ORIGINAL ARTICLE

The impact of overweight on diverticular disease: a cross-sectional multicenter study

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KEY WORDS

diverticulitis, diverticulosis, obesity, overweight

ABSTRACT

INTRODUCTION The prevalence of colonic diverticulosis and diverticulitis has significantly increased in recent years. Obesity is a well-known risk factor for diverticulitis, but far less is known about the association between diverticulitis and overweight.

OBJECTIVES We aimed to examine the association between overweight and diverticulitis and to study the potential relationship between body mass index (BMI) and disease severity.

PATIENTS AND METHODS We conducted a retrospective, multicenter study. Patients diagnosed with diverticulosis confirmed by colonoscopy were included. The diagnosis of diverticulitis was confirmed by computed tomography. Weight status was defined as normal in the case of BMI in the range of 18.5– 24.9 kg/m^2, overweight when BMI was 25–29.9 kg/m^2, and obesity with BMI equal or above 30 kg/m^2.

RESULTS The study included 592 patients. Among them, 157 (26.5%) had normal BMI, 191 (32.3%) were overweight, and 244 (41.2%) were obese. Patients with BMI above the normal range, overweight and obese were at higher odds of acute diverticulitis as compared with those with normal BMI. This was evidenced by the values of odds ratio (OR) 3.10 (95% CI, 2.00–4.73; P <0.001) for weight above the normal range, OR 1.85 (95% CI, 1.14–3.00; P = 0.01) for overweight, and OR 4.50 (95% CI, 2.84–7.12; P <0.001) for obese patients.

CONCLUSIONS Overweight was associated with an increased risk of diverticulitis among patients with diverticulosis. Since overweight is a modifiable factor, this observation has preventive importance.

INTRODUCTION The prevalence of colonic diverticulosis has increased in recent years, particularly in the older population. It has reached 75% among individuals above 80.[1,2] Although most cases of diverticulosis are asymptomatic, some may progress to serious complications that include acute diverticulitis, colonic bleeding and perforation.[3] A nationwide inpatient study from the United States reported that the proportion of hospitalizations due to complications of colonic disease increased by 26% between 1998 and 2005.[4] Risk factors for diverticulitis include modifiable ones such as high intake of red meat and fat and low intake of fiber, lack of physical activity, and smoking.[5]

Obesity prevalence is increasing dramatically worldwide[6] and is associated with disabling comorbidities including ischemic heart disease, hypertension, diabetes mellitus, metabolic syndrome, and cancer.[7,8] The association between obesity and diverticulitis was studied and confirmed previously.[6] However, data are lacking regarding any potential association between obesity and diverticulitis severity and between overweight and diverticulitis and its severity. In this multicenter study, we aimed at evaluating the association between obesity or overweight and diverticulitis rate among patients with diverticulosis. Furthermore, we evaluated the relationship between the above-normal body mass index (BMI) and the severity of diverticulitis.

PATIENTS AND METHODS We conducted a retrospective, cross-sectional study at 2 Israeli regional academic medical centers (Galilee Medical Center and EMMS Nazareth Hospital). Adult

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WHAT'S NEW?

The main finding of this study is a possible link between overweight and increased risk of acute diverticulitis among patients with asymptomatic diverticulosis. This observation has special practical implications since overweight is a modifiable factor. The findings of this study open horizons for prospective studies on the effects of weight loss as an optional treatment for symptomatic diverticular disease.

patients diagnosed with diverticulosis confirmed by colonoscopy between January 1, 2010 and December 31, 2020 were included in the study. Extracted data included demographic variables (age, gender), BMI, medical history (hyperlipidemia, hypertension, chronic renal failure, congestive heart failure, diabetes mellitus, and smoking). The primary outcome of the study was the assessment of the association between overweight or obesity, as measured by BMI, and the rate of diverticulitis (as diagnosed by computed tomography [CT] scans), and recorded in electronic files according to the International Classification of Diseases 9 and 10 up to 6 months before and after the colonoscopy. The secondary outcome was the search for the association between BMI and severity of diverticulitis as assessed by Hinchey classification: Hinchey 0: mild clinical diverticulitis with mild bowel wall inflammation; Hinchey I: localized abscess (para-colonic); Hinchey II: pelvic abscess; Hinchey III: purulent peritonitis; and Hinchey IV: feculent peritonitis.[9]

Patients who presented with Hinchey grades 0 and I were considered to have mild disease, while those with Hinchey grades II, III, and IV were considered to have moderate to severe, complicated diverticulitis.

Exclusion criteria were a diagnosis of colorectal cancer, presence of inflammatory bowel disease, history of colorectal surgery, and a lack of confirmatory colonoscopy following diverticulitis.

BMI was calculated by dividing the person's weight in kilograms by their height in meter squared. Weight status was defined as normal for patients with BMI 18.5–24.9 kg/m^2, overweight with BMI 25–29.9 kg/m^2, and obese with BMI equal or greater than 30 kg/m^2.

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board (approval 1110-20-NHR) on May 19, 2020. Written informed consent was waived by the local ethical committee due to the retrospective, noninterventional nature of the study.

Statistical analysis Categorical variables were presented as frequencies and percentages and were analyzed by application of the χ^2 test. Continuous variables were analyzed and reported as mean (SD) through the use of a 2 sample *t* test. A univariable model analysis was performed to assess the association between BMI groups and diverticulitis, reporting odds ratios (ORs) and CIs. Further backward selection logistic regression model was applied to adjust for potential confounders. Variables with *P* values below 0.05 were considered significant. Statistical analyses were performed using a commercial software Statistical Package for Social Sciences (SPSS version 24.0, IBM, Chicago, Illinois, United States).

RESULTS Overall, 592 patients with documented diverticulosis were included in the study. Among them, 157 patients (26.5%) had normal BMI, 191 patients (32.3%) were overweight according to their BMI, and 244 patients (41.2%) were obese. The average age in the normal, overweight and obese BMI groups was 73.1 (6) years, 69.4 (8.2) years, and 69.8 (7.6) years, respectively. More than half of the patient cohorts in all groups were male (58% for normal BMI, 59.2% for overweight BMI, and 62.3% for obesity BMI groups). The most common site for diverticulosis was the left colon (71.3%, 76.4%, and 66.8%, in normal, overweight, and obese BMI groups, respectively). TABLE 1 reports the demographics and baseline characteristics of the included population.

Association between BMI groups and diverticulitis A total of 33 patients (21%) in the normal BMI group had diverticulitis, as compared with 63 patients (33%) in the overweight group and 133 obese patients (54.5%). BMI in both the overweight and obese group was significantly associated with diverticulitis. The univariable analysis revealed a significantly higher odds of diverticulitis in obese patients than in those with normal BMI (OR, 4.50; 95% CI, 2.84–7.12; *P* <0.001). Similarly, patients classified as overweight according to BMI had a significantly higher odds of diverticulitis as compared with those with normal BMI (OR, 1.85; 95% CI, 1.14–3.00; *P* = 0.01). Further univariable analysis, performed to reveal parameters associated with increased risk of diverticulitis other than overweight and obesity, indicated a significant association with diabetes mellitus (OR, 3.56; 95% CI, 2.50–5.10; *P* <0.001), while chronic renal failure (OR, 0.43; 95% CI, 0.19–0.96; *P* = 0.03), congestive heart failure (OR, 0.45; 95% CI, 0.20–1.00; *P* = 0.05) and age (OR, 0.96; 95% CI, 0.95–0.98; *P* <0.001) were associated with lower odds of developing diverticulitis.

The data in TABLE 2 represent a univariable analysis of parameters associated with diverticulitis. After adjustment for potential confounders including diabetes mellitus and age, and using a backward selection logistic regression model, both overweight and obesity remained significantly associated with diverticulitis, as compared with the normal BMI group (OR, 1.68; 95% CI, 1.10–2.78; *P* = 0.04 and OR, 2.56; 95% CI, 1.50–4.37; *P* = 0.005, respectively) (TABLE 3). Moreover, there was no association

TABLE 1 Demographic and baseline characteristics of the study population

Variable		Normal BMI	Overweight BMI	Obesity BMI
Patients, n		157	191	244
Age, y, mean (SD)		73.1 (6)	69.4 (8.2)	69.8 (7.6)
Gender, n (%)	Male	91 (58)	113 (59.2)	152 (62.3)
	Female	66 (42)	78 (40.8)	92 (37.3)
Medical history, n (%)	Hyperlipidemia	72 (45.9)	98 (51.3)	153 (62.7)
	Hypertension	101 (64.3)	116 (60.7)	184 (75.4)
	Chronic renal failure	7 (4.5)	18 (9.4)	23 (9.4)
	Congestive heart failure	12 (7.6)	13 (6.8)	17 (7)
	Diabetes mellitus	11 (7)	47 (24.6)	60 (24.6)
Smoking, n (%)		35 (22.3)	39 (20.4)	72 (29.5)
Alcohol, n (%)		3 (1.9)	13 (6.81)	8 (3.28)
NSAIDs, n (%)		12 (7.64)	7 (3.74)	19 (7.9)
Aspirin, n (%)		62 (39.5)	82.3 (43.1)	127 (51.9)
Site of diverticulosis, n (%)	Left side location	112 (71.3)	146 (76.4)	163 (66.8)
	Right side location	7 (4.5)	9 (4.7)	22 (9)
	Pancolonic location	38 (24.2)	36 (18.8)	59 (24.2)
Experienced diverticulitis, n (%)		33 (21.02)	63 (33)	133 (54.5)

Abbreviations: BMI, body mass index; NSAIDs, nonsteroidal anti-inflammatory drugs

TABLE 2 Univariable analysis of parameters associated with diverticulitis

Parameter	OR	95% CI	*P* value
Gender male vs female	0.78	0.56–1.09	0.10
Age	0.96	0.95–0.98	<0.001
Hyperlipidemia	0.84	0.60–1.17	0.30
Hypertension	0.74	0.52–1.06	0.10
Smoking	1.38	0.94–2.02	0.10
Alcohol	0.43	0.16–1.15	0.09
NSAID use	0.93	0.47–1.83	0.83
Aspirin use	1.02	0.73–1.43	0.90
Chronic renal failure	0.43	0.19–0.96	0.03
Congestive heart failure	0.45	0.20–1.00	0.05
Diabetes mellitus	3.56	2.49–5.10	<0.001

Abbreviations: see TABLE 1 and 2

TABLE 3 Univariable and multivariable adjustment analysis of body mass index groups associated with diverticulitis

Parameter	OR	95% CI	*P* value
Obesity BMI vs normal BMI	4.50	2.84–7.12	<0.001
Overweight BMI vs normal BMI	1.85	1.14–3.00	0.01
After adjustment for diabetes mellitus and age			
Obesity BMI vs normal BMI	2.56	1.50–4.37	0.005
Overweight BMI vs normal BMI	1.68	1.10–2.78	0.04

Abbreviations: OR, odds ratio; others, see TABLE 1

between diverticulitis severity and BMI, as 66 patients with mild diverticulitis (Hinchey grades 0 and I) had average BMI of 31.8 kg/m^2, whereas 47 patients with moderate to severe diverticulitis (Hinchey grades II, III, and IV) had average BMI of 31.7 kg/m^2 (P = 0.40).

Association between diverticulosis location and diverticulitis Overall, we collected data regarding location in 229 patients with diverticulitis, and 363 patients without diverticulitis. The location of colonic diverticulosis is shown in TABLE 4. There was no association in diverticulitis occurrence with left side and pancolonic location (OR, 0.88; 95% CI, 0.62–1.25; P = 0.47 and OR, 0.88; 95% CI, 0.59–1.32; P = 0.54, respectively). On the other hand, right side location was significantly associated with diverticulitis (OR, 1.97; 95% CI, 1.1–3.62; P = 0.02). Further analysis revealed that BMI in right side colonic diverticulosis complicated with diverticulitis was significantly higher than in patients with right side colonic diverticulosis without diverticulitis (mean [SD] 31.1 [4.2] kg/m^2 vs 28.2 [4.1] kg/m^2, respectively; P = 0.01), suggesting that obesity is a risk factor for diverticulitis among patients with right side colonic diverticulosis (TABLE 4).

DISCUSSION

Colonic diverticulosis is a highly prevalent condition globally.[9,10] While most patients never show symptoms, an increasing incidence of diverticulitis with increasing morbidity has been reported, causing a substantial burden on national health services.[11] Complications of diverticulitis may require surgical intervention in about one-fifth of cases at their first presentation.[12,13]

The current impact of diverticular disease raises the question of possible unidentified etiologies and risk factors. Several risk factors have been recognized in previous studies and they include age, use of proton pump inhibitor drugs,[14] smoking, diabetes mellitus, chronic renal failure, congestive heart failure, and obesity.[5] The identification of new risk factors is of paramount importance in order to reduce or stop the growing incidence of diverticulitis.

Our study showed that obesity and overweight were associated with increased risk of diverticulitis among patients with diverticular disease. Notably, the observed risk factor retained its power after adjustment for possible confounders, such as diabetes mellitus. Previously, obesity had been shown to be a risk factor for diverticulitis, concomitant with the global increase of obesity rates.[6] Strate et al[15] performed a prospective large cohort study of male health professionals to assess the development of acute diverticulitis and found that obesity was a significant risk factor (relative risk, 1.78; 95% CI, 1.08–2.94). A Swedish prospective study of a large community-based sample of middle-aged men, showed that overweight and obesity were associated with the risk of future episodes of acute

TABLE 4 Location of diverticulosis among patients with and without diverticulitis

Location	With diverticulitis (n = 230)	Without diverticulitis (n = 362)	95% CI	*P* value
Left side diverticulitis vs no diverticulitis	162 (70.4)	259 (71.5)	0.62–1.25	0.47
Right side diverticulitis vs no diverticulitis	19 (8.3)	19 (5.2)	1.1–3.62	0.02
Pancolonic diverticulitis vs no diverticulitis	49 (21.3)	84 (23.2)	0.59–1.32	0.54

Data are presented as number (percentage) of patients unless otherwise indicated.

diverticulitis leading to hospitalization.[16] Notably, in our study, both overweight and obesity were associated with diverticulitis. This finding was in line with the previous observation by the Swedish group.[16]

Pathophysiological mechanisms that may link obesity or overweight with the development of diverticulitis include the release of cytokines that promote inflammation in subcutaneous abdominal fat.[17] Moreover, obesity induces variations in the colonic microbiome that may predispose a patient to diverticulitis. Obesity and diverticulitis are associated with alterations in gut microbiota (such as an increased ratio of *Firmicutes* to *Bacteroidetes*).[18] Obesity is also linked with other dietary and lifestyle factors that may be associated with diverticulitis, for example, low consumption of dietary fiber and sedentary lifestyle.[19] A recent review discussed the role of diet in diverticulosis, and concluded that higher consumption of red meat was associated with a mild increase in the risk of acute diverticulitis, while higher consumption of white meat did not pose such a risk.[20]

Overweight is an under-reported health-related factor in studies on the link between BMI and various medical conditions. The focus is always on obesity, while the effect of overweight on health issues is less well defined.

In a recent study Lukosiene et al[21] reported risk factors for diverticulosis and diverticulitis and showed that older age, obesity, and bowel movement habits were associated with an increased likelihood of diverticulosis, while the feeling of incomplete bowel evacuation and a higher educational level were associated with a higher rate of diverticulitis. Moreover, Covino et al[22] developed and validated a 6-item simple score to differentiate patients with the greatest risk of developing complicated, acute diverticulitis. The items were male sex, constipation, hemoglobin levels below 11.9 g/dl, C-reactive protein levels above 80 mg/l, severe obesity, and absence of proton pump inhibitor use. Positive scores for all 6 items produced an area under the receiver operating characteristic curve of 0.674.

From a public health perspective, our findings are of paramount importance, since overweight is a modifiable risk factor and the observed link may promote a public health care policy that identifies individuals with diverticulosis at an increased risk of experiencing diverticulitis.[23] Recently, Makar et al[24] reported that obesity led to adverse outcomes, and several surgical interventions and morbid obesity were associated with higher mortality rates among patients with acute diverticulitis. Furthermore, a study by Koziel et al[25] showed that among patients with established coronary artery disease, there was a gradual increase in BMI and waist circumference. These findings strengthen the data regarding the worst clinical consequences of obesity in this specific population.

Remarkably, another interesting finding of our study was that older age, chronic renal failure and heart failure were associated with lower likelihood of developing acute diverticulitis. These findings are in contrast with those reported in previous studies.[26-28] On the other hand, a recent study demonstrated that older patients showed reduced likelihood of developing acute diverticulitis than younger patients,[21] which was similar to our observations. However, we could not find other data regarding the likelihood of acute diverticulitis among patients with renal or heart failure, and thus further studies are warranted to confirm our findings. Additionally, we noticed that right side diverticular location was associated with higher occurrence of diverticulitis (OR, 1.97; $P = 0.02$). BMI was significantly higher in these patients than in those with right side colonic diverticulosis but without diverticulitis (31.1 vs 28.2 kg/m^2, respectively; $P = 0.01$). A previous study reported that rectosigmoid location is an important factor for recurrence and for acute diverticulitis prognosis.[29] Therefore, further studies are needed to accurately assess the impact of diverticulosis location on the rate and prognosis of diverticulitis.

The main limitation of this study was its retrospective design. However, the potential heterogeneity that arises from this fact is diminished since all physicians in all centers followed the same protocols for both data collection and the use of the diagnostic algorithm. Furthermore, for the last 20 years, all patient files have been recorded in a digital form. Therefore, our data were complete and homogeneous. An additional limitation was that, due to the retrospective design, we were unable to assess the dietary habits of the patients whose data were studied. Nonetheless, since we live in a Mediterranean region,

we assumed that the patients followed similar dietary menu, as the Mediterranean diet is accessible and affordable to people living in Israel.[30] The Mediterranean diet is characterized by a high intake of green vegetables, cereals, whole grains and olive oil, and moderate consumption of alcohol, red meat, and dairy products.[31,32] Moreover, we could extract neither the data on other medications prescribed nor other diverticulosis associated complications, such as bleeding.

The main strengths of this study were the multicenter design and a relatively large number of included patients.

In conclusion, our findings point out a possible link between overweight and increased risk of acute diverticulitis among patients with asymptomatic diverticulosis. This observation has special preventive importance since overweight is a modifiable factor. Prospective international multicenter studies should be performed to confirm our observations.

ARTICLE INFORMATION

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CONTRIBUTION STATEMENT AM, WS and TK contributed to the conceptualization and methodology of the study. WA and HH contributed to the data analysis validation and curation. AM, TK, WS and RP contributed to writing and original draft preparation. AM, TK and RP contributed to reviewing and editing of the manuscript. AM, TK and RP performed scientific criticism and visualization of the study. All authors approved the final version.

CONFLICT OF INTEREST None declared.

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