Surgery and medical therapy in Crohn’s disease

de Groof, E.J.

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Abdominal abscess in Crohn’s disease: multidisciplinary management

E.J. de Groof, C.F. Carbonnel, C.J. Buskens, W.A. Bemelman

Abstract

Crohn’s disease (CD) is characterised by full-thickness inflammation of the bowel. For this reason, perforating complications such as intra-abdominal abscesses or fistulas are common. A concomitant intra-abdominal abscess with active CD of the small bowel is a challenging dilemma for gastroenterologists and surgeons. Since there is active and severe disease, this should be treated with immunosuppressive drugs. However, in the presence of an intra-abdominal abscess, immunosuppression can be dangerous. There are several treatment options for intra-abdominal abscesses in CD. Nowadays, the first-line treatment is antibiotic therapy with or without percutaneous drainage. Historically, patients were treated with surgical drainage. With the development of percutaneous drainage, treatment shifted to a more nonsurgical approach. Success rates for percutaneous drainage in the literature vary from 74 to 100%, and it is considered to be a relatively safe procedure. It has been reported that surgery can be avoided after successful percutaneous drainage in a variable number of patients (14-85%). If sepsis is controlled, CD medication should be started to prevent recurrence. It is important to monitor the effect upon CD lesions to avoid further perforating complications. Finally, an undrainerable or small abscess can be treated with antibiotics alone, although high recurrence rates have been described with this approach. Patients with a concomitant stenosis, an enterocutaneous fistula or refractory active disease are likely to require surgery. Percutaneous drainage in combination with delayed surgery is useful to improve the patient’s condition prior to surgery and is associated with less morbidity, a lower stoma rate and more limited resection. In conclusion, when feasible, percutaneous drainage and antibiotics should be the treatment of choice in patients with an intra-abdominal abscess in CD. If surgery is inevitable, this must be delayed to reduce postoperative septic complications and high stoma rates.
Introduction

Crohn’s disease (CD) is a chronic condition that can manifest in any part of the gastrointestinal tract. The most commonly affected part of the bowel is the small bowel. CD is characterized by full-thickness inflammation of the bowel. Therefore, perforating complications such as an intra-abdominal abscess or a fistula, due to transmural translocation of bacteria from the diseased bowel to contiguous tissue, are common and should be regarded as serious complications during the disease course in these patients. In the literature, occurrence rates for intra-abdominal abscesses vary from 10 to 30%. A concomitant intra-abdominal abscess in patients with active CD of the small bowel can be challenging in decision-making and poses a dilemma for the multidisciplinary team. Active disease warrants medical treatment, but the presence of an abscess contraindicates immunosuppressive medication.

There are several treatment options for intra-abdominal abscesses in CD. Historically, patients were treated with surgical drainage and bowel resection simultaneously. Since the availability of percutaneous drainage, the treatment strategy for intra-abdominal abscesses has shifted towards this nonsurgical approach. Although antibiotics are mostly part of the treatment in both approaches, medical treatment of CD must be individualised.

Decision-making is complex when active CD is associated with intra-abdominal abscesses. The role and timing of medication and surgery need to be discussed in a multidisciplinary setting with gastroenterologists, colorectal surgeons and radiologists.

Treatment Options for Intra-Abdominal Abscesses

Surgical Drainage

Traditionally, surgical drainage of abdominal abscesses in CD has been the first treatment option. This procedure includes exploration of the abdominal cavity and pelvis with evacuation of all abscess contents. Surgical drainage of an intra-abdominal abscess in combination with resection of small bowel has often resulted in extensive resections, including ‘healthy’ organs incorporated in the inflammatory mass. Surgical drainage is associated with considerable morbidity and can be complicated by wound infections, ‘burst abdomen’, small bowel fistula and anastomotic leakage if resection and anasto-
mosis are performed. Since this procedure is frequently performed in an acute setting in fragile patients, a defunctioning ostomy is often considered to be necessary.

**Percutaneous Drainage**

Percutaneous abscess drainage is defined as draining a fluid collection by positioning a catheter or drain under imaging guidance and maintaining it in place to provide continuous drainage. Drainage can be guided by ultrasound or CT and it is usually combined with antibiotic therapy. Percutaneous drainage became popular after publications on the procedure in the late 1980s and 1990s, raising the expectation that surgery could be avoided. Although the literature suggests that surgery can be avoided in 14-85% of patients, this technique is currently more frequently used as a bridge to elective surgery. This allows patients to recover from septic complications and malnutrition. However, not all abscesses are ‘drainable’ or ‘accessible’. Effectiveness depends on abscess characteristics, such as etiology, location, number, size, presence of fistulas or close proximity to vital structures. The literature shows that percutaneous drainage can be performed successfully in 74-100% of patients with spontaneous or postsurgical intra-abdominal abscesses in CD. However, multiple percutaneous drainage procedures have been required in 8-20% of patients. Clinical improvement should be seen within 3-5 days after starting antibiotics and percutaneous drainage, with a decrease in drainage production. If a patient’s condition does not improve, reevaluation and imaging are indicated to determine whether the abscess has been adequately drained. If not, repositioning of the drain or surgical intervention is required.

Percutaneous drainage appears to be a relatively safe procedure. Although catheter insertion could damage vital structures in close proximity to the abscess, severe hemorrhage or damage to vital organs is rare. Complications of percutaneous drainage, for both spontaneous and postsurgical abscesses (not specified for CD), occur in approximately 10%. Major complications such as sepsis, small bowel fistulas with colon perforation and death (due to sepsis or hemorrhage) have been described in 5-11% of cases. Minor complications (such as bacteremia or infection at the site of the catheter insertion) occur in approximately 3%.

**Medical Treatment**

Management of intra-abdominal abscesses in CD mostly includes antibiotic therapy. Some studies have shown that small (<3 cm) abscesses can be treated with antibiotics
alone, especially in cases without associated fistulas or in immunomodulator-naive patients.\textsuperscript{6,7,8} It is important to closely observe the clinical condition of the patient and to intervene in case of any deterioration.

Antibiotic therapy in patients with CD should be adapted to the sensitivity of the bacteria (and sometimes fungi) to antibiotics. If drainage is not feasible and bacteria cannot be analysed, antibiotics should cover Gram-negative bacteria and anaerobes. Therefore, a combination of fluoroquinolones or third-generation cephalosporin and metronidazole is appropriate.\textsuperscript{9} The appropriate duration of antibiotic therapy is unclear. The recurrence rates after medical treatment of intra-abdominal abscesses in CD in the literature vary from 37 to 50%.\textsuperscript{4}

**Percutaneous versus Surgical Drainage**

Several studies retrospectively assessed outcomes of percutaneous drainage as compared to surgical drainage of intra-abdominal abscesses. Complication rates were significantly higher in patients treated with surgical drainage (69 vs. 20%, $p = 0.036$).\textsuperscript{10} Ultimate stoma creation rates were also significantly higher in patients that underwent initial surgical drainage as compared to initial percutaneous drainage (9/13 vs. 1/10, $p = 0.01$).\textsuperscript{10} Nguyen et al. reported shorter hospital stay in patients treated with percutaneous drainage compared to surgical drainage (5.0 vs. 15.5 days, $p = 0.001$).\textsuperscript{11} However, the results could be biased by differences in severity of illness and the presence of multiple abscesses between the groups.\textsuperscript{11} This difference in length of stay was also observed by Kim et al.\textsuperscript{12} Although there are no randomized controlled trials comparing percutaneous drainage with surgical drainage in patients with CD-related abscesses, consensus favors percutaneous drainage, provided the abscess is technically drainable.\textsuperscript{3} Occasionally, abscesses are not amenable for percutaneous drainage due to their location or size and do not respond to antibiotic therapy. Under these circumstances, a defunctioning ileostomy might cool down the inflammatory mass (fig. 1).

To guide clinical decision-making, Feagins et al. suggested an algorithm for the management of intra-abdominal abscesses in patients with CD (fig. 2).\textsuperscript{4}
Figure 1: Undrivable abscess in a female patient with CD. Conglomerate of pathological small bowel loops and several small intra-abdominal abscesses. After nonresponse to antibiotic therapy alone, a deviating ostomy was created.

Figure 2: Algorithm suggested by Feagins et al."
Combined Surgical Resection with Drainage or Percutaneous Drainage Followed by Delayed Resection?

Small bowel resections, especially in the case of perforating ileitis in CD, are associated with postoperative morbidity. Complications can vary from anastomotic leakage and abscesses to fistula formation. The overall risk of severe intra-abdominal septic complications, following bowel resection in CD patients, ranges between 9 and 13%. The risk of intra-abdominal septic complications increases significantly in the presence of intra-abdominal abscesses at the time of surgery. For ileocecal resections specifically, this complication rate increased from 7.2 to 40%. In a retrospective cohort study, Müller-Wille et al. assessed whether percutaneous abscess drainage prior to surgery reduced the number of severe postoperative septic complications in patients with CD. It was shown that percutaneous drainage could significantly reduce the occurrence of severe intra-abdominal septic complications as compared to patients without percutaneous drainage (25 vs. 69%, p = 0.04). Zerbib et al. also retrospectively analysed the results of preoperative management consisting of nutritional support, intravenous antibiotics, weaning of steroids, immunosuppressive drugs and biologicals, and drainage of abscesses (leaving the drain in situ). They concluded that this preoperative management of penetrating CD allowed ileocecal resection with low rates of postoperative morbidity and fecal diversion in only 7%. The overall morbidity rate was 18% (Clavien-Dindo >3 in only 5.3% of patients).

Most importantly, percutaneous drainage prior to surgery provides surgeons a better opportunity to create a primary anastomosis without a deviating ostomy. In CD, a laparoscopic approach is recommended due to short- and long-term patient-related advantages. This can sometimes even be performed with a single-port approach. Wu et al. assessed the operative outcomes of patients undergoing laparoscopic ileocolonic resection for penetrating CD compared to uncomplicated CD. There were no differences in conversion rates, postoperative morbidity or recovery time observed between the groups. Goyer et al. also performed a prospective study assessing these outcomes in patients undergoing ileocolonic resection. There were no differences in postoperative morbidity and hospital stay in patients with penetrating compared to noncomplicated primary CD. However, they observed an increased operative time, an increased risk of conversion and a higher rate of diverting stoma creation in the patients with penetrating CD.
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Is Resection Necessary after Treatment of Intra-Abdominal Abscesses?

There is a paucity of data regarding the question whether percutaneous or surgical drainage should be followed by delayed resection. Most authors favor a delayed elective resection, but there is no consensus. Twenty to 77% of patients with abscesses initially treated with percutaneous drainage are thought to require surgery. The available literature shows that small bowel resection is more likely in the presence of a stenosis with obstructive complaints or an enterocutaneous fistula. Other parameters favoring surgery are limited disease (<30 cm) and recurrent abscesses while adequately treated with anti-TNF. Patients that had a defunctioning ileostomy to cool down the inflammatory mass are also eligible for delayed resection.

Recurrence of Intra-Abdominal Abscesses after Treatment

In a retrospective study, Nguyen et al. evaluated the 5-year cumulative probability of abscess recurrence among patients with CD that had either surgical or percutaneous drainage. The recurrence rates were similar: 31.2% in patients who underwent percutaneous drainage as compared to 20.3% in patients who had surgery (p = 0.25). They also showed that a history of perianal disease and active ileal disease at the time of abscess diagnosis were significantly associated with time to abscess recurrence (HR = 2.58, 95% CI: 1.18-5.65, p = 0.02, and HR = 3.02, 95% CI: 1.37-6.66, p = 0.01, respectively). Age, length of hospital stay, medical therapy prior to drainage, history of penetrating disease (excluding perianal disease), abscess size, initial drainage and corticosteroid use at the time of abscess resolution were not associated with intra-abdominal abscess recurrence in this study. Efficacy of medical therapy in reducing abscess recurrence was also explored. Administration of anti-TNF agents after drainage reduced the risk for abscess recurrence (p = 0.001). There was also a trend towards abscess recurrence prevention in patients treated with immunosuppressive monotherapy as compared to patients with no therapy, although this was not statistically significant. However, in this study, 22% of the patients eventually required surgery during the follow-up period for recurrent internal penetrating disease.
Prevention of Postoperative Disease Recurrence

Recurrent CD after surgery is high in perforating disease. One year after ileocecal resection, endoscopic evidence of recurrence at the site of the anastomosis can be found in 73-93% of cases. Clinical recurrence rates (without therapy) are much lower and vary from 20 to 30%. Therefore, ileocolonoscopy for monitoring and evaluation of recurrence within 1 year after surgery is recommended.

Risk factors for postoperative disease recurrence have been identified in the literature. Smoking, a history of prior intestinal surgery, a perforating phenotype of CD, perianal localization and previous extensive small bowel resection (>50 cm) are associated with early postoperative recurrence. A spontaneous CD abscess indicates perforating disease and must be considered a risk factor for recurrence. The ECCO guidelines recommend that prophylactic medical therapy be started within 2 weeks after surgery, although there is no data indicating that an early start is superior to a later start. Therapy should be continued for at least 2 years. In addition, patients should be encouraged to quit smoking at all times.

Mesalazine and Antibiotics

The literature has shown that mesalazine reduces the rate of endoscopic recurrence by 18% [number needed to treat (NNT) = 5.5]. Regarding clinical recurrence, the overall risk difference was 15% (NNT = 6.6). Prophylaxis with mesalazine is an option for patients without risk factors for relapse. Administration of imidazole antibiotics postoperatively has been shown to be effective in the prevention of recurrence, but their side effects limit their use.

Thiopurines

For patients with one or more risk factors for early postoperative recurrence, azathioprine or mercaptopurine postoperatively is widely recommended. Peyrin-Biroulet et al. published a meta-analysis of four controlled trials that showed thiopurines were more effective as compared to placebo in preventing recurrence rates at 1 year (mean difference = 8%, 95% CI: 1-15, \( p = 0.021 \), NNT = 13) and at 2 years after surgery (mean difference = 13%, 95% CI: 2-24, \( p = 0.018 \), NNT = 8). In sensitivity analyses in this study, the efficacy of thiopurines was superior as compared to placebo for the prevention of postoperative recurrence at 1 year (mean difference = 13%, 95% CI: 2-25, \( p = \)
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0.025, NNT = 7). Nevertheless, higher adverse event rates (17 vs. 10%, \( p = 0.021 \)) were observed in the thiopurines group, which led to drug withdrawal. The ECCO guidelines of 2010 stated that thiopurines are more effective for preventing recurrence, both clinical and endoscopic, than mesalazine or imidazole antibiotics alone.

Anti-TNF Agents

Anti-TNF agents can also be administered as prophylactic therapy. A randomized controlled trial comparing adalimumab, azathioprine and mesalamine showed that the administration of adalimumab following intestinal resection was highly effective in preventing endoscopic and clinical recurrence of CD. Endoscopic recurrence rates were significantly lower in the adalimumab treatment group (6.3%) compared to the patients receiving azathioprine (64.7%, \( OR = 0.036, 95\% CI: 0.004-0.347 \)) and mesalamine (83.3%, \( OR = 0.013, 95\% CI: 0.001-0.143 \)) [28]. Moreover, the proportion of patients with clinical recurrence was significantly lower in the adalimumab group (12.5%) than in the azathioprine (64.7%, \( OR = 0.078, 95\% CI: 0.013-0.464 \)) and mesalamine groups (50%, \( OR = 0.143, 95\% CI: 0.025-0.819 \)).

A pilot randomised controlled trial with a small sample size (24 patients) showed that patients treated with infliximab had a lower endoscopic recurrence rate as compared to placebo postoperatively (9 vs. 85%). This effect was also seen in other small prospective cohort studies and case series. Currently, a randomised controlled trial (PREVENT trial, NCT01190839) is comparing infliximab and placebo in CD patients undergoing surgical resection who are at risk of recurrence.

Conclusion

Percutaneous drainage and antibiotics are the treatments of choice in patients with intra-abdominal abscesses in CD. The role of acute surgical resection or drainage is limited due to advances in percutaneous drainage and its superior results. In the rare occasion that percutaneous drainage with antibiotic therapy fails, a defunctioning ileostomy can be indicated as a last resort to cool down the inflammatory mass. If sepsis is controlled, medication should be started with monitoring of the effect. Patients who fail medical management should preferably have resection after resolution of sepsis and optimization of their preoperative condition. Nonsurgical management is likely to fail
in the presence of a stenosis, an enterocutaneous fistula or refractory active disease. Surgery should not be viewed as a ‘failure’ when it can be the swiftest, safest and most effective route to physical and psychosocial rehabilitation.
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References


