

Colonic diverticulitis with comorbid diseases may require elective colectomy

Kevin CW Hsiao, Joseph G Wann, Chien-Sheng Lin, Chang-Chieh Wu, Shu-Wen Jao, Ming-Hsin Yang

Kevin CW Hsiao, Chang-Chieh Wu, Shu-Wen Jao, Division of Colorectal Surgery, Department of Surgery, Tri-Service General Hospital, National Defense Medical Center, Taipei 114, Taiwan
Joseph G Wann, Department of Physiology, College of Medicine, National Taiwan University, Taipei 106, Taiwan
Chien-Sheng Lin, Department of Emergency and Critical Care Medicine, Cheng Hsin Rehabilitation Medical Center, Taipei 112, Taiwan

Ming-Hsin Yang, Department of Emergency, Tri-Service General Hospital, National Defense Medical Center, Taipei 114, Taiwan

Author contributions: Hsiao KCW, Wann JG, Lin CS, Wu CC, Jao SW, Yang MH perform the research; Hsiao KCW, Yang MH analyzed the data and wrote the paper.

Correspondence to: Min-Hsin Yang, MD, Department of Emergency, Tri-Service General Hospital, National Defense Medical Center, Taipei 114, Taiwan. dr.hsiao@msa.hinet.net
Telephone: +886-2-87923311 Fax: +886-2-87927411

Received: April 27, 2013 Revised: September 11, 2013

Accepted: September 16, 2013

Published online: October 21, 2013

were performed to identify the relevant risk factors correlating to colectomy.

RESULTS: The mean age of the 246 patients was 69.5 years (range, 24-94 years). Most diverticulitis could be managed with conservative treatment ($n = 227$, 92.3%), and urgent colectomy was performed in 19 patients (7.7%). There were three deaths in the surgical group and four deaths in the nonsurgical group. The overall mortality rate in the study was 1.7% among patients with conservative treatment and 15.7% among patients undergoing urgent colectomy. Multiple logistic regression analysis indicated that comorbidities were risk factors for urgent colectomy for diverticulitis.

CONCLUSION: To avoid high mortality and morbidity related to urgent colectomy, we suggest that patients with colonic diverticulitis and comorbid diseases may require elective colectomy.

© 2013 Baishideng. All rights reserved.

Abstract

AIM: To investigate the comorbid disease could be the predictors for the elective colectomy in colonic diverticulitis.

METHODS: A retrospective chart review of 246 patients with colonic diverticulitis admitted between 2000 and 2008 was conducted, and 19 patients received emergent operation were identified and analyzed. Data were collected with regard to age, sex, albumin level on admission, left or right inflammation site, the history of recurrent diverticulitis, preoperative comorbidity, smoking habits, medication, treatment policy, morbidity, and mortality. Preoperative comorbid diseases included cardiovascular disease, diabetes, pulmonary disease, peptic ulcer disease, gouty arthritis, and uremia. Medications in use included non-steroidal anti-inflammatory drugs, acetylsalicylic acid (Aspirin), and corticosteroids. Univariate and multivariate logistic regression analyses

Key words: Colonic diverticulitis; Colectomy; Comorbid disease

Core tip: Colonic diverticulitis can usually be managed with conservative treatment. However, in select groups of patients with recurrent persistent infection causing life-threatening septic shock, emergent and risky surgical management may be necessary. Elective colectomy for diverticulitis has been discussed in many reports. However, the criteria for elective surgery for colonic diverticulitis still remain controversial. Our data indicate that diverticulitis with comorbid disease increases the operative risk in urgent surgery. Therefore, if a patient has diverticulitis with comorbid disease, an elective colectomy may prevent the consequences of an urgent operation.

Hsiao KCW, Wann JG, Lin CS, Wu CC, Jao SW, Yang MH.

Colonic diverticulitis with comorbid diseases may require elective colectomy. *World J Gastroenterol* 2013; 19(39): 6613-6617 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v19/i39/6613.htm> DOI: <http://dx.doi.org/10.3748/wjg.v19.i39.6613>

INTRODUCTION

Diverticular disease of the colon has an overall prevalence of less than 10% in individuals under 40 years old and an estimated 50%-66% prevalence in individuals 80 years old or older^[1-4]. A diverticulum is the herniation of the mucosa and submucosa through the muscular layers of the colon and occurs because of increased intraluminal pressure and weakness in segments of the colonic wall^[5]. Overall, 10%-25% of patients with diverticular disease will experience diverticulitis and its complications^[6,7]. Diverticulitis is the inflammation of a diverticulum or diverticula and can be classified as uncomplicated or complicated. Cases involving abscesses, perforation, obstruction, fistula formation or peritonitis are defined as complicated diverticulitis^[8]. They may require percutaneous drainage of an abscess or emergent surgery. On the other hand, elective colectomy is recommended if an episode of complicated diverticulitis was treated non-operatively^[5,6]. Elective colectomy to prevent recurrent attacks of diverticulitis or emergent surgery was previously advised^[6]. However, newer recommendations have called for a revision of the practice of aggressive surgical resection in patients with uncomplicated disease, despite recurrence or age^[8]. The basis of these arguments is that a majority of patients do not appear to progress from uncomplicated to complicated disease over time^[9,10]. Moreover, recurrent diverticulitis has not been demonstrated to be a risk for emergency surgery^[8,9]. The aim of this study was to identify which comorbid diseases could be risk factors for urgent colectomy to aid in the management of colonic diverticulitis. Using this information, we can identify patients who may benefit from early elective colectomy.

MATERIALS AND METHODS

The charts of 246 patients who had been admitted to the Tri-Service General Hospital, Taipei, Taiwan, between 2000 and 2008 with a diagnosis of diverticulitis were reviewed, and 19 patients who received emergent operations were identified and analyzed retrospectively.

Data were collected with regard to age, sex, albumin level on admission, left or right inflammation site, history of recurrent diverticulitis, preoperative comorbidity, smoking habits, medication, treatment policy, morbidity, and mortality. The diagnosis of colonic diverticulitis was based on the findings of computed tomography, which has a high diagnostic sensitivity of approximately Ninety-three percent to ninety-seven percent and a specificity of

approximately 100%^[4]. Urgent colectomy was indicated in patients with peritonitis that could not be corrected by medical treatment or drainage. Preoperative comorbid diseases included cardiovascular disease (*e.g.*, hypertensive cardiovascular disease and coronary artery disease), diabetes, pulmonary disease (*e.g.*, chronic obstructive pulmonary disease and asthma), peptic ulcer disease (*e.g.*, gastric ulcer and duodenal ulcer), gouty arthritis, and uremia. Medications in use included non-steroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid (aspirin), and corticosteroids.

The mean values were compared using an independent *t* test, and χ^2 or Fisher's exact test was used to compare proportions. A value of $P < 0.05$ was considered statistically significant. Data were analyzed using SPSS version 15.0 (SPSS Inc., Chicago, IL, United States) for Windows.

RESULTS

In total, 246 patients were admitted with a diagnosis of colonic diverticulitis. The mean age was 69.5 years (range, 24-94 years); 144 of the 246 patients were men (58.5%), and 102 were women (41.5%). Most episodes could be managed with conservative treatment consisting of antibiotics and bowel rest ($n = 227$, 92.3%), but urgent colectomy was performed in 19 patients (7.7%) (Table 1). All of these patients received Hartmann's operation. However, there were three deaths in the surgical group, two from postoperative lobar pneumonia complicated with septic shock and acute respiratory distress syndrome and the other from urinary tract infection. There were four deaths in the non-surgical group. Two deaths (ages 81 and 79 years; the patient's family refused surgical intervention in both cases) in the nonsurgical group were the result of uncontrolled intra-abdominal infection complicated with septic shock during hospitalization. The other two deaths were due to lobar pneumonia (Table 2). The overall mortality rate was 2.8% ($n = 7$), and it was 15.7% ($n = 3$) in the group that underwent urgent colectomy. Ten patients had wound infections after colectomy, and four were returned to the operating room for surgical debridement. The morbidity rate in the urgent surgery group was 52.6% ($n = 10$) (Table 3).

Univariate analysis with logistic regression indicated that the factors associated with a greater likelihood of having an urgent colectomy were albumin level on admission (OR = 13.488, $P < 0.001$), comorbidity with cardiovascular disease (OR = 3.203, $P = 0.019$), type 2 diabetes (OR = 3.311, $P = 0.019$) or gouty arthritis (OR = 9.777, $P < 0.001$), and use of anticoagulants (OR = 3.200, $P = 0.023$) or NSAIDs (OR = 9.603, $P < 0.001$; Table 4). According to the multivariate analysis with logistic regression, only the albumin level, comorbidity with type 2 diabetes, the use of NSAIDs, and smoking remained risk factors for urgent colectomy for colonic diverticular disease (Table 5).

Table 1 Characteristics of patients with colonic diverticulitis *n* (%)

	Surgery group (<i>n</i> = 19)	Non-surgery group (<i>n</i> = 227)	<i>P</i> value
Age (yr)	66.21 ± 15.77	69.81 ± 12.36	0.344
Sex			0.670
Male	12 (36.6)	132 (58.1)	
Female	7 (63.2)	95 (41.9)	
Smoking			0.005
Yes	6 (31.6)	23 (10.1)	
No	13 (68.4)	204 (89.9)	
Albumin			< 0.001
< 3	11 (57.9)	21 (9.3)	
≥ 3	8 (42.1)	206 (90.7)	
Aspirin			0.017
Yes	7 (36.8)	35 (15.4)	
No	12 (63.2)	192 (84.6)	
NSAIDs			< 0.001
Yes	7 (36.8)	13 (5.7)	
No	12 (63.2)	214 (94.3)	
Steroids			0.138
Yes	2 (10.5)	8 (3.5)	
No	17 (89.5)	219 (96.5)	
Cardiovascular disease			0.014
Yes	8 (42.1)	42 (18.5)	
No	11 (57.9)	185 (81.5)	
DM			0.014
Yes	7 (36.8)	34 (15.0)	
No	12 (63.2)	193 (85.0)	
Liver disease			0.862
Yes	1 (5.3)	10 (4.4)	
No	18 (94.7)	217 (95.6)	
Uremia			0.997
Yes	1 (5.3)	12 (5.3)	
No	18 (94.7)	215 (94.7)	
Gout			< 0.001
Yes	5 (26.3)	8 (3.5)	
No	14 (73.7)	219 (96.5)	
Pulmonary disease			0.658
Yes	2 (10.5)	18 (7.9)	
No	17 (89.5)	209 (92.1)	
Peptic ulcer disease			0.694
Yes	2 (10.5)	21 (9.3)	
No	17 (89.5)	206 (90.7)	

DM: Diabetes mellitus; NSAID: Non-steroidal anti-inflammatory drug.

DISCUSSION

Emergent surgery should be considered for diverticulitis when the patient has peritonitis from perforation or obstruction causing unstable vital signs, when the patient fails to respond to conservative treatment within the first week of hospitalization, and when the patient presents with a large abscess (> 5 cm) that is undrainable by interventional radiology^[11]. Approximately 5.5% of patients who recover from an initial episode of diverticulitis require emergency surgical intervention^[12]. Although the mortality and morbidity rates are low, in a previous study, as in our study, they are higher when an urgent operation was performed. The mortality and morbidity rates were high in our operated group (15.7% and 52.6%, respectively). These results are in agreement with previous reports that indicated that patients who require surgical intervention have high mortality and morbidity rates of

Table 2 Characteristics of mortality case

Case	Age (yr)	Sex	Risk factors
Surgery			
1	75	Male	Gout, low albumin level, NSAIDs
2	60	Male	Uremia, DM
3	77	Female	Pulmonary disease, low albumin level
Non-surgery			
1	81	Male	DM, uremia
2	79	Male	NSAIDs, low albumin level, uremia
3	68	Male	Pulmonary disease, DM
4	74	Female	Pulmonary disease, uremia

DM: Diabetes mellitus; NSAID: Non-steroidal anti-inflammatory drug.

Table 3 Surgical complication of urgent surgery *n* (%)

Complications	<i>n</i> = 19
Wound infection	10 (52.6)
Wound infection needing debridement	4 (21.0)
Pneumonia complicated with acute respiratory distress syndrome	2 (10.5)
Urinary tract infection	1 (5.2)
Mortality	3 (15.7)

Table 4 Risk factors for urgent colectomy for colonic diverticulitis according to univariate analysis

Variables	B	SE	OR (95%CI)	<i>P</i> value
Smoking	1.409	0.540	4.094 (1.420-11.805)	0.009
Albumin	2.602	0.518	13.488 (4.886-37.232)	< 0.001
Aspirin	1.163	0.510	3.200 (1.178-8.693)	0.023
NSAIDs	2.262	0.555	9.603 (3.237-28.485)	< 0.001
CV disease	1.164	0.495	3.203 (1.214-8.454)	0.019
DM	1.197	0.511	3.311 (1.217-9.009)	0.019
Gout	2.280	0.633	9.777 (2.826-33.823)	< 0.001

DM: Diabetes mellitus; NSAID: Non-steroidal anti-inflammatory drug; CV: Cardiovascular.

approximately 4.5%-16.7% and 27.2%-71.1%, respectively^[1-3]. Hartmann's operation is a potential choice for the surgical intervention if the patient has diverticulitis with necrotic perforation. However, laparoscopic washout with diversion may be used if the patient has diverticulitis without necrotic perforation. In our study, all patients were subjected to Hartmann's procedure because they had diverticulitis with necrotic perforation.

To prevent a delay in treatment or consequent resource waste, elective surgery for patients with comorbidities may be recommended. In the previous practice parameters for sigmoid diverticulitis, elective surgery was recommended after two episodes of diverticulitis^[6]. Richards *et al*^[13] demonstrated that prophylactic colectomy is associated with increased life expectancy and quality-of-life years when performed after the third attack. However, Ricciardi *et al*^[14] found that the decline in the surgical treatment for diverticulitis is not associated with an increase in complicated diverticulitis, which indicates that elective surgery has a minimal effect on preventing

Table 5 Risk factors for urgent colectomy for colonic diverticulitis according to multivariable analysis

Variables	B	SE	OR (95%CI)	P value
Age	-0.046	0.662	0.955 (0.261-3.497)	0.944
Sex	0.001	0.025	1.001 (0.953-1.050)	0.983
Smoking	2.169	0.873	8.747 (1.580-48.405)	0.013
Albumin	3.467	0.806	32.049 (6.599-155.644)	< 0.001
Aspirin	-0.873	1.382	0.418 (0.028-6.270)	0.527
NSAIDs	3.323	1.212	27.745 (2.578-298.594)	0.006
Steroids	0.785	1.313	2.193 (0.167-28.780)	0.550
CV disease	1.320	1.262	3.745 (0.316-44.390)	0.295
DM	1.810	0.726	6.109 (1.473-25.333)	0.013
Liver disease	-0.291	1.373	0.748 (0.051-11.028)	0.832
Uremia	0.898	1.250	2.454 (0.212-28.416)	0.473
Gout	0.470	1.335	1.600 (0.117-21.911)	0.725

DM: Diabetes mellitus; NSAID: Non-steroidal anti-inflammatory drug; CV: Cardiovascular.

emergency colectomies. The recent recommendation of the American Society of Colon and Rectum Surgeons stated that “the decision to recommend elective sigmoid colectomy after recovery from acute diverticulitis should be made on a case-by-case basis”^[15]. The decision should be made based on the age and the medical condition of the patients, the frequency and severity of the attacks, whether there are persistent symptoms and the suspicion of the malignancy^[15]. Furthermore, elective surgery is also recommended if an episode of complicated diverticulitis is treated nonoperatively. The predictors of diverticulitis requiring surgery have not been determined, which is still a vexing problem confronting surgeons.

Our study was a retrospective analysis of 246 patients with colonic diverticulitis treated at a single medical center over 9 years. No difference was found in the distribution of colonic diverticulitis between the sexes ($P = 0.671$), and this trend was the same for cases requiring emergent surgery. The ages of patients with diverticulitis had no significant association with surgery ($P > 0.344$). Patient nutritional status upon admission affected the length of hospital stay for patients with colonic diverticulosis. Serum albumin levels correlated negatively with the length of hospital stay^[16,17]. Moreover, it is well known that there is a correlation between malnutrition and infection, poor wound healing, and the overgrowth of bacteria in the alimentary tract. In the present study, 57.9% of colonic diverticulitis patients in the emergent surgery group had albumin levels below 3 g/dL, whereas this was true of only 9.3% of patients in the non-surgery group. All patients with low albumin (< 3 g/dL) levels had parenteral nutrition.

Among the comorbidities, type 2 diabetes mellitus independently increased the severity of diverticulitis ($P = 0.019$). It is well established that diabetes mellitus has a negative effect on immunity. Polymorphonuclear leukocyte function, leukocyte adherence, chemotaxis, and phagocytosis are all affected in patients with diabetes mellitus^[18]. Gouty arthritis have also been demonstrated to be a risk factor of urgent operation ($P < 0.001$). How-

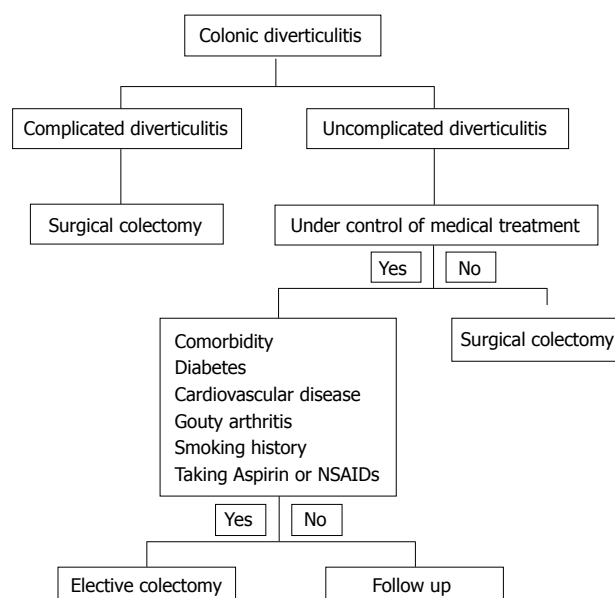


Figure 1 Management of patients with colonic diverticulitis. NSAIDs: Non-steroidal anti-inflammatory drugs.

ever, this relation may be because of the medication used in treatment because patients with these diseases take NSAIDs for pain control. It is known that there is a correlation between NSAIDs and perforation of colonic diverticula. Several reports have indicated that patients with perforated diverticular disease are significantly more likely to be taking NSAIDs than patients without disease^[19-21]. The inhibition of cyclo-oxygenase 1 (COX-1) results in deficient levels of prostaglandins, which are related to the protection of bowel mucosa. On the other hand, COX-2 inhibition leads to the failure of the immune response to localize a microperforation. In these patients, continuation of their non-steroidal anti-inflammatory treatments is highly likely to impair colonic mucosal repair^[19-21]. Cardiovascular disease has also been shown to be associated with urgent colectomy in diverticulitis. In the present study, all of the patients with cardiovascular diseases were taking acetylsalicylic acid, known as aspirin, as an anti-coagulant for preventive treatment. Aspirin is also classified as an NSAID because of its inhibition of platelet COX activity and is considered to predict colonic perforation^[22]. Smoking was one of the independent factors associated with emergent operation. Smoking may enhance or precipitate the inflammatory process in diverticulitis. Nicotine in cigarettes is a smooth muscle relaxant, which may counteract the colonic muscle spasm that correlates with the pathogenesis of diverticular disease^[23]. Nicotine may also decrease mucosal immunity by inhibiting the synthesis of proinflammatory cytokines such as interleukin α and tumor necrosis factor α in colonic mucosa. Smoking could also cause systemic sepsis via the promotion of oxidative damage by generating oxygen free radicals^[23]. Steroid treatment also has a negative effect on mucosal regenerative activity^[24]. In our study, it did not significantly predict diverticular perforation. This

is most likely because the number of patients with steroid treatment in our series was small.

Our results indicated several comorbid diseases are risk factors to urgent colectomy. There were 7.7% of patients with colonic diverticular disease who had to receive urgent colectomy despite conservative treatment including antibiotics and bowel rest. Preoperative comorbid diseases may increase the operative risk in urgent surgery, and the outcome is poor. The mortality and morbidity rates are up to 15.7% and 52.6%, respectively. To avoid high mortality and morbidity related to urgent colectomy. We suggested that patients with colonic diverticulitis and comorbid disease may require elective colectomy (Figure 1).

COMMENTS

Background

Colonic diverticulitis with comorbid disease may get fatal complication after urgent surgery. Therefore, To avoid high mortality and morbidity related to urgent colectomy, the authors suggest that patients with colonic diverticulitis and comorbid diseases may require elective colectomy.

Research frontiers

This study is designed to clarify the predictors of elective colectomy for colonic diverticulitis.

Innovations and breakthroughs

Comorbid disease could be the predictors of elective colectomy for colonic diverticulitis.

Applications

Provide a possible policy of surgical management for the patients with colonic diverticulitis.

Peer review

This is an interesting paper stressing the importance of comorbidities in the treatment of diverticulitis.

REFERENCES

- Oomen JL, Engel AF, Cuesta MA. Mortality after acute surgery for complications of diverticular disease of the sigmoid colon is almost exclusively due to patient related factors. *Colorectal Dis* 2006; **8**: 112-119 [PMID: 16412070 DOI: 10.1111/j.1463-1318.2005.00848.x]
- Funari G, Binjınan V, Seicean R. Urgent surgery for complicated colonic diverticula. *J Gastrointest Liver Dis* 2006; **15**: 37-40 [PMID: 16680231]
- Issa N, Dreznik Z, Dueck DS, Arish A, Ram E, Kraus M, Gutman M, Neufeld D. Emergency surgery for complicated acute diverticulitis. *Colorectal Dis* 2009; **11**: 198-202 [PMID: 18462249 DOI: 10.1111/j.1463-1318.2008.01546.x]
- Jacobs DO. Clinical practice. Diverticulitis. *N Engl J Med* 2007; **357**: 2057-2066 [PMID: 18003962 DOI: 10.1056/NEJMc-p073228]
- Almy TP, Howell DA. Medical progress. Diverticular disease of the colon. *N Engl J Med* 1980; **302**: 324-331 [PMID: 6985709 DOI: 10.1056/NEJM198002073020605]
- Wong WD, Wexner SD, Lowry A, Vernava A, Burnstein M, Denstman F, Fazio V, Kerner B, Moore R, Oliver G, Peters W, Ross T, Senatore P, Simmang C. Practice parameters for the treatment of sigmoid diverticulitis--supporting documentation. The Standards Task Force. The American Society of Colon and Rectal Surgeons. *Dis Colon Rectum* 2000; **43**: 290-297 [PMID: 10733108 DOI: 10.1007/BF02258291]
- Colcock BP. Surgical management of complicated diverticulitis. *N Engl J Med* 1958; **259**: 570-573 [PMID: 13578107 DOI: 10.1056/NEJM195809182591204]
- McCafferty MH, Roth L, Jorden J. Current management of diverticulitis. *Am Surg* 2008; **74**: 1041-1049 [PMID: 19062658]
- Chapman JR, Dozois EJ, Wolff BG, Gullerud RE, Larson DR. Diverticulitis: a progressive disease? Do multiple recurrences predict less favorable outcomes? *Ann Surg* 2006; **243**: 876-830; discussion 880-3 [PMID: 16772791 DOI: 10.1097/01.sla.0000219682.98158.11]
- Nelson RS, Velasco A, Mukesh BN. Management of diverticulitis in younger patients. *Dis Colon Rectum* 2006; **49**: 1341-1345 [PMID: 16897326 DOI: 10.1007/s10350-006-0655-6]
- Floch CL. Emergent and elective surgery for diverticulitis. *J Clin Gastroenterol* 2008; **42**: 1152-1153 [PMID: 18936656 DOI: 10.1097/MCG.0b013e3181893648]
- Anaya DA, Flum DR. Risk of emergency colectomy and colostomy in patients with diverticular disease. *Arch Surg* 2005; **140**: 681-685 [PMID: 16027334]
- Richards RJ, Hammit JK. Timing of prophylactic surgery in prevention of diverticulitis recurrence: a cost-effectiveness analysis. *Dig Dis Sci* 2002; **47**: 1903-1908 [PMID: 12353827]
- Ricciardi R, Baxter NN, Read TE, Marcello PW, Hall J, Roberts PL. Is the decline in the surgical treatment for diverticulitis associated with an increase in complicated diverticulitis? *Dis Colon Rectum* 2009; **52**: 1558-1563 [PMID: 19690482 DOI: 10.1007/DCR.0b013e3181a90a5b]
- Rafferty J, Shellito P, Hyman NH, Buie WD. Practice parameters for sigmoid diverticulitis. *Dis Colon Rectum* 2006; **49**: 939-944 [PMID: 16741596 DOI: 10.1007/s10350-006-0578-2]
- Wunderlich SM, Tobias A. Relationship between nutritional status indicators and length of hospital stay for patients with diverticular disease. *J Am Diet Assoc* 1992; **92**: 429-433 [PMID: 1556344]
- Yoo PS, Garg R, Salamone LF, Floch MH, Rosenthal R, Longo WE. Medical comorbidities predict the need for colectomy for complicated and recurrent diverticulitis. *Am J Surg* 2008; **196**: 710-714 [PMID: 18954602 DOI: 10.1016/j.amjsurg.2008.07.017]
- Joshi N, Caputo GM, Weitekamp MR, Karchmer AW. Infections in patients with diabetes mellitus. *N Engl J Med* 1999; **341**: 1906-1912 [PMID: 10601511 DOI: 10.1056/NEJM199912163412507]
- Goh H, Bourne R. Non-steroidal anti-inflammatory drugs and perforated diverticular disease: a case-control study. *Ann R Coll Surg Engl* 2002; **84**: 93-96 [PMID: 11995772]
- Morris CR, Harvey IM, Stebbings WS, Speakman CT, Kennedy HJ, Hart AR. Anti-inflammatory drugs, analgesics and the risk of perforated colonic diverticular disease. *Br J Surg* 2003; **90**: 1267-1272 [PMID: 14515298 DOI: 10.1002/bjs.4221]
- Piekarek K, Israelsson LA. Perforated colonic diverticular disease: the importance of NSAIDs, opioids, corticosteroids, and calcium channel blockers. *Int J Colorectal Dis* 2008; **23**: 1193-1197 [PMID: 18679693 DOI: 10.1007/s00384-008-0555-4]
- Lanas A, Serrano P, Bajador E, Esteve F, Benito R, Sáinz R. Evidence of aspirin use in both upper and lower gastrointestinal perforation. *Gastroenterology* 1997; **112**: 683-689 [PMID: 9041228 DOI: 10.1053/gast.1997.v112.pm9041228]
- Papagrigoriadis S, Macey L, Bourantas N, Rennie JA. Smoking may be associated with complications in diverticular disease. *Br J Surg* 1999; **86**: 923-926 [PMID: 10417566 DOI: 10.1046/j.1365-2168.1999.01177.x]
- Carpani de Kaski M, Rentsch R, Levi S, Hodgson HJ. Corticosteroids reduce regenerative repair of epithelium in experimental gastric ulcers. *Gut* 1995; **37**: 613-616 [PMID: 8549934 DOI: 10.1136/gut.37.5.613]

P- Reviewers Bulut O, Misiakos EP, O'Dwyer P, Ribas Y
S- Editor Wen LL L- Editor A E- Editor Ma S





Published by **Baishideng Publishing Group Co., Limited**
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road, Wan Chai, Hong Kong, China
Fax: +852-65557188
Telephone: +852-31779906
E-mail: bpgoffice@wjgnet.com
<http://www.wjgnet.com>



ISSN 1007-9327

