

ACUTE ABDOMEN IN CROHN'S DISEASE PATIENTS: SHORT- AND LONG-TERM OUTCOMES

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Communicated by Dainis Krieviņš

The aim of the study was to determine long-term outcome in Crohn's disease patients hospitalised for acute abdominal pain. Retrospective chart review was made of consecutive Crohn's disease patients hospitalised for acute abdominal pain at the tertiary referral centre in Eastern Europe. Between 2015 and 2020, 65 patients with Crohn's disease were admitted at least once to the emergency room because of acute abdominal pain. Thirteen were admitted twice, eight — three times, three — four times, and three — five times. Most patients had ileal involvement. There were two intra-abdominal abscesses. Fifty-three of 65 underwent abdominal imaging. Forty-five were treated with antibiotics (65%), 17 with steroids (26%), eight received a nasogastric tube and three — parenteral nutrition. Six underwent an intestinal resection during the initial hospitalisation (9%). The hospitalisation length median was eight days and significantly longer in those who underwent surgery (28 vs. 9, $p = 0.003$). The median follow-up time was 42.8 months. During the follow-up period, 26 (40%) readmitted for abdominal emergencies, 14 underwent surgery — either at the initial or later hospitalisation (21%). Thirteen of 14 surgeries were emergencies, and three were concluded by ostomy formation (21%). One developed postoperative intra-abdominal complication, and two died postoperatively (14%). Complicated disease was associated with hospital readmission (HR, 5.8, 95% CI: 1.4–23.3; $p = 0.013$) and enhanced probability to undergo intestinal surgery (HR, 10.3, 95% CI: 2.4–44.1; $p = 0.002$). An elevated CRP was associated with decreased risk of hospital readmission (HR, 0.08, 95% CI: 0.01–0.55; $p = 0.010$). Ileocolic disease was the main cause of hospitalisation for acute abdominal pain. Complicated (stricturing or penetrating) disease should be diagnosed early and surveilled closely.

Keywords: emergency, repeated hospitalisation, intestinal surgery, stricturing, penetrating, abdominal pains, perforation, IBD.

INTRODUCTION

Acute abdomen is a disorder that must be treated immediately. An infection, inflammation, vascular occlusion, and intestinal obstruction are all potential causes of an acute abdomen. Usually, the patient will experience an abrupt onset of stomach pain along with accompanying nausea or vomiting. In the emergency department (ED), acute abdominal

pain is a common presenting symptom, comprising 5–10% of all ED visits (Powers *et al.*, 1995; Kamin *et al.*, 2003).

However, there are no specific data on how many patients are hospitalised exactly due to Crohn's disease (CD) and acute abdomen, since the natural history of the disease, which is characterised by intra-abdominal inflammation and intestinal obstruction, is expected to lead to an increase in the incidence of abdominal emergencies.

The South-Limburg population cohort (The Netherlands) showed that the hospitalisation rate due to Crohn's disease decreased from 65.9% to 44.2% and the surgery rate from 42.9 to 17.4% at five years, respectively (both $p < 0.01$) (Jeuring *et al.*, 2017). The global trends in hospitalisation for Crohn's Disease and Ulcerative Colitis in the 21st century showed that the hospitalisation rate due to CD depends on the stage of industrialisation of the country, and varies from 3.62 to 10.94% (Buie *et al.*, 2022). Toxic colitis with or without megacolon, massive haemorrhage, free perforation, acute abscess (either intraabdominal or perianal) with sepsis, and intestinal obstruction are examples of acute surgical emergencies (Berg *et al.*, 2002). The data collected in that study (Berg *et al.*, 2002) did not differentiate between acute abdomen and other reasons for hospital admissions, but one might expect that acute abdominal pain was a reason for hospitalisation in a significant proportion of cases.

The guidelines of WSES (World Society of Emergency Surgery) state that CD can present with acute complications that require emergency surgery in approximately 6 to 16% of hospitalised cases (Gisbert *et al.*, 2018). Acute surgical emergencies in patients with Crohn's disease can have a high morbidity, so knowledge of the prognosis and natural history of these emergencies is of paramount importance.

According to the existing literature, the risk of surgery at one, five, and ten years after CD diagnosis is 16.3%, 33.3%, and 46.6%, respectively (Rolkis *et al.*, 2013). About 10–13% of intestinal resections are performed as emergency surgeries (Iesalnieks, 2008), although the incidence is probably decreasing.

Patients who require emergency surgery are generally in a critical condition and have intra-abdominal sepsis or intestinal obstruction. Compromised immunity and malnutrition expose them to even a higher risk of complications and mortality (Chiarello *et al.*, 2022).

In this retrospective analysis, our objective was to discuss not only acute complications of CD and their treatment, but more importantly, to determine: what happened with patients after an episode of acute abdomen, how often patients are readmitted, and is it possible to decrease the rate of repeated hospitalisations by elective surgery?

PATIENTS AND METHODS

A retrospective study was conducted in consecutive patients with Crohn's disease who were admitted emergently to an academic referral centre for acute abdominal pain between 2015 and 2020. Demographic data, symptoms at presentation, current medication, results of abdominal imaging techniques, laboratory values, and history of the disease were obtained by retrospective chart review. The disease phenotype was classified in each case according to the Montreal classification of Crohn's disease (Rocha *et al.*, 2021), based on abdominal imaging. If no abdominal imaging had been performed at the first hospitalisation, clinical behaviour was

obtained by intraoperative finding or data from diagnostic studies performed during the follow-up period. The main variables of the Montreal classification are the location of the disease (L1 — terminal ileum disease, L2 — colonic disease, L3 — disease of both the ileum and the colon, and L4 — disease of the gastrointestinal tract close to the terminal ileum. L4 is a modifier that can be added to L1–L3 when concomitant upper gastrointestinal disease is present) and the clinical behaviour (B1 — not stricturing /not penetrating disease, B2 — stricturing, and B3 — penetrating disease). Penetrating disease (B3) is defined as the presence of an intra-abdominal fistula, abscess, and/or an inflammatory mass. The mere presence of perianal fistulae is not considered as “penetrating disease”. B2 and B3 are exclusive: clinical behaviour is classified as B3 in patients with intra-abdominal fistula, abscess, or inflammatory mass, even if there is concomitant stricture. Severe anaemia was defined as haemoglobin level of less than 10 g/dl.

Telephone interviews with patients and primary care physicians were conducted to obtain follow-up data. Additionally, data from hospital records were used in the case of repeat hospitalisations at the Rīga East Clinical University Hospital.

The primary end point of the study was the determination of risk factors for hospital readmission due to Crohn's disease. The secondary endpoint of the study was the risk of intestinal resection for Crohn's disease.

Statistics. The Mann–Whitney test was applied in the case of no normal distribution for continuous variables. Comparisons between patient groups were made using the Fisher's exact test for categorical variables. Variables associated with hospital readmission and surgery risk in a univariate analysis with a $p < 0.2$ were included in a multivariate analysis using a stepwise logistic regression model with reverse elimination. $p < 0.05$ was considered to indicate statistical significance (two-tailed test). The Statistical Package for the Social Sciences version 20 (IBM, Chicago, IL, United States) was used.

RESULTS

Between 2015 and 2020, 65 patients with Crohn's disease were admitted at least once to the emergency department because of acute abdominal pain. Thirteen patients were admitted twice, eight three times, three patients four times and three patients five times. The time until the onset of complaints was variable, starting from one to 360 hours. Mean time was 19 hours (IQR 12). Table 1 shows the characteristics of the patients and the diseases of the study population. There was a very high proportion of smokers. Additionally, the intake of immunosuppressive drugs was apparently rare; therefore, most patients have been treated with 5-ASA alone. Most patients had ileal involvement. Two patients presented with an intra-abdominal abscess. Fifty-three of the 65 patients underwent abdominal imaging during hospitalisation.

Table 1. Patients with Crohn's disease attending the emergency department for acute abdominal pain: demographics and disease characteristics

Variable	Number
Female sex	35 (54%)
Age, years (mean, range)	42.6 (18–89)
Smokers	35 (58%)
Previous intestinal surgeries	9 (14%)
Medication at the time of hospital admission	
- Systemic steroids	8 (12%)
- Azathioprine	6 (9%)
- Budesonide	4 (6%)
- Biologicals	1 (1.5%)
- No medication other than 5-ASA	50 (77%)
Vomiting at the initial presentation	23 (35%)
Diarrhea at the initial presentation	34 (52%)
Laboratory values	
- Elevated C-reactive level > 5mg/d	53 (83%)
- Elevated leucocyte count > 10/nl	34 (52%)
- Severe anemia	12 (18%)
Disease localisation	
- L1 – ileitis	28 (42%)
- L2 – colitis	11 (17%)
- L3 – ileocolitis	26 (41%)
Clinical behaviour	
- B1 – no stricturing /non-penetrating	34 (61%)
- B2 – stricturing	6 (11%)
- B3 – penetrating	16 (29%)
Total	65 (100%)

After hospital admission, 45 patients were treated with antibiotics (65%), 17 with steroids (17%), eight patients started their treatment with nasogastric tube and three with parenteral feeding. Six patients underwent an intestinal resection during initial hospitalisation (9%). The median duration of hospitalisation was eight days (range, 1 to 115) and was significantly longer in those who underwent surgery (mean 28 days vs. 9 days, $p = 0.003$).

Follow-up information was obtained for all patients and the median follow-up time was 42.8 months. During the follow-up period, 26 patients (40%) were readmitted for abdominal emergencies. Fourteen patients underwent surgery — either in the initial or later hospitalisation stages (21%). Thirteen of 14 surgeries were emergencies — bowel resections because of perforation and peritonitis or obstruction, and three were concluded by enterostomy formation (21%). One patient developed a postoperative intra-abdominal complication, and two patients died postoperatively, one of them because of toxic megacolon perforation and pneumonia (14%).

Tables 2 and 3 depict the results of the univariate analysis of factors associated with the risk of repeat hospitalisations and surgery. By multivariate analysis, complicated disease (stricturing or penetrating) was associated with hospital re-admission (Hazard ratio, 5.8, 95% CI: 1.4–23.3; $p = 0.013$). An elevated level of C-reactive protein was associated with a decreased risk of hospital readmission (Hazard ratio, 0.08, 95% CI: 0.01–0.55; $p = 0.010$). Furthermore, complicated disease (stricturing or penetrating) was associated with an increased probability of undergoing intestinal surgery (Hazard ratio, 10.3, 95% CI: 2.4–44.1; $p = 0.002$).

Table 2. Risk of hospital readmission after hospitalisation for acute abdominal pain in Crohn's disease patients

Variable	Number (%)	<i>p</i>
Age		
< 40 years	16 of 36 (44%)	0.45
≥ 40 years	10 of 29 (34%)	
Sex		
Female	11 of 30 (37%)	0.8
Male	15 of 35 (43%)	
BMI at the time of hospitalisation		
< 20 kg/mg ²	10 of 19 (53%)	0.16
≥ 20 kg/mg ²	14 of 44 (32%)	
Smokers		
Yes	15 of 38 (39%)	1.0
No	11 of 27 (41%)	
C-reactive protein level at hospitalisation		
< 5 mg/l	8 of 11 (73%)	0.018
> 5 mg/l	17 of 53 (32%)	
Severe anaemia		
Yes	6 of 12 (50%)	0.52
No	20 of 53 (38%)	
Clinical behaviour		
No stricturing /non-penetrating	10 of 34 (29%)	0.05
Penetrating or stricturing	13 of 22 (59%)	
Ileal involvement		
Yes	23 of 54 (43%)	0.5
No	3 of 11 (27%)	
Previous intestinal surgeries		
Yes	6 of 9 (66%)	0.14
No	20 of 56 (36%)	

Table 3. Risk of to undergo surgery after hospitalisation for acute abdominal pain in Crohn's disease patients.

Variable	Number (%)	<i>p</i>
Age		
< 40 years	7 of 36 (19%)	0.76
≥ 40 years	7 of 29 (24%)	
Sex		
Female	5 of 30 (17%)	0.54
Male	9 of 35 (26%)	
BMI at the time of hospitalisation		
< 20 kg/mg ²	5 of 19 (26%)	0.48
≥ 20 kg/mg ²	7 of 44 (16%)	
Smokers		
Yes	9 of 38 (24%)	0.76
No	5 of 27 (18%)	
C-reactive protein level at hospitalisation		
< 5 mg/l	2 of 11 (18%)	1.0
≥ 5 mg/l	12 of 53 (23%)	
Severe anaemia		
Yes	3 of 12 (25%)	0.71
No	11 of 53 (21%)	
Clinical behaviour		
No stricturing /non-penetrating	3 of 34 (9%)	0.001
Penetrating or stricturing	11 of 22 (50%)	
Ileal involvement		
Yes	14 of 54 (26%)	0.10
No	0 of 11 (0%)	
Previous intestinal surgeries		
Yes	2 of 9 (22%)	1.0
No	12 of 56 (21%)	

DISCUSSION

The present study demonstrated a high risk of hospital readmission (40%) and surgery (21%) during the first 4–5 years after hospital treatment of acute abdominal pain for Crohn's disease. There was a significant risk of emergent surgery, ostomy formation at surgery and mortality, if immediate emergent surgery could not be avoided or at least postponed to be performed electively. Complicated disease (stricturing or penetrating) was significantly associated with hospital readmission (59%) and risk of surgery (59%).

Despite the lack of studies specifically looking at patients with Crohn's disease attending the emergency department for acute abdominal pain, there is some data supporting our findings (Meima-van Praag *et al.*, 2021). The study of the results of early surgery in 497 patients with Crohn's disease (Sarikaya *et al.*, 2022) found that surgery performed during an acute flare-up of Crohn's disease was associated with a higher risk of complications, reoperation, and anastomotic leaks, compared to surgery performed during a period of remission. However, the study also found that surgery performed during an acute flare-up was not associated with a higher risk of mortality. Another study (Mayumi *et al.*, 2021) evaluated the outcomes of emergency surgery in patients with Crohn's disease. The study found that emergency surgery was associated with a higher risk of complications, including wound infections and intestinal obstructions, compared to elective surgery. The study also found that patients who underwent emergency surgery had a higher risk of reoperation and a longer hospital stay.

However, in some cases, emergent surgery may be necessary to manage acute symptoms and prevent complications. In fact, 13 of 14 patients in our study underwent emergent surgery, but eight of these operations were performed during one of the next hospital admissions for acute abdominal pain. This underscores the importance of choosing the right patient for elective surgery after successful medical treatment of acute abdominal symptoms. The presence of stricture or penetrating disease that is seen in the distal ileum much more frequently than in the colon should be a strong factor in planning surgery in order to avoid further hospitalisations and emergent surgeries.

The optimal time for hospitalisation for surgery due to Crohn's disease with acute abdominal pain depends on several factors, including the patient's clinical condition, the severity and location of the disease, and the presence of complications. In some cases, emergency surgery may be necessary, such as when there is a bowel perforation or complete bowel obstruction. In these situations, surgery must be performed as soon as possible to prevent life-threatening complications. Unfortunately, there is a lack of studies determining the risk of emergent surgery in patients with Crohn's disease. In our study, 6 of 65 patients underwent emergent surgery at initial hospitalisation, i.e. the risk of emergent surgery was 9%.

Since emergent surgery is associated with an increased morbidity, as clearly demonstrated by the present and above-

mentioned studies, patient management in the emergency room should be aimed to recognise patients who need immediate surgery from those who will probably recover after medical treatment, to facilitate deciding when to postpone the decision to operate. There are no internationally established guidelines for abdominal emergencies in Crohn's disease; thus, only some thoughts could be discussed. Steroids are often given in patients with acute abdominal pain due to Crohn's disease. In our study, 17% of patients received steroids as an initial treatment. Steroids might reduce the swelling in the strictured intestinal segment, relieving the signs of obstruction. However, surgery will be performed under high steroid dosage in cases when the steroids fail. In patients with penetrating disease, initial steroids should not be administered to avoid the risk of septic derangement. Instead, antibiotics and fluid resuscitation might be the best primary choice. Abdominal cross-sectional imaging should be performed at the acute presentation to differentiate between complicated and uncomplicated disease and between stricturing and penetrating disease. Abscesses should be drained percutaneously. An abscess drainage — when technically feasible — might be one of the best tools to avoid emergent surgery; however, there were only two patients with acute abdomen having an intra-abdominal abscess in our study, and many abscesses are too small or not accessible for percutaneous drainage (Schill, 2013).

If the decision for elective surgery has been made, some type of preoperative optimisation strategies will probably be the right choice, since impairment of general health and, in particular, nutritional status, might be expected in many patients who are experiencing acute abdominal pain that requires in-hospital treatment.

In our study, an elevated level of CRP was associated with increased risk of hospital readmission. Patients with higher inflammatory markers were more likely to be considered more acute, as confirmed by radiological examinations. Further tactics were chosen in favour of surgical treatment. Therefore, this provides one more confirmation that surgical treatment is associated with a lower risk of re-hospitalisation in the long term.

The low number of patients and lack of abdominal imaging in 12 patients during the initial hospitalisation stage are limitations of our study. Also, we were unable to analyse the value of particular treatment strategies. The results may be different in other hospitals or countries. There was a very high number of smokers in our study. Also, there was obviously a low use of immunosuppressive treatment in the current population, as most patients were treated with only 5-ASA medications. Mesalamine is not superior to conventional corticosteroids; however, it is not a contraindication for an exacerbation of Crohn's disease (Lim *et al.*, 2010). Since the present study is of a retrospective manner, the proportion of patients with successful initial medical treatment might have been higher if avoiding emergent surgery was the primary goal of treatment. Physicians with less experience with Crohn's disease may have more difficulty predicting the natural history of abdominal emergency in this particular population.

CONCLUSION

Complicated Crohn's disease should already be recognised early in the emergency department in order to discuss the indications for operative therapy following recovery after successful emergent medical treatment.

ETHICS

The study was accepted by the local ethics committee of the University of Latvia.

DATA AVAILABILITY STATEMENTS

Data are available on requests from the authors. The data that support the finding of this study are available from the corresponding author [J.O.] upon reasonable request.

CONFLICT OF INTEREST

There is no conflict of interest.

AUTHORS CONTRIBUTION

All authors contributed to the conception and design of the study. Material preparation, data collection, and analysis were performed by Jānis Opincāns, Agris Rudzāts, and Zurabs Keczaja, Aleksejs Kaminskis, and Igors Ivanovs. The first draught of the manuscript was written by Jānis Opincāns and Igors Iesalnieks, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

FUNDING

No funding was obtained for this study.

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Received 27 February 2024

Accepted in the final form 13 June 2024

AKŪTS VĒDERS KRONA SLIMĪBAS PACIENTIEM: ĪSTERMIŅA UN ILGTERMIŅA REZULTĀTI

Komplicēta Krona slimība ir jāatpazīst jau agrīni uzņemšanas nodaļā, lai apspriestu indikācijas operatīvai terapijai pēc veiksmīgas konservatīvas terapijas neatliekamās medicīniskās palīdzības etapā.