Original Research Article

Factors Associated With The Recurrence Of Complicated Diverticular Disease

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Abstract

Colonic diverticula is observed in over 60% of the western population aged over 80 where up to 30% will eventually be symptomatic and may develop complications. The natural history and etiology of colonic diverticula have been well described. However, predictive indicators of complicated diverticular disease are not known thus preventing the prophylactic treatment of this subset of patients,. The aim of this study was to observe patients with complicated diverticular disease in order to identify common factors associated with recurrent complications. All hospital admissions from January 2005 to December 2008 for complications of diverticular disease were recruited. Using logistic regression, demographic data and factors such as clinical presentation, nature of complication, lifestyle, concomitant medical illness and medications that may be associated with recurrent episodes of complications were analyzed. A total of 121 patients were diagnosed with complicated diverticular disease during the study period with 24 patients having recurrent complications. Logistic regression analysis performed after controlling for confounders found active smoking (p=0.006) and alcohol consumption (p=0.036) along with underlying diabetes (p=0.031) and dyslipidemia (p=0.039) significantly associated with an increased risk of recurrent complications. We therefore concluded that smoking, alcohol consumption, diabetes mellitus and dyslipidemia are associated with recurrent complicated colonic diverticular disease. As these are modifiable risk factors, they should be sought for during the presentation of the first attack. Aggressive control of these factors will help in reducing the risk of recurrent complications.

Key Words: Colon, disease, diverticulitis, bleeding, surgery, risk.

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Introduction

Diverticular disease is a clinical spectrum of conditions ranging from latent colonic diverticulosis to symptomatic disease with potentially lethal complications. Asymptomatic diverticula are a common entity with a rising prevalence. It has no gender preponderance and is seen in up to 60% of those aged over 80 years (1), Industrialization and migrating populations are believed to contribute to the increased incidence of this condition globally (2).

The exact aetiology of colonic diverticula is not well elucidated although high intraluminal pressure and a weak colonic wall at the sites of nutrient vessel penetration are thought to contribute to its formation (3). Deficiency in dietary fibre has been widely accepted as a contributing factor with higher incidences of diverticular disease seen in subjects on low fibre diets (4). Interestingly, the anatomical distribution of colonic diverticula is also different in Asian and Western populations suggesting a genetic predilection (5, 6).

Factors contributing to the formation and complication of diverticular disease have been extensively studied. High fat and low fibre diet, smoking, immuno-compromise and a poor pre-morbid state have all been implicated although there are others that have reported the opposite (7, 8). Local epidemiological studies have also observed a trend of racial predisposition despite a rather similar dietary regime among the different races (9). This has raised the question of a genetic predisposition in the incidence of this disease.

The spectrum of disease presentation ranges from asymptomatic diverticula to diverticulitis, bleeding or other troublesome complications such abscesses and fistulas (10). Although most cases of complicated diverticular disease are self remitting and have a generally good outcome, patients who recover from a complication of diverticular disease tend to have an increased risk of developing future recurrence of symptoms (11, 12). Hence surgical management is advocated in this subset of patients.

Guidelines such as that proposed by the American Society of Colon and Rectal Surgery would advocate surgical intervention only after one or more attacks of diverticulitis (13). However, some of these patients may not survive the second or subsequent attacks. An earlier study has showed that multiple attacks of diverticulitis does not alter or predict a poorer outcome, instead they observed that patients with certain predisposing factors are at a higher risk regardless of the number of recurrence (14).

The aim of this retrospective cross sectional study was to observe patients with complicated diverticular disease, particularly those who developed recurrent complications. This study also aimed to identify causative factors such demography, co-morbidities or lifestyle factors that may be associated with recurrent complications.

Materials and Methods

The ward censuses for admissions to the surgical wards of Universiti Kebangsaan Malaysia Medical Centre (UKMMC) during a four year period from January 2005 till December 2008 was screened for patients admitted with a suspected complication of diverticular disease. Patients diagnosed clinically, radiologically, surgically or endoscopically based on the WHO ICD 10 classification for complicated diverticular disease were considered for recruitment by a single investigator who reviewed the case files to confirm the diagnosis of a complication of diverticular disease. Patients who failed to meet the diagnostic criteria or without complete hospital case notes were excluded.

Demography

Age at the time of complication and gender was included as prevalence studies on diverticular disease has shown a predilection towards elderly males, however studies looking at similar demographics in complicated diverticular disease showed a

higher incidence among younger men (15, 16). Similarly racial distribution was also observed to determine if any ethnic predominance exists not only in the prevalence but also in the complications of diverticular disease in the study population. Papagrigoriadis et. al concluded in their observational study that smoking may be an independent risk factor for complications (17).Keeping in view the above facts, the patient's smoking status at the time of diagnosis was recorded. The duration and amount of cigarette consumed were not categorized and patients were grouped into only two distinct groups. Although evidence directly implicating alcohol with complicated diverticular disease is still lacking, it has been established as a causative agent for other gastrointestinal pathologies including relapsing inflammatory bowel disease (18, 19). A Danish registry study has also independently implicated alcohol consumption with admissions for diverticulitis (20). Due to the lack of data from the case notes only active consumption was considered for analysis.

Co-morbid associations

Only co-morbidities with proven associations to diverticular disease and those usually associated with poor outcome scores in general were assessed. Diabetes was included in the analysis as the pro-inflammatory state it induces would render these patients more susceptible to recurrent complications (21). Ischemic heart disease or hypertension is associated in poorer outcomes for patients with complicated diverticular disease. Dyslipidemia was also included as it may indirectly be associated with a high fat diet and a sedentary lifestyle where previous studies have strongly linked these factors with a higher risk of developing diverticulosis. Medications with a risk for gastrointestinal related morbidity including non steroidal anti inflammatory drugs (NSAID), antiplatelets such aspirin, clopidogrel or ticlopidine, steroids were also included in the analysis. Traditional herbal remedies due to the presence of steroids in these preparations were also assessed.

Definitions and follow up

All patients diagnosed with a complication of diverticular disease were assessed for recurrence and previous attacks of complications. The patient's final outcome were measured into two distinct groups namely those with recurrence and those without. A recurrent attack of complication is defined as any hospital admission for a complication of diverticular disease with a documented previous episode of complicated diverticular disease.This was the basis for our data analysis as the main objective of the study was to compare the two groups with regards to factors that may predispose recurrence.

Statistical Analysis

Pearson's Chi-Square and Student T-test were used to look at possible relationship between these variables with recurrent complicated diverticular disease. Although there were some variables that had a statistically significant association on univariate analysis, they would pose little clinical significance if not assessed together on a multivariate basis. Hence, logistic regressions were used for all the variables from the data that was assessed previously irrespective of their significance level when assessed with the univariate analysis to form a more concrete conclusion from this analysis.

Results

Variable	**No of Patients**
Mean Age (yrs)	
Male	65.5
Female	68.2
Sex Ratio (N=121)	
Male	72
Female	49
Ethnicity	
Malay	56 (46.3%)
Chinese	59 (48.8%)
Indian	6 (5.0%)
Average weight (kg)	
Male	69.5

Female	57.1
Smoker	
Yes	64(52.9%)
No	57(47.1%)
Alcohol	
Yes	30(24.8%)
No	91(75.2%)
Co-morbidity	
Hypertension	82(67.8%)
Diabetes	55(45.5%)
IHD	37(30.6%)
Dyslipidemia	70(57.9%)
Haemorrhoids	46(38.0%)
Medications	
NSAIDS	26(21.5%)
Antiplatelets	43(35.5%)
Steroids	9(7.4%)
Traditional Medications	17(14.0%)
Laxatives	7(5.8%)
Complication	
Bleeding	79(65.3%)
Diverticulitis	42(34.7%)
Side of pathology	
Left	55(45.5%)
Right	66(54.5%)

Table 1: Characteristics of the 121 patients with complicated diverticular disease

Two hundred and eighteen patients were identified from a preliminary assessment of the ward with censuses between January 2005 to December 2008 but only 182 case files were retrievable for further analysis. The remaining 36 patients were hence automatically excluded from the study. Of these 182 case files, only 121 patients met the criteria for diagnosis of a complicated diverticular disease and these patients' data were then subjected for further analysis.

The general demography and clinical characteristics of these patients were summarized in Table 1. It was observed that there was a slightly higher male preponderance (59.5%) consistent with previous epidemiologic studies in diverticular disease. The mean age at diagnosis of a complication was 66.6 yrs.

Meanwhile, the ethnic distribution of complicated diverticular disease was observed to be similar among the Malays and Chinese whereas Indians made up only 5%. Social habits such as smoking and alcohol consumption were assessed based on the patient's history of active usage at the time of admission. The quantity and duration of use were not specifically measured hence the patients were only categorized into two groups.

There was an almost 2:1 ratio of bleeding to diverticulitis. It was also observed that there were more complications of the right colon as compared to the left. There were a total of 32 patients (26.4%) who required surgery and these varied from partial to total colectomies with or without stoma. 24 patients (19.8%) had a recurrence of either bleeding or diverticulitis after their initial discharge from hospital however none of the 121 patients analyzed died of the complications.

Pearson's Chi-Square test was used to determine the association of the studied variables with recurrent attacks. Here, it was demonstrated that there was a statistically significant association between recurrence of complication with smoking (χ^2_{1df}=3.87, p=0.049) and diabetes (χ^2_{1df}=10.54, p=0.001). Other variables were however not significantly associated with recurrent attacks as illustrated in *table 2*.

Factor	**Chi-Square (χ^2_{1df})**	***p* value**
Age	t=0.10	0.992
Gender	0.017	0.896
Race		
Weight	t=0.963	0.339
Alcohol	2.426	0.119
Smoking	**3.87**	**0.049***
Hypertension	1.29	0.720
Diabetes	**10.54**	**0.001***
IHD	0.028	0.867
Dyslipidemia	0.954	0.329
NSAIDS	3.071	0.080

Antiplatelets	0.050	0.822
Type of complication	0.103	0.749
Side of pathology	0.173	0.677

Independent samples t-test was used to assess age and weight
p value of <0.05 is considered as a significant association

Table 2: Summary of analysis of factors using Pearson's Chi-Square

The results were then used to construct a model predicting the recurrence of complication based on the same factors analyzed above. Race was excluded as it violated the assumption of Chi-Square with less than 80% of cells having an expected count of 5 or more. This was because there were only a total of six Indian patients identified with complication of diverticular disease and none had a recurrence of complication. All other variables used in the model met the assumptions of a multiple logistic regression analysis. A summary of the results was tabulated (Table 3).
After controlling for other confounding variables in the model it was observed that active smoking, alcohol consumption along with underlying diabetes and dyslipidemia were significantly associated with an increased risk of recurrence of complication. The Wald statistics suggests that smoking is the highest independent risk factor in predicting the recurrence of complications.

Viable	Coefficient (□)	Standard error	Wald (□^{2})	df	Sig. (*p* value)	Exp (B)
Age	-.011	.042	.064	1	.800	.989
Gender	.545	1.221	.200	1	.655	1.725
Weight	-.135	.080	2.856	1	.091	.874
Smoker	**3.852**	**1.398**	**7.590**	**1**	**.006***	**47.088**
Alcohol	**-5.649**	**2.687**	**4.419**	**1**	**.036***	**.004**
Hypertension	-.862	1.436	.361	1	.548	.422
Diabetes	**4.022**	**1.869**	**4.631**	**1**	**.031***	**55.789**
IHD	-2.050	2.046	1.004	1	.316	.129
Dyslipidemia	**-3.687**	**1.790**	**4.240**	**1**	**.039***	**.025**
Type of complication	.569	1.054	.291	1	.589	1.767
Side of pathology	2.131	1.154	3.412	1	.065	8.421
NSAID	-22.897	7993.805	.000	1	.998	.000
Antiplatelets	2.024	1.871	1.171	1	.279	7.571

Table 3: Summary of logistic regression equation predicting factors associated with recurrence of complicated diverticular disease

Discussion

The complications of diverticular disease can bring about severe consequences. Not only is it debilitating to patients but treating these complications may have an impact on the healthcare budget as well. Many studies have been performed to look at the factors that may predict the development of complications, patient's outcome and indeed the recurrence of these complications. It was on this basis of earlier studies that this study was designed.
In general, this retrospective cross sectional study looked at 121 patients with a confirmed diagnosis of complicated diverticular disease. Of these, there were a total of 24 (19.8%) cases of recurrent episodes of complications requiring hospital admission. This figure is quite low compared to earlier audits by

researchers which showed recurrence figures of about 35% (22,23). A possibility for this large discrepancy is the duration of follow up whereby their audit span spread over at least 10 years.

The effect of smoking on the risk of developing colon cancer has been well established. However, the effect of smoking on diverticular disease has been reported with mixed results. This study showed that smoking contributed to recurrent attacks of complicated diverticular disease. The ratio of smokers to non-smokers was almost equal at 1.1:1 among the study sample hence eliminating a selection bias. However smokers and non-smokers were separated only based on their current smoking status with no considerations made for ex smokers nor were the active smokers classified into distinct groups based on the quantity or duration of exposure and this may have impaired the significance of the analysis. The consensus on the effect of smoking on complicated diverticular disease has been conflicting. An earlier study reported an increased risk of complication in smokers in his case control study but a larger cohort by Aldoori however has instead shown no significant relationship (24). The effect of smoking on diverticular disease is still unclear but a delay in colonic motility has been demonstrated among smokers (25). The slower transit time which translates to increased intraluminal pressure and hence increased risk of developing colonic diverticula may also increase the risk of symptomatic disease too. The possible effect of smoking on the enteric circulation may also play a role although this requires further validation.

There were 24.7% active consumers of alcohol among the 121 patients in this study. Separation between the groups was only based on active alcohol consumption at the time of developing recurrence and no effort was made to classify the active consumers into groups based on the quantity, duration or the type of spirit consumed due to lack of data from the case files. It was noted that alcohol by itself posed no increase in the risk of developing recurrent complications, but its association was significant when confounders were controlled for. Not many studies have looked at the relationship between alcohol and symptomatic diverticular disease. The few sporadic studies that looked into the possibility of its association have so far shown conflicting results. The reason behind why alcohol may be significant is not yet to be established and further research is warranted .

Underlying co-morbidities has been associated with poorer outcomes in cases of acute diverticulitis. Among these, cardiovascular and renal diseases were reported to adversely affect survival and increase morbidity during an attack of diverticulitis or during recurrence (26). In this study, diabetes was demonstrated as a significant factor affecting recurrent complications. It may be possible that this significant result was due to the general lack of awareness and diabetic care in the local population. The less optimal blood sugar control in the diabetic population here compared to the western world may be the reason why diabetics with symptomatic diverticular disease are more susceptible to recurrent disease. The role of diabetes in promoting pro-inflammatory states, impairing wound healing, affecting microvasculature circulation in the gut and its other systemic effects are the likely reasons that leads to this. There is also perhaps a role of diabetes in exacerbating the effects of other co-morbidities although this was not observed in this study. The effect on microcirculation by diabetes may also potentiate that caused by smoking and vice-versa.

There are no previous studies that specifically reported dyslipidemia as a risk factor for complicated diverticular disease. The rationale for choosing dyslipidemia as a variable was its possible relationship with high fat diet and lack of physical activity and these factors has been reported to be associated with higher risks of developing a complications. It is an established fact that dyslipidemia is a modifiable risk factor for cardiovascular disease because of the role of cholesterol in atherosclerosis. Perhaps there is a similar role of dyslipidemia in atherosclerosis of the mesenteric blood supply that may impair

blood supply to the diseased colon rendering it susceptible to repeated attacks.

Nevertheless there are indeed many flaws with this hypothesis. Firstly, a high fat diet is not the only factor that may influence the development of dyslipidemia. Then there is also the subset of the population with familial hypercholesterolemia who may not necessarily conform to the above mentioned assumptions. Another shortcoming in the analysis for dyslipidemia was that the patients were grouped based on a documented diagnosis of dyslipidemia without considering the lipid profile of the patients or lipid lowering medication adopted.

There was no significant difference of age between the groups in this study. It is important to note that in the other studies that implicated age as a factor for developing complications, their primary end point was either the development of symptomatic disease or morbidity following an attack of complication. Since the prevalence of colonic diverticula increases with age it may be quite obvious that advanced age would be associated with a higher incidence of symptomatic disease. Moreover, the elderly would more likely be plagued with other co-morbidities and poorer general health hence their outcome following an acute attack may be less favorable.

Analyzing race as a possible risk factor was challenging due to the limited number of Indians in the study. There were also no Indians in the recurrent group making multivariate analysis difficult as well. It was also not appropriate to categorize the Indians together with one of the other two races. Therefore, the data on race was only used descriptively for this study.

There have been studies that linked lack of physical activity and obesity with both the development of colonic diverticula and the risk of developing symptomatic disease (27, 28). In order to assess the effect of obesity on diverticular disease, an objective measurement tool has to be available to properly assess it without encountering the bias of gender. Basal metabolic index (BMI) has been widely accepted as a clinically measurable tool which would also indirectly reflect lifestyle and physical activity. It would be interesting to observe the effect BMI would have on the multivariate analysis as well. An attempt was made to collect this data for analysis, however due to poor record keeping, there were less than 50% of data available for both height and weight at the time of diagnosis to enable an accurate measurement of BMI of all patients at that time hence BMI was not analyzed.

There was a slightly higher number of right sided diverticular disease and more cases of bleeding complications in the study population. The grouping of left versus right for this study was based on the main site of pathology as referenced from the blood supply of that part of the bowel. It has widely been accepted that the distribution of diverticulum in the Asian population has a right sided preponderance and it has also been observed that right sided colonic diverticulum has a higher tendency to bleed. (29). However, the type of complication did not influence likelihood of developing recurrent disease. This was also observed in the analysis of the site of pathology where no particular part of the colon was more susceptible to recurrence.

Of the 121 patients in this study, there were no reported deaths within the period of follow up. Although none of them died during their admission and none of the 24 patients in the recurrence group succumbed during their readmission, it cannot be confirmed if any of these patients had suffered lethal recurrence later nor if the 36 patients who's case files were not traceable had actually died from their disease. It would have been beneficial to have these patients identified as an analysis of factors associated with more adverse outcome following recurrence could have been carried out.

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