

ORIGINAL PAPERS

## Colonic diverticulosis and the metabolic syndrome: an association?

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### ABSTRACT

**Background and objectives:** Colonic diverticulosis (CD) is related to advanced age and a lack of dietary fiber. Recently, several studies have shown that metabolic syndrome (MS) is also implicated in the etiopathogenesis of CD. This study aimed to assess the association between MS, obesity and CD.

**Methods:** This was a prospective study of a one-year duration. The MS was defined according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III). Demographic data, risk factors for MS and endoscopic findings of patients who underwent a total colonoscopy in the department were collected. Obesity was defined as a body mass index  $\geq 30$  kg/m<sup>2</sup>. Informed consent was obtained. The local Ethics Committee and National Data Protection Committee approved the study. Statistical analysis was performed with SPSS 21 and statistical significance was defined as  $p < 0.05$ .

**Results:** The study included 203 patients, 95 males with a mean age of 65.5 years. CD was diagnosed in 30.5% of patients. Univariate analysis showed that age, hypertension, increased waist circumference and hyperlipidemia were associated with colonic diverticulosis. There was no association with gender, obesity or type 2 diabetes mellitus. Multivariate analysis showed that age and a greater waist circumference increased the risk of diverticulosis. Age-adjusted analysis showed that MS was associated with diverticulosis. The prevalence of adenoma in patients with CD was similar to that in patients without CD.

**Conclusion:** In this series, MS was significantly associated with CD. The identification of risk groups is important since diverticulosis can have serious and potentially fatal complications. To our knowledge, this is the first Southern European prospective study evaluating the association between MS and CD.

**Key words:** Colonic diverticulosis. Metabolic syndrome. Risk factors.

### INTRODUCTION

Diverticulosis is a frequent benign condition of the colon with a prevalence ranging from 10% to 66% of the population; the frequency increases with age (1-3).

Diverticulosis results from the herniation of the mucosa and submucosa through the muscular layer of the colonic wall. However, the etiopathology is not fully understood. In Western societies, diverticulosis generally affects the left colon (4). The clinical spectrum of diverticular disease is vast, varying from asymptomatic (in about 80% of affected individuals) to symptomatic disease with severe complications (4,5). A study by Peery et al. (6) has shown that diverticular disease costs an estimated amount of 2.6 billion dollars per year in the USA.

Although studies are controversial, some factors have been associated with a higher risk of colonic diverticulosis and its associated complications. It is thought that colonic wall structure abnormalities, disordered intestinal motility, and environmental, genetic, dietary and behavioral factors influence diverticulosis development. A low-fiber diet was traditionally considered to be a major risk factor for diverticular disease (7). However, recent studies have found no evidence of an effect of dietary fiber intake on the development of diverticulosis (8,9). Constipation was believed to be a risk factor for diverticulosis due to an increased intraluminal pressure (7). However, recent studies have not found an association between diverticulosis and less frequent bowel movements or other classic symptoms of constipation such as straining or incomplete bowel movement (8,10,11). Smoking (12), red meat ingestion (13) and insufficient physical activity (14) have also been identified as potential factors that increase the risk of diverticular disease. A genetic study in twins has recently demonstrated that genetic susceptibility contributes significantly to the development of diverticulosis (15). The role of obesity and metabolic factors has also been studied, but the results are heterogeneous (16,17). The aim of this study was to evaluate the possible role of the metabolic syndrome (MS) as a risk factor for diverticulosis.

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## METHODS

This was a prospective study with a series of patients who underwent a screening colonoscopy at the Gastroenterology Department of Centro Hospitalar de Setúbal, Portugal, between March 2013 and March 2014. This study was approved by the institution's Ethics Committee and National Data Protection Committee. Informed consent was obtained from all patients.

A colonoscopy was performed that reached at least the cecum, and the colonoscopic features of diverticulosis and colonic polyps were identified. Diverticulosis was classified as pancolonic, left-diverticulosis or right diverticulosis according to the location.

A standardized questionnaire was performed during the medical consultation in order to collect the following data: sex, age, height (m), weight (kg), body mass index (BMI) (kg/m<sup>2</sup>), waist circumference (cm) measured 1 cm above the umbilicus at minimal respiration, medical history of hypertension, type 2 diabetes mellitus, hyperlipidemia and medication. In the absence of these data, a laboratory evaluation of the following data was obtained prior to the colonoscopy: fasting glucose, triglyceride, and HDL cholesterol levels. Obesity was defined as a BMI  $\geq 30$  kg/m<sup>2</sup>.

MS was diagnosed according to the NCEP-ATP III (18) if three or more of the following criteria were present: a) waist circumference  $\geq 102$  cm in men and  $\geq 88$  cm in women; b) hypertriglyceridemia  $\geq 150$  mg/dl; c) low HDL cholesterol  $< 40$  mg/dl in men and  $< 50$  mg/dl in women; d) high blood pressure  $\geq 130$  mmHg systolic or  $\geq 85$  mmHg diastolic; and e) high serum fasting glucose  $\geq 110$  mg/dl.

## Statistical analysis

Statistical analysis was performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). The Chi-squared test was used for the comparison of discrete variables and the Student's t-test for the comparison of continuous variables. Variables found to be associated with colonic diverticulosis in the univariate analysis were reassessed using logistic regression analysis. A p-value  $\leq 0.05$  was considered as statistically significant.

## RESULTS

Two hundred and three patients were included; 95 were males (47%) with a mean age of  $65.5 \pm 9.2$  years. CD was present in 62 patients (30.5%), 79% of CD patients had left-sided diverticulosis, 3% had right-sided diverticulosis and 18%, pancolonic diverticulosis.

In addition, 84% of patients had elevated blood pressure, 84% had hyperlipidemia and 47%, diabetes mellitus; 67% presented an increased waist circumference and 43% were obese. MS was present in 72% of patients. Table 1 shows the characteristics of patients with and without diverticulosis.

Patients with diverticulosis were significantly older than patients without diverticulosis ( $68.9 \pm 8.3$  years vs  $64.0 \pm 9.2$  years,  $p < 0.001$ ). There was no difference with regard to gender between groups; 48% of patients in the diverticulosis group and 46% in the no diverticulosis group were males ( $p = 0.764$ ). Among patients with and without diverticulosis, 47% and 41%, respectively, were obese ( $p = 0.47$ ).

A positive association with colonic diverticulosis was found for increased waist circumference (77% vs 62%,  $p = 0.039$ ), elevated blood pressure (94% vs 81%,  $p = 0.021$ ) and hyperlipidemia (91.9% vs 80.9%,  $p = 0.046$ ). There was no difference with regard to the prevalence of diabetes mellitus between patients with or without diverticulosis (48% vs 47%,  $p = 0.836$ ).

All the characteristics that comprise the MS were evaluated and MS was more frequent in patients with diverticulosis (87%) than in patients without diverticulosis (65%) ( $p = 0.003$ ). The variables included in the multivariate analysis were age, hypertension, increased waist circumference and hyperlipidemia. An association with diverticulosis was found for age ( $p = 0.001$ , OR 1.068, 95% CI 1.027-1.111) and increased waist circumference ( $p = 0.049$ , OR 2.129, 95% CI 1.005-4.510).

**Table 1. Characteristics of the study population**

	Total (n = 203)	Diverticulosis (n = 62)	Controls (n = 141)	p value
Age, years $\pm$ SD	65.5 $\pm$ 9.2	68.9 $\pm$ 8.3	64.0 $\pm$ 9.2	< 0.001
Male gender n (%)	95 (46.8)	30 (48.4)	65 (46.1)	0.764
BMI $\geq 30$ n (%)	87 (42.9)	29 (46.8)	58 (41.1)	0.470
Hypertension n (%)	172 (84.7)	58 (93.5)	114 (80.8)	0.021
Hyperlipidemia n (%)	171 (84.2)	57 (91.9)	114 (80.9)	0.046
Diabetes mellitus n (%)	96 (47.2)	30 (48.4)	66 (46.8)	0.836
Increased waist circumference n (%)	136 (67.0)	48 (77.4)	88 (62.4)	0.039
Metabolic syndrome n (%)	146 (71.9)	54 (87.1)	92 (65.2)	0.001
Colorectal adenomas n (%)	80 (39.4)	22 (35.5)	58 (41.1)	0.448

BMI: Body mass index.

MS adjusted for age was evaluated and there was an association with colonic diverticulosis ( $p = 0.002$ , OR 3.682, 95% CI 1.587-8.546). There was no difference in the prevalence of colorectal adenomas between patients with colonic diverticulosis (36%) and control patients (41%) ( $p = 0.448$ ).

## DISCUSSION

Colonic diverticulosis is a prevalent condition with an unknown etiology. Colonic diverticulosis can result from a weakness of supporting connective tissue and a subsequent increase in intraluminal pressure, which occurs with aging (19).

The prevalence of diverticulosis in this study was 30.5%, which is similar to other studies (2,20), and it increased with age, as previously demonstrated in other studies (21,22). The majority of patients with diverticulosis had left-sided diverticulosis, which is consistent with other European studies (23,24). Asian studies, in contrast, found a higher prevalence of right-sided diverticular disease (17,25).

There was no correlation between gender and diverticulosis. Initial studies have demonstrated a male preponderance for colonic diverticulosis (26). However, more recent studies found a higher rate of diverticular disease in females, especially in advanced ages (27). A study of the incidence of complicated diverticular disease based on gender and age by McConell et al. (28) found that strictures and obstructions occur more commonly in females, while diverticular bleeding occurs more often in men.

Although some studies found an association between obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) and asymptomatic colonic diverticulosis (16), others did not find such an association (17). Other studies have found that obesity increased the risk of symptomatic diverticular disease (29-31). In this study, obesity did not represent a risk factor for diverticulosis development. However, increased waist circumference was associated with diverticulosis. A Portuguese study by Afonso et al. (32) that assessed visceral and subcutaneous fat by ultrasound demonstrated an association between diverticulosis and visceral fat. In addition, two other studies that assessed central obesity via computed tomography (CT) scan demonstrated that visceral fat area, but not BMI, was an independent risk factor for diverticulosis (25,33). Furthermore, the study by Yamata et al. (34) showed that patients with left sided diverticula that developed diverticulitis were more likely to have a visceral fat area  $\geq 100$  cm than patients with asymptomatic diverticulosis. Some studies have shown that visceral fat produces elevated serum levels of several proinflammatory cytokines that induce chronic subclinical inflammation (35,36). In addition, nitric oxide synthase elevation (35) can lead to a decrease in the action of nonadrenergic and noncholinergic inhibitory nerves that induces colonic segmentation and contributes to diverticulosis development (37,38).

There is controversy with regard to the association of other metabolic factors in the development of colonic diverticulosis. A study by Kopylov et al. (16) demonstrated that *diabetes mellitus* was a protective factor for colonic diverticulosis and found no association with hypertension or hyperlipidemia. By contrast, a study by Sakuta et al. found that *hypertension* and diabetes mellitus frequency rates were higher among patients with diverticulosis than in control patients (39). The study by Rosemar et al. (31) demonstrated that elevated blood pressure was also a risk factor for symptomatic diverticular disease. Another study by Joaquim et al. (40) found no association between hypertension, hyperlipidemia or DM and recurrence of diverticular bleeding. In this series, hypertension, diabetes mellitus and dyslipidemia were not independent risk factors for diverticulosis, and the prevalence of colonic adenoma or adenocarcinoma was similar in patients with or without diverticulosis, which is similar to the findings from other studies (16).

There are several limitations with regard to this study. Firstly, other potential confounders such as smoking, intake of dietary fiber, physical activity and constipation were not assessed. Secondly, the study population included patients who underwent a screening colonoscopy after referral from a general practitioner or a specialist physician rather than subjects from the general population, which may constitute a selection bias. In addition, data collection of some metabolic factors such as arterial hypertension, hyperlipidemia and diabetes mellitus was performed using the patients' medical history, medication reports and recent laboratory analysis. New laboratory tests were performed only when this information was not available.

In summary, this study demonstrated an association between age, increased waist circumference and MS with diverticulosis development. Studies assessing the relation between MS and diverticulosis are scarce. This study supports the hypothesis that MS plays a role in diverticulosis development. However, further studies are needed to confirm these results and to understand the importance of several metabolic factors in the pathogenesis of diverticular disease.

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