MANAGEMENT OF DIVERTICULITIS AND PREVENTION OF RECURRENCE

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ABSTRACT

Acute diverticulitis is an acute inflammation of colonic diverticulae that is associated with an episode of severe, prolonged, lower abdominal pain (usually on the left side), changes in bowel movements, low-grade fever, and leukocytosis. Acute diverticulitis is a significant burden in industrialised societies, accounting for 313,000 hospitalisations in the USA alone, and a trend of rising incidence has been observed. Despite the high prevalence, the management of diverticulitis and post-diverticulitis is largely based on consensus more than evidence derived from randomised clinical trials. In this review we will focus on the diagnosis and management strategies for diverticulitis and post-diverticulitis.

Keywords: Diverticular disease, diverticulitis, management, risk factors, therapy.

INTRODUCTION

The prevalence of colonic diverticulae in the general population is estimated to range from 20–60%.[1,2] The mere presence of colonic diverticulae is defined as diverticulosis. The term 'diverticular disease' (DD) implies that the diverticulae have given rise to illness. An acute inflammation of colonic diverticulae is defined as acute diverticulitis.[2] The natural history of DD is poorly understood. Early population-based, retrospective studies showed that patients with diverticulosis display a 10–25% lifetime risk of developing acute diverticulitis.[2,3] A recent population-based cohort study reappraised the risk of developing diverticulitis: in a survival analysis of 2,222 patients with diverticulosis incidentally discovered during colonoscopy, only 95 patients (4.3%; 6 cases per 1,000 patient-years) developed diverticulitis over an 11-year follow-up period.[4] However, DD accounts for 313,000 hospitalisations in the USA and is the fifth most common reason for ambulatory care visits.[1]

CLINICAL FEATURES OF ACUTE DIVERTICULITIS

Acute diverticulitis is associated with an episode of severe, prolonged, lower abdominal pain (usually on the left side), changes in bowel movements, low-grade fever, and leukocytosis.[5,6] The true incidence of diverticulitis is unknown because population studies have only considered patients admitted to hospital, whereas many patients without a systemic inflammatory response or known diagnosis of DD are treated for episodes of abdominal pain in primary care, which leads to an underestimation of the true incidence of the disease.[5] However, several studies have reported an increase in the incidence of acute diverticulitis, with an overall age-adjusted increase in hospital admissions from 61.8 per 100,000 hospitalisations to 75.5 per 100,000 hospitalisations in the USA from 1998–2005.[7]

RISK FACTORS

Lifestyle factors and ageing are considered two major risk factors for the development of diverticulitis and its complications. The following lifestyle factors have been evaluated in terms of

the risk of symptom development: physical activity, diet (including fibre content and nut, corn, and popcorn consumption), smoking, and obesity. Strate et al.[8] evaluated the role of physical activity in DD during an 18-year follow-up and found that men in the highest quintile of vigorous physical activity had a 25% risk reduction for developing diverticulitis compared with men who exercised the least.

The EPIC-Oxford study has examined the relationship between dietary fibre intake and risk of hospitalisation for DD. A cohort of 47,033 healthy individuals was followed-up for 5 years and showed that patients with a high fibre intake (>25 g/day) had a 41% lower risk of hospitalisation compared to those with the lowest fibre intake (<14 g/day).[9] Regarding the consumption of certain foods, Strate et al.[10] reported that the consumption of nuts, corn, and popcorn does not increase the risk of diverticulitis and its complications.

Tobacco consumption is associated with several inflammatory conditions. In the EPIC-Oxford cohort, individuals who smoked <15 cigarettes per day had a relative risk of hospitalisation for DD of 1.34, whereas those who smoked ≥15 cigarettes per day had a relative risk of 1.86, compared with non-smokers.[9] Similarly, in a retrospective Italian study, current smokers had an increased risk of diverticulitis compared with non-smokers (odds ratio: 2.79; 95% confidence interval: 1.30–5.96).[11]

Obesity has also been established as a major risk factor for diverticulitis. Men with a body mass index (BMI) >30 kg/m^2 displayed a 78% higher risk of diverticulitis compared with men with a BMI <21 kg/m^2 in an 18-year follow-up of 47,000 men.[12]

Several studies have also shown an association between drug use and diverticulitis. These findings have important clinical implications given the prevalence of DD in the elderly. In a large prospective study, an increased risk of diverticulitis and diverticular bleeding was observed among users of aspirin and non-steroidal anti-inflammatory drugs (NSAIDs).[13] Furthermore, there is evidence that the use of opiate analgesics and oral corticosteroids is associated with an increased risk of diverticulitis complications, such as perforation.[14]

CLINICAL PRESENTATION

The clinical manifestations of acute diverticulitis vary with the extent of the inflammatory process. In classical cases, patients report abdominal pain that localises to the left lower quadrant, which may be associated with nausea or vomiting and a change in bowel habits (diarrhoea or constipation). Suprapubic or right-sided pain may also be reported by some patients with a large and redundant sigmoid colon. Diffuse abdominal pain associated with peritoneal signs suggests complicated disease, such as free perforation, whereas absolute constipation may be due to an underlying obstruction. Dysuria is a common symptom reported by patients and is secondary to irritation of the bladder by the inflammatory process.

On physical examination, findings vary according to the severity of the inflammation: fever and tachycardia may be present. The patient may present with pain and localised rigidity in the left lower quadrant, whereas patients may present with a rigid board-like abdomen in cases with inflammatory extension of the peritoneum. Bowel sounds may be depressed (paralytic ileus) or increased (obstruction). Table 1 shows the clinical features observed in a study reviewing 741 cases of acute diverticulitis.[15]

Several other diseases can have a similar presentation and mimic acute diverticulitis. For this reason, alternative diagnoses for lower abdominal pain must be considered. In particular, it may be necessary to rule out appendicitis, inflammatory bowel disease, colon cancer, cystitis, pelvic inflammatory disease, and infectious colitis.[5]

Table 1: Clinical features of acute diverticulitis.[15]

Clinical feature	Frequency (N=741)
Abdominal pain	97.6%
Pain in lower abdomen	82.7%
Pain not limited to lower abdomen	17.3%
Nausea	38.0%
Vomiting	16.2%
Diarrhoea	23.2%
Constipation	14.0%
Rectal bleeding	6.8%
Abdominal tenderness	89.2%
Fever	30.1%
Leukocytes >11,000/mm^3	58.5%

DIAGNOSIS

In cases of abdominal pain, laboratory tests should be performed in order to evaluate the inflammatory state and to exclude other potential causes. Blood tests such as a full blood count, creatinine, C-reactive protein, amylase, and lipase are required, as is urine analysis to exclude urinary tract infection. The double-contrast enema is not currently in use because the extramural component of inflammation is more important than the intramural inflammation for the staging of acute diverticulitis. Computed tomography (CT) is considered as the initial radiological examination because of its high sensitivity (93–97%) and a specificity for diagnosis approaching 100%,[16] but also because CT allows the physician to evaluate the extent and complications of diverticulitis.[17] Alternatively, evidence supports the role of ultrasound (US) examination in the management of diverticulitis. The primary advantage of US is that it does not require exposure to radiation and is widespread. However, the accuracy of US is often dependent on the skill of the examiner. In addition, CT has the potential to provide more information on alternative causes of abdominal pain. In a comparative study, the sensitivity of CT was slightly superior (91% versus 85%) whilst US displayed slightly superior specificity (85% versus 77%).[18]

In recent years, magnetic resonance imaging (MRI) has also been introduced for the diagnosis of DD and acute diverticulitis. In a study conducted in Germany, the sensitivity and specificity of MRI colonoscopy were calculated as 86% and 92%, respectively.[19] As with double-contrast enema, colonoscopy does not provide information about the extramural component of inflammation. In addition, colonoscopy should be avoided in acute diverticulitis because of the risk of perforation.

STAGING

The most commonly used criteria for scoring the severity of diverticulitis is Hinchey's system. Hinchey's classification categorises peritonitis as one of four stages.[20] Patients with Stage 1 have small, confined, pericolic abscesses. Stage 2 disease is characterised by larger abscesses, often confined to the pelvis. Stage 3 disease is present when a peridiverticular abscess has ruptured, leading to a purulent peritonitis. Lastly, Stage 4 is characterised by faecal contamination of the peritoneal cavity. Although it does not consider the systemic inflammatory response or patient features (i.e. age, immunosuppression, and comorbidities), Hinchey's classification is useful in clinical practice: the risk of death is <5% for patients with Stage 1 or 2 diverticulitis, 13% for those with Stage 3, and 43% for those with Stage 4.[21]

TREATMENT

Management and treatment approaches depend on the severity and complexity (i.e. presence of an abscess, fistula, and/or perforation) of the condition. For patients with mild acute diverticulitis, outpatient therapy with oral, broad-spectrum antibiotics is reasonable. A combination of metronidazole and ciprofloxacin is often used, but other regimens are also effective (Table 2). A review of 92 publications identified the following criteria for hospitalisation in cases of mild acute diverticulitis: significant inflammation, intolerance to oral fluids, no response to oral antibiotic therapy, age >80–85 years, and presence of immunosuppression or comorbidities (e.g. diabetes, chronic renal failure, malignant haematological diseases, HIV infection, chemotherapy, steroid therapy, or transplantation).[22]

Table 2: Drug regimens commonly used to treat diverticulitis.[21]

Oral regimens	Intravenous regimens
Metronidazole (500 mg every 6-8 hr) + quinolone (e.g. ciprofloxacin 500-750 mg every 12 hr)	Metronidazole (500 mg every 6-8 hr) + quinolone (e.g. ciprofloxacin 400 mg every 12 hr)
Metronidazole (500 mg every 6-8 hr) + trimethoprim–sulfamethoxazole (160 mg trimethoprim and 800 mg sulfamethoxazole every 12 hr)	Metronidazole (500 mg every 6-8 hr) + third-generation cephalosporin (e.g. ceftriaxone 1-2 g every 24 hr)
Amoxicillin–clavulanate (875 mg every 12 hr)	Beta-lactam with a beta-lactamase inhibitor (e.g. ampicillin–sulbactam 3 g every 6 hr)

All clinical guidelines recommend hospitalisation, bowel rest, and broad-spectrum antibiotics in severe and/or complicated acute diverticulitis not in need of emergency surgery. These patients should be treated with intravenous antibiotics active against aerobic and anaerobic bacteria. Recommended drug combination regimens are based more on clinical consensus than on evidence from randomised clinical trials (RCTs; Table 2).[6]

For patients in whom diverticulitis is complicated by peridiverticular abscess, the size of the abscess is an important determinant of treatment success: small pericolic abscesses (<4 cm in diameter) can be treated conservatively with bowel rest and antibiotics, while larger abscesses (>4 cm) are more likely amenable to CT-guided percutaneous drainage.[6]

Despite the lack of RCTs comparing antibiotic treatment with no antibiotic treatment, conservative management with bowel rest and antibiotics is considered the standard of care for non-complicated acute diverticulitis. However, in recent years several studies have compared antibiotic treatment with no antibiotic treatment in mild acute diverticulitis. In a retrospective audit of 311 patients hospitalised for acute diverticulitis at a single hospital in Sweden, Hjern et al.[23] observed that managing acute diverticulitis without antibiotics leads to no increase in adverse events compared with antibiotic management, with a similar rate of recurrence also observed. In a recent multicentre RCT in Sweden, 623 patients with CT-verified, acute, uncomplicated, left-sided diverticulitis were randomised to treatment with or without antibiotics. The results of the study reveal that antibiotic use does not reduce the risk of complications (abscess or perforation) or the 1-year recurrence rate, and nor does it accelerate recovery.[24] Although suggestive, at the present time there is not yet enough evidence for this strategy to be adopted into clinical practice. Further data will accrue from another large, pragmatic, multicentre RCT (the DIABOLO trial) comparing treatment with and without antibiotics. Patients will be randomised to a conservative strategy (antibiotics for 10 days, hospital admission, and supportive measures) or to a liberal strategy (no antibiotics, supportive measures, and admission on clinical grounds only if necessary).

PREVENTION OF RECURRENCE

The natural history of DD is not fully understood. Few studies have explored the course of acute diverticulitis and the recurrence rate of diverticulitis. A retrospective study analysing 337 patients with uncomplicated diverticulitis and 165 with complicated diverticulitis, with a median follow-up of 101 months, reported an overall recurrence rate of 18.8% for one episode of recurrence and 4.7% for two or more episodes, with no statistically significant difference between the two patient groups in terms of the rate of recurrence.[25] In a study performed using the California Office of Statewide Health Planning and Development database, 179,649 patients admitted for diverticulitis and managed medically were analysed and, of these, 27,450 (16.3%) suffered a second episode of diverticulitis. The risk factors for recurrence included: age <50 years, smoking, obesity, female sex, complicated presentation, previous diagnosis of diverticulosis, and chronic use of NSAIDs.[26]

The primary goal in the management of patients with a history of diverticulitis is the prevention of a subsequent episode. However, there are many issues in this field because of the lack of studies regarding secondary prevention of acute diverticulitis. In addition, the studies available are often of low quality and include a small number of patients. To date, the management of post-diverticulitis is based more on consensus than on RCT data.[27] A high daily fibre intake, especially insoluble fibre, appears to be a good strategy, although no clear evidence is available.[6]

The use of antibiotics may promote the selection of non-pathogenic strains of intestinal bacterial flora, thereby reducing the risk of diverticulitis. A recent, multicentre, randomised, open trial studied the efficacy of rifaximin, in addition to a high-fibre dietary regimen, in the secondary prevention of acute diverticulitis. Rifaximin plus high-fibre proved to be more effective than high-fibre alone in the secondary prevention of acute diverticulitis, with a recurrence rate at 12 months of 10.4% in patients given rifaximin plus high-fibre versus 19.3% in patients receiving high-fibre alone (p=0.033).[28] Further studies are needed to confirm these results.

Several studies have investigated the role of mesalazine in the secondary prevention of diverticulitis. However, two Phase III, double-

blind, placebo-controlled, multicentre RCTs have evaluated the efficacy of multimatrix mesalazine versus placebo for the prevention of recurrent diverticulitis in 590 (PREVENT1) and 592 (PREVENT2) adult patients with ≥1 episodes of acute diverticulitis in the previous 24 months.[29] No significant difference in the rate of diverticulitis recurrence was observed among treatment groups at Week 104. In addition, mesalazine did not reduce the time to recurrence, and the proportion of patients requiring surgery was comparable between treatment groups. Given this evidence, there is no clear proof that mesalazine reduces the rate of diverticulitis recurrence.[6]

ELECTIVE SURGERY

In the past, statements from scientific associations agreed on the need for a prophylactic sigmoidectomy after two previous episodes of acute diverticulitis.[30,31] Recent studies have shown a more benign natural history of DD, with a low rate of recurrence. Therefore, a less aggressive surgical policy has been suggested.[32] In fact, elective surgery should be recommended in patients with symptomatic, complicated DD (e.g. fistula, stenosis). In other cases, the indication to perform elective colectomy resection should not be based on the number of previous episodes of diverticulitis but should be evaluated by balancing the severity of symptoms, risk of severe recurrences, and morbidity due to surgery.[6]

CONCLUSION

Acute diverticulitis is a significant burden in industrialised countries. Despite the high prevalence of the disease, there are many issues regarding therapeutic management. It is known that lifestyle factors (diet, obesity, smoking, drug use) play a critical role in the development of the first episode and recurrence. The optimal clinical management of an episode of acute diverticulitis is currently under debate; bowel rest and broad-spectrum antibiotics are the most common strategies. Preliminary data on management without antibiotics support this strategy for mild diverticulitis. Complicated diverticulitis needs a case-by-case evaluation and further studies are needed to understand the best medical management strategy.

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