Colorectal Disease

Position Statements:
Management of Anal Fissure
Management of Acute Severe Colitis

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Contents

Position Statements

The Management of Anal Fissure: ACPGBI Position Statement

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Introduction

Anal fissure is a linear ulcer in the squamous epithelium of the anal canal located just distal to the dentate line. It is usually located in the posterior midline but occurs anteriorly in a fifth or more or patients. It typically causes pain during defaecation which may last for 1–2 h afterwards [1]. The most consistent finding on physical examination is spasm of the anal canal due to hypertonia of the internal anal sphincter. It has been postulated that this may either be due to or be the result of ischaemia [2]. All management options aim to reduce anal tone. They include general measures such as dietary fibre supplements, adequate fluid intake, and topical analgesics, medical treatments such as glyceryl trinitrate(GTN) ointment, calcium channel blockers (eg diltiazem cream) and botulinum toxin. Surgery includes lateral sphincterotomy, advancement flap procedures and fissurectomy. This position statement recommends evidence-based practice associated with these treatment options.

Methodology

Searches of the Cochrane Database, Pub Med MEDLINE and EM-BASE were performed using keywords relevant to each section of this position statement. They were limited to English language articles. Additional publications were retrieved from the references cited in articles identified from the primary search of the literature. All evidence was classified according to an accepted hierarchy of evidence and recommendations graded A–C on the basis of the level of associated evidence and/or noted as Good Practice and/or part of NICE/SIGN recommendation or Rapid Technology Appraisal (Table 1).

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Aetiology

Fissures associated with internal anal sphincter hypertonia are probably ischaemic in nature (Level IIb, Grade B).

The aetiology of the typical fissure is not clear. Trauma from passing a large or hard stool is a common initiator [3], but many traumatic fissures heal and others do not. Resting anal pressure is higher in patients with an anal fissure [4]. Ambulatory manometry has shown persisting high anal resting tone interpreted as due to hypertonia of the internal anal sphincter with poor spontaneous relaxation in patients with a chronic fissure [5]. In a study examining the influence of ischaemia, it was found that the higher the sphincter pressure, the lower the anodermal bloodflow. This was most pronounced posteriorly where most fissures occur and was followed by a return of normal bloodflow after sphincterotomy [6]. It was postulated that the pain caused by anal fissure was because of ischaemic ulceration, perhaps due to sphincter spasm reducing the blood flow in vessels penetrating the internal anal sphincter [7] Although this has never been proved with certainty, it remains the most commonly supported theory.

The aetiology of fissure formation in females who have had a vaginal delivery whether complicated or assisted or in patients with a rectocele may be different. Scar formation may be associated with ischaemia and poor healing, but in addition resting sphincter pressure is low [8].

If the fissure is not situated in the midline or if it is multiple or painless, the association with other pathologies should be considered. These include Crohn's disease, ulcerative colitis, HIV and associated secondary infections, tuberculosis, syphilis, and neoplasia including leukaemia or carcinoma.

Table 1 Levels of evidence and grades of recommendation.

Level of evidence		Grade of evidence	
I	Evidence obtained from a single randomized controlled trial or from a systematic review or meta-analysis of randomized controlled trials	A	Evidence of type I or consistent findings from multiple studies of type IIa, IIb or III
IIa	Evidence obtained from at least one well-designed controlled study without randomization	B	Evidience of type IIa, IIb or III and generally consistent findings
IIb	Evidence obtained from at least one other well-designed quasi-experimental study	C	Evidence of type IIa IIb or III but inconsistent findings
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies	D	Little or no systematic evidence
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities, case reports	GP	Recommended good practice based on the clinical experience of the expert group and other professionals*

Adapted from Eccles M, Mason J[1] and NHS Executive. Clinical Guidelines: Using Clinical Guidelines to improve patient care within the NHS. London: 1996.

*Previous experience and the literature in this area suggests that given the relative lack of evidence for many health care procedures, expert opinion and professional consensus are likely to be an important part of this process.

Diagnosis

Diagnosis is made from the history and examination (Level IV, Grade GP).

Anal Fissure is common. It occurs mostly between the second and fourth decades of life with an equal distribution between men and women with a lifetime incidence of 11.1% [9]. The diagnosis is usually suspected on the history alone. The symptoms include anal pain during and after defaecation which may last several hours. Bleeding is common and tends to be bright red and is often seen on the toilet paper. The patient may complain of periodic episodes indicating chronicity.

In most patients physical examination by inspection on gentle traction of the buttocks will show the fissure. A sentinel tag at the distal pole of the fissure, a hypertrophied anal papilla at its proximal extent and the appearance of the circular fibres of the internal sphincter muscle in its base indicate that the fissure is chronic. The majority of fissures are in the midline posteriorly, 8% occur both posteriorly and anteriorly [10,11].

Digital rectal examination or endoscopy should be not be carried out in most patients at the time of the initial consultation owing to the likelihood of causing pain. If the fissure is seen on inspection then treatment can be initiated. If it is not apparent then an examination under anaesthetic should be advised to make the diagnosis and also to exclude anorectal sepsis which is associated with fissure or may be present in its own right.

The presence of diseases associated with fissure as listed above should be suspected if the patient reports general symptoms of weight loss or weakness or abdominal symptoms referable to the gastrointestinal track. A family history of inflammatory bowel disease or a morphologically unusual fissure away from the midline should be regarded with suspicion. At the time of the initial consultation it is possible to pass a paediatric proctoscope to determine whether the rectal mucosa is inflamed. This is usually pain free.

Treatment

Conservative

Conservative treatment will heal a proportion of acute anal fissures (Level I, Grade A).

Conservative treatment includes increasing liquid intake, stool softeners and topical analgesics. In a prospective trial dietary bran supplements (5 g three times a day) and warm sitz baths were superior with fewer recurrences than topically applied local anaesthetic or hydrocortisone cream [12]. Recurrence rates were reduced from 68–16% at 1 year following continued conservative management [13].

Medical Therapies

Relaxation of internal anal sphincter tone is achieved by the reduction of intracellular calcium in the

smooth muscle cells thereby reducing muscle tone. This can be achieved by nitric oxide donation using GTN or by direct intracellular calcium depletion using calcium channel blockers (diltiazem or nifedipine). Irreversible acetylcholine neuromuscular blockade using botulinum toxin also reduces resting tone.

Glyceryl trinitrate

Topical GTN heals anal fissure better than placebo, irrespective of dose but is associated with headache in around 25% of patients (Level 1, Grade A).

Glycerine trinitrate is a vasodilator and causes relaxation of smooth muscle. When applied topically to the anus two to three times daily, the internal sphincter is relaxed and the fissure heals significantly better than placebo. Healing occurs in only 60% of patients in the short-term, with recurrence rates of around one-third over 18 months. Patients with recurrence may respond to further GTN, but a proportion will require sphincterotomy [14]. The dose of GTN (0.2% or 0.4%) does not influence the efficacy but increases the incidence of side effects, particularly headache which occurs in about a quarter of patients [15,16]. Commercially available GTN ointment ('Rectogesic' 0.4%) is often more easily available than 0.2% GTN ointment, Loder, 1994 p. 51 Watson, 1996 p. 173 [17] and [18]. Meta-analysis has shown that topical GTN twice daily is effective although the placebo response is around 30% (Fig. 1).

Calcium channel blockers

Topical diltiazem has similar efficacy to GTN but with fewer side effects and should be recommended as first line treatment in the management of anal fissure. Patients should be warned about pruritis ani (Level 1, Grade A).

Calcium channel blockers, such as diltiazem and nifedipine improve fissure healing by inhibiting calcium ion entry through voltage-sensitive areas of vascular smooth muscle causing muscle relaxation and vascular dilatation. In a randomized comparison of topical diltiazem 2% with topical GTN 0.2% applied twice daily there was no difference in healing rates [20]. Diltiazem is, however, rarely associated with headache, and only occasionally associated with pruritis ani [21]. Diltiazem 2% and GTN 0.2% are unlicensed so individual drug and therapeutics hospital guidelines will dictate availability. Oral nifedipine has been shown to give good healing rates, but is associated with greater systemic side effects than the topical preparation [22]; a similar finding was seen with oral diltiazem [23].

Botulinum toxin

Botulinum toxin is associated with a similar rate of healing of anal fissure as GTN but is more expensive. It may be used for a fissure resistant to topical GTN or diltiazem. The technique, dose and site of injection do not affect the rate of healing (Level 1, Grade A).

Contraction of the internal sphincter is mediated by sympathetic neuronal activation. Botulinum toxin irreversibly binds to presynaptic nerve terminals preventing acetylcholine release and thereby stopping neural transmission. Botulinum toxin thus induces a relative hypotonia, reducing resting anal canal pressure. This effect lasts for 2–3 months until acetylcholine reaccumulates in the nerve terminals [24].

There are many different published techniques for injecting botulinum toxin. The dose has varied from 10–100 u (mean 23 u based on 20 trials) with a mean healing rate of 75.6% and a range of 44–100% irrespective of the technique. Most frequently the injection has been

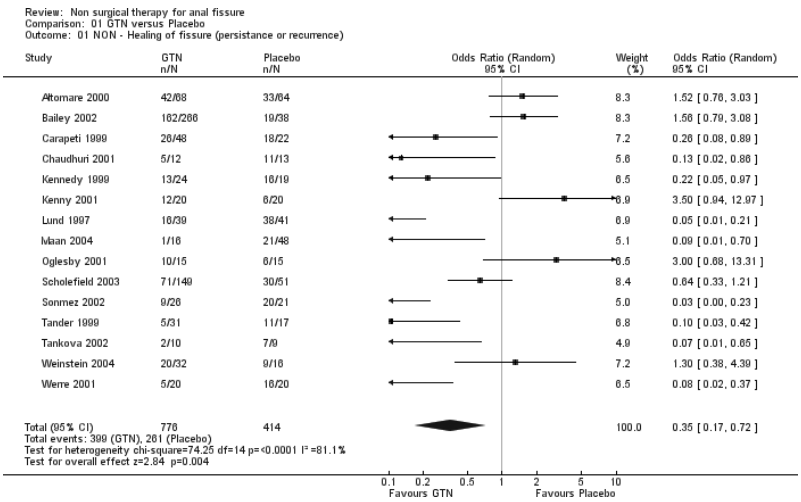


Figure 1 Topical glyceryl trinitrate: fissure healing. (Courtesy of Professor Nelson[19].)

carried out on either side of the fissure into the internal sphincter. Botulinum toxin has been shown to be as effective than GTN in the primary healing of fissure [25,26], and appears to be as effective for a fissure resistant to GTN [27]. There is no difference in healing rates between the different commercially available products including Botox or Dysport [28]. Botox costs approximately £200/100 u. Grouping of patients on the same operating list and follow-up at the same outpatient clinic improves cost effectiveness, as one vial can be used to treat four patients.

Suggested recommendation for medical management
An acute fissure should initially be treated with increased intake of oral fluids, fibre, stool softeners and analgesics combined with the local application of diltiazem 2% cream. A chronic fissure should be managed with diltiazem 2% topically twice daily for 6–8 weeks where such a prolonged treatment schedule is clinically more acceptable. Failure or recurrence after the application of a topical preparation should be treated with botulinum toxin 20–25 u in two divided doses injected into the internal sphincter on either side of the fissure. Failed medical management or recurrence warrants anorectal physiological testing in females, or in males having had previous anal surgery.

Surgery

The aim of surgery is to reduce resting anal canal tone due to the internal anal sphincter thereby increasing blood supply to the anoderm to improve healing. Surgical options include lateral sphincterotomy, fissurectomy and advancement flap procedures. In the past anal dilatation, posterior sphincterotomy have been used, but there is little evidence to support their continued use. In patients with a low resting pressure an anal advancement flap is a logical option.

Lateral sphincterotomy
Lateral sphincterotomy heals more anal fissures with lower recurrence than medical management but is associated with a significantly higher rate of incontinence to flatus. It should be reserved for patients who fail medical treatment (Level 1, Grade A).

Lateral sphincterotomy has been shown to be more effective than medical management (Fig. 2). One study reported an 85% cure rate, with 5% showing persistence and 10% recurrence. There was however a significant continence disturbance with 30% of patients having difficulty controlling flatus, 20% soiling, and 3–10% having episodes of leakage which appeared to depend on whether a closed or open lateral sphincterotomy had been carried out. Overall there was a 90% patient satisfaction rate [29]. A meta-analysis of the four randomized controlled trials assessing open *vs* closed lateral sphincterotomy found no significant difference, but there was a trend to greater healing and greater flatus incontinence in the open group [29]. By limiting the sphincterotomy to the length of the fissure, healing rates are not reduced but the frequency of incontinence is lessened [31].

Based on the evidence, the optimal surgical technique should involve the use of an anal retractor to identify the intersphincteric groove followed by an incision over the groove at 3 o'clock with blunt dissection of the internal sphincter away from the mucosa. The internal sphincter is then divided to the length of the fissure, but for no more than half the length of the sphincter. No difference in healing or complications has been found whether the anal skin incision is closed or not.

Fissurectomy
Fissurectomy with or without posterior sphincterotomy has been found to be useful when the fissure is associated with a fistula [32], but posterior sphincterotomy has lost favour as it may cause a 'keyhole deformity' resulting in mucous leakage in up to a third of patients [33]. Fissurectomy includes excision of the fibrotic edge of the fissure, curettage of its base, and excision of the sentinel pile and/or anal papilla if present. When used in association with botulinum toxin in the treatment of a chemically resistant fissure, it appears to enhance healing while, avoiding the risk of a sphincterotomy [34].

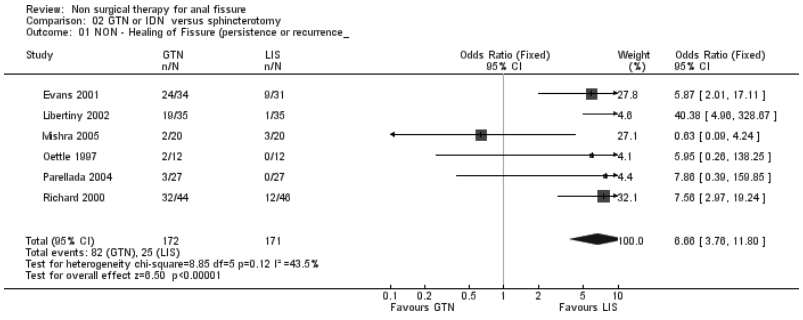


Figure 2 Glyceryl trinitrate *vs* sphincterotomy: fissure healing. (Courtesy of Professor Nelson [30]).

Anal dilatation

Anal dilatation heals fewer fissures and is associated with higher rates of incontinence than lateral sphincterotomy and is normally not indicated in the management of anal fissures (Level 1, Grade A).

Manual dilatation of the anus does not appear to heal anal fissure although it may lead to significant symptomatic relief. However, when uncontrolled, digital anal stretch can cause sphincter disruption and incontinence [35]. Different techniques of anal dilatation have been tried. These include the use of an anal dilator as outpatient treatment [36], dilatation in conjunction with sphincterotomy [37] and gentle dilatation under total neuromuscular blockade [38]. The last of these reported a retrospective review which showed minimal incontinence. In a meta-analysis anal dilatation caused significantly more incontinence and healed fewer fissures than sphincterotomy [30].

Anal advancement flap

An anal advancement flap is effective in healing an anal fissure and is followed by minor complications only. It should be recommended in patients with a low resting anal pressure (Level 1, Grade A). Various flaps have been described but a rotational or V–Y flap may reduce complications (Level III, Grade B).

An island flap in which a circumcised area of perianal skin is advanced proximally to cover the fissure has been shown to be effective in healing with no incidence of incontinence [39,40]. An alternative to this is a V–Y advancement flap or a rotational flap, which are both associated with lower rates of donor site wound complications, reported to be as high as 60% [41].

'Ideal' management recommendations

Lateral sphincterotomy should be used when medical management fails in men or women with normal to high resting tone. An alternative may be fissurectomy and botulinum toxin. In patients with low anal resting tone an anal advancement flap is a preferable option (see management algorithm).

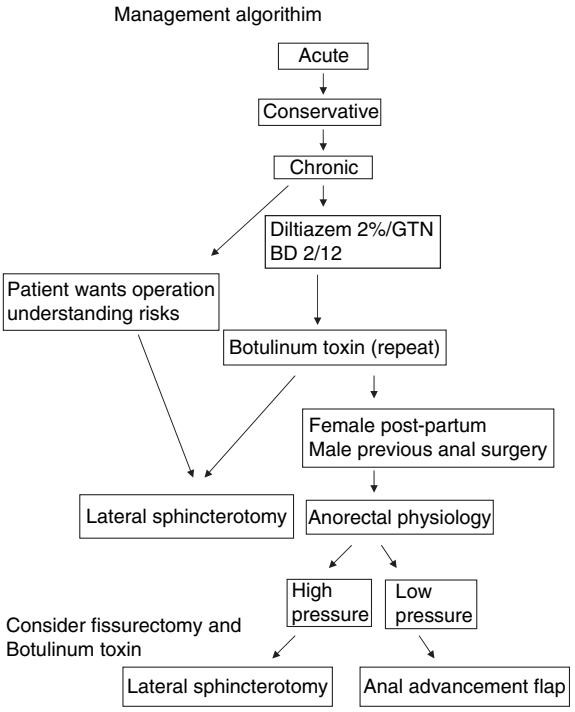
Anal fissure in children

Fissure in children should be treated conservatively initially. If it fails to respond, local GTN or calcium channel blockers should be tried. Lateral sphincterotomy or fissurectomy should be reserved for those failing to heal with medical treatment (Level IIa, Grade B).

Most fissures occur in children aged between 6 and 24 months usually as a result of a mechanical tear. If chronicity develops, associated underlying pathologies should be ruled out as in adults. Diagnosis is by the history and examination. Stool negativism i.e. the deliberate reluctance to defaecate is not uncommon. It is important to palpate the abdomen for signs of faecal loading. An acute fissure usually heals in 10–14 days with conservative management, including dietary modification and osmotic laxatives [42]. If the fissure persists for 6–8 weeks chemical sphincterotomy should be considered. GTN 0.2% topically twice daily has been shown to be effective in treating children [43]. There is little information on diltiazem or botulinum toxin treatment in children.

Surgery is rarely indicated. Anal dilatation in the management of constipation and faecal soiling has not been found to be beneficial and is associated with a high rate of recurrence [44]. For an indolent fissure resistant to healing, fissurectomy and lateral sphincterotomy have been found to be beneficial [45,46]. The surgical technique is the same as for adults.

For further full text reference information, please refer to the recently published systematic review by Bhardwaj R and Parker MC [47].



Conflicts of Interest

None declared

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The Management of Acute Severe Colitis: ACPGBI Position Statement

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Introduction

'Acute severe colitis' (formerly known as fulminant colitis) is a potentially life-threatening condition that constitutes a medical and surgical emergency. The majority of cases are due to ulcerative colitis (UC), although other causes such as Crohn's colitis and pseudomembranous colitis (PMC) can result in a similar clinical picture. The condition is common; the prevalence is around 15% [1]. As a very rough estimate for the UK, there are about 2500 admissions per year [2,3] or around one patient per 22 000 population (about 12 patients per year for a District General Hospital). More precise data will result from the UK National IBD Audit (http://ibdaudit.rcplondon.ac.uk/2006/).

To understand the implications of current medical and surgical therapy, the management first needs to be placed in historical context. In 1933, the mortality in the first year after acute presentation was 75% [4] and of the order of 50% following ileostomy. With the introduction of excision of the disease by colectomy by Miller *et al.* [5] towards the end of the 1940s, the mortality rate fell to 5%. This was achieved by other units at the time, although, in some, mortality was still over 20% in the early 1950s [6]. In 1955, the introduction of steroid therapy was reported to reduce the mortality of severe colitis from 24% to 7%, [7] and it is now less than 1% in specialist centres [8]. Nevertheless, the response to steroids of severe colitis has remained unchanged for 50 years [9]. Furthermore, nonspecialist management of severe colitis still carries high risk. Of 32 admissions (in 25 patients) for severe colitis under general physicians in a small UK district general hospital between 1994 and 2000, six patients died [10].

Perhaps more than any other condition, severe acute colitis requires the highest level of cooperation between surgeon and physician and specialist management for the most favourable outcome. This position statement sets out to examine the current literature on this condition and to provide an evidence-base upon which practitioners can base individual management.

Methodology

Organized searches of the Cochrane Database, MEDLINE and EM-BASE were performed using keywords relevant to each section of this position statement. Searches were limited predominantly to English language articles. Additional publications were retrieved from the references cited in articles identified from the primary search of the literature. All evidence was classified according to an accepted hierarchy of evidence and recommendations graded A–C on the basis of the level of associated evidence and/or noted as Good Practice and/or part of NICE/SIGN recommendation or Rapid Technology Appraisal (Table 1) [11,12]. The five main sections addressed within this statement are medical diagnosis and assessment (ST), pathological diagnosis (NH), radiological diagnosis (JH) nonsurgical management (ST) and surgical management (BG).

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Table 1 Grading scheme for assessing submitted evidence.

Level of evidence		Grade of recommendation	
I	Evidence obtained from a single RCT or systematic review/meta-analysis of RCTs	A	Evidence of type I or consistent findings from multiple studies of type IIa, IIb or III
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III	Evidence obtained from well-designed nonexperimental descriptive studies, e.g. comparative studies, correlation studies and case studies	D	Little or no systemic evidence
IV	Evidence obtained from expert committee reports/opinions ± clinical experiences of respected authorities, case reports	GP	Recommended good practice based on the clinical experience of the expert group and other professionals*

All evidence will be classified according to an accepted hierarchy of evidence that was originally adapted from the US Agency for Healthcare Policy and Research Classification. Recommendations will then be graded A–D on the basis of the level of associated evidence and/or noted as a Good Practice and/or as part of NICE/SIGN recommendation or Rapid Technology Appraisal.
Adapted from Eccles and Mason [11] and NHS Executive [12].
*Previous experience and the literature in this area suggests that given the relative lack of evidence for many healthcare procedures, expert opinion and professional consensus are likely to be an important part of this process.

A. Medical diagnosis and assessment

Findings

It is essential to define what is meant by acute severe colitis in order to diagnose and manage patients with the disease (Level I).

Recommendations

Acute severe colitis should be defined as six or more bloody stools daily with evidence of systemic toxicity as demonstrated by fever, tachycardia, anaemia or an elevated erythrocyte sedimentation rate (ESR) (Grade A).

Although the term 'fulminant' colitis is often used to describe patients with severe colitis, 'acute severe colitis' is preferred because it has defined objective measures for diagnosis, defines a course of action and has reported outcomes. The term 'fulminant colitis', coined in 1950, referred to a single attack going on to death within 1 year [2], which no longer has relevance today. Nevertheless, the term 'fulminant' has frequently been used for patients with severe colitis and signs of systemic toxicity, especially in the USA. This has created confusion, most manifest in the Active Colitis Trials (ACT) of infliximab (IFX) that used the term 'severe' colitis for outpatients with treatment-refractory active colitis [13].

The American College of Gastroenterology defines acute severe colitis according to Truelove and Witts' criteria [14], as has the European Crohn's and Colitis Organisation [15] (Table 2).

Table 2 Diagnosis of severe ulcerative colitis (modified from [7]).

Criteria	Severe
Bloody stool frequency	> 6/24 h and
Pulse rate	> 90 bpm, or
Temperature	> 37.8°C, or
Haemoglobin	< 10.5 g/dl, or
ESR	> 30 mm/h

Only one additional criterion in addition to a bloody stool frequency > 6/day is needed to define a severe attack, because the number of additional criteria is unrelated to the outcome of individual episodes [2,8].

Findings

It is important to exclude other causes of symptoms associated with acute severe UC (Level III).

Recommendations

A combination of clinical, endoscopic, histological and radiological criteria should be used to exclude other differential diagnoses (Grade B).

Recommendations

Every patient should have his or her full blood count (FBC), inflammatory markers (C-reactive protein (CRP) or ESR), electrolytes and liver function tests measured, along with a stool sample for culture and sensitivity as well as assay of Clostridium difficile *toxin (Grade B).*

The diagnosis of UC is made according to conventional criteria, combining clinical, endoscopic, histological and radiological criteria [16]. Patients with a severe attack may look deceptively well: a tachycardia and tender colon may be the only physical signs. However, many of these patients are obviously ill, with fever, salt and water depletion, anaemia and evidence of weight loss [17]. There may be oral candidiasis, aphthous ulceration, leuconychia and peripheral oedema. The abdomen may be distended, with reduced bowel sounds and marked tenderness.

Infective colitis must be excluded, especially *C. difficile* and cytomegalovirus (CMV) infection when patients with established colitis (especially those on immunomodulators) have a severe relapse. In a small proportion with atypical features, Crohn's colitis, colitis yet-to-be classified or drug-induced colitis should also be considered (see section B).

Recommendations

All patients with severe colitis should have a plain abdominal radiograph (Grade B).

A plain abdominal radiograph will not only exclude colonic dilatation (> 5.5 cm), but can also estimate the extent of disease and identify features that predict response to treatment (see section C).

Recommendations

A flexible sigmoidoscopy is appropriate to confirm the diagnosis and exclude infection (Grade B).

Flexible sigmoidoscopy will often confirm the diagnosis of UC and exclude most other causes. Endoscopic criteria for severe colitis have been described, including extensive mucosal abrasions, deep ulcerations, mucosal detachment on the edge of these ulcerations and well-like ulceration [17,18]. Phosphate enema preparation is considered safe, but is probably best avoided in patients with a dilated colon. For such patients, gentle flexible sigmoidoscopy by an experienced endoscopist using minimal insufflation in an unprepared colon is more appropriate.

Full colonoscopy in patients with acute severe colitis cannot be recommended, because all the endoscopic criteria for severe colitis can be assessed at flexible sigmoidoscopy. A purgative preparation can provoke dilatation, while colonic perforation is a real hazard of colonoscopy during active disease.

Findings

Careful assessment during admission predicts outcome and aids management (Level III).

Recommendations

Regular monitoring of stool frequency, pulse and temperature and daily physical examination is essential (Grade B).

Monitoring after admission includes measuring the pulse rate and temperature four times daily and a stool chart to record the number of bowel movements, including the presence or absence of blood. Measurement of FBC, ESR or CRP, serum electrolytes, serum albumin and liver function tests should be performed every 24–48 h. Electrolyte disturbance should be corrected and the CRP may contribute to the objective evaluation of response to treatment.

Daily physical examination is appropriate to evaluate abdominal tenderness and rebound tenderness. In the presence of a dilated colon, twice daily examination is appropriate and evaluation by a gastroenterologist and colorectal surgeon together is an aid to decision making about the timing of colectomy.

Recommendations

Radiological monitoring should be considered and may predict the need for colectomy (Grade C).

Daily abdominal radiography is appropriate if signs of colonic dilatation (transverse colon diameter > 5.5 cm) are detected (see section C). Once the colonic diameter decreases or a decision is made to proceed to surgery, radiographic monitoring can cease. Repeat abdominal radiography is also appropriate if there is any deterioration (such as a rise in pulse rate or temperature) during intensive treatment of severe colitis.

Recommendations

Stool frequency should be monitored and may predict the need for colectomy (Grade B).

A stool frequency > 12/day on day 2 was associated with 55% colectomy [19], while a frequency > 8/day on day 3 of intensive treatment predicted colectomy in 85% on that admission [8]. In a prospective study, a stool frequency 3–8/day in conjunction with a CRP > 45 mg/l on day 3 of intensive treatment ('Oxford

index') also predicted colectomy in 85% [8]. This index has been prospectively validated in an independent cohort: the 'Sweden index' or 'fulminant colitis index'. When the stool frequency × 0.14 of the CRP value was > 8 on day 3 (equivalent to a stool frequency of > 4/day and CRP > 25 mg/l on day 3), this predicted colectomy in 75% [20]. The predictive criteria of stool frequency, CRP and temperature on day 3 have also been validated in a paediatric cohort to develop a Paediatric Ulcerative Colitis Activity Index [21].

Recommendations

Biochemistry should be monitored regularly and may predict the need for colectomy (Grade C).

Biochemical markers that may predict the outcome include CRP, albumin and pH. An ESR > 75 mm/h or a pyrexia > 38°C on admission have been associated with a five- to ninefold increase in the need for colectomy in a prospective study of 67 patients [22]. In this study, lack of response to steroids was predicted by < 40% reduction in stool frequency within 5 days. Nevertheless, indices that provide relative values are not that clinically useful. Patients (and their doctors) prefer to have an absolute estimate of the likelihood of colectomy, rather than a relative measure. A retrospective study of 167 patients, in whom a high proportion (40%) came to colectomy, developed a numerical score combining the mean stool frequency over 3 days, the presence or absence of colonic dilatation and hypoalbuminaemia (< 30 g/l) on admission that was associated with the need for colectomy in up to 85% [23]. This 'Edinburgh fulminant colitis index' needs prospective validation.

Genetic markers are in their infancy. Between 1% and 3% of the general population express HLA DRB1*103, while 16% of those who come to colectomy express this haplotype [24]. A polymorphism in the gene for the multidrug resistance (MDR-1) efflux pump, which is associated with drug resistance in chemotherapy, is also associated with steroid resistance and colectomy in UC [25]. Although genetic polymorphisms have the potential to predict the outcome of disease in an individual from the time of diagnosis, they cannot be used for decision making when colectomy is imminent.

Indices exist to be applied as a threshold for triggering appropriate action at an early stage. This means surgical consultation and assessment by a stomatherapist, in addition to augmenting medical treatment. A CRP > 45 mg/l and stool frequency 3–8/day [8] are the simplest objective measures, but are neither immutable nor always reproduced. Other criteria may do as well, but must be as straightforward. The most important issue is to have the objective measures of response integrated into the clinical strategy, so that patients with severe colitis are not blighted by delays in medical or surgical decision making.

Findings

Outcome of patients with acute severe colitis is influenced by the experience of the medical and nursing staff caring for the patient (Level IV).

Recommendations

Patients diagnosed with severe colitis should be managed by staff experienced in caring for patients with gastrointestinal disorders (Grade GP).

There is broad agreement among clinicians that patients with severe colitis are best cared for jointly by a gastroenterologist and colorectal surgeon. A high mortality is associated with nonspecialist care by general physicians [10]. Care should ideally be on a ward with nursing staff experienced in caring for patients with gastrointestinal disorders. Other factors associated with either an optimal or poor outcome are likely to be identified by the UK National IBD Audit. Until the audit reports, no definitive recommendations can be made, but it is reasonable to recommend a system by which patients admitted with acute colitis are automatically transferred to the care of a specialist gastroenterologist and a gastroenterology ward. Colorectal surgical assessment is recommended for all such patients at an early stage, at least by the third day of intensive therapy in patients who have objective evidence of a poor response to conventional therapy.

B. Histological diagnosis

The pathologist plays two important roles in the management of acute severe colitis. The first is as an aid to the diagnosis of the cause of the colitis in the acute phase. The second is as an aid to the definitive diagnosis after the acute phase has settled or after the patient has undergone colectomy. Both roles have a decisive influence on management. For instance in the acute phase, a diagnosis of infective colitis will alter medical therapy while after colectomy, the diagnosis of Crohn's colitis or ischaemic colitis will influence the choice of subsequent surgery including an ileo-anal pouch procedure. Only the role of the pathologist in the setting of acute severe colitis will be discussed.

Findings

The histological confirmation of a diagnosis of UC in acute severe colitis can be difficult (Level IV).

Recommendations

Histological data should be combined with clinical, microbiological and radiological data in order to reach a diagnosis (Grade B).

Ulcerative colitis is primarily a mucosal disease, but may affect the superficial part of the submucosa. The serosa in the majority of cases appears either normal or congested. Rarely, with toxic megacolon, perforation may be seen. On naked eye appearance of acute severe colitis, the mucosa is generally congested and there are variable degrees of ulceration. Classically, the patchy ulcerations undermine adjacent intact mucosa forming mucosal projections erroneously called pseudopolyps. Characteristically, the ulcers are linear in distribution and are predominantly situated along the course of the taenia coli. They are usually superficial and do not penetrate through the muscularis propria except in toxic megacolon.

One characteristic feature of UC is continuous inflammation. The disease typically involves the rectum and extends proximally in a continuous and symmetrical fashion to involve a variable extent of the colon up to the ileocaecal valve. On occasion there is backwash ileitis, which is a superficial inflammation of the terminal ileum 10–25 cm proximal to the ileocaecal valve. This is attributed to the pancolitis leading to a dysfunctional valve and reflux of colonic content into the terminal ileum. Backwash ileitis resolves following colectomy and has no clinical significance apart from potential confusion with Crohn's disease and a possible predilection for pouchitis after ileoanal pouch surgery [26]. Appendiceal involvement is seen in over half of the cases of colectomy specimens from patients with pancolitis and may simply represent the continuous inflammatory process. However, in less extensive colitis, appendiceal inflammation may still be seen in a high proportion of patients (15–86%) [27] as indeed may a peri-appendiceal caecal patch of inflammation [28].

Histologically, the hallmark of activity in UC is the presence of neutrophilic infiltrate. This concentration of the neutrophils relate to the level of activity of the disease. Crypt abscess formation (collection of neutrophils in the crypt lumen) is the natural progression of cryptitis (neutrophilic infiltrate involving the crypt epithelium). On occasions, the crypt ruptures leading to seepage of mucus, which initiates a histocytic response sometimes with the formation of a granuloma. This is called leakage granuloma and must be differentiated from the more classical sarcoid type granuloma of Crohn's disease.

The natural evolution of crypt abscesses is either resolution or progression to ulceration and these ulcers may spread into the submucosa to undermine adjacent intact mucosa, leading to the macroscopic appearance of acute severe colitis. In acute severe colitis, the ulcers are usually large and extend into the muscularis propria but not beyond except in toxic megacolon.

Mucus depletion is a feature of activity and regeneration. It has no diagnostic significance in active colitis other than this, although it is probably more commonly seen in UC than in Crohn's disease. Hyperaemia and vascular telangiectasia are other features of active severe inflammation.

Despite the classical macro- and microscopic features described, it is often difficult to classify the aetiology of acute severe colitis on histological analysis of biopsies alone. This is due to a variety of factors, which includes the following.

1 Lack of clinical information available to the pathologist at the time of reporting. It is important to realize that the diagnosis of IBD is a strictly clinico-pathological diagnosis and does not rely solely on the pathologist [29,30]. Other clinical and imaging data are essential in most cases to reach the final diagnosis. A multidisciplinary meeting to include all involved clinicians may be helpful in this situation [31], or if this is not possible, a detailed pathological request form may improve the accuracy of pathology reporting [32].
2 The clinical and pathological features, which are acute and severe, are not always pathognomic of a specific diagnosis. Having said that the diagnosis of UC should be questioned when rectal bleeding is absent, or rectal mucosa spared (see below) during an acute attack. Diarrhoea without bleeding is more common in Crohn's colitis.
3 The colonic mucosa responds in a limited way to various injuries and there is no single histological criterion that is invariably present.
4 Many other conditions in the colon that mimic UC and some of them may present as acute severe colitis (see Table 3 [33,34]).

Although the definitive histological diagnosis is often difficult, some conditions in the differential diagnosis do have pathognomic histological features. *Clostridium difficile* infection may be identified histologically by 'summit' lesions representing a fibrin cap above inflammation, as well as the endoscopic features of pseudomembrane formation. Note, however, that these lesions are seen in only a portion of the colitic area and absence does not exclude PMC. Sometimes such lesions are seen in ischaemia and other infections.

Cytomegalovirus infection is characterized by multiple intranuclear inclusion bodies on haematoxylin and eosin (H&E) staining, which is the most reliable way of identifying CMV infection [35] particularly if confirmed with immunohistochemistry. Either *C. difficile* or CMV

Table 3 Differential diagnosis of severe ulcerative colitis.

Condition	Comment
Infective colitis	Usually short duration; may complicate existing colitis (especially CMV)
Campylobacter sp.	
Shigella sp.	
Clostridium difficile	
Escherichia coli 0157 H7	
CMV	
Amoebiasis	
Crohn's colitis	
Colitis yet-to-be classified	Having features of both UC and Crohn's colitis; the term 'indeterminate colitis' should be reserved for colectomy specimens
Ischaemic colitis	Exceptionally rarely affects the rectum
Diverticular colitis	Never affects the rectum
NSAID colitis	May be impossible to discriminate from UC: ask about NSAID ingestion and alert the pathologist

CMV, cytomegalovirus; UC, ulcerative colitis; NSAID, nonsteroidal anti-inflammatory drug.

infection on top of UC is an important diagnostic consideration in acute severe colitis. On the rare occasion that there is a strong suspicion that CMV is responsible for deterioration (such as a patient on immunomodulators, in association with a high fever and elevated alkaline phosphatase), it is appropriate to request urgent histopathology. An answer can be available within 24 h allowing antiviral therapy to be initiated if appropriate.

C. Radiological investigation

The radiologist plays three key roles in the diagnosis and management of patients with severe acute colitis. The first is the diagnosis of colitis in a patient presenting for the first time with acute abdominal symptoms. The second, often combined with the first, is the differentiation of various causes of acute colitis (for instance, PMC compared with UC or Crohn's disease). The third role is the monitoring of patients with disease as an aid to the effectiveness of medical therapy and the need for surgery. Plain films and more recently computed tomography (CT) scanning are utilized, but it should be remembered that radiology is only an adjunct to management. It is not a substitute for careful clinical assessment by a gastroenterologist and colorectal surgeon. It would be wrong to give the impression that a radiologist reporting a CT scan will tell the surgeon and physician when to operate.

Findings

The diagnosis of an acute presentation of colitis in a previously well patient may be aided by plain abdominal radiography and CT scanning (Level III).

Recommendations

A CT scan may aid the diagnosis of colitis in the patient presenting for the first time with severe acute colitis and give an indication of the underlying aetiology (Grade B).

A significant minority of patients (about 5–8%) present for the first time with acute severe colitis. Diagnosis may be difficult and involves a combination of clinical, endoscopic, microbiological and radiological techniques. CT scanning is a useful adjunct in confirming the diagnosis of colitis, as well as helping to determine the extent of the colitis and detecting complications that may not otherwise be apparent.

Certain specific CT features help with the diagnosis of colitis in this situation [36] and may even indicate the type of colitis.

- The normal colonic wall thickness (measured when the gut is distended and imaged transaxially) should be no more than 3 mm [37]. A wall thickness of greater than 4 mm in any segment of small bowel and colon is abnormal [38]. There is considerable overlap between the CT features seen in Crohn's and UC. Both show bowel wall thickening, but that seen in UC (7.8 mm ± 1.9 mm) is typically less than in Crohn's disease (11 mm ± 5.1 mm) [41]. PMC appears to cause the greatest thickening with mean thicknesss of up to 14 mm [39–41]. This condition deserves specific mention as the incidence is increasing and it may be associated with significant morbidity and a mortality of over 3.5% [42,43]. Early diagnosis and appropriate treatment are essential for preventing these adverse outcomes [44], and the radiologist may be the first person to entertain the possibility of the condition.
- In severe colitis, peri-colonic inflammatory change and ascites may be seen [45].
- The 'target' or 'halo' sign is specific for inflammatory disease [46], although it is not a useful sign for differentiating types of colitis [47–49]. It is best seen on postcontrast scans where the inner and outer high-attenuation areas correspond to the enhancing mucosa and muscularis propria and/or serosa respectively, and the middle low-attenuation layer is thought to represent the submucosa, which is oedematous or inflamed [48,50].
- The 'Accordion' sign was originally described as showing alternating oedematous haustral folds separated by transverse mucosal ridges filled with oral

contrast material, simulating the appearance of an accordion [40,51]. This finding has been reported to be a specific sign of severe PMC, with the degree of wall thickening caused by the pseudomembranes and submucosal oedema being the cause of the sign's specificity [51,52]. Subsequent studies have shown that the accordion sign may be detected in a variety of inflammatory and oedematous conditions that affect the colon, not just in PMC [53].

- The distribution of the colitis can also be useful in narrowing down the differential diagnosis. UC typically affects the colon in a continuous fashion, extending from the rectum proximally and not affecting the small bowel, although backwash ileitis may be seen as thickening on CT. Crohn's colitis may show segmental and even small bowel thickening on CT. Most infectious colitides cause a pancolitis, with some (salmonella, *Yersinia*, tuberculosis and amoebiasis) being more limited to the right colon and even terminal ileum. Others such as schistosomiasis and shigellosis affect mainly the left side of the colon. Neutropenic colitis or typhlitis affects the caecum and proximal ascending colon. Here, the history should make the diagnosis clear [54]. Ischaemic colitis typically affects the elderly and appears as a segmental thickening around the splenic flexure or recto-sigmoid region on CT, although the entire colon may be involved in up to 11% [55].

Findings

Reliable and rapid information about the extent and intensity of mucosal inflammation is important for the proper management of patients with acute severe colitis. Plain abdominal radiographs provide some of this information and may help to predict prognosis (Level III).

Recommendations

All patients with suspected acute severe colitis should have a plain abdominal radiograph (Grade B).

Although a CT scan may be indicated for a patient with acute colitis where the diagnosis is not clear, the plain abdominal radiograph is usually the first radiological investigation performed. It is therefore important that the features of a severe colitis are properly interpreted to allow prompt diagnosis and appropriate treatment. The typical features of severe UC on a plain abdominal radiograph include thickening of the colonic wall, mucosal irregularity and thickening or loss of the haustrations [56–58]. In the presence of severe disease, 'mucosal islands' (small, circular opacities representing residual mucosa isolated by surrounding ulceration) may also be seen, which represent oedematous mucosal remnants due to deep and extensive surrounding ulceration. These are recognized as soft tissues projecting into the gas-filled lumen of the bowel [58,60]. These features are only seen in segments of colon containing luminal gas and may not be visualized in collapsed segments. Note that absence of haustra in the left colon can be a normal finding.

The plain abdominal radiograph may also be used to estimate the extent of disease [60]. Inflamed colon does not usually contain faecal material, so the proximal extent of disease can be estimated by the distal distribution of faecal residue and by the presence of mucosal ulceration and alteration of the haustral pattern. The extent of colitis on the admission radiograph in 51 acute episodes was correct within one colonic segment in 74% of cases, with the extent of disease being overestimated by two or more colonic segments in 18% and underestimated in 8% [8].

Besides aiding the diagnosis of acute severe colitis, the plain film may provide some prognostic indicators:

- The presence of mucosal islands. Several series show that this predicts increased risk of colectomy during the acute admission. Fifty per cent of patients with mucosal islands present on the plain film 2 days after admission went on to require colectomy, compared with only 10% of patients without mucosal islands [8]. Eighty per cent (eight of 10) patients with mucosal islands required colectomy in another study [60]. Mucosal islands are also a predictor of impending dilatation and toxic megacolon [19,59,61].
- The distribution of gas throughout the bowel. Chew *et al.* [61] found that the presence of small bowel distension, defined as the presence of three or more gas-filled loops of small bowel on the plain abdominal radiograph in a patient with severe UC, may predict a poor response to medical treatment. Seventy-three per cent (24 of 33) of those who failed medical therapy and required colectomy had small bowel distension, whereas this was only seen in 43% (18 of 42) of those who settled on medical therapy. Other investigators have also shown that persistent gaseous distension of the gastrointestinal track (stomach, small bowel and large bowel) characterizes a subgroup of patients with a poor response to medical treatment and an increased risk of developing toxic megacolon [62]. Seven of 31 patients with increased small bowel gas developed toxic megacolon, whereas this was not seen in 38 patients with normal bowel gas distribution [63].

The use of an air enema has been advocated as a safe and effective way of assessing the depth of ulceration and the potential for failure of medical therapy [64]. Plain abdominal radiography after gentle air insufflation identified 42/49 patients with deep ulcers that were associated with the need for colectomy. However, this technique is not commonly used in UK clinical practice.

Findings

Toxic megacolon is a complication of acute severe colitis and may influence the timing of colectomy in the correct clinical situation (Level III).

Recommendations

All patients with severe acute colitis and signs of colonic distension should have daily abdominal radiographs to monitor for toxic megacolon, until there is clinical and radiological improvement or the decision has been made to perform a colectomy (Grade B).

Toxic megacolon as a complication of UC was first described in 1950 [65]. It simply represents the end of a spectrum of severe colitis that has been unrecognized or undertreated. It is defined as the total or segmental nonobstructive dilatation of the colon associated with systemic toxicity [66]. After studies by Hywel Jones and Chapman in 1969 [67], a limit of > 5.5 cm is commonly taken as the indicator of significant dilation.

The incidence has never been studied systematically. About 5% of patients with acute severe colitis admitted to hospital will have toxic dilatation [68]. Earlier diagnosis, more intensive medical management and earlier surgery has reduced the incidence of toxic megacolon complicating UC, but the incidence for infective colitis is rising, reflecting the increasing prevalence and severity of PMC [69].

The measurement of the diameter of the colon can be made on any segment of the colon, although the transverse colon is usually the dilated segment due to its more anterior-dependent position when the abdominal radiograph has been taken supine [67,70], not because it is more diseased than the remainder of the colon. Gas within the transverse colon has been shown to redistribute into the descending colon preferentially and some into the ascending colon on turning the patient prone [71].

D. Nonsurgical management

Findings

The management strategy of patients with acute severe colitis should discriminate between early identification of patients requiring surgery and those who will improve with intensive medical management (Level IV).

Recommendations

There should be joint care between specialist gastroenterologist and colorectal surgeon (Grade GP).

The two principal clinical dilemmas in managing acute severe colitis are how to identify at an early stage those who are likely to need colectomy and when to start rescue medical therapy in time so that surgery, if it becomes necessary, is not inappropriately delayed. The two are not mutually exclusive and management demands the most taxing clinical judgement. As therapeutic options increase [ciclosporin (CsA), IFX or visilizumab among others], so too does the opportunity for deferring a decision about surgery. Only a single patient need die as a result of complications caused by operating too late, to negate the benefits of medical therapy.

Specific medical therapy: corticosteroids

Recommendations

Intravenous corticosteroids remain the mainstay of conventional medical therapy (Level I).

Treatment with corticosteroids should not be delayed awaiting microbiological results for possible infective causes. Treatment is usually given for about 5 days.

The landmark paper of Truelove in 1955 showed a reduction in mortality from 24% in the placebo group to 7% in the steroid treated group [7]. Corticosteroids are generally given as hydrocortisone 100 mg four times daily or methylprednisolone (MeP) 60 mg daily. Higher doses (including 500 mg–1 g MeP) are no more effective, but lower doses are less effective [9,72]. Bolus injection is as effective as continuous infusion [73]. Extending therapy beyond 7–10 days has no benefit [9].

The response to intensive treatment with steroids has not changed for 50 years [9,74]. In a systematic review of the 32 trials of steroid therapy for acute severe colitis involving 1991 patients from 1974–2006, the overall response to steroids (intravenous hydrocortisone, MeP or betamethasone) was 67% (1429/1991, 95% CI: 65–69) [7]. Twenty-nine per cent (565/1991, 95% CI: 28–31) came to colectomy. Mortality was 1% (22/1991, 95% CI: 0.7–1.6) and none of these outcomes changed between 1974 and 2006 ($R^2 = 0.07$, $P = 0.8$). Because of substantial heterogeneity, it was not possible to discriminate between complete response and partial response to steroids. Only a minority (100/1991) of patients received CsA (see below). These data are supported by serial results (1955, 1974 and 1996) from a single centre. When complete response to steroids was defined as a stool frequency ≤ 3/day without visible bleeding on day 7, 41–42% had a complete response, 27–31% had a partial response and the remainder (28–32%) came to colectomy on that admission [7,8,75]. This centre's figures most closely match the mean colectomy rate of all studies [9], and are similar to those from a prospective study of 116 patents in 29 hospitals enrolled over 3 months [3,9].

Recommendations

In addition to intravenous steroids, other measures should be considered.

1 Intravenous fluid and electrolyte replacement to correct and prevent dehydration or electrolyte imbalance (Grade B).

Potassium supplementation of at least 60 mmol/day is almost invariably necessary [8]. Hypokalaemia or hypomagnesaemia can promote toxic dilatation [68].

2 Blood transfusion to maintain a haemoglobin > 10 g/d. (Grade GP).

3 Subcutaneous heparin to reduce the risk of thromboembolism [76] (Grade B).

4 Enteral nutritional support if the patient is malnourished (Grade B).

Enteral nutrition is most appropriate and associated with significantly fewer complications than parenteral nutrition in acute colitis (9% *vs* 35%) [77]. Bowel rest through intravenous nutrition does not alter the outcome [78], but some centres use a food challenge after 5 days to discriminate between complete and partial responders intensive therapy.

5 Withdrawal of anticholinergic, antidiarrhoeal agents, NSAID and opioid drugs (Grade B).

These drugs may precipitate colonic dilatation [68].

6 Topical therapy (corticosteroids or mesalazine) if tolerated and retained (Grade C).

There have been no systematic studies in acute severe colitis, although topical therapy is part of the regimen of some centres [75].

7 Intravenous antibiotics only if infection is considered (such as in the acute, first attack of short duration or after recent admission to hospital), or immediately prior to surgery (Grade B).

Controlled trials of metronidazole, tobramycin, ciprofloxacin or oral vancomycin in acute severe colitis have shown no significant benefit [79,80].

Other drugs

Findings

Since a complete response to steroids occurs in only 40% of patients with acute severe colitis, evaluation of rescue therapies is appropriate, but await adequately powered randomized controlled trials (Level IV).

Recommendations

A single attempt at rescue therapy with CsA or IFX should be considered before colectomy after careful discussion with the patient by a gastroenterologist and colorectal surgeon (Grade GP).

No individual patient wants a colectomy, but it is becoming easier for physicians to discuss other therapeutic options with patients as their availability increases. The question is how to do this safely. There are two principal options (CsA and IFX), with others on or below the horizon (tacrolimus or visilizumab).

Recommendations

It is not possible to determine the most useful rescue therapy for intravenous steroid-resistant UC (IVSR-UC) without a properly powered randomized controlled trial. At present either CsA or IFX are suitable options, although colectomy without trial of either therapy is appropriate for some patients (Grade B).

Ciclosporin emerged as the most useful rescue therapy for IVSR-UC after a placebo-controlled trial in 1994 [81]. This demonstrated that intravenous CsA at 4 mg/kg could prevent urgent colectomy. Nine of 11 patients failing steroids improved on CsA whilst all nine on placebo failed to improve. Subsequent studies have shown high initial response rates (over 80% in some series), but 1 year relapse rates have exceeded 50% [82–84]. The narrow therapeutic index of CsA and its side-effect profile has limited acceptability. In 2001, out of the 116 consecutive patients admitted to 29 UK hospitals with severe UC, only 17 (15%) received CsA, and only seven (21%) of 33 who came to colectomy had received CsA [2]. Preliminary results from the National audit of IBD 2006 (http://ibdaudit.rcplondon.ac.uk/2006/) show that only 150/2074 (7.2%) patients admitted with acute severe colitis to 180 UK hospitals received CsA and 37 received anti-TNF therapy. Treatment was started at a median of 6 days [interquartile range (IQR) 4–10 days] and 10 days (IQR 7–14) after admission for CsA and IFX respectively, which is a measure of delay in medical decision making. Clinical remission rates were 55% and 54% respectively. In nine studies that used CsA as the rescue therapy in the systematic review of steroids, only 100/622 (16%) patients received CsA [9]. The short-term response in this series was 51% (95% CI: 41–60) and 29% still came to colectomy (95% CI: 25–32). Concerns about early toxicity have been partly addressed by low dose (2 mg/kg iv) induction therapy. In the largest randomized study of CsA to date, 73 patients were randomized to either 2 mg/kg or 4 mg/kg of intravenous CsA [85]. Response rates at 8 days were similar in both groups (83% and 82% respectively), with 9% coming to colectomy in the 2 mg/kg group and 13% in the 4 mg/kg group.

CsA monotherapy and oral dosing

Ciclosporin monotherapy (4 mg/kg iv) was as effective as intravenous MeP (40 mg/day) for severe UC (response in 10/15 CsA patients *vs* 8/15 MeP patients) [86]. Monotherapy with CsA is an option when steroids are

best avoided, such as in patients susceptible to steroid-psychosis (schizophrenics or previous psychosis), concomitant osteoporosis, diabetes or personal good responses to both intravenous doses of 2–4 mg/kg and oral 5 mg/kg daily, without serious side effects [87]. An oral dose of CsA 5 mg/kg/day is broadly equivalent to intravenous 2 mg/kg/day. Oral microemulsion CsA (Neoral® Novartis Pharmaceuticals, Sumey, UK) does not contain the chromophore in intravenous CsA that causes seizures in patients with hypocholesterolaemia (≤ 3 mmol/l) or hypomagnesaemia (0.5 mmol/l). When either oral or intravenous CsA is used, the aim is a whole-blood trough concentration of 100–200 ng/ml using a monoclonal radioimmunoassay.

Outcome of CsA

Colectomy is usually delayed rather than avoided by CsA. In two series, 58% of 76 patients [83] and 88% of 142 patients [84] came to colectomy over 7 years. CsA was associated with the three deaths from opportunistic infections in the latter series [84], two from *Aspergillus* sp. infection and one from *Pneumocystis carinii*. Debate continues about *Pneumocystis* prophylaxis, but it should not be considered mandatory. When responders received oral CsA for a limited period (3 months) in one large series, no opportunistic infections (other than oral *Candida*) or deaths occurred [83]. Nevertheless, a study from Pennsylvania found that the highest costs, longest length of stay and highest number of overall complications occurred in 18/41 patients who failed CsA and required colectomy on that admission [88]. This illustrates the potential consequences of CsA delaying colectomy, although others have found no increase in septic complications after CsA and surgery [89].

Recommendations

Infliximab as a single dose (5 mg/kg) is also effective rescue therapy (Grade B).

Evidence of efficacy is based largely on a single controlled trial. A Swedish–Danish study treated 45 patients with acute severe colitis who had not responded to 3–7 days intravenous steroids with IFX 5 mg/kg as a single dose, or placebo and continued intravenous betamethasone [90]. No patient died. Seven in the IFX group and 14/21 in the placebo group had a colectomy within 3 months ($P = 0.017$; OR: 4.9; 95% CI: 1.4–17). The results merit appraisal. Two different scores were used to identify patients at high risk of colectomy before randomization to IFX or placebo. The Sweden index calculated on day 3 [stool frequency × (0.14 × CRP)] broadly predicts that patients with a CRP > 25 mg/l have a 75% chance of colectomy [20], while the Seo index calculated on days 5–7 is a complex collection of variables akin to the Crohn's Disease Activity Index, whereby a value < 150 is consistent with remission [91]. The two are different, as those patients randomized on the basis of the Seo index had less active disease than those randomized through the Sweden index. It was this group with less active disease after 5–7 days of intravenous steroids who benefited most from IFX. The benefit of avoiding colectomy after IFX appears to be maintained at 24 months (unpublished data Jarnerjot G). There have been other studies of IFX for acute severe colitis refractory to steroids, but all too small to show a difference in colectomy [92–94]. Open label experience, reporting up to 75% colectomy after IFX [95,96], is a clear sign that a large controlled trial is needed. The literature is confused by liberal use of the term 'severe' to refer to outpatients with moderately active refractory colitis. Inpatients with severe colitis in the Swedish study [90] represent a very different patient population to the outpatients in the ACT 1 and 2 studies [13].

Infliximab vs ciclosporin

A definitive recommendation on the best choice between CsA and IFX is not possible until the two have been compared in a randomized controlled trial. This comparison is currently the subject of controlled trials in France and the UK (2008). Both have a rapid onset of action. Although it is possible that CsA works more rapidly, the median times to response of CsA and IFX have not been published in a form that can be compared. The short-term safety profile may favour IFX, since it does not provoke seizures or hypertension, while the longer-term safety profile of both drugs is at present not known. The real advantage of CsA, however, is that it has a short half-life compared with IFX. This means that if CsA is not working, it is only a matter of hours before it disappears from the circulation, while IFX will circulate for weeks. This may matter if colectomy is performed, since septic complications are the major cause of postoperative morbidity and mortality. Although IFX is reported not to increase postoperative sepsis [97], no data are available that relate to emergency colectomy alone for patients with acute severe UC. In a Scottish survey, 13/39 patients came to colectomy after IFX treatment for acute severe colitis. One patient who initially responded to IFX died of septic shock from bronchopneumonia 3 weeks after treatment, and another had severe postoperative sepsis resistant to antibacterial therapy and only responding to intensive antifungal treatment [98]. Other considerations about the choice of IFX or CsA include the severity of the attack (which favours CsA if colectomy is imminent and a rapid response to rescue therapy is needed) and diagnostic

confidence. If a precise distinction between UC and Crohn's is not possible at the time of severe colitis, then IFX is favoured because it works in Crohn's colitis while CsA does not. What should be self-evident, however, is that using both CsA and IFX within weeks of each other increases the risks of serious infection. In a worrying report, 20 patients received CsA (for a mean 3.8 months, range 0.5–12.2) before IFX, or IFX (mean two infusions, range 1–3) before CsA for severe steroid-refractory colitis [99]. One patient died from *Escherichia coli* septicaemia, another became jaundiced and another developed herpetic oesophagitis. Such therapy in combination to avoid colectomy carries high risks and cannot be recommended.

Other agents

Tacrolimus is a calcineurin inhibitor acting through a mechanism similar to CsA. One randomized controlled trial has been performed in UC that included 27/60 patients with acute severe colitis [100]. Nine of 16 had a partial response to 0.05 mg/kg/day adjusted to trough levels (up to 15 ng/ml), compared to 2/11 on placebo and the remainder had no response. Results did not reach significance. Case series have shown broadly similar results to CsA after both intravenous (0.01–0.02 mg/kg) and oral (0.1–0.2 mg/kg) administration (Table 4). It carries many of the risks and side effects (including nephrotoxicity) of CsA, so it is hard to see a therapeutic advantage.

Visilizumab (Nuvion® PDL Biopharma, Redwood City, California, USA) was an IgG2-humanized monoclonal antibody that binds to CD3 on human T cells. Open-label studies showed a response in nearly 80% of patients with severe colitis resistant to intravenous steroids, with around 30% going into remission after 5 μg/kg intravenously on 2 consecutive days [104]. Controlled trials were stopped in 2007 for adverse events and lack of effect.

Leucocytopheresis is a technique in which white blood cells are selectively removed from the circulation via an extracorporeal circuit. A single randomized study has compared leucocytopheresis to intravenous steroids for severe colitis, but the definitions of severe colitis equated to moderate colitis, and remission equated to mildly active disease [105]. At present, the only role for this therapy is as part of a trial.

Toxic megacolon

Findings

Toxic megacolon is the end of the spectrum of severe colitis and requires aggressive medical therapy and early surgical decision making (Level IV).

Recommendations

Intensive medical therapy should be instituted for 24 h and continued only if there is radiological and clinical evidence of improvement (Grade GP).

The key aspects of management of toxic megacolon are aggressive medical therapy and early surgical decision making. It is no different to conventional therapy for acute severe colitis, with the exception that antibiotics (metronidazole 500 mg three times daily and ciprofloxacin 500 mg twice daily) are appropriate in the case of an infective aetiology. The combination of steroids and antibiotics is safe even for infective colitis; steroids reduce inflammation in PMC [106]. Nasogastric suction cannot be expected to decompress the colon and is unnecessary. An experienced surgical opinion is best sought on the day of admission. It should be made clear that there is a 24-h window of opportunity for medical treatment to work and that if there is no improvement, then early colectomy is obligatory.

On the day after admission, the plain abdominal radiograph should be repeated. If the diameter has decreased, then medical treatment can be continued and the radiograph repeated the following day. If the diameter has increased, or if it remains unchanged with an accompanying tachycardia or temperature, then urgent colectomy is indicated. If there is doubt, or if

Table 4 Case series of tacrolimus (tacro) for steroid-refractory ulcerative colitis, compared to a case series of ciclosporin therapy in similar patients.

			Colectomy at			
Series	*n*	Response	1–3 months	1 year	2 years	References
Ciclosporin (Oxford)	76	56/76	10/76	16/76	16/76	83
Tacro iv 0.01/oral 0.2 mg/kg	38	18/38	3/38	12/38	19/38	101
Tacro iv 0.01 mg/kg	23	22/23		2/23	3/23	102
Tacro oral 0.15 mg/kg	9	9/9	1/9	–	3/9	103

there is focal tenderness, then a CT scan to look for localized perforation is appropriate. Management decisions should be made jointly between an experienced gastroenterologist and colorectal surgeon.

There are no randomized trials and it should be understood that the condition is potentially fatal. The mortality increases markedly if perforation occurs, while inappropriate persistence with medical treatment 'because the patient is too sick for surgery' is a self-fulfilling prophecy. Around 50% of patients with toxic megacolon due to UC will respond to medical therapy [68].

Long-term outcome of medical therapy

Findings

The proportion of patients with acute severe acute UC who eventually undergo colectomy is high, especially after an incomplete response to intensive medical therapy (Level III).

Recommendations

Patients, physicians and surgeons should be aware of the long-term outcome when deciding on medical or surgical management (Grade B).

The long-term outcome after admission with acute severe UC is not good. It is necessary that patients, their physicians and surgeons understand this, although measured outcomes of medical and surgical treatment are different and not directly comparable. To determine the outcome of patients admitted with severe UC who avoided colectomy on the index admission, a small prospective cohort of patients from a single centre was examined over 15 years [107]. Main outcome measures were colectomy-free survival, time to colectomy and duration of steroid-free remission. 6/19 complete responders to intravenous steroids (32%) came to colectomy compared with 10/13 incomplete responders ($P = 0.015$; odds ratio 7.2, 95% CI: 1.4–36.2). This means that just 1 week after admission with severe UC in the pre-biologic era, incomplete responders can be advised that the chance of colectomy may be 50% within a year and 80% within 5 years. The maximum duration of steroid-free remission in complete responders was about five times longer than incomplete responders, but a third still come to colectomy.

Timing of surgical intervention

Findings

The decision of when to abandon medical therapy in favour of surgical intervention is paramount in influencing the outcome of any subsequent therapy (Level IV).

Recommendations

An objective predictive index is a useful guide to optimal timing of surgical intervention (Grade A).

Medical indecision reflects the difficulty in making the irrevocable recommendation for colectomy, which neither the patient, nor physician, nor indeed the surgeon wants. As a general rule, patients who do not respond to steroids within 3–5 days should have medical 'rescue therapy', as there is a predictable failure of continued steroids in these poor responders. An objective predictive index is best used. Several indices exist (see above). The simple measures of CRP > 45 mg/l and stool frequency 3–8/day, or a stool frequency > 8/day on day 3 [8] are a ready guide. The figures are easy to remember, simple to apply and define an approach to treatment. At the very least, patients meeting these criteria should have a joint consultation with physician and surgeon, as well as being introduced to a stomatherapist. The patient can be prepared for possible surgery in a timely manner, so that emergency colectomy and the need for a stoma are both anticipated. This contingency planning helps patients come to terms with the possibility of medical failure. For CsA, the median time to response is 4 days [85], and for IFX it is about 7 days [13], so failure to respond by this time is usually an indication for colectomy. Despite these general guidelines, such early decision making is a long way from being achieved in practice. In 187 of 2074 patients who received rescue therapy with either CsA (150) or IFX (37) after failure to respond to intravenous steroids, treatment was started at a median of 6 days (IQR 4–10 days) or 10 days (IQR 7–14) after admission (http://ibdaudit.rcplondon.ac.uk/2006/). Surgeons should encourage their physicians to make early decisions, rather than contribute to delay and risk perforation or postoperative complications.

E. Surgical management

Absolute indications for surgery are perforation and massive bleeding, both of which are rare. Toxic dilatation carries a high risk of perforation and is almost an absolute indication for surgical assessment, with at least half coming to colectomy. If there is objective evidence of response to intensive medical treatment within 24 h, then emergency surgery may sometimes be avoided (see above).

Unresponsiveness to medical therapy is the most common indication for surgery, but unfortunately is difficult to define precisely. If there is no improvement after 3 days of high-dose intravenous and rectal steroids,

it is common to initiate rescue therapy with either CsA or IFX. If there is still no improvement in 5–7 days after admission, then surgical treatment is required.

The most difficult and potentially dangerous group of patients are those who appear to respond partially to medical therapy. There are no trials to assist management in this situation. A low threshold for surgery risks excessive surgical morbidity. Continued medical therapy risks creating a progressively unwell, malnourished, immunosuppressed patient with the associated mortality and morbidity of medical treatment and/or delayed surgery. The mortality of emergency colectomy is difficult to evaluate, because only specialist centres report large series. In these, the mortality of managing acute severe colitis (including surgical mortality) is < 1% [8,75]. Preliminary results from the UK National IBD audit, however, indicate that it is higher than this (http://ibdaudit.rcplondon.ac.uk/2006/). Of 2074 patients admitted as emergency with acute UC, 318 came to emergency colectomy. This is a low rate and indicates potential selection bias during the first retrospective phase of the audit. Another 397 patients had elective surgery for UC and 15 patients died after surgery. This means that the perioperative mortality is between 2.1% and 4.7% (15/715 or 15/318).

General recommendations to optimize management for acute severe colitis have already been detailed but should be re-emphasized:

1 joint care by specialist gastroenterologist and colorectal surgeon;
2 regular clinical assessment with documentation of temperature, pulse rate, abdominal examination and stool frequency;
3 daily abdominal X ray until an objective response has occurred;
4 daily measurement of full blood count, CRP, ESR and albumin;
5 exclusion of infective colitis;
6 early assessment by stomatherapist.

In deciding whether or not to proceed to surgery, it is helpful to consider the state of the colon and quality of medical therapy prior to the acute attack. If, for example the patient had pre-existing chronic UC despite optimal medical therapy with immunomodulators, then there is little prospect of avoiding colectomy. In this situation, surgery should be undertaken promptly after explanation and careful discussion with the patient and family. Alternatively, if there is a history of mild colitis, with long periods of steroid-free remission, or if immunomodulators have not been given, then there is a greater chance of avoiding colectomy. It should be remembered, however, that of the group of partial responders to medical therapy, 60% will come to colectomy within the next year and 80% within 5 years [6,107].

Findings

If the decision to operate has been reached, there is a need to carry out a procedure that is likely to result in the rapid resolution of the disease process with minimal compromise to an already very ill patient (Level II).

Recommendations

Subtotal/total colectomy and ileostomy with preservation of the rectum should be considered the standard operation for patients who require surgery for acute severe colitis (Grade B).

Once the decision to operate has been made, there are theoretically four surgical options available:

(A) defunctioning ileostomy alone;
(B) restorative proctocolectomy (RPC) and ileoanal pouch anastomosis (±covering ileostomy);
(C) proctocolectomy and permanent ileostomy;
(D) subtotal/total colectomy and ileostomy with preservation of the rectum.

(A) There is no place for a defunctioning ileostomy alone in the management of acute severe UC, nor infective colitis. If the patient has known Crohn's colitis, this may be considered in exceptional circumstances [108].

(B) Several groups have reported satisfactory results with RPC in patients with acute colitis, but great care should be taken before opting for this approach. Patients with acute severe colitis have usually been on high doses of steroids, may be nutritionally compromised and often hypoalbuminaemic. The risk of complications is high and this has the potential to affect long-term pouch function. Ziv *et al.* [109] reported their experience of 737 patients undergoing RPC, 12 of whom had acute disease requiring intravenous steroids but not hypotension, tachycardia or megacolon. No early septic complications occurred in this small selected subset. Harms *et al.* [110] reported their results of RPC in 20 patients with acute severe colitis, but without sepsis or medical comorbidity. There were no deaths and no pelvic sepsis. Other complications included pancreatitis (10%), anastomotic leak (5%), adrenal insufficiency (15%), gastrointestinal bleed (5%) and small bowel obstruction (15%).

There are no randomized trials comparing subtotal colectomy with ileostomy *vs* RPC in the acute setting. Heyvaert *et al.* [111] compared emergency *vs* elective patients in a consecutive series of patients undergoing RPC. The complication rate was higher in the emergency group [morbidity 66% *vs* 27% ($P < 0.06$)] as was the

anastomotic leak rate [41% *vs* 11% ($P < 0.08$)]. The authors conclude that RPC is contraindicated in emergency circumstances, especially in patients with signs of sepsis on high-dose steroids. This represents the opinion of many experienced colorectal surgeons [15].

(C) Before the advent of pouch surgery, emergency proctocolectomy with permanent ileostomy was considered as optimal surgical treatment of acute severe colitis. In the 1970s, there was considerable debate, but no trials, over the issue of proctocolectomy *vs* subtotal colectomy for acute severe colitis. Binder *et al.* [112] favoured emergency proctocolectomy, claiming that the morbidity and mortality was no higher than colectomy (Table 5). But this view was put forward over 30 years ago and before RPC became available. It is thus not appropriate to extrapolate these results into the modern surgical era, except to suggest that the results of emergency colectomy with ileostomy may not be very different to those of proctocolectomy and permanent ileostomy. These procedures are the only techniques that allow resection of the majority of the diseased colon and at the same time avoiding the morbidity associated with an anastomosis in a patient likely to be very sick. It could be argued that selected patients with acute severe colitis, in whom there is no prospect of future pouch reconstruction (e.g. very elderly or those with major sphincter damage) may benefit from a proctocolectomy and permanent ileostomy in the acute phase. There are no recent studies to support this approach, but it merits discussion with selected patients.

(D) A subtotal/total colectomy avoids the morbidity associated with the pelvic dissection. It allows the patient to recover his/her general health and to stop anti-inflammatory medication. The patient regains self-confidence and is able to return to normal activity including work. All future surgical options are left open. Subtotal/total colectomy and ileostomy is the standard operation for the majority of patients who require surgery for acute severe colitis [113–115].

Table 5 Comparison of proctocolectomy with colectomy for acute colitis [112].

	Proctocolectomy ($n = 37$)	Colectomy ($n = 43$)
Indications		
Perforation	4	10
Toxic megacolon	9	7
Bleeding	4	1
Failed medical therapy	20	25
Results		
Deaths	3	3
Hospital stay (days)	27.6	33.3
Nonseptic complications	10	18
Septic complications	10	14

Technique of colectomy and ileostomy

Much of the technique of colectomy is standard. Subtle variations do exist most of which are anecdotal. Examples are discussed below. Other variations, such as what to do with the rectal remnant and whether laparoscopic resection is feasible, do have some evidence base and are discussed in more detail.

For the open incision, a midline incision is favoured by the majority of surgeons, allowing wide access to the abdomen and avoiding compromising potential stoma sites. Others favour a low transverse (or pfannensteil) incision claiming a better cosmetic result; an important factor in a commonly young body image-conscious patient group. However, access to the flexures may be difficult even after bowel shortening seen particularly in long-standing disease.

It is usually preferable to make the trephine for the ileostomy before making the incision, with the perceived advantages of minimal distortion of the rectus muscle and a cosmetically better stoma with reduced hernia formation.

Mobilization of the colon is standard but some advocate ligation of the ileocolic vessels close to the bowel with preservation of the mesenteric vascular arcade of the right colon (as it arises from the middle colic artery). Preservation of these vessels allows other mesenteric vessels (such as the ileo-colic or, in exceptional circumstances, even the superior mesenteric artery) to be ligated without compromising the terminal ileal blood supply [116,117]. Obviously intestinal viability should be tested with soft clamps before irreversible ligation of these major vessels. Some advocate omentectomy to reduce the incidence of adhesional obstruction [118,119]. A large retrospective study of 645 pouch patients suggests that the omentum should be preserved as the incidence of postoperative sepsis was reduced while the incidence of adhesional obstruction was unchanged [120].

Findings

A major contribution to postoperative morbidity after colectomy relates to the retained rectal stump (Level IV).

Recommendations

Closure of the rectal stump either at the pelvic brim with transanal rectal drainage, or subcutaneous closure with transanal drainage, are appropriate options for most

patients requiring subtotal colectomy and ileostomy for acute severe colitis. An open mucous fistula may occasionally be necessary when severe inflammation prevents safe closure. Closure of the rectum below the pelvic brim is not recommended (Grade C).

The surgical options to manage the retained rectum after subtotal colectomy and ileostomy are (Fig. 1):

1 open mucous fistula;
2 subcutaneous closed mucous fistula;
3 intrapelvic 'Hartmann's' closure at pelvic brim;
4 low closure at pelvic floor.

There are no trials comparing one technique with another. In occasional situations, one technique may be manifestly more appropriate. For instance, if the distal sigmoid/rectosigmoid is so friable that it cannot safely be closed, then an open mucous fistula would be appropriate. Published data on the different techniques are shown in Table 6.

Whilst none of these studies is randomized, some trends emerge. In early studies, the debate was principally over whether it was reasonable to close the retained rectum and avoid a second stoma, which had been standard practice previously. Later reports considered the technical aspects of subsequent ileal pouch anal anastomosis.

It may be concluded that closure of the retained rectum either as a Hartmann's type closure at the pelvic brim, or as a subcutaneous closed mucous fistula, is reasonable. Neither result in excessive rates of pelvic

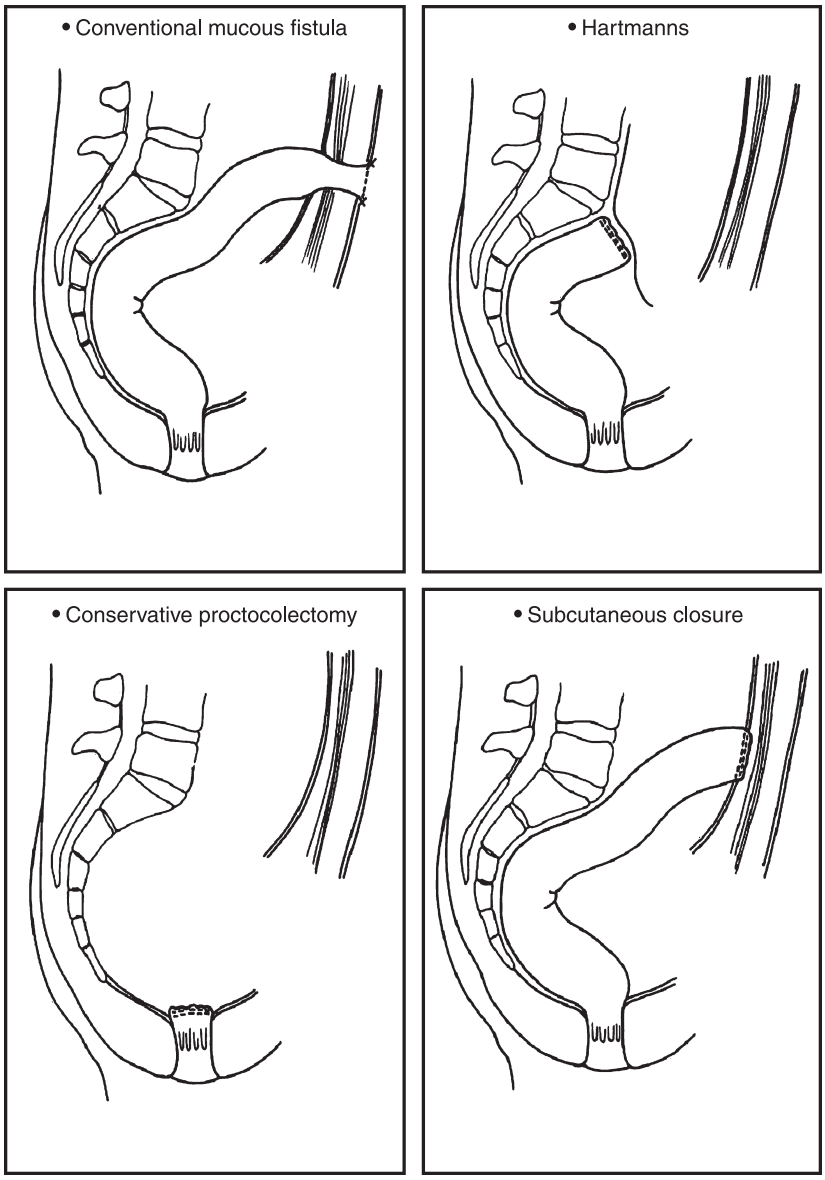

Figure 1 Methods of 'dealing' with the rectal stump.

Table 6 Studies of rectal stump after colectomy and ileostomy.

Study	Procedure	Results	Comments
Carter *et al.* [121]	55 s/c 30 open 51 Hartmann's	Hartmann's higher pelvic sepsis + more difficult after dissection. 19/55 s/c closures re-opened causing 7/55 wound infections	
Kyle *et al.* [122]	7 open 23 Hartmann's	2/23 (8.9%) pelvic sepsis after Hartman's	Subsequent rectal surgery uncomplicated in 18
Ng *et al.* [123]	32 s/c	7/32 complications (2/32 re-operation, 5 minor wound)	Easy to locate rectal stump
Karch *et al.* [124]	114 Hartmann's	3 pelvic sepsis due to rectal stump leak	0/41 leakage/sepsis if transanal drain
McKee *et al.* [125]	53 long closed stump 9 short closed stump	1/53 leak from long stump 3/9 leak from short stump	Careful closure above peritoneal reflection recommended
Wojdemann *et al.* [126]	147 Hartmann's	3 pelvic abscess due to leak	No difficulty finding rectal stump subsequently
Randall *et al.* [127]	54 s/c 26 Hartmann's	4/54 wound abscess after s/c closure 2/26 pelvic abscess + 1/26 abdominal abscess after Hartman's	Consequences of stump leakage more severe after Hartmann's cf. s/c closure
Brady *et al.* [128]	159 Hartmann's	5 (3.1%) stump dehiscence 8 (5%) abdominal/pelvic abscess	Hartmann's associated with low sepsis + high success of later pouch surgery

s/c, subcutaneous closure.

sepsis or problems locating the rectum at subsequent surgery. Either closure should be accompanied by transanal rectal decompression during the early postoperative period [124]. Closure of a short rectal stump is not recommended. It is possible that subcutaneous closure of the rectal remnant is associated with an increased risk of wound infection, although there is weak evidence that it may reduce the risks of more major intra-abdominal or pelvic sepsis.

Findings

There is evidence to suggest that colectomy could be carried out laparoscopically. Nonrandomized data suggest an earlier return to bowel function and shorter hospital stay compared with open surgery. No differences in early complication rates have been demonstrated and late results are not yet available (Level IIb).

Recommendations

Laparoscopic colectomy for acute severe colitis may be undertaken safely in centres with appropriate laparoscopic experience (Grade B).

The debate in 2007 is whether colectomy and ileostomy should be undertaken by open, laparoscopic or laparoscopic-assisted surgical approaches. An early study by Wexner *et al.* [129] demonstrated the feasibility of laparoscopic colectomy but demonstrated no benefit over conventional open surgery. Several subsequent studies have compared laparoscopic colectomy with case-matched controls or same-institute controls. There are no randomized controlled trials comparing procedures.

Two series published by the same group from Japan (n = 10 and n = 21) contrasted laparoscopic total colectomy with institutional open-colectomy controls [131,132.]. The group included colectomy for familial adenomatous polyposis rather than acute severe colitis specifically. The results are summarized in Table 7.

Dunker *et al.* [132] assessed the feasibility and safety of laparoscopic colectomy for acute severe colitis. In a consecutive series of 42 patients, 10 underwent a laparoscopic-assisted procedure and 32 underwent open colectomy. Outcomes were compared (Table 8). Laparoscopic-assisted surgery took longer even when corrected for multiple comparisons, and this is a potential logistic constraint on emergency theatre time. The same conclusion that laparoscopic colectomy took appreciably longer than open colectomy was reached by Seshadri *et al.* [133], who compared 37 patients undergoing laparoscopic total colectomy (all indications) over a 9-year period with institutional open-colectomy controls (Table 9). The prospect of a shorter postoperative stay after laparoscopic-assisted colectomy may apply to elective procedures, but may not be transferable to acute severe colitis.

Table 7 Laparoscopic colectomy compared to open-colectomy for all patients (same institution controls).

Araki *et al.* [130,131]	Laparoscopic *n* = 10 [91], *n* = 21[92]	Open *n* = 29 [91], *n* = 11 [92]	*P*
Blood loss (ml)	321, 218	471, 238	NS, NS
Duration of surgery (min)	282, 215	274, 198	NS, NS
Time to bowel function (days)	1.9, 1.7	5.2, 5.4	0.01, 0.05
Time to oral intake (days)	3.3, 3.3	6.8, 6.1	NS, 0.05
Hospital stay (days)	43, 32	46, 39	NS, NS
Mortality	0/10, 0/21	1/29, 1/11	NS, NS
Morbidity	5/10, 11/21	18/29, 7/11	NS, NS

First figures in each box represent Ref. [131], second figures Ref. [132].

Table 8 Laparoscopic-assisted colectomy compared to open colectomy for acute severe colitis (same institution).

Dunker *et al.* [132]	Laparoscopic-assisted (*n* = 10)	Open (*n* = 32)	*P*
Blood loss (ml)	531	435	NS
Duration of surgery (min)	271	150	0.001
Re-operation	2/10	5/32	NS
Time to bowel function (days)	3.1	2.3	NS
Time to oral intake (days)	3.4	4.9	NS
Hospital stay (days)	14.6	18	0.05
Morbidity	6/10	24/32	NS

Table 9 Laparoscopic colectomy for all indications compared with open colectomy over a 9-year period with institutional case-matched controls.

Seshadri *et al.* [133]	Laparoscopic (*n* = 37)	Open (*n* = 36)	*P*
Duration of surgery (min)	270	178	0.001
Hospital stay (days)	6	9	0.001
Mortality	1/37	0/36	NS
Morbidity	9/37	24/36	NS

Similar findings have been reported by Pokala *et al.* [134], who compared 34 patients undergoing laparoscopic colectomy (for all indications) over a 4-year period with institutional case-matched controls (Table 10). Another series by Marcello *et al.* [135] compared 19 patients undergoing laparoscopic colectomy for acute severe colitis (UC or Crohn's disease) with 29 institutional case-matched controls (Table 11). The most recent and largest series on laparoscopic *vs* open colectomy for acute severe colitis has been reported by Marceau *et al.* [136]. Forty patients undergoing laparoscopic colectomy for acute or severe colitis (UC and Crohn's) were compared with 48 institutional case-matched controls (Table 12).

Table 10 Laparoscopic colectomy for all indications compared with open colectomy over a 4-year period with institutional case-matched controls.

Pokala *et al.* [134]	Laparoscopic (*n* = 34, 4 conversions)	Open (*n* = 34)	*P*
Duration of surgery (min)	187	126	0.001
Hospital stay (days)	3	6	0.001
Blood loss (ml)	168	238	0.001
Complications (%)	26.5	38.2	NS
Re-admissions (%)	11.8	14.7	NS
Re-operations (%)	8.8	11.8	NS
Death	1/34	0/34	NS

Table 11 Laparoscopic colectomy for acute severe colitis (ulcerative colitis or Crohn's) compared with institutional case-matched controls.

Marcello *et al.* [135]	Laparoscopic (*n* = 19)	Open (*n* = 29)	*P*
Blood loss (ml)	100	150	NS
Duration of surgery (min)	210	120	0.001
Time to bowel function (days)	1	2	0.003
Hospital stay (days)	4	6	0.04
Complications	3 (16%)	7 (24%)	NS

All these studies are subject to selection bias, but some trends emerge. As might be expected, most studies show that laparoscopic colectomy takes longer than open colectomy, although the most recent French series shows no difference. One study showed less blood loss with laparoscopic colectomy, although three studies showed no difference. Time to return of bowel function and time

Table 12 Laparoscopic colectomy for acute severe colitis (ulcerative colitis or Crohn's) compared with institutional case-matched controls.

Marceau *et al.* [136]	Laparoscopic (n = 40, 2 conversions)	Open (n = 48)	P
Duration of surgery (min)	253	231	NS
Morbidity (%)	35	56	NS
Hospital stay (days)	9	12	NS

to oral intake were superior in the laparoscopic group in two of three studies, which adequately reported this, and no difference in one. Hospital stay was significantly shorter following laparoscopic colectomy in all but one of the studies. Complication rates showed no differences between laparoscopic and open procedures in any study, although the trend for fewer complications always favoured laparoscopic colectomy. Late complications such as incisional hernia and adhesive small bowel obstruction rates are not reported, although these are important to patients. If it could be shown that laparoscopic (-assisted) colectomy shortened the length of stay or reduced later episodes of adhesional obstruction compared to open colectomy, then the argument would be won.

Conflicts of interest

None declared.

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