

# World Journal of *Clinical Cases*

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## Retrospective Study

## Age, alcohol, sex, and metabolic factors as risk factors for colonic diverticulosis

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## Abstract

**BACKGROUND**

The pathogenesis of colonic diverticulosis is not well understood. Moreover, only a few studies on colonic diverticulosis have been reported in mainland China.

**AIM**

To evaluate the prevalence of and risk factors for asymptomatic colorectal diverticulosis in Eastern China.

**METHODS**

From August 2016 to July 2020, 6180 asymptomatic individuals were enrolled in this cross-sectional study. These individuals had undergone physical examinations, laboratory testing, and colonoscopy. Data regarding the baseline characteristics and their general health status were obtained through interviews.

**RESULTS**

The prevalence of colonic diverticulosis was 7.3% (449/6180). Colonic diverticulosis was detected predominantly on the right side of the colon (88.4%). Logistic regression analysis revealed that an age  $\geq 60$  years (adjusted odds ratio [OR] 2.149, 95% confidence interval [CI] 1.511-3.057,  $P < 0.001$ ), male sex (adjusted OR: 1.878, 95% CI: 1.373-2.568,  $P < 0.001$ ), obesity (adjusted OR: 1.446, 95% CI: 1.100-1.902,  $P = 0.008$ ), alcohol intake (adjusted OR: 1.518, 95% CI: 1.213-1.901,  $P < 0.001$ ), hypertension (adjusted OR: 1.454, 95% CI: 1.181-1.789,  $P < 0.001$ ), hypertriglyceridemia (adjusted OR: 1.287, 95% CI: 1.032-1.607,  $P = 0.025$ ), and hyperuricemia (adjusted OR: 1.570, 95% CI: 1.257-1.961,  $P < 0.001$ ) significantly increased the risk of colonic diverticulosis.

**CONCLUSION**

Advanced age, male sex, alcohol intake, obesity, and other metabolic-related factors, such as hypertension, hypertriglyceridemia, and hyperuricemia, were independent risk factors for colonic diverticulosis. Understanding the true

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prevalence of colonic diverticulosis and its associated risk factors will aid in its prevention and treatment.

**Key Words:** Aged; Alcohol drinking; Colonic diverticulosis; Hypertension; Obesity

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**Core Tip:** This cross-sectional study revealed that advanced age, male sex, alcohol intake, obesity, and other metabolic-related factors, such as hypertension, hypertriglyceridemia, and hyperuricemia, were independent risk factors for colonic diverticulosis. The prevention and management of these risk factors may aid in reducing the risk of colonic diverticulosis development and decreasing the incidence of colonic diverticulosis.

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## INTRODUCTION

Colonic diverticulosis is characterized by herniation of the mucosa and submucosa through defects in the muscle layer, covered only by the serosa[1]. The distribution of diverticula within the colon showed geographic and racial variability. In the Western population, colonic diverticulosis is commonly observed and is predominantly left-sided[2]. In contrast, the prevalence of diverticulosis is lower and predominantly right-sided in Asian populations[3-5].

The prevalence of colonic diverticulosis has increased worldwide over time. Recently, a study in Northern China reported that the diverticulosis rate markedly increased from 3.8% in 2011 to 4.98% in 2015[6]. The elevated incidence of colonic diverticulosis in China may result from an aging society, a more westernized diet, and an increase in CT scans or colonoscopy screening. In approximately 15% of cases of asymptomatic colonic diverticulosis, complications such as bleeding, diverticulitis or peritonitis may develop during a patient's lifetime[7,8]. Colonic diverticulosis may, therefore, become a substantial socioeconomic burden because of the increasing incidence, followed by increasing hospital admission rates and costs. The pathogenesis of diverticulosis is not completely understood to date. Several risk factors, such as age, obesity, diet, and physical inactivity, have been identified for colonic diverticulosis[9-12]. Other than the known factors, recent studies have implied that low-grade inflammation and gut microbiota may influence the development of diverticulosis[7,13]. To the best of our knowledge, only a few studies have focused on colonic diverticulosis in mainland China. Therefore, this cross-sectional study aimed to assess the prevalence of and the risk factors associated with asymptomatic colorectal diverticulosis in Eastern China.

## MATERIALS AND METHODS

### Patient selection

From August 2016 to July 2020, 6312 consecutive asymptomatic individuals underwent health check-ups at the First Affiliated Hospital of Wenzhou Medical University. All these individuals underwent physical examination, blood biochemical examination, and colonoscopy. The patients' baseline characteristics and general health status were obtained through face-to-face interviews. The exclusion criteria were a history of colitis, colorectal cancer, and colonic surgery. Finally, 6180 individuals were enrolled in the study.

This study was approved by the Institutional Review Board and Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. It was performed in compliance with the 1964 Helsinki declaration and its later amendments. The

requirement for informed consent was waived owing to the retrospective nature of the study.

### Diagnostic criteria

Colonoscopy was performed with a CF-H250AI colonoscope. The location of the diverticula was defined as right-sided (cecum, ascending colon, or transverse colon) and left-sided (splenic flexure, descending colon, or sigmoid colon). All examinations were performed on the same day.

### Statistical analysis

The statistical analysis was performed using SPSS 23. Continuous variables are presented as the means  $\pm$  standard deviations (SDs), and between-group differences were evaluated using *t* tests. The chi-square test was used for categorical variables. Odds ratios (ORs) and 95% confidence intervals (CIs) were obtained by logistic regression analysis. Statistical significance was established for two-sided *P* values  $< 0.05$ .

## RESULTS

The prevalence of colonic diverticulosis was 7.3% (449/6180). Colonic diverticulosis was detected predominantly on the right side of the colon in 88.4% (397/449), on the left side in 6.2% (28/449), and bilaterally in 5.3% (24/449) of the individuals. **Table 1** shows the characteristics of the colonic diverticulosis (+) group and colonic diverticulosis (-) group. Subjects with colonic diverticulosis were significantly older than those without colonic diverticulosis ( $50.57 \pm 10.116$  years *vs.*  $47.92 \pm 10.533$  years,  $P < 0.001$ ). The mean body mass index (BMI) was higher in the colonic diverticulosis (+) group than in the colonic diverticulosis (-) group ( $25.03 \pm 3.226$  *vs.*  $23.84 \pm 3.131$ ,  $P < 0.001$ ). Obesity (BMI  $\geq 28$ ) was more frequently noted in the colonic diverticulosis (+) group than in the colonic diverticulosis (-) group ( $P < 0.001$ ). Smoking and alcohol consumption rates were higher in the colonic diverticulosis (+) group than in the colonic diverticulosis (-) group ( $P < 0.001$ ). Additionally, the systolic and diastolic blood pressures ( $P < 0.001$  for both) and the triglyceride ( $P < 0.001$ ), total cholesterol ( $P = 0.001$ ), fasting blood glucose ( $P = 0.001$ ), and uric acid ( $P < 0.001$ ) levels differed significantly between the colonic diverticulosis (+) group and colonic diverticulosis (-) group. Hypertension ( $P < 0.001$ ), hypertriglyceridemia ( $P < 0.001$ ), hypercholesterolemia ( $P = 0.001$ ), hyperglycemia ( $P < 0.001$ ), and hyperuricemia ( $P < 0.001$ ) were more frequently observed in the colonic diverticulosis (+) group than in the colonic diverticulosis (-) group.

Variables showing a significant association on the univariate analysis were included in the logistic regression analysis. Logistic regression analysis revealed that an age  $> 60$  years (adjusted OR: 2.149, 95%CI: 1.511-3.057,  $P < 0.001$ ), male sex (adjusted OR: 1.878, 95%CI: 1.373-2.568,  $P < 0.001$ ), obesity (adjusted OR: 1.446, 95%CI: 1.100-1.902,  $P = 0.008$ ), alcohol intake (adjusted OR: 1.518, 95%CI: 1.213-1.901,  $P < 0.001$ ), hypertension (adjusted OR: 1.454, 95%CI: 1.181-1.789,  $P < 0.001$ ), hypertriglyceridemia (adjusted OR: 1.287, 95%CI: 1.032-1.607,  $P = 0.025$ ), and hyperuricemia (adjusted OR: 1.570, 95%CI: 1.257-1.961,  $P < 0.001$ ) were significantly associated with an increased risk of colonic diverticulosis (**Table 2**).

## DISCUSSION

In this study, the prevalence of colonic diverticulosis was 7.1%, which is lower than that reported for asymptomatic populations in neighboring areas, such as Taiwan (13.5%)[14], Japan (18.8%)[15], and South Korea (8.7%)[16]. This difference may be attributed to the differences in the mean age, genetic predispositions, dietary habits, and lifestyles of the study cohorts. In this study, colonic diverticulosis was predominantly right-sided, similar to that reported in other Asian countries. In contrast, in Western populations, colonic diverticulosis was predominantly left-sided and was particularly detected in the sigmoid colon. This difference may be due to the genetic predispositions of the subjects. Choe *et al* [17] performed a genome-wide association study in South Korea and found that the *WNT4*, *RHOA*, and *OAS1/3* genes might be the underlying cause of the development of right-sided diverticulosis.

Table 1 Baseline characteristics of the subjects

Parameter	Diverticulosis (+), 449	Diverticulosis (-), 5731	P value
Mean Age	50.57 ± 10.116	47.92 ± 10.533	< 0.001
Age < 40	60	1203	
60 > Age ≥ 40	300	3669	
Age > 60	89	859	< 0.001
Male gender	382 (85.1%)	3622 (63.2%)	< 0.001
Mean BMI	25.03 ± 3.226	23.84 ± 3.131	< 0.001
Obesity (BMI ≥ 28)	77 (17.1%)	528 (9.2%)	< 0.001
Smoker	190 (42.3%)	1601 (27.9%)	< 0.001
Alcohol	185 (41.2%)	2158 (37.7%)	< 0.001
Systolic blood pressure, mmHg	132.07 ± 18.608	125.19 ± 17.995	< 0.001
Diastolic blood pressure, mmHg	78.82 ± 12.27	74.14 ± 12.278	< 0.001
Hypertension, (BP ≥ 130/80mmHg )	183 (40.8%)	1447 (25.2%)	< 0.001
TG, mmol/L,	2.38 ± 2.277	1.80 ± 1.549	< 0.001
Hypertriglyceridemia, (TG ≥ 2.3 mmol/L)	166(37.0%)	1272(22.2%)	< 0.001
TC, mmol/L	5.49 ± 1.122	5.32 ± 1.090	0.001
Hypercholesteremia, (TC ≥ 6.2 mmol/L)	116(25.8%)	1087(19.0%)	0.001
FBG, mmol/L	5.08 ± 1.270	4.88 ± 1.229	0.001
Hyperglycemia, (FBG ≥ 6.1 mmol/L)	56(12.5%)	421(73.5%)	< 0.001
UA, umol/L	388.73 ± 90.508	344.57 ± 87.70	< 0.001
Hyperuricemia, (UA ≥ 420umol/L)	160(35.6%)	1074(18.7%)	< 0.001

Continuous variables are reported as mean ± SD; categorical variables are reported as *n* (%). BMI: Body mass index; BP: Blood pressure; TC: Total cholesterol; TG: Triglyceride; FBG: Fasting blood glucose; UA: Uric acid.

Multivariate logistic regression analysis further indicated that advanced age, male sex, obesity, alcohol intake, hypertension, hypertriglyceridemia, and hyperuricemia were independent risk factors for colonic diverticulosis. Age was previously reported to be an important risk factor for colonic diverticulosis[15,18]. Our results suggest that the risk of colonic diverticulosis increases with age. Individuals aged > 60 years were more likely to develop colonic diverticulosis than those aged < 40 years. Age-related degeneration of the mucosal wall and segment was proposed to increase the pressure in the colon, resulting in the bulging of sites with weak tissue[7]. This study revealed a strong positive association between male sex and colonic diverticulosis. This finding was consistent with those of published studies from Japan[15], Taiwan[14], and Israel [19]. Alcohol intake was also identified as a risk factor for colonic diverticulosis. This may be because alcohol inhibits colonic motility through the activation of the nuclear factor-kB pathway and the subsequent upregulation of inducible nitric oxide synthase expression, thus resulting in increased intracolonic pressure and colonic diverticulosis [20,21]. We identified various metabolic factors that play a substantial role in the development of colonic diverticulosis. The mean BMI in the colonic diverticulosis (+) group was significantly higher than that in the colonic diverticulosis (-) group. Multivariate analyses indicated that obesity increased the risk of colonic diverticulosis, which is consistent with the findings of studies on other Asian and Western populations. Strate *et al*[22] conducted a large long-term follow-up study and identified obesity as a major risk factor for diverticulosis. Although the precise mechanism underlying the association between obesity and diverticulosis development is unclear, the altered cytokine profile[23], altered microflora[24], and increased intra-abdominal pressure in obese individuals may play important roles. Other metabolic-related factors, such as hypertension, hypertriglyceridemia, and hyperuricemia, also pose increased risk for colonic diverticulosis. Vascular changes may explain the association between these metabolic-related factors and diverticulosis.

**Table 2** Logistic regression analysis for the risk factors of diverticulosis

	Adjusted OR	P value	95%CI
Age			
< 40	1	1	1
60 > Age ≥ 40	1.489	0.007	1.112-1.993
Age ≥ 60	2.149	< 0.001	1.511-3.057
Male gender	1.878	< 0.001	1.373-2.568
Obesity	1.446	0.008	1.100-1.902
Smoker	1.175	0.154	0.941-1.466
Alcohol	1.518	< 0.001	1.213-1.901
Hypertension	1.454	< 0.001	1.181-1.789
Hypercholesteremia	1.244	0.064	0.988-1.567
Hypertriglyceridemia	1.287	0.025	1.032-1.607
Hyperglycemia	1.281	0.121	0.937-1.750
Hyperuricemia	1.570	< 0.001	1.257-1.961

Logistic regression analysis adjusted for age, male sex, body mass index, smoking habit, alcohol consumption, hypertension, hypercholesteremia, hypertriglyceridemia, hyperglycemia, hyperuricemia.

The anatomical characteristics of the colon are fragile spots in the circular layer where the blood vessels penetrate the colon[25,26]. These factors cause endothelial injury and arteriosclerosis, resulting in blood vessel degeneration, thereby leading to a further substantial decrease in the blood supply to the fragile colonic wall[27].

This study has some limitations. First, the study lacked data on dietary habits, physical activity, and daily bowel movements, which are important confounding factors for colonic diverticulosis. Second, this was a cross-sectional study; therefore, a causal relationship between the risk factors and colonic diverticulosis could not be confirmed. Third, data on smoking and alcohol intake should be quantified. Finally, all subjects were enrolled from an asymptomatic population undergoing health examinations, which is indicative of a better economic status of the study population; therefore, the presence of selection bias cannot be disregarded.

## CONCLUSION

Colonic diverticulosis is considered a major health burden because of its potentially serious complications[28-30]. Therefore, the prevention and management of alcohol intake, obesity, and other metabolic factors, such as hypertension, hypertriglyceridemia, and hyperuricemia, may aid in reducing the risk of colonic diverticulosis development and in decreasing the incidence of colonic diverticulosis.

## ARTICLE HIGHLIGHTS

### Research background

The pathogenesis of colonic diverticulosis is not well understood.

### Research motivation

Only a few studies on colonic diverticulosis have been reported in mainland China. Understanding the true prevalence of colonic diverticulosis and the risk factors associated with it will aid in the prevention and treatment of this disease.

### Research objectives

To evaluate the prevalence of and risk factors for asymptomatic colorectal divertic-

ulosis in mainland China.

### Research methods

From August 2016 to July 2020, 6180 asymptomatic individuals were enrolled in this cross-sectional study.

### Research results

Logistic regression analysis revealed that an age  $\geq 60$  years (adjusted odds ratio [OR] 2.149, 95% confidence interval [CI] 1.511-3.057,  $P < 0.001$ ), male sex (adjusted OR: 1.878, 95%CI: 1.373-2.568,  $P < 0.001$ ), obesity (adjusted OR: 1.446, 95%CI: 1.100-1.902,  $P = 0.008$ ), alcohol intake (adjusted OR: 1.518, 95%CI: 1.213-1.901,  $P < 0.001$ ), hypertension (adjusted OR: 1.454, 95%CI: 1.181-1.789,  $P < 0.001$ ), hypertriglyceridemia (adjusted OR: 1.287, 95%CI: 1.032-1.607,  $P = 0.025$ ), and hyperuricemia (adjusted OR: 1.570, 95%CI: 1.257-1.961,  $P < 0.001$ ) significantly increased the risk of colonic diverticulosis.

### Research conclusions

Advanced age, male sex, alcohol intake, obesity, and other metabolic-related factors, such as hypertension, hypertriglyceridemia, and hyperuricemia, were independent risk factors for colonic diverticulosis.

### Research perspectives

Our findings are of educative value and are likely to aid clinicians in the management of patients with this disease entity.

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