

# Clinical characteristics, natural history, and outcomes of Crohn's-related intra-abdominal collections

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## Abstract

**Background:** Intra-abdominal collections in the form of abscesses or matted bowel loops, called phlegmons, might occur in patients with Crohn's disease (CD). The clinical characteristics and management of such conditions are not well described. We aim to characterize CD-related intra-abdominal collections clinically, and identify predictors of need for surgical interventions and the time to surgery.

**Methods:** We utilized the Saudi Inflammatory Bowel Disease Information System (IBDIS) database to identify all patients treated for radiologically proven intra-abdominal abscesses or phlegmons since inception. Demographics, clinical data, clinical course, and treatment outcomes were recorded. Logistic regression analysis and survival analysis were used to identify predictors of surgical resection and differences in time to surgery between patient subgroups, respectively.

**Results:** A total of 734 patients with a diagnosis of CD were screened and 75 patients were identified. The mean age was  $25.6 \pm 9.9$  years and 51% were males. Nearly 60% of patients had abscesses larger than 3 cm while 13% had smaller abscesses and 36% had phlegmons. On presentation, the most commonly reported symptom was abdominal pain (99%) followed by weight loss (27%). About 89% of patients were treated with antibiotics during hospitalization for an average of 2.7 weeks. Steroids were prescribed for 52% of patients and tumor necrosis factor alpha (TNF-alpha) antagonists for 17%. Surgical resection was required for 33 patients (44% of the cohort) while 51% were managed with antibiotics and/or percutaneous drainage. The most common surgical intervention was ileocecal resection (45%). Although patients who underwent follow-up imaging were more likely to require early surgical intervention ( $P = 0.04$ ), no statistically significant predictor of surgery could be identified from this cohort. Time to surgery varied numerically according to abscess size (HR = 1.18, 95% CI = 0.62–2.27,  $P = 0.61$ ).

**Conclusions:** Although the majority of patients with CD-related intra-abdominal collections underwent surgical resection in this cohort, no obvious predictors of surgical intervention could be identified. The decision to perform early surgery appeared to be influenced by the findings observed on cross-sectional imaging during the follow-up of these collections.

**Keywords:** Abscess, collection, Crohn's disease, outcome, phlegmon, surgery

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## INTRODUCTION

Crohn's disease (CD) is an autoimmune bowel disorder characterized by chronic transmural inflammation that can affect any part of the gastrointestinal system. It has the potential for progressing to local and systemic complications secondary to unopposed inflammation.<sup>[1]</sup> Local complications of CD include fistulas, abscesses, strictures, and bowel perforation depending on disease phenotype and location.<sup>[2]</sup> The disease can manifest as one of three phenotypes: inflammatory, fibro-stenotic, or penetrating behavior as defined by the Montreal classification.<sup>[3]</sup> CD involves the ileocolonic region in up to 45% of cases.<sup>[4,5]</sup> These factors in addition to age and gender might play a role in the formation of local disease complications.<sup>[6]</sup>

Conventional step-up therapy is an appropriate treatment approach for CD patients with low-risk features. Early introduction of biologics is more effective in patients with high-risk features such as fistulizing phenotype and early age at the time of diagnosis.<sup>[7]</sup> It is not clear if early treatment influences important outcomes such as the development of intra-abdominal collections.<sup>[8]</sup>

Intra-abdominal collections such as abscesses and phlegmons are not well characterized in the literature. Although a standardized definition does not exist, phlegmons are generally described as inflammatory masses that are composed of matted loops of bowel without any clear fluid collection. This is how they are distinguished from abscesses on cross-sectional imaging. The latter has a clearly defined collection with or without matted loops of bowel.

Treatment options in cases of intra-abdominal collections include a conservative approach with percutaneous drainage and antimicrobial therapy or surgical intervention. The natural history and correct treatment of phlegmons are not well-characterized. Whether or not phlegmons can be effectively and safely treated with TNF antagonists is uncertain. A small retrospective analysis by Cullen *et al.* suggested that anti-TNF therapy might be effective for phlegmons.<sup>[6,9]</sup> However, some experts suggest that surgical resection should always be performed in cases of phlegmons due to the high recurrence rates.<sup>[10-15]</sup> Furthermore, predictors of the need for surgical intervention in phlegmon remain unknown.

This study aims to characterize CD-related intra-abdominal collections and to identify predictors of the need for surgical resection.

## PATIENTS AND METHODS

The Inflammatory Bowel Disease Information System (IBDIS) is a centralized database that is used to register all the patients (total number 1294) diagnosed with IBD enrolled in major medical centers in the Kingdom of Saudi Arabia (KSA). IBDIS (www.ibdis.net) is a web-based documentation system comprising of multiple blocks of information including IBD-related parameters such as demographics, risk factors, diagnosis, disease location and behavior, course of the disease, extra-intestinal manifestations, complications, pregnancy, surgical, and conservative therapy (defined as antibiotics and or percutaneous drainage). Further description of the registry has been outlined in a previous publication.<sup>[4,16-20]</sup>

From the IBDIS registry, we identified all patients who had a radiologically confirmed diagnosis of abscess or phlegmon based on ultrasound (US), computed tomography (CT), or magnetic resonance imaging (MRI) of the abdomen. A phlegmon was defined as a spontaneously occurring inflammatory mass adjacent to an area of inflamed/matted bowel loops that lacks any evidence of a fluid collection<sup>[9]</sup> and an abscess as any extra-luminal fluid collection.

Patient demographics and clinical data at the time of phlegmon diagnosis were recorded. This included their age, gender, duration of disease, disease phenotype according to the Montreal classification, disease extent/location, past and present medications including steroids, immunosuppressives, antibiotics, or TNF-alpha antagonist use, cigarette smoking, and clinical symptoms. Laboratory and radiology investigations including complete blood count (CBC), C-reactive protein, and erythrocyte sedimentation rate (ESR), were also recorded.

### Outcomes

Surgical resection of small or large bowel segments due to the presence of an inflammatory mass or fluid collection was considered the main outcome. Time to surgery was considered the secondary outcome.

### Statistical analysis

Convenient sample size was utilized for analysis. Baseline means and standard deviations (SD) were calculated for continuous variables, while frequencies and percentages were calculated for categorical variables.

Simple logistic regression analysis was used to identify predictors of surgical resection. When permitted, multiple logistic regression analysis was attempted depending on the number of variables and observations, and multinomial

logistic regression analysis was used if the dependent variable had more than two categories with relative risk (RR) ratios reported. A Kaplan-Meier curve was used to estimate and compare time to surgery among groups of patients. Cox proportional regression analysis was used to compare time to events using hazard ratio (HR) estimates. The precision of point estimate was estimated using 95% confidence intervals (CI). STATA 11.2 (StataCorp, Texas, USA) with a significance level of 5%.

### Ethical approval

This study was conducted in accordance with the protocol and principles of the Declaration of Helsinki. The study was approved by the Ethical Committee of the Institute for IBD Database registry with IRB project No. E-11-538.

## RESULTS

### Baseline characteristics

The baseline characteristics of 75 included patients are described in Table 1. The mean age was  $25.6 \pm 9.9$  years, 54% of patients in this cohort were older than age 40, and 51% were males. The mean duration of disease was  $28 \pm 43$  months and the most common form of disease distribution was an ileocolonic disease (54%). About 60% of patients had abscesses that had a diameter larger than 3 cm. Smaller abscesses were found in 13% while 36% of patients had a phlegmon. On presentation, the most commonly reported symptoms were abdominal pain (99%) and weight loss (27%). Use of corticosteroids, azathioprine (AZA), and 5-ASA agents were reported in 50%, 48%, and 42%, respectively and only 11% of patients were on a TNF-alpha antagonist at the time of diagnosis of an intra-abdominal collection. The average duration of follow-up following the diagnosis of an intra-abdominal collection was  $0.5 \pm 0.6$  years.

### Predictors of abscess formation

Males were more likely to have smaller abscesses (RR = 11.2, 95% CI = 0.81–16,  $P = 0.07$ ) and phlegmons (RR = 41.6, 95% CI = 2.21–784.28,  $P = 0.01$ ) compared to females. A numerically higher percentage of patients had vomiting as the presenting symptom of phlegmon formation compared to patients with large abscesses (RR = 8.24, 95% CI = 0.86–78.62,  $P = 0.07$ ).

### Hospital course and outcomes

The average duration of hospitalization was  $16.3 \pm 10.5$  days. Antibiotics were prescribed to 89% of patients. Corticosteroids were prescribed for 52% while AZA was prescribed for 72% of the cases. Only 17% of the patient cohort received anti-TNF therapy (Supplementary Figure 1).

**Table 1: Baseline characteristics of 75 patients with Crohn's-related intra-abdominal collections**

Age (mean±SD)	25.6±9.9
- <40 (A1)	46%
- >40 (A2)	54%
BMI (mean±SD)	18.8±4.5
Disease duration in months (mean±SD)	28±42.5
Male gender (%)	38 (51)
Cigarette smoking (%)	11 (15)
Disease location (%)	
Ileal (L1)	34 (45)
Colonic (L2)	1 (1)
Ileocolonic (L3)	40 (54)
Lesion Type (%)	
Abscess > 3 cm	44 (59)
Phlegmon	21 (28)
Abscess ≤ 3 cm	10 (13)
Symptoms (%)	
Abdominal pain	74 (99)
Weight loss	20 (27)
Diarrhea	15 (20)
Vomiting	13 (17)
Abdominal Mass	9 (12)
Fever	7 (9)
Vital signs on presentation (Mean±SD)	
Heart rate	99±20
Respiratory rate	20.5±1.2
Temperature	37.5±4.5
Medications at baseline (%)	
5-ASA	33 (44)
Corticosteroids	32 (43)
Azathioprine	31 (41)
Anti-TNF agents	7 (9)
Laboratory investigations	
Hemoglobin (g/dL)	108.5±25.9
Platelets	453±146.7
WBC count	9.9±4.6
CRP	72±78.5
ESR	55±32.6
Duration of follow-up in months (mean±SD)	6±7.2

\*SD: Standard deviation, BMI; body mass index, ASA; aminosalicilic acid, WBC; white blood cell, CRP; C-reactive protein, ESR; erythrocyte sedimentation rate

The average time to surgical intervention, which was required for 44% of patients, was  $4.1 \pm 9.4$  weeks and the most common surgical intervention was ileocecal resection (45%). Perforation occurred in 4% of patients. For patients who completed 1 year of follow-up, 56% were surgery-free following conservative therapy, 36% eventually required surgery, and 5% underwent a second surgical intervention. Radiological follow-up of intra-abdominal collections occurred in 70% of cases. Patients who underwent follow-up imaging were more likely to require early surgical intervention ( $P = 0.04$ ). Hospital course and treatments are described in Table 2.

### Predictors of surgical resection

On simple and multiple regression analysis, no statistically significant predictor of the need for surgical resection could be identified. The only exception was weight loss; defined as a 15% decline in body weight within the preceding 2 months, which was statistically significant according to

**Table 2: Treatment and hospitalization course of 75 patients with Crohn's disease**

Duration of treatment in weeks (mean±SD)	2.7±1.7
Corticosteroids (%)	39 (52)
Duration of treatment in weeks (mean±SD)	4.1±9.4
Dosage in milligrams (mean±SD)	17.8±16.5
Azathioprine (%)	54 (72)
Anti-TNF (%)	13 (17)
Adalimumab 40 mg once weekly	1 (8)
Adalimumab 40 mg every 2 weeks	1 (8)
Infliximab 5–10 mg/kg	11 (84)
Duration of hospitalization in days	16.3±1.4
Types of Surgical resection (%)	33 (44)
Ileocecal resection	16 (48)
Ileal resection	6 (19)
Right hemicolectomy	3 (10)
Vesico-enteric fistula repair	3 (10)
Small bowel resection	2 (6)
Total colectomy	2 (6)
Subtotal colectomy	1 (3)
Left hemicolectomy	1 (3)
Time to Surgery in weeks (mean±SD)	4.1 + -9.4
Timing of surgery (%):	
- None	42 (56)
- < 2 months	24 (32)
- > 2 months	9 (12)
Perforation (%)	3 (4)
Follow-up imaging (%)	37 (49)
Outcome after 1 year of follow-up:	
- Need for surgical intervention	33 (44)
- Resolution with conservative therapy	42 (56)
- Need for surgery following conservative treatment	15 (36)
- Need for a second surgery	4 (5)

\*SD; standard deviation, TNF; tumor necrosis factor

simple (OR = 3.8, 95% CI = 1.29–1.22) but not to multiple logistic regression analysis [Table 3].

### Time to surgery

Time to surgical resection was stratified according to the type of intra-abdominal collection using the Kaplan-Meier curve [Figure 1]. A large variation was observed between the three groups with the longest time to surgery observed with large abscesses (>3 cm). However, based on Cox proportional regression analysis, no statistical significance was observed when comparing time to surgery between the three types of collections (HR = 1.18, 95% CI = 0.62 to 2.27,  $P = 0.61$ ).

### DISCUSSION

Persistence of disease activity is associated with the development of intra-abdominal abscesses and phlegmons in patients with CD. This could be attributed to the transmural nature of inflammation seen in CD. Limited data suggest that phlegmons can be safely treated with TNF antagonists<sup>[9]</sup> in the presence of antibiotics. The use of TNF antagonists in this population did not lead to an increase in the size of abdominal collections. Nonetheless, many physicians will be concerned about abscess expansion and the development of complications such as perforation with

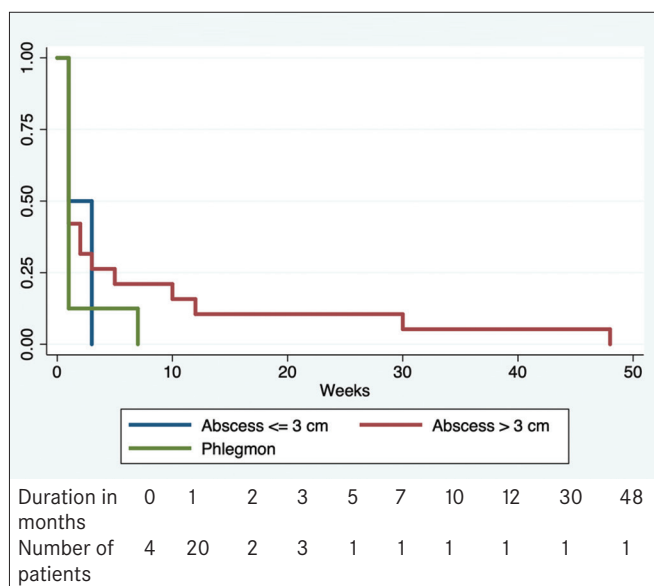
immunosuppressive treatment.<sup>[21]</sup> Therefore, it is essential to differentiate intra-abdominal and pelvic collections from phlegmons. While cross-sectional imaging can accurately differentiate between these lesions and help estimate their sizes,<sup>[22]</sup> it is difficult to distinguish between them clinically. In our cohort, the only symptom found to be predictive of phlegmon formation when compared to abscesses was vomiting, which likely occurs due to obstructed bowel.

Generally, larger lesions are considered at higher risk for free perforation. Based on our data, most collections developed in the ileocecal region and were larger than 3 cm in diameter. Furthermore, men appeared to have smaller collections compared to female patients and perforation, a fearful complication of intra-abdominal collections occurred in only 9% of the cases. Moreover, consequences of leaving an abscess without drainage or relying solely on antibiotics for treatment are not well-studied, yet available data suggests that treatment with antibiotics alone can lead to resolution of up to two-thirds of abscesses but with a recurrence rate that exceeds 50%.<sup>[23-25]</sup> In addition to antimicrobial therapy, both image-guided percutaneous drainage and surgical resection are treatment options with comparable outcomes.<sup>[14,26,27]</sup> While no randomized controlled studies have compared the two approaches, surgical resection is believed to be superior to percutaneous drainage based on retrospective data.<sup>[28]</sup> Nevertheless, the perioperative morbidity and mortality associated with surgical resection during the acute stages is the main reason why percutaneous drainage should first be attempted.<sup>[29]</sup> In a multicenter study that involved 128 CD patients with intra-abdominal abscesses, surgical intervention appeared to be the most effective treatment strategy compared to

**Table 3: Simple and multiple linear regression analysis of predictors of surgical resection for intra-abdominal collections**

Variable	Univariate OR (95% CI)	Multivariate OR (95% CI)
Type of collection	0.94 (0.44,1.93)	19.81 (0.52,759.98)
Gender	0.89 (0.37, 2.35)	840.66 (0.025, 2.84e+07)
Duration of disease in months	0.99 (0.98, 1.00)	0.99 (0.91, 1.08)
Smoking	1.22 (0.33, 4.41)	0.12 (0.001, 15.16)
Weight loss	<b>3.8 (1.29, 11.22)</b>	562.55 (0.036, 8774450)
Age	0.99 (0.95, 1.04)	1.68 (0.72, 3.95)
Extent of disease	1.01 (0.63, 1.61)	9.58 (0.38, 239)
Baseline use of 5-ASA	0.43 (0.31, 2.28)	0.02 (0.0001,2.46)
Baseline use of AZA	0.52 (0.19, 1.41)	0.02 (0.00002,36.67)
Baseline use of steroids	0.30 (0.22, 1.62)	0.24 (0.006,9.40)
Baseline use of TNF antagonists	0.96 (0.19, 4.69)	26.42 (0.02,31802)
Baseline CRP	1.00 (0.99, 1.01)	1.03 (0.98,1.09)
Duration of antibiotics use	1.05 (0.79, 1.41)	1.84 (0.12,27.23)

OR; odds ratio, CI; confidence interval, ASA; aminosalicic acid, AZA; azathioprine, TNF; tumor necrosis factor, CRP; C-reactive protein



**Figure 1:** Time to surgery based on the type of intra-abdominal collection

percutaneous drainage and antibiotic therapy. Antibiotic therapy was more likely to fail in the presence of larger abscesses (OR = 1.65; 95% CI 1.07–5.4;  $P = 0.02$ ), fistulas (OR = 5.43; 95% CI 1.18–24.8;  $P = 0.02$ ), and treatment with immunosuppressants (OR = 8.45; 95% CI = 1.16–61.5;  $P = 0.03$ ).<sup>[30]</sup> Nearly 44% of our patient cohort underwent surgery; most of which involved the right side of the colon and terminal ileum. Conservative therapy including antibiotic use in combination with percutaneous drainage led to the resolution of abscesses in 51% of patients, surgical intervention was required following treatment with antibiotics in 36% of cases, and 7% required a second operation. Although our results showed that patients who underwent follow-up imaging were more likely to require early surgical intervention ( $P = 0.04$ ), likely due to selection bias i.e., symptomatic patients were more likely to undergo follow-up imaging and hence more likely to have positive findings that would require surgery, no obvious predictors of surgery could be identified in this cohort nor were there any significant differences observed between times to surgery based on collection size. Endoscopic intervention has been proposed as a novel method for draining collections in patients with CD. This remains an experimental method and should be restricted to research settings.

We acknowledge that our results might be biased due to the retrospective method of collecting data and small sample size. Large, prospectively conducted studies are needed to better evaluate outcomes of CD-related intra-abdominal collections and compare different types in treatment.

## CONCLUSIONS

Crohn's-related intra-abdominal collections are difficult to identify clinically without cross-sectional imaging of the abdomen and differentiating between abscesses and phlegmons using clinical evaluation remains challenging. The majority of this cohort required surgical intervention within 1 year of presenting with a collection, including those treated conservatively (51/75), and for those who did require surgical intervention, no obvious clinical markers could be relied upon to predict average time to surgery. Large randomized controlled trials are needed to identify the optimal treatment approach for phlegmons and abscesses.

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## Conflicts of interest

There are no conflicts of interest.

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**Supplementary Figure 1:** Treatment of Crohn's disease-related intra-abdominal collections