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Increasing Diverticulosis in an Aging Population: A Colonoscopy-Based Study of 5-Year Trends in 26 463 Patients in Northern China

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background:

Because such data are scarce in northern China, the purpose of this study was to determine trends in diverticulosis over the past 5 years.

Material/Methods:

A total of 26 463 patients (27 558 examinations, including 1095 repeated colonoscopies) performed between January 2011 and December 2015 were reviewed respectively. The distributions of diverticulosis were recorded, which were classified as right-sided, left-sided, and bilateral type. The trends in diverticulosis were analyzed in terms of aging and yearly increase. Additionally, associations of the occurrence of diverticulosis with age (\leq 39, 40–59, and \geq 60 years) and sex were determined using a logistic regression model.

Results:

We identified 1045 patients with colonic diverticulosis, with an overall prevalence of 3.8% (1045/27 558). A preponderance of right-sided diverticulosis was demonstrated, accounting for 72.9% (693/951) of included subjects. The proportion of colonic diverticulosis increased significantly (P < 0.001 for trend), from 2.78% (112/4028) in 2011 to 4.98% (309/6208) in 2015. The proportion of patients of all age groups with diverticulosis increased significantly (P < 0.001 for trend) in correlation with yearly increase. There was a greater proportion of diverticulosis, regardless of the distribution, in patients aged ≥ 60 than in younger age groups (P < 0.001 for trend). Multivariate analysis showed older age and male sex (P < 0.001) were independent risk factor for diverticulosis. Colonic diverticulosis has been increasing in northern China, where rapid aging is ongoing.

Conclusions:

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MeSH Keywords:

Aging • Diverticulosis, Colonic • Risk Factors

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Background

Diverticulosis comprises various entities related to the presence of diverticula of the colon, referring to herniations through a weak site on the bowel wall, resulting in a bulging pouch. Several factors may contribute to the pathogenesis of diverticulosis, including age, diet, intestinal motility, and genetic factors, as well as intestinal innervation [1]. The prevalence of diverticulosis is highly heterogeneous due to ethnic and geographic variability [2]. A western lifestyle characterized by a low-fiber diet and a lack of physical activity probably contributes to a rise in the incidence for diverticulosis [3]. However. more recently, a large cross-sectional study failed to identify low-fiber diets or physical inactivity as risk factors for diverticulosis [4]. In the U.K., data demonstrated a dramatical increase from 49 000 cases of diverticulosis in 2000 to more than 70 000 in 2006 [5]. A similar trend regarding prevalence of diverticulosis was also reported in Asian countries, although it is still low in comparison with western countries [6-10]. Recently, a study in Japanese by Nagata et al. [7] found the diverticulosis rate gradually increased from 18% in 2003 to 23% in 2011. Additionally, a study from Taiwan indicated a prevalence of 13.5% in the asymptomatic population [9].

Concerns have been raised about the stressful epidemiologic and economic burden of diverticular disease [1]. Patients with diverticulosis may develop symptoms, including abdominal pain, diverticulitis, peritonitis, ileus, or abscess formation. These complications were estimated to cost over 4 billion dollars for in 2004 in the U.S. [11]. Furthermore, the prevalence of diverticular complications may continue to rise owing to the aging and growing population [12]. As the world's most populated country, China is facing a challenge due to an aging society. The elderly (aged 60 and older) population in China is expected to exceed 400 million by 2050, accounting for 30% of the total population [13]. Surprisingly, studies of

epidemiological trends in colonic diverticulosis from mainland China are scarce. Recently, a colonoscopy-based survey from southern China demonstrated a still very low prevalence of diverticulosis, without a yearly change in trends [14].

Therefore, we conducted the present retrospective study of patients undergoing a complete colonoscopy within the last 5 years at our high-volume endoscopy center. We aimed to investigate the rates of diverticulosis in a rapidly aging population in northern China.

Material and Methods

Study population

From January 2011 to December 2015, consecutive patients aged ≥18 years old undergoing a colonoscopy at the Endoscopy Center, Department of Gastroenterology and Hepatology, Tianjin Medical University General Hospital, were included in the current study. All patients provided informed consent prior to examination. This study was approved by the Ethics Committee of Tianjin Medical University General Hospital. All procedures were conducted in accordance with the Declaration of Helsinki. We excluded patients with a prior diagnosis of inflammatory bowel disease, a previous history of colectomy, incomplete colonoscopy procedure (including cases without cecum intubation and any severe complication), or poor bowel preparation (Figure 1).

Colonoscopy procedure

All colonoscopies were performed by endoscopists at our institution. An electronic endoscope (CF-Q260, Olympus Optical Co., Tokyo, Japan) was used during the study period. Bowel preparation was obtained by using 2.0 L of polyethylene glycol the day before the examination.

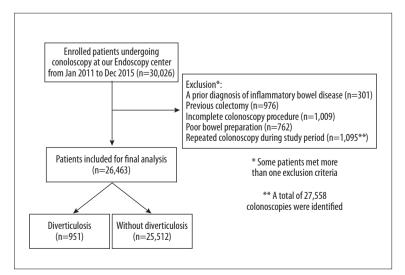


Figure 1. Flow diagram for patients included in the current study.

We regarded complete colonoscopy as cecal intubation followed by identification of the ileocecal valve. The location of diverticula was defined as right-sided (involving the cecum, ascending colon, or transverse colon); left-sided (involving the splenic flexure, descending colon, or sigmoid colon); or bilateral (involving the entire colon). The distribution and type of diverticulosis were recorded carefully in our electronic database by the endoscopists.

Statistical analysis

Data are given as mean \pm standard deviation (range) or simple proportion, as appropriate. We used the chi-square test to assess the patient characteristics (age and sex) and increase over time in diverticulosis. Logistic regression models were used to evaluate the association of the presence of diverticulosis with age (\leq 39, 40–59, and \geq 60 years old) and sex. The trends with respect to age growth and yearly increase were determined by using the Cochran-Armitage test. We calculated odds ratio (OR) and 95% confidence intervals. We regarded a *P* value <0.05 as statistically significant. STATA 12.0 (Stata Corp., College Station, Tex., U.S.) and SPSS 18.0 (SPSS Inc., Chicago, IL., U.S.) were used for all analyses.

Results

Patient characteristics

The baseline characteristics of investigated patients are shown in Table 1. Of the 26 463 patients enrolled, 13 738 (51.9%) were female and the mean age was 53.1±14.0 years (range 18-94 years). The majority of the study population were outpatients (22 310/26 463, 84.3%) and underwent colonoscopies for diagnosis (17 911/26 463, 67.7%). As shown in Figure 2, the proportion of participants aged ≥60 years significantly increased from 31.2% in 2011 to 38.5% in 2015 (P<0.001 for trend), whereas no significant difference was found in terms of sex (P=0.67 for trend). We identified 1045 patients with colonic diverticulosis, with an overall prevalence of 3.8% (1045/27 558 total examinations), including 576 males (60.6%) and 375 females (39.4%). The mean age was 58.0±13.1 years (range 19–93 years) for subjects with diverticulosis, and 450 (47.3%) were aged ≥60 years. Diverticulosis was located bilaterally in 145 (15.2%), in the left side of the colon in 113 (11.9%), and in the right side in 693 (72.9%).

Change in proportion of diverticulosis according to age growth and yearly increase

As shown in Figure 3, the proportion of colonic diverticulosis increased significantly (*P*<0.001 for trend) from 2.78% (112/4028) in 2011 to 4.98% (309/6208) in 2015. The proportion of patients

Table 1. Baseline characteristics of included patients.

	Total (n	=26,463)	
Age (years)	53.1±14.	0 (18–94)	
Gender, n (%)			
Male	12725	(48.1)	
Female	13738	(51.9)	
Outpatients			
Baseline indication	22310	(84.3)	
Screening	1508	(5.7)	
Endoscopic intervention	6879	(26.0)	
Diagnosis/Surveillance	17911	(67.7)	
Others	165	(0.6)	
Overall proportion, n (%)	3.8% (104	1045/27,558)	
Distribution of diverticula, n (%)			
Right-sided	693	(72.9)	
Left-sided	113	(11.9)	
Bilateral	145	(15.2)	

of all age groups with diverticulosis increased significantly (P < 0.001 for trend) according to year. Right-sided and bilateral diverticulosis rates increased significantly (P < 0.001 for trend), from 2.09% (84/4028) and 0.35% (14/4028) in 2011 to 3.58% (222/6208) and 0.85% (53/6208) in 2015, respectively, but were not significantly changed with respect to left-sided (P = 0.21 for trend) diverticulosis.

When stratified by age, a very rapid increase in the diverticulosis rate was observed in the study population (P < 0.001 for trend) (Figure 4A). Of participants aged ≤ 39 years, only 1.88% showed any evidence of diverticulosis, while it was present in 4.84% of patients aged 60 years and above. The diverticulosis rate reached a peak in the ≥ 60 year age group (5.13% for males and 4.55% for females). There was a greater proportion of diverticulosis, regardless of the distribution, in patients aged ≥ 60 than in other younger age groups (P < 0.001 for trend) (Figure 4B).

Associations of age and sex with the presence of diverticulosis

Univariate analysis showed that increasing age was correlated with the presence of diverticulosis. Patients in older age groups (40–59 year and \geq 60 year age groups) were more likely to have diverticulosis compared with those under 40 years (P<0.001). Additionally, men were more likely to have diverticulosis than

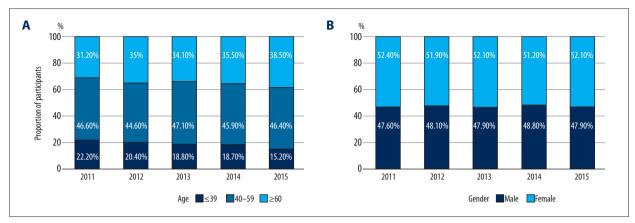


Figure 2. Age and sex distribution of the study population. (A) Age distribution of the study population. The proportion of participants aged ≥60 years significantly increased (P<0.001 for trend). (B) Sex distribution of the study population. No significant difference was found in terms of sex (P=0.67 for trend).

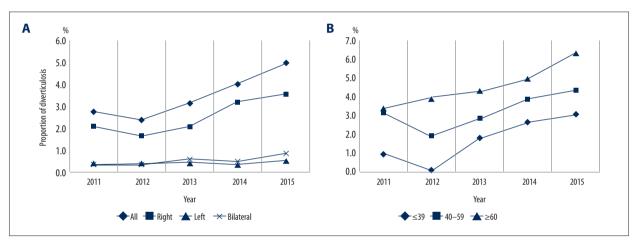


Figure 3. Change in the proportion of diverticulosis according to yearly increase. (A) Colonic diverticulosis increased yearly (P<0.001 for trend). Yearly right-sided and bilateral diverticulosis rates increased with time (both P<0.001 for trend). (B) Annual proportion of patients of all age groups with diverticulosis increased over time (all P<0.001 for trend).

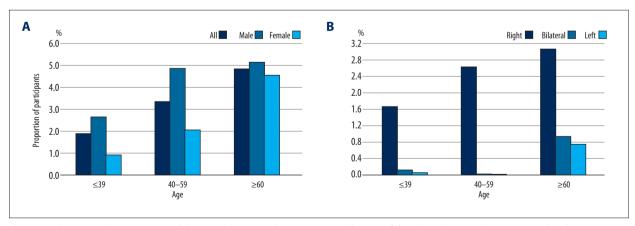


Figure 4. Change in the proportion of diverticulosis according to age stratification. (A) Colonic diverticulosis increased with age in both males and females (P<0.001 for trend). (B) A greater proportion of diverticulosis was observed in the ≥60 year group (P<0.001 for trend).

Table 2. Logistic regression analysis of age and gender regarding the presence of diverticulosis.

	Div(–)* (n=25,512)	Div(+)** (n=951)	OR	Univariate 95% CI***	P value	OR	Multivariate 95% CI	P value
Age (years)								
≤39 (n=4,958)	4,865 (19.1)	93 (9.8)	1	Reference		1	Reference	
40-59 (n=12,200)	11,792 (46.2)	408 (42.9)	1.84	1.46–2.31	<0.001	1.93	1.54–2.43	<0.001
≥60 (n=9,305)	8,855 (34.7)	450 (47.3)	2.69	2.15-3.38	<0.001	2.82	2.25–3.55	<0.001
Gender								
Female (n=13,738)	13,363 (52.4)	375 (39.4)	1	Reference		1	Reference	
Male (n=12,725)	12,149 (47.6)	576 (60.6)	1.68	1.47-1.92	<0.001	1.74	1.52–1.99	<0.001

^{*} Div(-) - patients without diverticulosis; ** Div(+) - patients with diverticulosis; *** CI - confidence interval.

their female counterparts, as shown by univariate analysis (P<0.001). Multivariate analysis with stepwise logistic regression showed older age (40–59 year group: OR 1.93, 95% CI 1.54–2.43; \geq 60 year group: OR 2.82, 95% CI 2.25-3.55; P<0.001) and male sex (OR 1.74, 95% CI 1.52–1.99; P<0.001) were independent risk factors for diverticulosis (Table 2).

Discussion

The prevalence of colonic diverticulosis is reported to be increasing throughout the world [7,15]. Diverticulosis is generally regarded as being a western disease, giving rise to the distinction concerning its racial and geographic incidence [2]. Until recently, the majority of detailed and large-scale studies were from North America and the developed countries of Europe. It is estimated that diverticulosis affects approximately 50% of the population aged 60 and over [15-18]. However, with the intensive penetration and incorporation of western lifestyle, as well as the remarkably increasing elderly population, there has been a dramatic increase of the incidence of diverticulosis among Asian countries. While still low in comparison to western countries, an increasing trend in prevalence was observed in Asia, including Japan, Singapore, Thailand, and Taiwan [7,9,10,19]. The literature on diverticulosis prevalence in mainland China is scant, which is surprising, as it is the most populated and rapidly aging country in the world [20]. Recent research from southern China has revealed an overall diverticulosis prevalence of 1.97%, without significant change during the last decade [14]. However, the aforementioned study is limited by its relatively small percentage of elderly people, and it did not reflect the diversity in lifestyle and dietary patterns between northern and southern China [21].

In the present study, a yearly trend of increasing diverticulosis rates was observed, from 2.78% in 2011 to 4.98% in 2015.

This result concurs with other studies, reflecting corresponding contributing to increased incidence of diverticulosis.

One issue that should be addressed is the changing proportion of included subjects with respect to age stratification. The clear increase of elderly participants over the survey period in our study is important, with the 38.5% rate recorded in 2015 being approximately 1.2-fold the rate in 2011. Generally, the occurrence of diverticulosis is associated with advancing age. Peery et al. found the incidence rose from <16% in patients aged <40 years to >63% among septuagenarians [4]. Likewise, Tanaka et al. also showed that women aged 90-99 years had an increased incidence of diverticulosis, but they found a slightly decreased incidence with age in men [22]. The prolonged time during which the connective tissue is exposed to intestinal contents (thereby increasing susceptibility various pathogenetic factors) may give rise to diverticulosis [23,24]. China, as the world's most populated nation, is now facing the challenges of a rapidly aging population. It is estimated that China's aging population (aged 60 and older) will increase by 6.2 million per year from 2020 to 2050, and is expected to exceed 400 million by 2050, accounting for 30% of its overall population [13]. Collectively, the tendency of increasing diverticulosis rates may last for many years, which is partly supported by results of the current study, since Tianjin is one of the most developed municipalities in northern China [25,26].

According to the age groups, our results indicate that onset of diverticulosis significantly increases with aging in both males and females. Additionally, males were more likely to have diverticulosis in any age group than were females. These findings are consistent with published reports from Japan and Taiwan, which revealed male sex as a risk factor for the development of diverticulosis [7,9]. Most recently, a screening study also showed a male preponderance for diverticulosis in the U.S. [4]. Although there is little consensus on sex differences

regarding the pathogenesis of diverticulosis, several extrapolations demand further investigation. Recent studies have suggested that diverticulosis is caused at least in part by alteration of gut microbiome composition, immunodeficiency, release of toxic metabolites, and damage to intestinal epithelium [27]. Moreover, Yazici et al. [28] demonstrated that methanogens probably participate in the development of diverticulosis, independent of age and other clinical factors. Taken together, it is plausible that gut microbiota may partly cause the sex disparity in diverticulosis formation due to natural sex-related differences [29].

The distribution pattern of diverticulosis differs between western and Asian countries. The general literature shows a preponderance of right-sided diverticulosis in Asian populations [6,7,9,10,14,19]. Our results are consistent with these observations, showing a 72.9% right-sided diverticulosis rate in the study population. We found that the increasing trend was stronger with the right-sided type than other types according to yearly increase and age growth. The left-sided and bilateral diverticulosis rates slightly declined in patients aged 40-59 years, but finally reached a peak in those age 60 and over. Takano et al. found that diverticulosis showed a strong tendency to rise and spread from the right side to both sides of the colon [30]. Furthermore, it is evident that left-sided type is predisposed to be acquired, meaning that it is more likely influenced by a low-fiber diet and intestinal dysmotility [31]. In this regard, Wang et al. [32] found a stable level of dietary fiber in Chinese adults age 40 and older, but found decreased fiber consumption in younger people. Collectively, our results and those of others suggest confounding factors and different underlying mechanisms in various patterns of diverticulosis regarding onset and development of the condition.

It is meaningful to compare the findings of our study with a recent observational study from southern China by Hong et al. [14]. After reviewing 63 282 colonoscopies, they concluded that the prevalence of diverticulosis was still low (1.97% overall prevalence) and that trends did not change during the survey years. The discrepancies between that study and ours should be interpreted as follows: (1) The proportion of elderly participants varied greatly between these 2 studies. The yearly trends of increasing diverticulosis in our study partly arise from a steadily increasing proportion of elderly people (≥60 years). (2) A disparity consistently exists

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between northern and southern China concerning dietary pattern. In support of this, He et al. [21] demonstrated a "Green Water" dietary pattern characterized by high intakes of rice and vegetables, and moderate intakes of seafood, pork, and poultry in southern China. Moreover, rapid economic growth in Tianjin has led to a rapid shift to a diet dominated by fat and animal products, with decreased consumption of grains and vegetables [25]. Intriguingly, Crowe et al. [33] confirmed that higher intake of fiber from grain was associated with reduced risk of diverticular disease. Another prospective study from Korea also suggested a positive correlation between a high-fat diet and high prevalence of colonic diverticulosis [6]. Although Peery et al. [4] showed that fat intake was not associated with increased prevalence of diverticulosis, their study mainly included asymptomatic subjects.

The present study is thus far the largest epidemiological study in northern China with colonoscopy-derived data, which is a powerful way to eliminate systematic bias arising from heterogeneous examination methods. However, our study still has several limitations. First, it is a retrospective review with selection bias due to the inclusion criteria. Actually, the indication for baseline colonoscopy covered screening, diagnostic, and therapeutic purposes, subsequently affecting the precision of evaluation. Due to flaws in non-screening designation, the current study was prone to clinical bias due to influences of practice and perspective. Second, we were largely unable to specify confounding factors in the increasing trend of diverticulosis, apart from changes over time and with increased age. Further prospective investigations are needed to determine risk factors of diverticulosis. Third, Tianjin is a major city with a heterogeneous population due to prospering economy and tourism and our electronic database included very few patients from the surrounding province, which would have tended to be local people. Fourth, our findings may not be generalizable to other regions due to the geographically uneven development of China. Finally, we cannot comment on the economic burden of diverticulosis due to the enrollment of both inpatients and outpatients in this retrospective review.

Conclusions

Colonic diverticulosis has been increasing in northern China, where rapid aging is ongoing.

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