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Proportion of Colonic Diverticulosis and Its Associated Factors among Patients Underwent Colonoscopy

Kolonoskopi Yapılan Hastalarda Kolonik Divertikülozis Oranı ve İlişkili Faktörler

Nik Ahmad Amru NIK MAZLAN[1,2]
0000-0003-4331-8329
Ahmad Shanwani MOHAMED SIDEK[3]
0000-0002-6369-2847
Andee Dzulkarnaen ZAKARIA[1,2]
0000-0002-4826-9725
Zaidi ZAKARIA[1,2]
0000-0003-1644-3546
Maya Mazuwin YAHYA[1,2]
0000-0002-3994-6608
Wan Zainira WAN ZAIN[1,2]
0000-0001-8019-6063
Mung Seong WONG[1,4]
0000-0002-8027-2166
Siti Rahmah HASHIM MERICAN[1,2]
0000-0002-8158-3601
Mohd Nizam MD HASHIM[1,2]
0000-0002-4066-6558
Ikhwan Sani MOHAMAD[1,2]
0000-0002-9825-0459
Wan Mokhzani WAN MOKHTER[1,2]
0000-0002-5622-0307
Zalina ZAHARI[5]
0000-0003-1459-8958
Michael Pak-Kai WONG[1,2]
0000-0001-9137-3096

[1]School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia
[2]Department of Surgery, Hospital Universiti Sains Malaysia, Kelantan, Malaysia
[3]Department of Surgery, Hospital Raja Perempuan Zainab II, Kelantan, Malaysia
[4]Department of Internal Medicine, Hospital Universiti Sains Malaysia, Kelantan, Malaysia
[4]Faculty of Pharmacy, Universiti Sultan Zainal Abidin, Terengganu, Malaysia

Corresponding Author
Sorumlu Yazar
Michael Pak-Kai WONG
michaelpkwong@usm.my
Zalina ZAHARI
zalinazahari@unisza.edu.my

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ABSTRACT

Aim: Diverticular disease is one of the most common gastrointestinal disorders to date, with a notable rising trend in developing countries. However, the proportion of colonic diverticulosis and its associated factors among patients who have undergone colonoscopy remains controversial. This study aimed to determine the local data on the proportion of diverticular disease in the community, its complications, the association of diverticulosis with diabetes mellitus and hypertension, as well as demographic characteristics.
Material and Methods: A retrospective review of medical records was performed among patients who had undergone colonoscopy between January and December 2019. Demographic and clinical characteristics, the presence of diabetes mellitus, hypertension, and diverticular disease and its complications were examined, and the association of diverticular disease and its complications with demographic and clinical characteristics were analyzed.
Results: Out of 221 patients, 12.7% (n=28) of them had diverticular diseases with a slightly predominant right-sided occurrence (42.9%, n=12). There were significant associations with age (p=0.002), ethnicity (p=0.011), and hypertension (p=0.036), but not with gender and diabetes mellitus (p=0.261, and p=0.334, respectively). There was no significant association between hypertension and recurrence of complicated diverticulitis (p=0.741), septic complications (p=0.678), and diverticular bleeding (p=0.243). Diabetes mellitus was significantly associated with diverticular bleeding complications (p=0.001) but not with septic complications (p=0.418) and recurrence of complicated diverticulitis (p=0.629).
Conclusion: This study showed almost a similar percentage of diverticulosis compared to previous local studies. Age, ethnicity, and hypertension were associated with the presence of diverticulosis, and diabetes mellitus was associated with diverticular bleeding.
Keywords: Diverticular disease; age; ethnicity; hypertension; diabetes mellitus.

ÖZ

Amaç: Divertiküler hastalık bugüne kadar en sık görülen gastrointestinal hastalıklardan biridir ve gelişmekte olan ülkelerde belirgin bir artış eğilimi göstermektedir. Ancak kolonoskopi yapılan hastalarda kolonik divertikülozis oranı ve bununla ilişkili faktörler tartışmalıdır. Bu çalışmada, toplumdaki divertiküler hastalık oranına ilişkin yerel verilerin, komplikasyonları, divertikülozisin demografik özelliklerin yanı sıra diyabet ve hipertansiyon ile ilişkisinin de incelenmesi amaçlandı.
Gereç ve Yöntemler: Ocak ve Aralık 2019 tarihleri arasında kolonoskopi yapılan hastaların tıbbi kayıtları geriye dönük olarak incelendi. Demografik ve klinik özellikler, diyabet, hipertansiyon ve divertiküler hastalık varlığı ve komplikasyonları incelendi ve divertiküler hastalık ve komplikasyonlarının demografik ve klinik özellikler ile ilişkisi analiz edildi.
Bulgular: 221 hastanın %12,7'sinde (n=28) divertiküler hastalıklar mevcuttu ve hafif baskın olarak sağ tarafta (%42,9, n=12) görülüyordu. Yaş (p=0,002), etnik köken (p=0,011) ve hipertansiyon (p=0,036) ile anlamlı ilişki vardı, ancak cinsiyet ve diyabet ile anlamlı ilişki yoktu (sırasıyla p=0,261 ve p=0,334). Hipertansiyon ile komplike divertikülit nüksü (p=0,741), septik komplikasyonlar (p=0,678) ve divertiküler kanama (p=0,243) arasında anlamlı bir ilişki saptanmadı. Diabetes Mellitus'un divertiküler kanama komplikasyonları (p=0,001) ile anlamlı düzeyde ilişkili olduğu ancak septik komplikasyonlar (p=0,418) ve komplike divertikülit nüksü (p=0,629) ile ilişkili olmadığı görüldü.
Sonuç: Bu çalışma önceki yerel çalışmalarla karşılaştırıldığında neredeyse benzer bir divertikülozis yüzdesi gösterdi. Yaş, etnik köken ve hipertansiyon divertikülozis varlığıyla, diyabet ise divertiküler kanamayla ilişkiliydi.
Anahtar kelimeler: Divertiküler hastalık; yaş; etnik köken; hipertansiyon; diyabet.

INTRODUCTION

Diverticular disease is one of the most common gastrointestinal disorders to date, where it is most prevalent in Western countries due to dietary habits, with a notable rising trend in developing countries. Despite being known to have less prevalence of colonic diverticular disease, the adoption of the Western diet into the Asian population may have led to an increment in the prevalence of cases (1). Diverticular disease is thought to be a disease of the elderly with a proportionate increment with age, where more than 60% of affected individuals are older than 80 years old, and only 10% of them are younger than 40 years old. However, the incidence of diverticular disease among younger populations appears to be arising. This poses a diagnostic challenge as 70% of these young patients require surgical intervention, whereas most of the elderly patients remain asymptomatic throughout their lives.

Many aspects of diverticular disease remained uncertain, making primary and secondary prevention seem impossible. Previous theories on the pathophysiology of diverticular disease support that of bacterial overgrowth causing infection, but recent reports indicate an inflammatory process initiated by the release of pro-inflammatory cytokines, as evidenced by the abundance of mast cells seen at all layers of histopathological sections of the diseased colonic wall. Other causes include alterations in colonic wall resistance, disordered colonic motility, and dietary deficiencies, especially fiber (2). This pro-inflammatory state is present in diabetes mellitus patients, whereas hypertension is associated with a worse prognosis for patients to develop complicated diverticular disease due to the increased pressure in blood vessels causing vascular endothelial injury and subsequently atheroma formation, leading to arteriosclerosis. This, in turn, will cause the affected blood vessels in the diverticula to be more fragile; elevating the risk of them to be ruptured leading to bleeding complications (3).

Recent studies have shown the association between metabolic disorders and colonic diverticular disease. The surge in the prevalence of hypertension and diabetes mellitus in the Malaysian population may contribute to an increase in the prevalence of colonic diverticulosis. Hypertension and diabetes mellitus patients are common in the Malaysian population, where the number of Malaysians suffering from both diseases increases proportionately with age. A similar trend is observed with the prevalence of diverticulosis. Several years have passed but the percentage of hypertensive patients in the Malaysian population has been in a plateau (around 30%) since 2011. Diabetes mellitus, on the other hand currently affects 1 in every 5 adults in Malaysia, with its prevalence on the rise as reported by NHMS 2019; 11.2% in 2011, 13% in 2015 to 18.3% in 2019 (4). A 2012 Israeli study reported that diabetes mellitus serves as a protective factor against the development of diverticulosis (5), contradicting a Japan-based study which found that more concomitant diabetes mellitus is discovered among patients with diverticulum than those without diverticulum (6), supported by a 2011 Malaysian-based study which reported that diabetes mellitus is associated with recurrent complicated diverticular disease (7). The same Israeli study also concluded that arterial hypertension is not related to diverticulosis whereas the same Japanese study found that more diverticulum patients have hypertension compared to those with no diverticulum.

Only 10-25% of patients have symptoms, thus the diagnosis of diverticular diseases is often incidentally detected by investigations of the lower gastrointestinal tract (8). Symptoms range from non-specific abdominal pain and feeling bloated to complications such as acute diverticulitis, bleeding, and perforations, which are also signs and symptoms for numerous other gastrointestinal disorders (2). Although most patients with complicated diverticular disease are self-remitting and have a generally good prognosis, they are at risk of disease recurrence and eventually need surgical intervention.

Diagnostic tools used to determine the presence of diverticulosis include CT colonography and/or CT abdomen, colonoscopy, barium enema, and ultrasonography; where all are with different sensitivity and specificity. CT colonography and/or abdomen ranked first, especially in diagnosing acute diverticulitis.

In this study, we aimed to obtain local data on the proportion of diverticulosis in the community, its complications, the association of diverticular disease to diabetes mellitus and hypertension, as well as demographic characteristics; and subsequently compare it with other regional statistics.

MATERIAL AND METHODS

This study is a retrospective review of the medical records in the Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan, and Hospital Raja Perempuan Zainab II (HRPZ II), Kota Bharu Kelantan from January to December 2019 involving all patients who had underwent colonoscopy that fulfilled the inclusion and exclusion criteria.

The list of patients was obtained from the colonoscopy room via admission records. During the whole span of 2019, a total of 862 colonoscopies were conducted in the HRPZ II while 770 colonoscopies were done in HUSM. Systematic random sampling where every 7^{th} record was chosen to be selected as subject (9). Details were then filled up into data collection forms (pro forma). The subjects were each assigned with unique subject ID and pro forma filled were kept in files only accessible by the investigator.

A total of 221 patients' records that fulfilled the criteria were enrolled in the study. Subjects are labeled with study code to maintain privacy and confidentiality. The inclusion criteria for this study included patients aged above 18 years old who underwent colonoscopy from January to December 2019. Cases with incomplete data of colonoscopy findings from records, incomplete colonoscopy, and patients who had undergone prior bowel resection were excluded.

The sample size was calculated using a single proportion formula for the first objective and two independent proportion formulas for the second objective, using PS: Power and Sample Size Calculation Version 3.0.4.3. To determine the proportion of colonic diverticular disease in Kelantan from January until December 2019, the sample size was determined based on parameter estimates obtained from Wong et al. (10).

For the second objective, which is to determine the factors associated with colonic diverticulosis in Kelantan from January until December 2019, the sample size was calculated using the parameter estimates obtained from Rajendra et al. (11) with a significance level of 0.05, and the power of the study of 80%. The final targeted sample size was determined by considering a 20% drop-out rate. The estimated sample size for this study was 221.

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008) as reflected in a priori approval by the Human Research Ethics Committee, Universiti Sains Malaysia in Kelantan, Malaysia (18.11.2020, USM/JEPeM/20080442).

Statistical Analysis

The data were descriptively analyzed in mean and standard deviation (SD) or median and interquartile range (IQR) for continuous data. For categorical data, frequency and percentage were used. The chi-square test and Fisher's exact test were used to determine the association between colonic diverticulosis and its complications with hypertension and diabetes mellitus, as well as patients' demographics, where appropriate. Data analyses were performed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). The level of significance was set at 0.05.

RESULTS

A total of 221 samples were randomly selected by systematic random sampling method which were enrolled from the colonoscopy records of both tertiary hospitals. The mean age of patients was 57.1±16.9 (range, 20-89) years, where the majority of patients (n=116, 52.5%) were >60 years old. Of the patients, 132 (59.7%) were male. The majority of the patients were Malay (n=186, 84.2%). This is consistent with demographic data of Kelantan, Malaysia population where more than 90% of the population is Malay. Hypertension and diabetes mellitus were present in 49.3% (n=109) and 28.1% (n=62) of the patients, respectively. Colonic diverticulosis was detected in 12.7% (n=28) of the study group. There was a slight predominance of right-sided diverticulosis (n=12, 42.9%) as compared to left-sided occurrence 35.7% (n=10), whereas 21.4% (n=6) have bilateral diverticulosis. (Table 1).

In those older than 60 years of age, 19.8% (n=23) were diagnosed with diverticulosis during colonoscopy. None of the patients aged younger than 40 years old have diverticulosis on colonoscopy, while only 7.8% (n=5) of the 41-59 age group have diverticular disease. There was a significant association between age and presence of diverticulosis (p=0.002).

Among the 89 female patients, 15.7% (n=14) were diagnosed with diverticulosis while only 10.6% (n=14) suffered from diverticulosis among males (Table 2). However, there was no statistically significant association between gender and the presence of diverticulosis (p=0.261).

While 18 (9.7%) of the Malay patients had diverticulosis, 10 (30.3%) Chinese had diverticulosis, whereas none of the Indians and other ethnicities had the disease. Statistical analysis indicated that race was significantly associated with the presence of diverticulosis (p=0.011).

Of the 109 patients with hypertension, only 19 (17.4%) had diverticulosis, while those without diverticulosis comprised 90 (82.6%) patients. In 112 non-hypertensive patients, only 9 (8%) were diagnosed with diverticulosis, whereas 103 (92%) patients had no diverticulosis. There was a significant association between hypertension and the presence of diverticulosis (p=0.036).

While 10 (16.1%) of the patients with diabetes mellitus had diverticulosis, 52 (83.9%) of these patients did not. Among 159 non-diabetic patients, only 18 (11.3%) of them suffered from diverticular disease, whereas 141 (88.7%) patients were free of it. However, there was no statistically significant association between diabetes mellitus and the presence of diverticular disease (p=0.334).

Among the hypertensive patients, 21.1% (n=4) had a history of acute diverticulitis prior to colonoscopy, while 15.8% (n=3) had recurrent complicated diverticulitis after colonoscopy (Table 3). Similar findings were also noted in the non-hypertensive group. There was no statistically significant association between hypertension and recurrence of complicated diverticular disease (p=0.741).

A similar finding was also noted among the diabetic and non-diabetic group of patients. Among the 20% (n=2) of diabetic patients with a previous history of acute diverticulitis, 10% (n=1) was found to have recurrent complicated diverticulitis after colonoscopy, while among the 22.2% (n=4) of non-diabetic with previous acute diverticulitis, 16.7% (n=3) developed complicated diverticulitis after colonoscopy (Table 3). However, there was no statistically significant association between diabetes mellitus and recurrence of complicated diverticular disease (p=0.629).

Hypertension was also not associated with septic complications (p=0.678), bleeding complications (p=0.243), or any complications of diverticular disease (p=0.483). Bleeding complications were present in 31.6% (n=6) of the hypertensive patients and 15.8% (n=3) had septic complications.

While 7 (70%) diabetic patients suffered from complicated diverticular disease, and 27.8% (n=5) of non-diabetics had the same disease (Table 3). Statistical analysis indicated that diabetes mellitus was significantly associated with

Table 1. Patient demographics and clinical characteristics

	All Patients (n=221)
Age (years), mean±SD	57.1±16.9
Age, n (%)	
<40 years	41 (18.6)
41-59 years	64 (29.0)
>60 years	116 (52.5)
Gender, n (%)	
Male	132 (59.7)
Female	89 (40.3)
Ethnicity, n (%)	
Malay	186 (84.2)
Chinese	33 (14.9)
Indian	1 (0.5)
Others	1 (0.5)
Hypertension, n (%)	109 (49.3)
Diabetes mellitus, n (%)	62 (28.1)
Diverticular disease, n (%)	28 (12.7)
Anatomical distribution of diverticular disease, n (%)	*(n=28)*
Left	10 (35.7)
Right	12 (42.9)
Bilateral	6 (21.4)

SD: standard deviation

Table 2. Presence of diverticular disease according to the patient demographics and clinical characteristics

	Age			p
	<40 years (n=41)	**41-59 years (n=64)**	**>60 years (n=116)**	
Presence of diverticular disease, n (%)	0 (0.0)	5 (7.8)	23 (19.8)	**0.002**

	Gender		p
	Male (n=132)	**Female (n=89)**	
Presence of diverticular disease, n (%)	14 (10.6)	14 (15.7)	0.261

	Ethnicity				p
	Malay (n=186)	**Chinese (n=33)**	**Indian (n=1)**	**Others (n=1)**	
Presence of diverticular disease, n (%)	18 (9.7)	10 (30.3)	0 (0.0)	0 (0.0)	**0.011**

	Hypertension		p
	Yes (n=109)	**No (n=112)**	
Presence of diverticular disease, n (%)	19 (17.4)	9 (8.0)	**0.036**

	Diabetes mellitus		p
	Yes (n=62)	**No (n=159)**	
Presence of diverticular disease, n (%)	10 (16.1)	18 (11.3)	0.334

Table 3. History of acute diverticulitis before colonoscopy, recurrent complicated diverticulitis after colonoscopy, septic and bleeding complications, and complicated diverticular disease according to hypertension and diabetes mellitus status

	Hypertension		p	Diabetes Mellitus		p
	Yes (n=19)	**No (n=9)**		**Yes (n=10)**	**No (n=18)**	
History of acute diverticulitis, n (%)	4 (21.1)	2 (22.2)	0.944	2 (20.0)	4 (22.2)	0.891
Recurrent complicated diverticulitis, n (%)	3 (15.8)	1 (11.1)	0.741	1 (10.0)	3 (16.7)	0.629
Septic complication, n (%)	3 (15.8)	2 (22.2)	0.678	1 (10.0)	4 (22.2)	0.418
Bleeding complication, n (%)	6 (31.6)	1 (11.1)	0.243	6 (60.0)	1 (5.6)	**0.001**
Complicated diverticular disease, n (%)	9 (47.4)	3 (33.3)	0.483	7 (70.0)	5 (27.8)	**0.030**

diverticular complications (p=0.030). Septic complications refer to acute diverticulitis and complicated diverticulitis such as diverticular abscess, perforation, and fistulas. When separated into septic and bleeding complications, only the bleeding complication is significantly associated with diabetes mellitus (p=0.418, and p=0.001, respectively). 10% (n=1) of diabetic patients have septic complications and 60% (n=6) have bleeding complications, whereas 22.2% (n=4) of non-diabetics suffered from septic complications, and only 5.6% (n=1) have bleeding complications.

DISCUSSION

The result of this study showed that 12.7% of patients were diagnosed with diverticular disease in 221 colonoscopy records examined. This is a slight increment compared to an earlier Malaysian-based study conducted in 2005 at a private institution which had a 10% prevalence of diverticular disease diagnosed using colonoscopy (11). Otherwise, this study showed a lower prevalence when compared to two Japanese studies that were conducted over 20 years (from 1990 to 2010) with a reported 18.8% prevalence (12), and 20.3% prevalence for a study conducted from 2003 to 2011 (13). On the other hand, another study in Japan conducted from 1965 to 1980 had a lower percentage (7.8%) of prevalence in the initial year that increased up to 12.3% during the last 3 years of the study (14). A Singaporean study showed a 45% prevalence of diverticular disease diagnosed with barium enema from the year 2001 to 2002 (15), a rising number as compared to an earlier study in a similar setting which reported a prevalence of 28% in the year 1988 till 1989 (16). An Indian-based study reported a 9.9% prevalence of diverticular disease. Western part of the world showed a prevalence of 5 to 10% in young age groups and this can increase up to 70% in the elderly (17).

Anatomic distribution of the colonic diverticular disease can be divided into the right (cecum, ascending, and transverse colon), left (entire colon distal to splenic flexure), or bilateral involvement (11). Of the 28 patients with colonic diverticulosis in our study, 10 (35.7%) were left-sided, 12 (42.9%) were right-sided and 6 (21.4%) were bilateral. There is a slight predilection to the right side of about 42.9% compared to the left side of 35.7%, although left-sided diverticular disease is still considered common. Various Asian-based studies have a right-sided diverticulum preponderance as compared to our Western counterparts (7). This finding is comparable to a study made in Brunei where the reported cases of right-sided diverticulum were 37.1%, left-sided diverticulum of 32.7%, and bilateral diverticulum of 26.1% (10). This is further supported by a study in Thailand using an analysis of barium enema involving a sample of 2877 subjects where a significant right-sided predominance was reported, with double the amount compared to left-sided diverticulum (18).

A Malaysian study conducted in 2010 reported a recorded number of 24 out of 121 patients (19.8%) having recurrent complicated diverticular diseases with a significant association with diabetes mellitus. The present study has shown that 10% of diabetic patients developed recurrent complicated disease after colonoscopy. A possible reason

for this is due to diabetes mellitus being known to cause pro-inflammatory conditions, delay wound healing, affect microvasculature circulations in the intestines, and various other systemic effects; where all these factors may have contributed to this finding (7). However, we did not include the data on diabetes mellitus control in this study group, which would have had effects on developing more complications related to diverticular disease.

Most of our study group were elderly patients, where this group of subjects are likely associated with more comorbidities and poorer general health, and therefore, may have a less favorable outcome following an acute attack of diverticulitis.

This study found that ethnicity was related to the presence of colonic diverticulosis. However, Indians and other ethnicity (Siamese, in this study) only constituted 1% of the study group and none of them were diagnosed with diverticular disease. Therefore, it is difficult to conclude the actual frequency among different racial groups.

Colonoscopy performed in the elderly can have its unique challenges which include poor bowel preparations, multiple comorbidities resulting in higher hypotensive episodes with the use of sedatives secondary to prolonged procedures, and a lesser number of completed colonoscopy procedures (19). As most of our study group was in the elderly group, this carries a risk of missing the presence of diverticular disease in the study group as an incomplete procedure has to be excluded from this study.

Complicated colonic diverticular disease can be seen as bleeding, acute diverticulitis, or segmental colitis (20,21). These complications can cause morbidity and mortality. One aspect we looked into was the association between the recurrence of complicated colonic diverticular disease with the presence of metabolic conditions; hypertension and diabetes mellitus. Our finding reported no association both hypertension and diabetes mellitus with the recurrence of complicated colonic diverticular disease. This result was supported by a previous study that reported a significant association between diabetes mellitus and the recurrence of complicated diverticular disease, and no significant association with hypertension (7). This study could probably be improved further by studying the population admitted to the ward for complicated colonic diverticular disease with a bigger sample size.

The present study reported a non-significant association between hypertension with septic or bleeding complications of colonic diverticular disease. However, a prospective case-control study on colonic diverticular bleeding conducted in Japan concluded that hypertension has an odds ratio (OR) of 2.2 to cause diverticular bleeding, thus considered an independent risk factor (3). The basis of risk factors for bleeding diverticular are conditions that are known to alter blood flow and angioarchitecture (22,23).

There is a significant association between diabetes mellitus and complicated diverticular disease (24), mainly towards bleeding diverticular (25). These results are not in accordance compared to a study that noted diabetes mellitus has no significant association with diverticular bleeding (26). Diabetes mellitus is associated with an immunocompromised state as it impairs blood circulation and adversely affects normal immunological response. However, in this study diabetes mellitus has no significant association with septic complications of diverticular disease. It is interesting to note that a study reported that obesity (a risk factor for diabetes mellitus) is associated with an increased incidence and severity of complicated diverticular disease, which is diverticulitis (27).

Our study is limited also by the absence of a sub-analysis of the severity of the comorbidity; hypertension and diabetes mellitus. We understood that some of the patients with multiple comorbidities would be on polypharmacy. This limitation hinders us from concluding the association of risk of bleeding and sepsis especially those with uncontrolled diabetes mellitus and those on anticoagulant or antiplatelet therapy. Perhaps in future studies, we could collect more detailed variables regarding this to perform a sub-analysis on the outcomes related to the severity of the comorbidities and medications towards the proportion of diverticulosis and its complications.

CONCLUSION

We conclude that this study reported almost similar percentage of diverticular disease compared to other previous local studies and that there were significant associations between age, ethnicity, and hypertension with the presence of diverticular disease but hypertension is not significantly associated with either septic or bleeding complications of diverticular disease. Diabetes mellitus is associated with diverticular bleeding. However, the presence of diabetes mellitus, as well as gender, are not significantly associated with diverticular disease. Some studies showed similar results but there are also contradicting outcomes, suggesting that further, more comprehensive study is needed to be done in the future. Understanding the connection between these comorbidities and diverticulosis allows healthcare professionals to more accurately assess the risks and benefits before initiating multidrug therapy. For example, since diabetes mellitus is associated with bleeding complications, it is crucial to advise patients that the initiation of anticoagulants or antiplatelets puts them at a higher risk of bleeding. This informed approach enables healthcare providers to make more precise decisions tailored to the individual's health profile.

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