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Crohn's Disease Complicated by an Intra-abdominal Abscess: Poke, Prod, or Cut?



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Crohn's disease is a chronic, inflammatory bowel disease characterized by transmural bowel inflammation that can involve any segment of the gastrointestinal tract. The natural progression of Crohn's disease results in penetrating complications, including abscesses. In the management of intra-abdominal abscesses, clinicians face a therapeutic dilemma where issues of management of disease activity with immunotherapy must be balanced with the risk of worsening infectious complications. Historically, the management strategies utilized included surgical drainage. Recent data has demonstrated the efficacy of antibiotics and percutaneous drainage followed by therapy with biologics. Considering the therapeutic quandaries associated with management, a multi-disciplinary approach to intra-abdominal abscesses in Crohn's disease is required. Herein, we review the current data regarding the management of intra-abdominal abscess complications in Crohn's disease. We highlight both medical and surgical management strategies. We also present an algorithmic strategy for the management of these complications.

INTRODUCTION

Crohn's disease (CD) is a chronic relapsing and remitting condition exemplified by transmural inflammation involving any part of the gastrointestinal tract. Moreover, the disease appears to be progressive, evolving from primary inflammatory disease to a disease with stenotic or penetrating complications in a majority

of patients.¹⁻³ Penetrating complications related to Crohn's disease include fistulae, perforations, and the development of intra-abdominal or pelvic abscesses.

The rates of intra-abdominal abscess (IAA) described in the literature has been estimated at approximately 20%.⁴ Abscess development can occur spontaneously or as a post-operative complication. In the context of active disease, abscess formation presents a therapeutic challenge for health care providers. The management of disease with immunosuppressive agents must

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be balanced by the potential risk of potentiating septic complications. Classically, the management strategy reserved for intra-abdominal abscess in Crohn's disease was surgical drainage, operative resection and potential ostomy creation. Recently, the management of abscess has changed with an increasing reliance on antibiotics with percutaneous drainage when possible.

Confounding a uniform management strategy is the fact that there are a paucity of evidence based data. As such, treatment approaches should ideally be individualized and decision-making should involve a multidisciplinary approach, involving teams of specialists. To aid, we summarize the evidence related to the management of IAA in Crohn's disease. We highlight the treatment pathways and provide an algorithmic approach for guidance in the management CD associated IAA.

Mechanism and Risk Factors for the Development of Intra-Abdominal Abscess in Crohn's Disease

Abscess development in CD is proposed to occur through three distinct mechanisms: direct extension of enteric bacteria from sites of transmural bowel inflammation with fistulae formation to adjacent structures, hematologic seeding in the setting of transient bacteremia for areas of diseased bowel, or peritoneal contamination at the time of surgical intervention. Corresponding to these mechanisms are the common sites of abscess formation. Most commonly, abscess formation appears to involve the peritoneum, often in dependent sites, and often associated with diseased bowel.^{4,5} Less often is abscess development observed in association with the retroperitoneum, abdominal wall, or liver.

Commonly, most abscess reveal polymicrobial isolates when cultured. A retrospective study of 97 patients with CD who developed IAA spontaneously demonstrated that 151 aerobic bacterial species. The most common associated bacteria isolated were *E. coli*, *K. pneumoniae*, and *E. faecium*.⁶ A subsequent newer study also suggested a similar microbial isolate from 92 patients with CD.⁷ Of the 174 isolated bacteria in the study, a minority showed a pattern of resistance to commonly administered antibiotics. Of note, therapy with corticosteroids was associated with quinolone-resistance *E. coli* species, leading to

inadequate antibiosis.

Risk factors associated with the development of spontaneous abscess in patients with Crohn's disease include the use of corticosteroids. Of note, a prior study has suggested that the use of oral corticosteroids was associated a 9-fold increased odds of developed an abdominopelvic abscess.⁸ A similar study has also suggested that the use of preoperative corticosteroids was associated with an increased risk of intra-abdominal septic complications in patients following operative resection.⁹

Smoking has long been associated with the development of penetrating complications in IBD, including abscess.¹⁰ The use of tobacco has also been linked to early recurrence of penetrating disease in Crohn's following operative remission.¹¹

Prior studies investigating the effect of medical therapies, including the previously mentioned study have suggested no increased risk of abscess formation in the setting of azathioprine use.⁸ In single center studies, there has been conflicting evidence regarding the development of post-operative abscess complications in Crohn's disease patients, who have been exposed to biologics.¹²⁻¹⁴ However, the PUCCINI study evaluated the effect of pre-operative anti-tumor necrosis factor alpha (TNF) in a multi-center, prospective cohort. TNF-inhibitor exposure was defined not only by patient-reported anti-TNF use but also through the detection of peri-operative TNF drug levels. 955 patients were included in the study, of which 574 had no exposure to anti-TNF and 382 patients had exposure 12 weeks prior to surgery. Frequency of any infection defined by a detectable anti-TNF was 19.7% in the unexposed cohort and 19.6 in the exposed cohort. The study suggested that exposure to ant-TNF within 12 weeks of surgery did not increase the risk of post-operative infectious complications.

Management of Intra-abdominal Abscess in Patients with Crohn's Disease

Initial Management

A standardized approach to initial intra-abdominal abscess management in patients with Crohn's disease has not been studied. However, a multidisciplinary approach, incorporating not only surgical and gastroenterology expertise, but

also consultation with radiologist and infectious disease specialists is warranted.

Upon the exclusion of alternative etiologies, anti-infective therapy should be initiated. Agents effective against enteric organisms, specifically gram-negative bacilli, anaerobic bacilli, and gram-positive bacteria are warranted. Considering the potential for possible resistant organisms, proposed agents included piperacillin-tazobactam, ticarcillin-clavulanate, cefoxitin, ertapenem, meropenem, moxifloxacin, or tigecycline as single agent therapy. Alternatively, a cephalosporin, second or third generation, or ciprofloxacin combined with metronidazole has also been suggested. Broad-based therapy is often initiated early in the course of illness and narrowed with the return of culture and sensitivity data. Parenteral antibiotics are preferred as evidence regarding the use of oral antibiotics in the acute setting is limited.

Supportive care including the use of resuscitative intravenous fluid management, non-opiate analgesics, anti-pyretics, and close clinical monitoring is also warranted. The management of sepsis may also require the need for vasopressor support, colloid administration, and intensive-care monitoring. In the setting of chronic corticosteroid use, discontinuation may need to be balanced with the potential for possible adrenal insufficiency. Nevertheless, in the acute setting, the withdrawal or de-escalation of agents is appropriate.

The duration of antibiotics is determined by the efficacy of the drainage procedures. For adequately drained abscess, antibiotics should be continued for 3-7 days. In the absence of appropriate drainage, long courses of antibiotics may be required with interval re-imaging to ensure appropriate resolution. Imaging techniques to consider include not only repeat computed tomography (CT) or magnetic resonance (MRI) imaging but potentially the use of contrast injection through drainage catheters to assess continuity of the fluid collection with the bowel. Additional diagnostics to also pursue include an ileocolonoscopy to assess the extent of disease. In terms of nutritional support, bowel rest is often warranted in the acute setting with the potential need for total parenteral nutrition.

Percutaneous Drainage

The drainage of fluid collections through radiologic means, either ultrasound or CT guidance, has significantly altered the management strategy of IAA in CD. Radiographic drainage is the first line therapy in combination with antimicrobial treatment. Initial usage of interventional drainage procedures was reported in short case reports.¹⁵ Nevertheless, with advancement in imaging techniques, the usage of percutaneous drainage (PD) for the management abscess has become more common. A claims-based study using the nationwide inpatient sample of 3926 hospitalization suggested an increase in the use of PD for the management of abscess from 7% in 1998 to 29% in 2007.¹⁶

PD has been assessed not only as an option to avoid surgery but also as a bridge, allowing for patient optimization for eventual surgical management. In the largest retrospective cohort study, 87 patients with Crohn's disease were managed with PD, the primary technical success was reported at 77%, with a subsequent increase in successful drainage with catheter manipulation to 84.3% without serious complications.¹⁷

From the perspective of safety, although the risk of injury to structures in close proximity to abscess collections exist as well as concern for potential hemorrhage, major complications associated with PD are rare and estimated at 5-10%.¹⁷ In rare instances, bacteremia along with the development of enterocutaneous fistulae have been reported in retrospective cohorts.¹⁸⁻²⁰ Considering the technical success as well as the relative safe profile of the PD, the strategy has been routinely recommended as the initial therapeutic option in patients with IAA.

Medical Management

There is limited data regarding medical management alone in the absence of surgical or radiologic drainage of abscesses in Crohn's disease. Antibiotics are often continued in these settings in longer courses with the need for re-imaging to assess recurrence or involution.

In a mixed cohort of patients without Crohn's disease, Kumar and colleagues performed a retrospective study at a single center assessing the factors associated with successful medical management in patients presenting with

Table 1. Studies Comparing Surgical Drainage to Medical Management (Percutaneous Drainage and Antibiotics) for the Management of Intra-abdominal Abscess

Reference	Study Design	Year	Number of Patients			Follow Up	Mean Abscess Size	Conclusions
			Total	PD	Surg			
Garcia J et al.	Retrospective	2001	56	25	31	45 Months	NR	Surgery more effective at preventing abscess recurrence than medical therapy (p=0.016) Medical management prevented surgery in 50% of cases
Gutierrez A et al.	Retrospective	2006	66	29	37	12 months	7.2 cm	Time to abscess resolution similar in PD compared to surgery A third of patients treated with PD required surgical drainage within one year Early PD improved time to abscess resolution
Kim DH et al	Retrospective	2009	27*	9	18	12 months	>4cm -13 non-Surgical -9 Surgical	Similar rates of abscess recurrence in PD compared to surgical drainage (27.8% vs. 30.8%, p=1.0)
de Luz Moreira et al.	Retrospective	2009	94	48	31	NR	NR	PD failure associated with ileocolonic phenotype, corticosteroids, and multiloculated/multiple abscess. Elective surgery following PD associated with reduced rates of stoma creation Initial PD was more cost-effective and provided more quality-associated life years than initial surgery
Xie Y et al.	Retrospective	2012	23	10	13	25 months	6.6 cm	Initial PD associated with lower rates of post-drainage complications and stoma creation compared to surgery (p=0.036 and p=0.01)
Nguyen D et al.	Retrospective	2012	95	55	40	43 months	7.2 cm	Abscess recurrence similar between PD and Surgery cohorts (31.2% vs. 20.3%, p=0.25) Perianal disease, active ileal disease associated with recurrence; whereas post-drainage anti-TNF therapy reduced recurrence
Bermejo F et al.	Retrospective	2012	74*	30	44	12 months	4.5 cm	Efficacy of PD compared to surgical drainage was 45% vs. 91%
Lobaton et al.	Retrospective	2013	44	22	22	12 months	10.5 cm	Higher therapeutic success rate with surgery compared to PD (95.5% vs. 27.2%, p<0.001) PD associated with treatment failure in multivariate analysis (OR: 88.26, 7.28-1055.28, p<0.001)
Liu et al.	Retrospective	2014	56 [§]	25	31	3 months	6.1 cm	Recurrence rates of abscess in PD vs. surgery group similar (64.0% vs. 58.1%, p=0.1) Lower rate of stoma creation in PD (20.0%) vs. surgery (58.1%), p=0.061

*Study also included a third arm, incorporating medical treatment without PD.

§Study included a third arm, incorporating a trocar puncture/sump drain. PD: Percutaneous Drainage

intra-abdominal abscess.²¹ In a cohort of 114 patients treated with parenteral antibiotics and bowel rest, 61 (54%) had clinical response and were discharged without percutaneous drainage. Of these patients, 58 had no documented evidence of recurrence. Factors associated with successful drainage included abscess size and admission presentation with fevers. Although this study showed the potential for successful management, clinical applicability is limited by its retrospective, single-center design as well and lack of inclusion of patients with CD.

A subsequent study, specifically assessed different management strategies IAA in patients with CD in a multicenter European retrospective study.²² In a cohort of 128 cases, 54 patients (40%) were treated solely with antibiotics. Of note, 77.8% of the patients treated with antibiotics were also co-managed with corticosteroids. The efficacy of this strategy was reported at 63%. Predictors of treatment failure with medical therapy included the need for immunosuppressant therapy, associated fistula visualized on imaging, and abscess size.

Management with bowel rest and antibiotics may be a potential option in patient with uncomplicated, small collections, unamenable to percutaneous drainage. From the data provided in studies above, the recurrence rates with medical therapy alone continues to be reported at 37-50%. The patient cohort that may best respond to antibiotics is unknown and at this point management solely with medical therapy is likely best attempted in a group of patients with expert consultation with infectious disease specialists and colorectal surgery.

Surgical Management

Historically, the management of IAA in CD involved surgical drainage. Currently, the estimated rates of surgery as a first line management approach to abscess range from 7%-25% in CD.^{23,24} Surgical drainage of an abscess often involves not only the evacuation of the abscess contents, irrigation with lavage, and debridement but often resection of the bowel and creation of an ostomy.

Surgical management has shown to have significant technical success in the management of abscess. In an early study, Garcia and colleagues compared the long-term outcome of medical,

percutaneous, and surgical management of abscess in 51 patients with Crohn's disease presenting to a single, tertiary care center over a 10 year period.²⁵ Of these patients, 10 were treated medically, 7 were provided with percutaneous drainage, and 34 underwent surgical drainage. Abscess recurrence occurred in 50% of patients treated with medical therapy alone, 67% in patients treated with percutaneous drainage, and in 12% of patients treated surgically. Although this suggested the superiority of potential surgical management as a strategy, the authors did not delineate the size or other aspects of the abscess. Additional studies have also suggested lower rates of abscess recurrence in patients treated initially with surgery.^{22,26}

Nevertheless, surgical drainage is not often an innocuous process. In frail patients, often malnourished from the catabolic burden of a chronic inflammatory process, risks of surgery include post-operative complications related to anastomotic leak and wound infection. Moreover, surgery is non-curative and rates of recurrence of CD in the absence of post-operative management continues to be high. Considering this, surgical management for IAA in CD is often utilized in cases not amenable to medical management or percutaneous drainage. Specifically, surgical drainage is often preferred in patients with IAA in locations unable to be accessed through percutaneous drainage, patients with multiple abscesses or large abscess, patients with long-standing or medically refractory disease, or patients with disease associated with stricture.

Comparisons Between Percutaneous and Surgical Drainage

The evidence comparing percutaneous drainage of Crohn's related IAA compared to surgical drainage is limited by study design. Considering the overall low incidence of abscess formation, the feasibility of a randomized comparative study may not be possible. Despite biases and the inherent heterogenous nature, several retrospective observational studies can provide guidance in comparing PD to surgical drainage. An overview of the pivotal studies comparing PD and surgical drainage with major conclusions is provided in Table 1.

The largest study comparative study reported the Mayo clinic experience including a total of 95

Table 2. Factors Associated with Surgery[‡] for Intra-abdominal Abscesses in Crohn's Disease

Ileal Disease, Ileocolonic or Upper GI Disease
Perianal Disease
Prior Surgery with Intestinal Anastomosis
Disease Duration > 1 year
Malnutrition
Corticosteroids
Multiple or Multilocular Abscesses
Fistulae
Spontaneous, non-Recurrent Abscess
Larger Abscess Size (>6cm)
Active Disease Segment < 15cm
Stenosis with Pre-stenotic Dilation ≥ 3cm
Bowel Wall Thickening > 6mm

patients with CD treated for IAA.²⁷ In this cohort, 55 patients underwent PD and 40 underwent surgical drainage. The study reported a median follow up of 3.5 years. Of the cohort that underwent surgical drainage, 22.5% had either a high severity of illness marked with hemodynamic instability or multiple abscesses; 17.5% had obstructive symptoms. The mean abscess size in the PD cohort was 6.9 cm and 7.4 cm in the surgical cohort.

The results of the study demonstrated that there was not a significant difference in the probability of abscess recurrence in the surgical group (20.3%) compared to PD (31.2%). In total, there were 25 cases of abscess recurrence, 17 occurred in the medical group and 8 in the surgical group. Abscess recurrence occurred in the first month of abscess drainage in 66% of patients. There was no significant difference in the rates of early abscess recurrence between cohorts. Twelve patients in the percutaneous group eventually requires surgical resection during the follow up period. Both a history of perianal disease as well as active ileal disease were significantly associated with abscess recurrence. In contrast, the use of an anti-TNF, as monotherapy or in combination, was protective against abscess recurrence.

Additional retrospective studies have compared the surgical drainage to PD. The results of these

Table 3. Factors Associated with Success of Medical Therapy (Antibiotics along with Percutaneous Drainage)

New Onset Crohn's Disease
Absence of Fibrostenotic Disease
Small Abscess Size (<4 cm)
Absence of Prior Surgery
Inflammatory Phenotype

studies were summarized in a recent meta-analysis, incorporating six studies and 333 patients, in whom percutaneous drainage was provided to 44.7% of patients and surgical drainage was provided to 55.3% of patients.²⁸ The range of follow up reported in the meta-analysis was 12-43 months. In contrast to the study by Nguyen and colleagues, the authors reported that PD significantly increased the likelihood of abscess recurrence compared to surgical drainage. The pooled proportion of patients who initially underwent PD that eventually required surgery was 70.7%. The remaining minority, 29.3%, of patients was able to avoid surgery. There was no significant difference between the complication rates.

Success of PD is often dependent on Crohn's disease history, abscess characteristics and associated complications.²⁹ A potential reason for the difference in the results presented by Nguyen and colleagues compared to the meta-analysis may be due to the heterogeneity in patient population and evolving expertise in PD. Of note, initial pre-operative PD followed surgery has been suggested as a cost-effective strategy with lower risks of complications compared to initial surgical drainage.^{30,31} Identifying the factors attributed with the greatest success in PD may provide an ideal strategy in patient allocation for PD or surgical drainage.

Several studies have suggested risk factors for failure of PD, including ileal disease, perianal disease, abscess size, utilization of corticosteroids, and multiple or multilocular abscesses. In a smaller study, Sahai and colleagues also reported that abscesses associated with fistulae were also associated with a higher risk of PD failure.¹⁹ In contrast, an initial spontaneous abscess responded favorably to PD compared to recurrent or

post-operative fluid collections. Table 2 lists the factors associated with PD failure and Table 3 list factors associated with success of PD.

A recent study sought to specifically identify the factors associated with the avoidance of future surgery in patients with nonoperatively managed IAA.³² In a retrospective cohort of 121 patients who were provided with non-operative management, 36.4% were able to avoid bowel resection within two years of mandated follow up. Indications for surgery included not only persistent abscess but also refractory disease. Factors associated with surgery within two years of index hospitalization for IAA included an abscess size greater than 6 mm, length of active disease segment greater than 15cm, a stricture with evidence of pre-stenotic dilatation greater than or equal to 3cm, and bowel wall thickening greater than 6 mm in size. Neither biologic medications in combination or as monotherapy nor PD at index hospitalization influenced the risk of future surgery in the analysis; however, this was attributed to colinear adjustments associated with abscess size and disease activity characteristics. Of note, although corticosteroid use was not associated with future surgery, only 14 patients were continued on corticosteroids at doses greater than 20mg following index hospitalization, limiting statistical modelling.

Subsequent Medical Management

Following the control of abdominal sepsis through drainage, either surgical or through radiologic means, the use of immunosuppressant agents is often recommended. In the aforementioned, Nguyen study detailing the Mayo experience, twelve patients were started on immunosuppressive therapy on the same date as abscess drainage.²⁷ Post-hoc analysis of randomized control data investigating the role of Anti-TNF in drained abscess have also suggested the lack of new abscess-associated complication in patients treated with anti-TNF therapy.³³

In patients with abscesses that are not drained, caution should be taken in term of continuing immunosuppressant agents. In older case series, the use of corticosteroids was not explicitly associated with significant complications.^{19,34} These case reports have significant limitations in widespread

application considering the small size of these studies, known risks of corticosteroid use, and subsequent trial suggesting conflicting results.²²

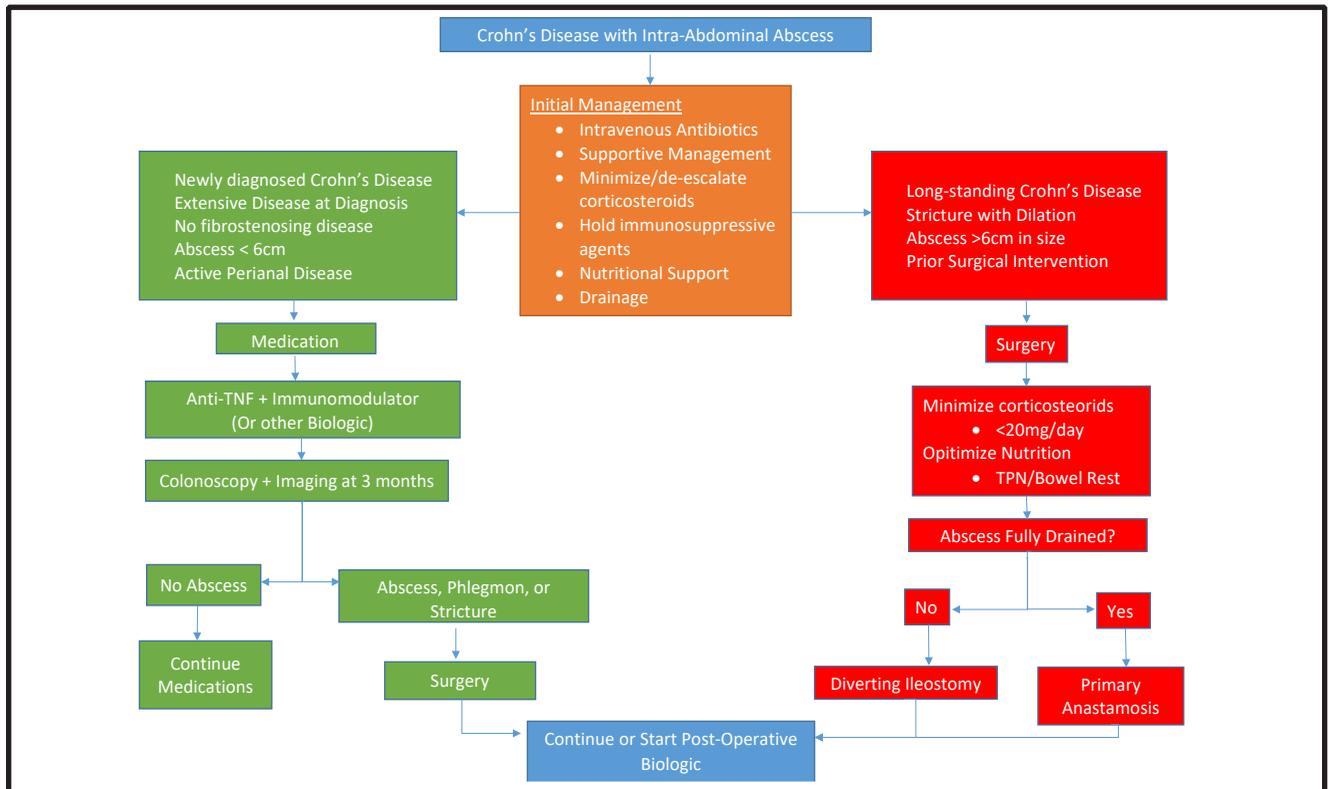
Although presented in abstract form, a recent study assessed the role of Adalimumab in 117 patients with Crohn's disease and IAA.³⁵ Following the resolution of abdominal sepsis, patients were provided with Adalimumab. In the study, only eleven patients had PD prior to the start of anti-TNF therapy. Of note, at baseline imaging, the median size of the abscess 2.5cm at time of inclusion with a fistula tract identified in 58% of patients. The primary composite outcome, adalimumab success, was defined as the lack of corticosteroids at week 12, no abscess recurrence, no intestinal resection and the lack of clinical relapse in follow up by week 24. The outcome was met in 74% of patients. At least one serious adverse event was reported in 40 patients, and 9% of patients has either abscess recurrence or required intestinal resection in the follow up period.

Thus, although there is some evidence for the use of immunosuppressive therapy in the absence of drainage, caution should be exercised. Following control of abdominal sepsis; however, it is our practice to de-escalate corticosteroid therapy and institute combination therapy with anti-TNF and immunomodulator or alternative biologic.

Published Guidelines

Several guidelines have commented on the management of IAA in Crohn's disease. The American College of Gastroenterology recommend abscess drainage prior to the initiation of treatment for Crohn's disease, but American expert consensus does not weigh on the choice of initial drainage procedure and suggest either PD or surgical drainage as potential options.³⁶ Both the European Crohn's and Colitis Organization (ECCO) and the British Society of Gastroenterology (BSG) recommend PD as the initial approach for all well-defined and accessible IAA in situations where expertise is available.^{37,38} Following adequate drainage, the ECCO experts suggest that medical management without surgery be considered with a low threshold for surgery be maintained. Additionally, the authors BSG guideline recommend against immediate resection in cases where surgical drainage is required.

Figure 1. Proposed Algorithm for the Management of Intra-Abdominal Abscess in Crohn's Disease



Proposed Algorithm

Several algorithms for the management of IAA in Crohn's disease have been proposed.^{30,39} The majority of these strategies incorporate cut-offs in abscess size as decision points to surgical or medical therapy. Considering newer relevant data, we propose a new algorithm for the management of IAA following drainage (Figure 1). The proposed algorithm incorporates not only abscess size, but patient and disease characteristics.

CONCLUSION

The natural history of Crohn's disease is associated with the development of penetrating complications. IAA is a complication of Crohn's disease that occurs in nearly 20% of patients. Although previously managed through surgical means, advances in imaging have resulted in an increased reliance on PD as an initial strategy for management. The evidence for the management of IAA is limited retrospective, cohort studies. Despite the recent advancements in PD, recent studies have suggested that roughly 30% of patients treated with PD are able to avoid future surgical

resection. Algorithmic approaches to management should incorporate not only characteristics of the presenting abscess but also patient and disease associated aspects that may impart the greatest success of medical therapy with PD. Considering the evidence available, a multidisciplinary approach to the management of IAA is recommended, incorporating gastroenterology, colorectal surgery, radiology, and, potentially infectious disease. ■

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