\pm$ 12) years (range of 33–93 years; median 62). In non-responders, 49% were female, with a mean ($\pm$ s.d.) age of 59 ($\pm$ 14) years. Using a logistic regression model to predict survey response, only a weak association with age was detected (OR for responding, per year of age = 1.02, 95% CI 1.01–1.02), with no association for gender (OR in women relative to men = 1.1, 95% CI 0.99–1.28). In the non-responders to the current survey who had responded to a previous mail containing questions defining IBS ($n = 852$), a similar, very modest association with age and gender was observed. Notably, the proportion of

responders vs. non-responders (to the second survey) reporting IBS on the first survey were very similar (11.6 % vs. 11.2 %, $P>0.5$).

Among the 2,298 responders, we excluded 31 subjects who had current, active intra-abdominal or pelvic malignancy ($n=13$), chronic colitis, including ulcerative colitis, Crohn's disease and microscopic colitis ($n=17$), or gastrointestinal amyloidosis ($n=1$) (Figure 1).

Reliability of diagnosis of diverticular disease

We assessed the reliability of the medical record review for the diagnosis of colonic diverticular disease. The observed percent agreement was 92.6 % between data abstractors and an experienced gastroenterologist (McNemar's test, $P>0.5$) and the κ coefficient was 0.84 (95 % CI 0.77 – 0.91), suggesting very good agreement.

Among the subjects who had any of the specified colon tests, 411 subjects had undergone a single colon test, 302 subjects had undergone two colon tests and 999 subjects had undergone three or more colon tests. The agreement of colonoscopy vs. abdominal CT scan was 67.4% (192/285), with a κ coefficient of 0.26 (95 % CI 0.15 – 0.37). The agreement and κ value of CT colonography with colonoscopy was 81.8% (9/11) for a κ of 0.56 (95 % CI 0.06 – 1.0), and for barium enema with colonoscopy was 60 % (9/15) for a κ of 0.21 (95 % CI 0–0.69).

Overall, 1,712 (76 %) out of the total number of 2,267 eligible responders underwent any of the specified colon tests (Table 1). Among them, 919 were women (54 %) and the mean age was 65 (± 11 years). Older age, high SSC, higher BMI, current alcohol use, and previous cholecystectomy were significantly associated with having one or more colon tests; however, no significant association with current smoking, marital status, and educational status was observed.

Colonic diverticular disease was identified by one or more of the tests in 44.4% (95% CI 42.1 – 46.8) of the subjects, with one or more diverticuli being identified in 670 and diverticulitis in 91 subjects. Among the 91 subjects with diverticulitis, 49 patients met the diagnostic criteria for definite diverticulitis and 42 were probable cases.

Association between colonic diverticular disease and clinical characteristics

Older age (≥ 65 years) was a significant predictor of colonic diverticular disease (OR=2.2, 95% CI 2.0–2.5, $P<0.001$), but no association with gender was detected (Table 2). After adjusting for age and gender, a higher SSC score was associated with colonic diverticular disease (OR=1.3, 95% CI 1.1–1.6, $P=0.01$), whereas smoking, alcohol, marital status, educational status, having constipation with use of fiber/laxatives, BMI, and previous cholecystectomy history were not associated (Table 2).

Association between colonic diverticular disease and IBS

Overall, 1,695 (99 %) of the 1,712 subjects undergoing colon tests had eligible symptom data recorded for defining IBS, and IBS was reported by 8.8 % (95% CI 6.9 – 11.0) of the men and 17.0 % (95 % CI 14.6 – 19.6) of the women. Among the subjects with IBS ($n = 223$), 114 (51.1%) had colonic diverticular disease. After adjusting for age and gender, the presence of IBS was associated with a significantly increased odds for diverticular disease (OR = 1.7, 95% CI 1.2–2.4, $P < 0.001$). This association was stronger among the subjects who had diverticulosis, but was not seen in the group with diverticulitis (Table 3).

Relative to the non-IBS subgroup, D-IBS and M-IBS each had significantly increased odds for diverticular disease (OR = 1.9, 95% CI 1.1–3.2, $P=0.02$; OR=2.6, 95% CI 1.0–6.4,

$P=0.04$, respectively) and diverticulosis. For diverticulitis vs. no diverticular disease, the association of IBS subtype and diverticulitis was not analyzed because of limited numbers in the IBS subtypes (Table 3).

Overall the odds for diverticular disease increased with age (Table 2) and modestly in subjects with IBS (Table 3, top 2 lines). In subjects < 65 years, IBS was not associated with an increased odds for diverticular disease. In subjects without IBS, the association with age was more pronounced than the overall age association, i.e., in the older age group (≥ 65 years) without IBS the odds for diverticular disease was strongly increased relative to younger subjects (<65) without IBS (OR=4.3, 95% CI 3.5 – 5.4). In contrast, in younger subjects, not much of an increment associated with IBS alone was observed (left most group in Figure 2), but a considerable increment was associated with both older age and IBS combined (rightmost group in Figure 2; Table 3).

Gastrointestinal symptoms in colonic diverticular disease

Based on abdominal pain characteristics, lower abdominal pain alone (OR 1.6, 95 % CI 1.2 – 2.2, $P=0.002$), separately, both upper and lower abdominal pain (OR 1.7, 95 % CI 1.1 – 2.5, $P=0.02$), moderate-to-severe pain, and an average pain duration of <2h were all significantly associated with a greater odds for having colonic diverticular disease, after adjusting for age and gender (Table 4). However, upper abdominal pain alone, as well as bloating, mucus, any blood in stool, and stool form were not significantly associated. Furthermore, both functional constipation and functional diarrhea were not significantly associated with colonic diverticular disease.

An analysis of the associations between colonic diverticulosis status (present vs. the no diverticular disease reference group) and specific bowel symptoms indicated lower abdominal pain, severe abdominal pain, abdominal pain duration of <2h, and chronic diarrhea all significantly increased the odds for colonic diverticulosis (Table 4). Alternatively, among the 670 subjects with colonic diverticulosis, frequent lower abdominal pain was reported by 110 (16.5 %), and altered bowel habit by 185 (28.5%), whereas among the 951 subjects without diverticular disease the corresponding proportions were 12.7 % and 24.1 %, respectively ($P=0.03$ and $P=0.05$, respectively, univariate chi square test for association).

DISCUSSION

We present new information on the association between IBS and colonic diverticular disease in the general population (2,28–30). Previous epidemiologic data were based on cases with known symptomatic diverticular disease, or presented the proportion with diverticular disease in the community without adequate symptomatic information (2,28,30). There are three major new findings in this study. The presence of IBS, especially D-IBS, was associated with a higher risk of having colonic diverticular disease. Second, this association between IBS and colonic diverticular disease was strongest in older people. Third, we observed that one-fourth of the subjects with diverticulosis had symptoms of abdominal pain or bowel habit changes.

Our study showed that in older age there was a strong association between IBS and diverticular disease, and this was not seen in the younger age group. This result could be explained by several possibilities. First, there might be power issue as a smaller proportion of the younger age group had colon testing (65 % vs. 86%), but this seems unlikely to be critical here. Still, the lower health-care-seeking rates in younger people might have distorted the link between IBS and diverticular disease. Alternatively, the association with IBS and colonic diverticular disease may be more obvious in older age; IBS may potentiate

the expression of colonic diverticular disease with changes in function of smooth muscle or excitatory or inhibitory neurons with ageing (31–33).

Chronic constipation and diarrhea were present in a similar proportion of subjects with colonic diverticular disease and the reference group in our study. Many assume that constipation is linked to diverticulosis, but this large population-based study indicates that amongst those with IBS, it was IBS-D that was the strongest predictor of colonic diverticular disease. IBS-D also more often follows colonic infection (13). A high somatization score was also an independent predictor of diverticular disease in the community. In post-infectious IBS, pre-existing anxiety or depression is associated with a significantly higher risk of developing IBS after bacterial gastroenteritis, and perhaps a similar mechanism operates in diverticular disease (13).

Chronic low-grade inflammation can influence the function of epithelial cells, smooth muscle, and enteric nerves, leading to changes in motility and sensation (34). Biopsy studies have shown that some patients without clinical diverticulitis have mild colitis in the diverticula, a finding that suggests the possibility of a relationship between diverticulosis and inflammation (35). Epidemiologic data have shown that a low-fiber diet is associated with a higher prevalence of colonic diverticular disease (36). Stasis of luminal contents occurs in colonic diverticula, resulting in local bacterial overgrowth (37). This may give rise to chronic low-grade inflammation, which sensitizes intrinsic primary afferent neurons in the submucosal and myenteric plexus, resulting in visceral hypersensitivity and changes in colonic motor function and perhaps symptoms of IBS in some cases (3,28,38).

Disturbances of large bowel motility have been suggested to be an important feature of IBS (35,36). Patients with diverticulosis have also shown abnormal motility and excessive colonic contractility, particularly in segments bearing diverticula (7,39). The tunica muscularis in the sigmoid is thicker than in the ascending colon, and this thickening is concentrated in inter-digitating diverticulæ (40). Such regional differences in compliance might influence colonic motility. Animal models have shown greater thickness of the external smooth muscle layers of the colon with aging because of alteration of the extracellular matrix (31). The lack of intrinsic inhibition, also, may contribute to impaired muscle relaxation in IBS and colonic diverticular disease (38,39). Other animal studies have revealed that nonadrenergic, noncholinergic relaxation in the rat colon was mediated by nitric oxide and also decreased with aging (32,33). These findings support our observations of the association between IBS and colonic diverticular disease being stronger in older age. Visceral hypersensitivity is an important pathophysiological abnormality in IBS (43,44). Symptomatic uncomplicated colonic diverticulosis patients have shown a heightened perception to distension, not only in the diverticula bearing sigmoid, but also in the unaffected rectum (15), which was not observed in asymptomatic diverticulosis patients. These findings suggest that a generalized hyper-perception of intestinal stimuli may occur in symptomatic diverticular disease, which resembles IBS.

This study has a number of strengths. First, it is population-based, which should minimize the effect of referral bias and improve the generalizability of the results. The majority of patients with colonic diverticular disease are believed to have no or minor symptoms and never seek medical attention (45). However, most of the studies have been based on hospital clinical practice (28,29). Another important issue is whether these data are generalizable to the whole population. The data resources of the REP are able to enumerate 96% of the population of Olmsted County, from which we drew our random sample, and we have the ability to link questionnaire data from people randomly selected in the community to their medical record; in the United States this linkage is relatively unique (20). Another strength is that we could ascertain colonic diverticular disease using objective testing in 76 % of the

survey respondents in this community. Third, we used multiple colon tests where available to identify the cases. The main limitation in the diagnosis of colonic diverticular disease is a potentially high false negative rate of testing for diverticulosis (47). The sensitivity and specificity of radiological or endoscopic definition for diverticulosis has traditionally been studied against an imperfect gold standard (46,47). Barium enema is generally accepted as a good imaging test for diagnosis of diverticular disease (46); however, the accuracy of barium enema or colonoscopy in differentiating diverticulosis from other concomitant lesions has been reported to be as low as 50 % (48,49), whereas CT scanning is more valuable for identifying diverticulitis (50). We defined colonic diverticulosis using any positive test to increase sensitivity, but this may have reduced specificity.

There are some potential limitations of this study. There are inherent problems in assessing the epidemiology of colonic diverticular disease as the diagnosis depends on imaging studies, which tend to introduce selection bias. In our study, notably aging, high somatic symptom score, high BMI, current alcohol use, and a cholecystectomy history increased the odds for undergoing colon testing. Second, diagnostic ascertainment for colonic diverticular disease in this study may have induced some limitations, but the agreement rate of 60–82 % between colon tests in our study is consistent with previous data (46–49). Another potential limitation was a relatively low response rate (55%) to the survey. However, we could not detect any major response bias comparing responders vs. non-responders. In those who had responded to a previous mail through which data on IBS were collected (19), a similar, very modest association of response with age but not gender was observed; however, the proportion of responders vs. non-responders (to the second survey) reporting IBS on the first survey was almost identical.

In conclusion, there is a significantly increased frequency of colonic diverticular disease in subjects with IBS in the US community. These results suggest that IBS and colonic diverticular disease may be etiologically connected.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Both colonic diverticular disease and irritable bowel syndrome (IBS) are common in the population.
- ✓ It is unknown how many people with IBS in the community have objective evidence of colonic diverticular disease.
- ✓ Moreover, any link between IBS subtypes and colonic diverticular disease is unclear.

WHAT IS NEW HERE

- ✓ The presence of IBS, especially diarrhea-predominant IBS, was associated with a higher risk of having colonic diverticular disease.
- ✓ The relationship between IBS and colonic diverticular disease was strongest in older people.

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Figure 1.

Study design. For each step of the survey, the number of subjects involved is indicated.

*Thirty-one subjects who had current, active gastrointestinal cancer ($n = 13$), chronic colitis, including ulcerative colitis, Crohn's disease, microscopic colitis ($n = 17$), and amyloidosis ($n = 1$), were excluded.

Figure 2.

The association of irritable bowel syndrome (IBS) with colonic diverticular disease according to age. The reference group was the younger age group (< 65 years) without IBS. Odds ratio (OR) was adjusted for gender. CI, confidence interval.

Table 1

Age- and gender-specific frequency ratios of colonic diverticular disease in Olmsted County, MN

Age (years)	≤49	50–59	60–69	70–79	≥80
<i>Men</i>					
Responders (n=1,068)	191	230	282	279	86
Colon test (n=793)	78	165	227	251	72
Diverticular disease ^a (n=363, 45.8%)	7 (9%)	43 (26%)	105 (46%)	158 (63%)	50 (69%)
<i>Women</i>					
Responders (n=1,199)	230	267	318	291	93
Colon test (n=1,712)	112	207	260	258	82
Diverticular disease ^a (n=398, 43.3%)	14 (13%)	42 (20%)	124 (48%)	162 (63%)	56 (68%)
<i>Total</i>					
Responders (n=2,267)	421	497	600	570	179
Colon test (n=1,712)	190	372	487	509	154
Diverticular disease ^a (n=761, 44.4%)	21 (11%)	85 (23%)	229 (47%)	320 (63%)	106 (69%)

^aThe proportion of colonic diverticular disease among the subjects who had undergone any colon tests.

Table 2

Association between colonic diverticular disease and clinical characteristics, Olmsted County, MN

	Diverticular disease, <i>n</i> =761	No diverticular disease, <i>n</i> =951	Odds ratio (95% CI)	<i>P</i> value
<i>Age (years) ^a</i>				
≥ 65 (<i>n</i> =898)	551 (61.4%)	347 (38.6%)	2.2 (2.0–2.5)	< 0.001
< 65 (<i>n</i> =814)	210 (25.8%)	604 (74.2%)	1.0 ^b	
<i>Gender</i>				
Female (<i>n</i> =919)	398 (43.3%)	521 (56.7%)	0.9 (0.7–1.1)	0.31
Male (<i>n</i> =793)	363 (45.8%)	430 (54.2%)	1.0 ^b	
<i>Median (± s.d.) SSC score ^c</i>				
≥ 0.50 (<i>n</i> =837)	394 (47.1%)	443 (52.9%)	1.3 (1.1–1.6)	0.01
< 0.50 (<i>n</i> =814)	330 (40.5%)	484 (59.5%)	1.0 ^b	
<i>Mean (±s.d.) BMI (kg/m²) ^d, <i>n</i> =1,627</i>				
	30.0±7.4	30.0±8.2	1.01 (0.99–1.0)	0.12
<i>Smoking</i>				
Current smoker (<i>n</i> =137)	55 (40.2%)	82 (59.8%)	1.06 (0.7–1.6)	0.78
Not current smoker (<i>n</i> =1,575)	706 (44.8%)	869 (55.2%)	1.0 ^b	
<i>Alcohol</i>				
User (<i>n</i> =809)	358 (44.2%)	451 (55.7%)	1.2 (0.9–1.4)	0.17
Non-user (<i>n</i> =903)	403 (44.6)	500 (55.4%)	1.0 ^b	
<i>Marital status</i>				
Married (<i>n</i> =1,351)	583 (43.2%)	768 (56.8%)	0.95 (0.7–1.2)	0.67
Not married (<i>n</i> =361)	178 (49.3%)	183 (50.7%)	1.0 ^b	
<i>Education status</i>				
Less than high school (<i>n</i> =108)	59 (54.6%)	49 (45.4%)	0.8 (0.5–1.2)	0.21
High school or college (<i>n</i> =937)	445 (47.5%)	492 (52.5%)	1.0 ^b	
Professional training (<i>n</i> =646)	242 (37.5%)	404 (62.5%)	0.8 (0.6–1.0)	0.06
<i>Laxative/fiber use</i>				
No constipation (<i>n</i> =673)	299 (44.4%)	374 (55.6%)	1.0 (ref)	
Constipation, no laxatives/fiber use (<i>n</i> =254)	93 (36.6%)	161 (63.4%)	0.6 (0.4–0.9)	0.003
Constipation, fiber/bran/prunes use (<i>n</i> =152)	70 (46.0%)	82 (54.0%)	0.9 (0.6–1.3)	0.43
Constipation, laxative use (<i>n</i> =633)	299 (47.2%)	334 (52.8%)	1.0 (0.8–1.3)	0.99
<i>Previous cholecystectomy</i>				
Yes (<i>n</i> =239)	119 (49.8%)	120 (50.2%)	1.02 (0.8–1.4)	0.92
No (<i>n</i> =1,473)	642 (43.6%)	831 (56.4%)	1.0 ^b	

BMI, body mass index; CI, confidence interval.

^aOdds ratio per ten years of age.^bReference.

^c Odds ratio per one unit of somatoform SSC.

^d Odds ratio per one unit of BMI.

All models adjusted for age and gender.

Table 3

Association of IBS and IBS subtypes with colonic diverticular disease, Olmsted County, MN

Total (n =1,695)	Diverticular disease (n=761)	Diverticulosis (n =670)	Diverticulitis (n=91)			
	OR (95% CI)	P value	OR (95% CI)	P value		
IBS						
No	1.0 (ref)		1.0 (ref)			
Yes	1.7 (1.2–2.4)	< 0.001	1.8 (1.3–2.4)	< 0.001	1.7 (0.9–3.2)	0.12
No IBS						
Age < 65	1.0 (ref)		1.0 (ref)		1.0 (ref)	
Age ≥ 65 ^a	4.3 (3.5–5.4)	< 0.001	4.4 (3.5–5.5)	< 0.001	4.0 (2.4–6.8)	< 0.001
IBS						
Age < 65 ^a	1.2 (0.8–1.8)	0.44	1.2 (0.8–2.0)	0.35	0.8 (0.2–2.8)	0.76
Age ≥ 65 ^a	9.4 (5.8–15.1)	< 0.001	9.3 (5.7–15.2)	< 0.001	9.6 (4.2–21.9)	< 0.001
No IBS	1.0 (ref)		1.0 (ref)		-	-
IBS subtype						
D-IBS ^b	1.9 (1.1, 3.2)	0.02	1.9 (1.1–3.3)	0.02	—	—
C-IBS ^b	1.5 (0.9, 2.6)	0.12	1.5 (0.9–2.6)	0.13	—	—
M-IBS ^b	2.6 (1.0, 6.4)	0.04	3.0 (1.2–7.4)	0.02	—	—
U-IBS ^b	1.5 (0.8, 2.8)	0.23	1.4 (0.7–2.7)	0.32	—	—

C-IBS, constipation-predominant IBS; D-IBS, diarrhea-predominant IBS; IBS, irritable bowel syndrome; M-IBS, mixed IBS; U-IBS, un-subtyped IBS.

^aOdds ratio compared with the younger group (< 65 years) without IBS.

^bOdds ratio compared with the no IBS group. Diverticular diseases (n=742) is the combination of the diverticulitis subgroup and the diverticulosis subgroup. The analysis of IBS subtype among the diverticulitis group was not done owing to limited numbers in these subgroups.

All models adjusted for age and gender.

Table 4

Association between CDD and gastrointestinal symptoms, Olmsted County, MN

Total (n=1,712)	Odds ratio (95% CI) for diverticular disease (n=761)	Odds ratio (95% CI) for diverticulosis (n=670)
<i>Location of abdominal pain</i>		
None (n=1,108)	1.0 ^a	1.0 ^a
Lower abdomen (n=244)	1.6 (1.2–2.2)	1.5 (1.1–2.0)
Upper abdomen (n=220)	1.2 (0.9–1.7)	1.1 (0.8–1.6)
Both upper and lower (n=121)	1.7 (1.1–2.5)	1.5 (0.98–2.3)
<i>Severity of abdominal pain</i>		
None or mild (n=1,250)	1.0 ^a	1.0 ^a
Moderate (n=376)	1.6 (1.2–2.1)	1.5 (1.1–1.97)
Severe/very severe (n=57)	2.5 (1.3–4.5)	2.1 (1.1–4.1)
<i>Frequency of abdominal pain</i>		
None (n=1,101)	1.0 ^a	1.0 ^a
≤1 Time/month (n=369)	1.4 (1.1–1.9)	1.3 (0.99–1.7)
2–5 Times/month (n=90)	1.8 (1.1–2.9)	1.6 (1.0–2.7)
≥6 Times/month (n=120)	1.5 (1.0–2.2)	1.4 (0.9–2.1)
<i>Duration of pain</i>		
None (n=1,101)	1.0 ^a	1.0 ^a
≤ 2 h (n=424)	1.5 (1.2–2.0)	1.5 (1.1–1.9)
>2 h (n=148)	1.3 (0.9–1.9)	1.1 (0.7–1.6)
<i>Functional constipation</i>		
No (n=1,499)	1.0 ^a	1.0 ^a
Yes (n=198)	0.9 (0.7–1.3)	0.95 (0.7–1.3)
<i>Functional diarrhea</i>		
No (n=1,589)	1.0 ^a	1.0 ^a
Yes (n=108)	0.97 (0.6–1.5)	1.0 (0.7–1.6)
<i>Chronic constipation</i>		
No (n=1,385)	1.0 ^a	1.0 ^a
Yes (n=313)	1.2(0.9–1.5)	1.2 (0.9–1.6)
<i>Chronic diarrhea</i>		
No (n=1,490)	1.0 ^a	1.0 ^a
Yes (n=208)	1.4(0.99–1.9)	1.5 (1.0–2.0)
<i>Blood in stool</i>		
No (n=1,512)	1.0 ^a	1.0 ^a
Yes (n=188)	1.1(0.8–1.5)	1.1 (0.7–1.5)
<i>Bloating</i>		
No (n=1,240)	1.0 ^a	1.0 ^a

Total (n=1,712)	Odds ratio (95% CI) for diverticular disease (n=761)	Odds ratio (95% CI) for diverticulosis (n=670)
Yes (n=460)	1.3 (0.99 –1.6)	1.2 (0.9 –1.5)
<i>Mucus</i>		
No (n =1,531)	1.0 ^a	1.0 ^a
Yes (n =159)	1.1 (0.8 –1.7)	1.1 (0.8 –1.7)
<i>Straining</i>		
No (n =1,244)	1.0 ^a	1.0 ^a
Yes (n =443)	1.0 (0.8 –1.3)	1.1 (0.8 –1.3)

CDD, colonic diverticular disease; CI, confidence interval; OR, odds ratio.

^a Reference level.

All models adjusted for age and gender.

“Diverticular diseases (n =761) is the combination of the “diverticulitis” subgroup and the “diverticulosis” subgroup.