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Computerized tomography features acting as predictors for invasive therapy in the management of Crohn's disease-related spontaneous intra-abdominal abscess: experience from long-term follow-up

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Abstract

Background Decision-making in the management of Crohn's disease (CD)-related spontaneous intra-abdominal abscess (IAA) is challenging. This study aims to reveal predictive factors for percutaneous drainage and/or surgery in the treatment of CD-related spontaneous IAA through long-term follow-up.

Methods Data were collected, including clinical manifestations, radiography and treatment strategies, in Chinese patients with CD-related IAA in a tertiary medical center. Univariate and Multivariate Cox analysis were conducted to identify predictors for invasive therapy.

Results Altogether, 48 CD patients were identified as having IAA through enhanced CT scans. The median follow-up time was 45.0 (23.3, 58.0) months. 23 (47.9%) patients underwent conservative medical treatment, and 25 (52.1%) patients underwent percutaneous drainage and/or surgical intervention (invasive treatment group). The 1-, 2-, and 5-year overall survival rates without invasive treatment were 75.0%, 56.1%, and 46.1%, respectively. On univariate Cox analysis, the computerized tomography (CT) features including nonperienteric abscess (HR: 4.22, 95% CI: 1.81–9.86, $p=0.001$), max abscess diameter (HR: 1.01, 95% CI: 1.00-1.02, $p<0.001$) and width of sinus (HR: 1.27, 95% CI: 1.10–1.46, $p=0.001$) were significantly associated with invasive treatment. Nonperienteric abscess was significantly associated with invasive treatment on multivariate Cox analysis (HR: 3.11, 95% CI: 1.25–7.71, $p=0.015$). A score model was built by width of sinus, location of abscess and max abscess diameter to predict invasive treatment. The AUC of ROC, sensitivity and specificity were 0.892, 80.0% and 90.9% respectively.

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Conclusions More than half of CD-related IAA patients needed invasive therapy within 5-year follow-up. The CT features including nonperienteric abscess, larger maximum abscess diameter and width of sinus suggested a more aggressive approach to invasive treatment.

Keywords Crohn's disease, Spontaneous intra-abdominal abscess, Percutaneous drainage, Surgery

Introduction

Crohn's disease (CD) is predominately characterized by transmural inflammation of the intestine, which may lead to fistulization and intra-abdominal abscesses (IAAs). It is estimated that 10–30% of CD patients develop IAA during their disease course [1], which results in a poor prognosis and imposes significant health care costs. The management of CD-related IAA necessitates a multidisciplinary approach, involving gastroenterologists, surgeons, radiologists, and nutritionists.

Several treatment options are available, including surgery, percutaneous drainage and conservative medical treatment. Conservative medical treatment, which may include antibiotics alone, can be effective in certain cases, offering satisfactory outcomes while circumventing invasive procedures. However the literature indicates that the use of immunomodulators at the time of diagnosis, the presence of detectable fistula in imaging, and a larger abscess size are factors that contribute to the failure of initial therapy with antibiotic treatment alone [2]. Recent ECCO guidelines recommended percutaneous image-guided drainage of well-defined accessible IAA as the primary approach [3]. While some abscesses were situated in the central abdominal cavity, lacking suitable puncture access. Researchers have pointed out that in abscesses with a diameter over 50 mm, surgery was superior to percutaneous drainage, although it was associated with a higher complication rate [4]. Meanwhile, the use of biologics has been shown to potentially heal intestinal fistulas, thereby eliminating the need for surgical intervention [5]. Thus determining the predictors for invasive medications is challenging and an urgent unmet need in clinical practice. This study aimed to clarify the predictive factors for percutaneous drainage and surgery in CD-related IAA patients and develop a predictive model for decision-making.

Methods

Study population

By searching the administration registration system of a tertiary medical center, all patients hospitalized from Jan 2014 to Mar 2021 and diagnosed with CD and abdominal abscess were selected for chart review and CT imaging review by experienced gastroenterologists and radiologists, respectively. The expert abdominal radiologist who was blinded to the clinical data reviewed all CT scans to confirm the diagnosis of abdominal abscess. Postoperative abscesses, which were defined as any abscess identified within 3 months after abdominal surgery, were specifically excluded.

Baseline characteristics and follow-up information were collected from the records of all patients and telephone interviews and confirmed by an expert gastroenterologist.

Patients who underwent percutaneous drainage and/or surgical intervention during follow-up were classified as the invasive treatment group. The other patients were classified into the conservative treatment group.

Clinical data

Medical history, laboratory results and treatment data were carefully obtained from the patient record system. Demographics, disease features, previous smoking habits, previous history of abdominal and/or pelvic surgery and perianal disease data of patients were also collected. Lab results included routine blood tests, serum albumin, erythrocyte sedimentation rate (ESR), and hypersensitive C reactive protein (hsCRP). Opportunistic infection tests, including cytomegalovirus (CMV) and Clostridium difficile (C. Diff), were also included. Medication use 3 months before diagnosis of IAA and during follow-up was obtained.

Imaging data

All enhanced CT scans with or without enterography were critically retrospectively reviewed by an expert abdominal radiologist (W L).

For CTE imaging, pre-imaging intestinal preparation was required. Following a 8-hour fasting period, all the patients were given 2000 mL isotonic mannitol solution (500 mL hyperosmotic mannitol solution plus 1500 mL drinking water) within 45–60 min to ensure adequate distension of the small bowel before CT imaging. For standard CT imaging, no intestinal preparation was needed before CT imaging.

All imaging work was conducted with multi-detector CT scanners (Sensation-64 or SOMATOM Definition Flash; Siemens Medical Systems, Erlangen, Germany). The scanning parameters were as follows: slice thickness, 5 mm; pitch, 1; kVp, 120; mAs, 250. Iohexol injection (GE Healthcare, Shanghai, China) was intravenously administered as a bolus (1.5 mL/kg) at a rate of 3–4 mL/sec using a power injector (Mark V ProVis, Medrad). A bolus-tracking program was used to obtain arterial phase CT data after the intravenous injection of contrast agent. The regions of interest (ROI) cursor for bolus tracking was placed at the abdominal aorta (the level of renal artery) for real-time serial monitoring triggered by threshold of 100 HU. Venous phase was commenced at 30 s after arterial phase scan. In addition, in order to evaluate perianal fistulas and abscesses, the scan was performed from the diaphragm to the perineum.

Abscess was defined as accumulation of purulent material with or without matted loops of bowel. Phlegmons which were inflammatory masses composed of matted loops of bowel without any clear fluid collection were excluded [6]. The location and maximal diameter of abscesses were recorded based on venous phase of CT scan. Based on the location in the CT scan, abscesses were divided into perienteric and nonperienteric abscesses; the latter group included mural abscesses, retroperitoneal abscesses and abscesses invading adjacent organs. The mural enhancement pattern, mesenteric fat turbidity, comb sign, maximal diameter of lymph nodes, length and width of sinus were also recorded based on venous phase of CT scan.

Statistical analysis

Statistical analysis was performed using SPSS version 25.0 statistical software (SPSS, Inc., Chicago, IL, USA). Statistical analysis included descriptive statistics and survival analysis. Continuous variables are expressed as the mean ± standard deviation or median plus interquartile range (IQR). Categorical variables are presented as percentages of the total group. Differences in categorical variables were compared with the χ^2-test (using Fisher's exact test when appropriate). Overall survival was calculated from the date of diagnosis until the date of percutaneous drainage or abscess-related surgical treatment or the last follow-up. Survival curves were plotted with the Kaplan–Meier method and compared with a log-rank test. A Cox proportional hazard model was used for the multivariate analyses to identify the significant or independent predictors for invasive therapy. A predictive model was established according to the coefficient in the regression analysis. The predictive performance of the model was measured by the area under the curve (AUC) of receiver operating characteristic (ROC) curve. *P* values were two-tailed, and the significance level was set at $P < 0.05$.

Results

Patient characteristics

Altogether, 48 CD patients were identified as having IAA through CT. There were 37 (77.1%) males and 11 (22.9%) females with a median age at disease onset of 23.5 (17.3, 33.8) years. The median age at admission was 29.0 (23.0, 37.0) years, and the range from onset to admission was 3.0 (1.0, 6.8) years. 23/45 of the patients were underweight (body mass index, BMI<18.5 kg/m2), with a median BMI of 17.5 (15.6, 20.9) kg/m2. The median follow-up time was 45.0 (23.3, 58.0) months. 23 (47.9%) patients underwent conservative medical treatment, and 25 (52.1%) patients underwent percutaneous drainage and/or surgical intervention (invasive treatment group). There was no difference in the percentage of underweight patients between conservative medical treatment and invasive treatment group ($p = 0.302$).

Imaging characteristics

Based on the enhanced CT scan, most lesions were segmental (31/47, 64.6%) instead of local. Mesenteric fat turbidity was found in each patient. Comb signs were found in 18 (37.5%) patients. Bowel stenosis was found in 39 (81.3%) patients, while bowel dilation was found in 12 (25.0%) patients.

Most abscesses were perienteric, accounting for 58.3% of all abscesses. Other abscesses were located in the retroperitoneal space, had access to the abdominal wall, or invaded adjacent organs, including the gallbladder or uterus and were classified as nonperienteric abscesses (Fig. 1). In 35 (72.9%) patients, single abscess was found while multiple abscessed were found in other patients. Fistulas were found in each patient. 16 (34.8%) patients had a single fistula, while 30 (65.2%) patients had 2 to more than 10 fistulas.

The invasive treatment group had more nonperienteric abscesses than the conservative medical treatment group (64.0% vs. 17.4%, $p = 0.001$). The median maximum abscess diameter was 49.0 (37.0, 71.0) mm. The maximum abscess diameter was larger in the invasive treatment group (61.0(39.5,96.0) mm vs. 39.0 (25.0, 58.5) mm), with a *p* value of 0.001. There was no difference in the number of fistulas between the two treatment groups. The maximum width of the sinus was larger in the invasive treatment group (8.9 ± 2.8 mm vs. 6.1 ± 1.9 mm), with a *p* value less than 0.001. Laboratory tests, infection conditions, imaging characteristics and treatment before IAA happened between the two groups were shown in Table 1.

Overall survival (OS) without invasive treatment and prognostic factors

The 1-, 2-, and 5-year overall survival rates without invasive treatment were 75.0%, 56.1%, and 46.1%, respectively. On univariate Cox analysis, nonperienteric abscess (HR: 4.22, 95% CI: 1.81–9.86, $p = 0.001$), max abscess diameter (HR: 1.01, 95% CI: 1.00-1.02, $p < 0.001$) and width of sinus (HR: 1.27, 95% CI: 1.10–1.46, $p = 0.001$) were significantly associated with invasive treatment. Nonperienteric abscess was significantly associated with invasive treatment on multivariate Cox analysis (HR: 3.11, 95% CI: 1.25–7.71, $p = 0.015$). (Table 2; Fig. 2).

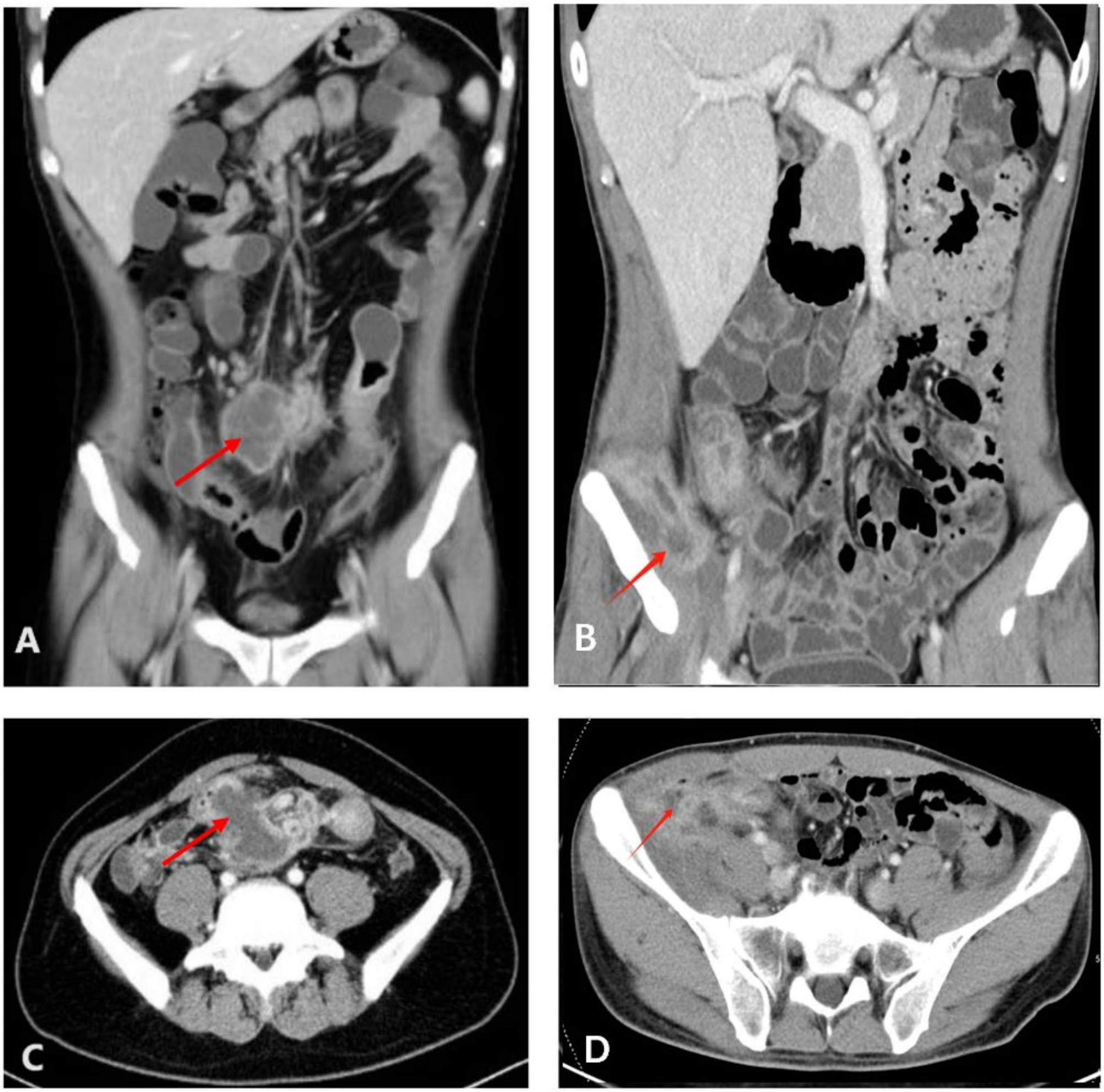

Fig. 1 Perienteric abscess and nonperienteric abscess
Left column: perienteric abscess in a patient with CD; **A**-coronal image, **C**-axial image, both portal phase of CT enterography
Right column: non perienteric abscess involving iliopsoas and posterior abdominal wall; **B**-coronal image, **D**-axial image, both portal phase of CT enterography

Score model for predicting invasive therapy

A score model was built by 0.423×width of sinus+2.194×location of abscess+0.035×max abscess diameter-7.722 to predict invasive treatment. The AUC of ROC were 0.892 (0.801–0.983). The sensitivity and specificity were 80.0% and 90.9% respectively (Fig. 3).

Discussion

CD is a chronic full-thickness inflammatory condition of the bowel; thus, when transmural translocation of bacteria occurs, perforating complications such as IAA or fistula occur. Longitudinal studies have shown that approximately half of patients will develop penetrating disease behavior 10 years after diagnosis [7]. Risk factors for penetrating disease are well recognized, such as terminal ileal disease, disease extent at baseline, number of

Table 1 Patient charateristics in conservative and invasive treatment group in Crohn's disease related intra-abdominal abscess

Items	Total patients (*N* = 48)	Conservative treatment group (*N* = 23)	Invasive treatment group (*N* = 25)	*p* value
Male, n(%)	37(77.1%)	20(87.0%)	17(68.0%)	0.173
Age at onset (years), IQR	23.5(17.3,33.8)	26.0(17.0,33.0)	22.0(17.5,39.0)	0.591
Age at admission (years), IQR	29.0(22.0,37.0)	27.0(21.0,36.0)	29.0(22.5,43.5)	0.326
Range from onset to admission (years), IQR	3.0(1.0,6.8)	1.0(1.0,5.0)	4.0(3.0,8.0)	0.027
Previous history of abdominal and/or pelvic surgery, n(%)	14(29.2%)	8(34.8%)	6(24.0%)	0.412
Perianal disease	23(47.9%)	11(47.8%)	12(48.0%)	0.990
BMI (kg/m2), IQR	17.5(15.6,20.9)	18.3(15.0,20.8)	17.4(15.9,21.5)	0.964
Underweight (BMI<18.5 kg/m2), n(%)	26 (54.1%)	11 (47.8%)	15 (60%)	0.302
WBC (×10^9/L), mean ± SD	8.9(6.2,11.7)	9.3(6.8,13.7)	8.4(5.9,10.8)	0.560
HGB (g/L), mean ± SD	112.9 ± 23.2	118.9 ± 24.9	107.4 ± 20.4	0.088
PLT (×10^9/L), mean ± SD	348.0(281.0,478.0)	360.5(280.0,487.0)	342.0(268.0,505.5)	0.483
Serum albumin (g/L), mean ± SD	37.2 ± 5.6	36.9 ± 5.7	37.4 ± 5.6	0748
ESR (mm/h), mean ± SD	40.0(27.0,62.0)	39.0(24.0,59.0)	40.0(27.5,63.5)	0.483
hsCRP (mg/dL), mean ± SD	54.1(25.3,95.0)	61.1(28.1,100.2)	52.8(20.1,85.3)	0.451
CMV infection, n(%)	1(2.2)	1(4.3%)	0(0%)	0.142
C.Diff infection, n(%)	8(17%)	3(13%)	5(20.8%)	0.492
Location, n (%)				0.001
perienteric abscess	28(58.3%)	19(82.6%)	9(36.0%)	
non perienteric abscess	20(41.7%)	4(17.4%)	16(64.0%)	
Number of abscess, n (%)				0.200
single	35(72.9%)	19(82.6%)	16(64.0%)	
multiple	13(27.1%)	4(17.4%)	9(36.0%)	
Max abscess diameter(mm), IQR	49.0(37.0,71.0)	39.0(25.0,58.5)	61.0(39.5,96.0)	0.001
Fistula, n (%)				0.216
single	16(34.8%)	6(26.1%)	10(43.5%)	
multiple	30(65.2%)	17(73.9%)	13(56.5%)	
Length of sinus(mm, x ± s)	15.8 ± 6.6	14.5 ± 6.2	16.9 ± 6.9	0.220
Width of sinus(mm, x ± s)	7.7 ± 2.8	6.1 ± 1.9	8.9 ± 2.8	<0.001
Treatment before IAA diagnosis				
glucocorticoid, n (%)	17(35.4%)	5(21.7%)	12(48.0%)	0.057
immunosuppresants, n (%)	6(12.5%)	2(8.7%)	4(16.0%)	0.668

IQR interquartile range, SD standard deviation, BMI body mass index, WBC white blood cell, HGB hemoglobin, PLT platelet, ESR erythrocyte sedimentation rate, hsCRP hypersensitive C reactive protein

Table 2 Univariate and multivariate cox analyses on predictors for invasive treatment

Items	Univariate cox analysis		Multivariate cox analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Non perienteric abscess	4.22 (1.81, 9.86)	0.001	3.11 (1.25, 7.71)	0.015
Max abscess diameter	1.01 (1.00, 1.02)	<0.001		
Width of sinus	1.27 (1.10, 1.46)	0.001		

HR hazard ratio, CI confdence interval

flares per year, active smoking and perianal disease [8]. Spontaneous intra-abdominal abscesses are a frequent complication of CD; however, there is limited evidence on the optimal management. In this study, we explored the clinical course and the radiological predictors for invasive therapy in the management of CD-related spontaneous IAA through long-term follow-up and developed a score model for decision-making.

Abscess location is important in decision-making. In a previous study, intra-abdominal fistulae were classified clinically into two groups: those that formed an internal connection between two bowel layers or segments and those that occurred between the intestine and other organs, such as entero-vesical, rectovaginal, or abdominal wall fistulae [9, 10]. Similarly, we divided IAA into two groups: those located between two bowel layers or segments were called perienteric abscesses, and those invading other organs, such as the abdominal wall, retroperitoneum, urinary bladder or uterus, were called nonperienteric abscesses. We found that nonperienteric abscesses were strong predictors for invasive therapy.

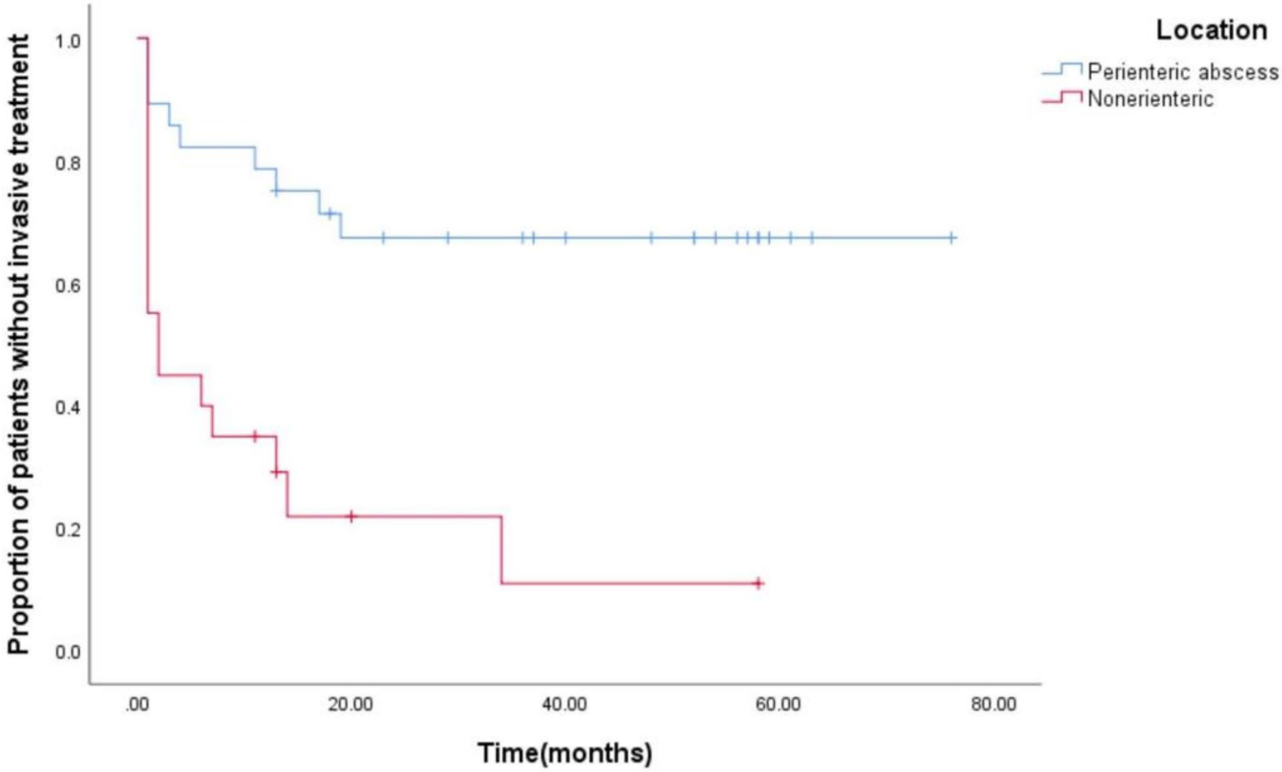

Fig. 2 Kaplan-Meier curves comparing the overall survival of patients without invasive treatment
Blue line indicated proportions of patients without invasive treatment diagnosed as perienteric abscess and red line indicated proportions of patients without invasive treatment diagnosed as non perienteric abscess

It seems consistent that the larger the diameter of the abscess is, the higher the risk of invasive therapy. In the algorithm suggested by Feagins et al. [11], if the abscess size was over 30 mm, percutaneous drainage and close clinical observation were needed, and if the clinical deterioration and abscess persisted, surgery to drain the abscess with or without bowel resection should be considered. In another study, doctors found that abscess sizes greater than 60 mm were independent risk factors for future surgery [12]. Graham found the same result in another cohort in which the mean abscess diameter was 32 mm in the medical treatment group versus 59 mm in the invasive treatment group [13]. In a multicenter study in Spain, researchers have also found that the size of the abscess was critical to the effectiveness of each treatment. In abscesses < 30 mm, the antibiotic was effective, however in abscesses > 50 mm, surgery was superior to percutaneous drainage [4].

A wider sinus width may also be a predictive factor. Although it is difficult and time-consuming to measure the sinus width on CT scans, it is still meaningful to measure it. We found no difference in the number of abscesses or fistulas between the two groups. Segmental/local lesions, bowel stenosis and bowel dilation were not associated with invasive treatment. However, in another study, researchers found that prestenotic bowel dilation of 30 mm or more was associated with surgery [12]. In a Korean cohort, the presence of intestinal stricture at development after diagnosis increased the risk of IAA and intestinal free-wall perforation [14]. More attention should be focused on bowel stenosis and bowel dilation in future studies.

Most percutaneous drainage occurred within 1 month after the detection of abscesses in our study. Zhao et al. published their single-center experience with CT-guided drainage for intraabdominal and pelvic abscesses [15]. The mean duration of drainage was 10.3 days, with a high percentage of complete resolution of abscess following drainage up to 92.7% and a low incidence of complications. Although some patients still need surgery after PD, we believe that PD can bridge the patient to surgical resection by optimizing nutrition and maturing the fistulous tract [16]. The presence of IAA at the time of surgery is a known independent risk factor for postoperative septic complications. Several studies have compared the clinical outcomes between percutaneous drainage and initial surgery for patients with CD-related IAA. Meta-analyses have revealed that the overall complication rate was significantly higher in patients undergoing initial surgery than in those undergoing initial percutaneous

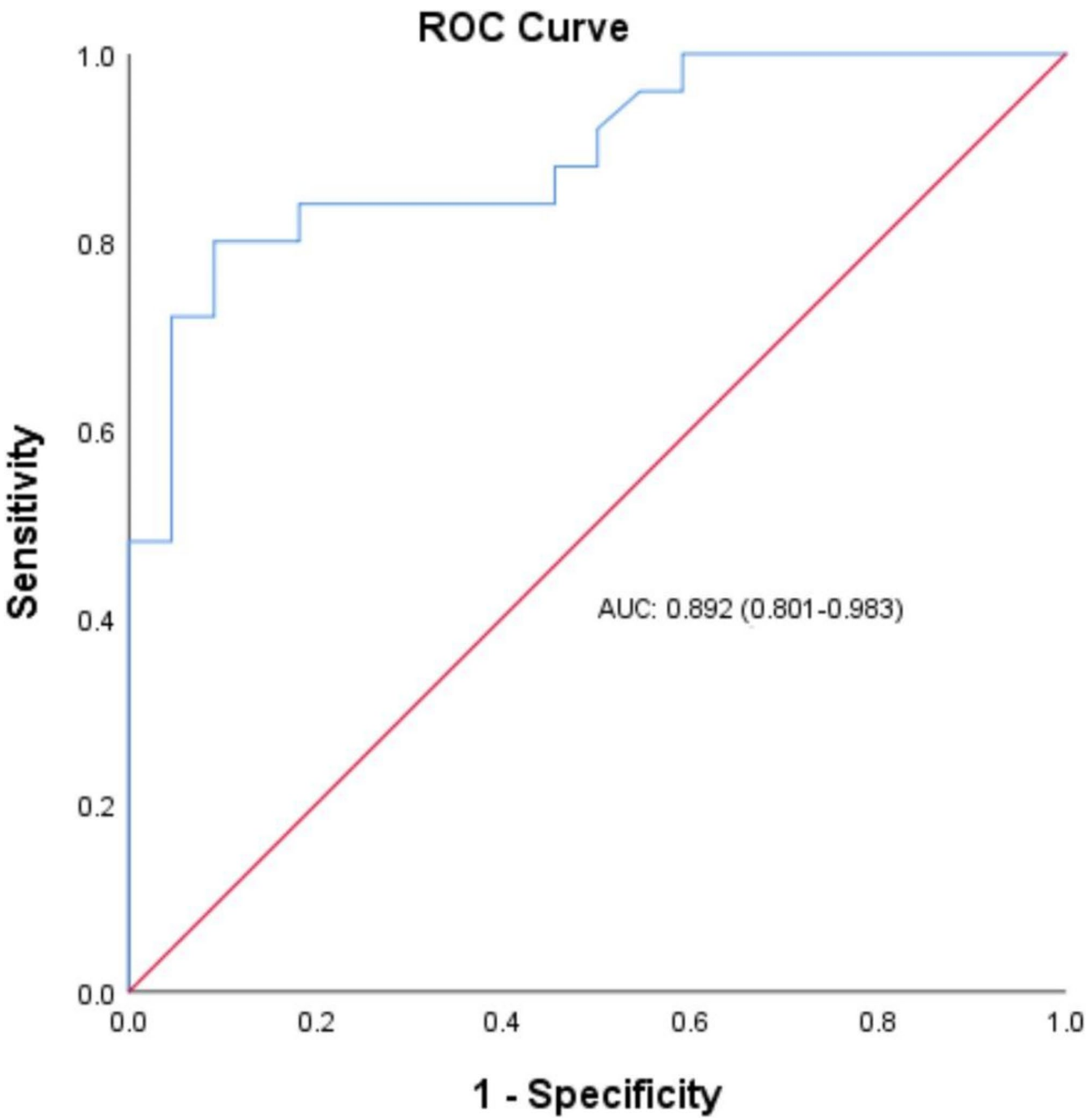

Fig. 3 Receiver operating characteristic curves (ROC) for the score model for predicting invasive therapy
The vertical axis represented sensitivity, and the horizontal axis represented 1-specificity. Different true positive rates and false positive rates corresponded to each point on the ROC curve. The AUC of ROC were 0.892 (0.801–0.983)

drainage, and PD performed prior to surgery can significantly reduce the occurrence of severe postoperative intra-abdominal septic complications [17]. Since immediate surgery will usually result in laparotomy and stoma or a high anastomotic leak rate if performing primary anastomosis, immediate surgical intervention should usually be reserved only for patients with generalized peritonitis, septic shock or clinical deterioration [18].

Antibiotics are fundamental in the treatment course and should cover gram-negative bacteria and anaerobes. In one study, the most frequently isolated pathogen was the gram-negative bacterium E.coli belonging to the family of Enterobacterales [19]. Therefore, a combination of fluoroquinolones or third-generation cephalosporin and metronidazole is appropriate [20]. And it seemed that patients receiving intravenous antibiotics demonstrated a decreased risk for nonsurgical readmission than patients receiving oral antibiotics [21]. The appropriate duration of antibiotic therapy is unclear, with the shortest term being 2–4 weeks. However, antibiotics are not enough. In 2015, Dotson et al. published a single-center series on young patients with CD, and in his study, 60% of patients with IAA required surgery. In addition, at the 1-year follow-up, 67% of patients who were managed with initial nonoperative management required surgical intervention [22]. When choosing conservative medical treatment, we recommend using strict indications and close clinical observation. Meanwhile, the long-term prognosis is dependent on the medical medications especially after the disappearance of abdominal abscess in luminal fistula CD patients, including biological agents and immunosuppressants [23]. Some studies have pointed out that the use of biotherapies could avoid surgery and long-term abscess recurrence [24].

This retrospective study was from a single tertiary medical center and had some limitations. First, treatment decision-making was uncontrolled. As this was not an interventional study, the choice of treatment type was subject to patient preference,, which could introduce bias. Some patients with a larger diameter of abscess might refuse surgery because of fear of complications or economic status, causing lingering of the disease. Second, the sample size was limited. However, we designed the follow-up period to be as long as possible to observe the final outcome of treatment options on CD-related IAA. Third, as a long-term follow-up study, the trend of medications might be changed, especially the increasing usage of biologics and immunosuppressants for CD patients in our center, which have been indicated to lower the incidence of surgery in other centers [25]. These factors were not taken into account in this retrospective study. Last, 42 patients included in our study received CT enterography and 6 patients received contrast-enhanced CT scans. Although it was reported that CTE could better evaluate the wall of small bowel [26], the type of examination did not affect the results when only analyzing the 42 patients with CT enterography in our study. A prospective, multicenter randomized trial would be beneficial to define the best technique for assessment and optimal treatment for CD-IAA.

When IAA occurs in CD patients, a careful and comprehensive evaluation of IAA should be conducted. In particular, an experienced radiologist should be asked to read the enhanced CT data to obtain the type of IAA and other information to make a better plan for treatment strategy. Our study highlighted that nonperienteric abscesses, including complicated mural abscesses, retroperitoneal abscesses and abscesses invading adjacent organs, often require invasive treatment, such as percutaneous drainage or surgery. The larger the maximum diameter of the abscess and the wider the width of the sinus, the higher the probability of invasive treatment. We also built a score model that could be a useful and convenient tool in clinical practice to help make medical decisions in CD-related IAA patients.

Conclusions

More than half of CD-related IAA patients needed invasive therapy within 5-year follow-up. The CT features including nonperienteric abscess, larger maximum abscess diameter and width of sinus suggested a more aggressive approach to invasive treatment.

Abbreviations

AUC	Area under the curve
BMI	Body mass index
C. Diff	Clostridium difficile
CD	Crohn's disease
CMV	Cytomegalovirus
CT	Computerized tomography
ESR	Erythrocyte sedimentation rate
hsCRP	Hypersensitive C reactive protein
IAA	Intra-abdominal abscess
IQR	Interquartile range
ROC	Receiver operating characteristic

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Author contributions

Yinghao Sun was involved in study design, data collection and analysis, and writing the manuscript. Wei Liu was involved in study design, reviewing all CT scans and analysis. Ye Ma was involved in statistical analysis. Hong Yang, Yue Li and Bei Tan participated in patient recruitment and clinical profile revision. Ji Li and Jiaming Qian designed and supervised the study, analyzed the data, and critically revised the manuscript. All authors have approved the final manuscript.

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Data availability

The data that support the findings of this study are available on reasonable request from the author(E -mail: liji0235@pumch.cn). The imaging data were not publicly available because of restrictions (containing information that could compromise the privacy of research participants).

Declarations

Ethics approval and consent to participate

This study was approved by the Ethical Committee of Peking Union Medical College Hospital (PUMCH) (No. S-K1709). Informed consent to participate was obtained from all of the participants in the study. We have two participants who was 14 years old when attending this study and informed consent was obtained from their mothers. Other participants were over 16 years old and informed consent was obtained from themselves.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

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