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RESEARCH

Direction of perforation predicts the failure of non-operative management in patients with acute diverticulitis

I. Iesalnieks[1] · M. Beyer[2] · A. Agha[3] · D. Hofmann[4] · Maximilian Sohn[5]

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Abstract

Aim To identify factors predicting the failure of non-operative treatment in acute complicated colonic diverticulitis.

Material and methods Consecutive patients hospitalized for non-operative treatment of acute complicated diverticulitis of the sigmoid colon between 2009 and 2015 were included in this retrospective analysis. Complicated disease was defined as the presence of extraluminal air or fluid collection within a computed tomography (CT) scan. The primary endpoint of the study was the need for emergent sigmoidectomy. The direction of perforation was assessed by CT scan and divided into 2 main groups: perforation towards the small bowel and perforation in other directions (abdominal wall, pelvic wall, retroperitoneum, urogenital organs).

Results A total of 140 patients were included. Of these patients, 25 patients did not respond to non-operative treatment and underwent rescue surgery (18%). CT revealed perforations towards the small bowel in 28 patients, 19 of whom did not respond to non-operative treatment (68%); in contrast, 6 of 112 (5%) patients with perforation in other directions experienced treatment failure. By multivariate analysis, perforation towards the small bowel (hazard ratio 75.0; 95% CI, 13.7–409.7, $p<0.001$) was associated with a significantly increased risk for a failure of non-operative management. The only other risk factor was the presence of an intra-abdominal abscess. Diverticular perforation towards the small bowel is associated with a very high risk for emergency sigmoidectomy due to failed non-operative treatment.

Keywords Acute sigmoid diverticulitis · Non-operative treatment · Emergency sigmoidectomy

Introduction

The majority of patients suffering from acute complicated diverticulitis of the left colon can be successfully treated non-operatively. Thus, emergent surgery, which might be associated with increased morbidity and stoma formation rates, can be avoided in most cases. Accordingly, German national guidelines recommend initial non-operative treatment for both acute uncomplicated and complicated disease (CD) [1, 2]. Similarly, the majority of international guidelines propose primary non-operative management in all patients with acute diverticular disease except those presenting with generalized peritonitis [3–6]. Most patients recover uneventfully after conservative treatment; however, a minority do not respond to medical treatment and undergo emergent surgery. Any delay in identifying patients not benefiting from non-operative management might be associated with increased morbidity. Some previous studies identified distant extraluminal air [7],and a particular abscess localisation [8–11] to be factors which were associated with failure

✉ Maximilian Sohn
Maximilian.sohn@isarklinikum.de

1 Klinik für Allgemein-, Viszeral- und Gefäßchirurgie, Evangelisches Krankenhaus Köln Kalk, Köln, Germany

2 Diagnostische und interventionelle Radiologie, Klinikum Mutterhaus der Borromäerinnen, Trier, Germany

3 Klinik für Allgemein-, Viszeral-, Endokrine- und minimalinvasive Chirurgie, München Klinik Bogenhausen, Germany

4 Klinik für Gastroenterologie, Hepatologie und gastroenterologische Onkologie, Isarklinikum München, Germany

5 Klinik für Allgemein-, Viszeral- und minimalinvasive Chirurgie, Isarklinikum München, Germany

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of primary non-operative treatment, thus indirectly pointing to the importance of perforation site as an independent risk factor. However, to our knowledge, no study exists to analyse the impact of the localization and direction of perforation in *all* patients with complicated diverticular disease and not only in those with abscesses or distant air. This retrospective study was conducted to determine the factors associated with the unsuccessful conservative treatment of acute complicated diverticulitis. Special attention was given to potential predictors in the initial CT scan.

Materials and methods

Consecutive patients hospitalized in the “München Klinik Bogenhausen” from October 2009 to November 2015 for non-operative treatment of acute complicated diverticulitis of the left-sided colon were included in the analysis. The exclusion criteria were generalized peritonitis requiring immediate emergency surgery, uncomplicated disease, diverticular bleeding, unavailable CT scan, and presence of concomitant colon cancer. The primary endpoint of the study was emergent sigmoid resection for failed non-operative management (“rescue surgery”). The decision to perform emergency surgery was made by surgeons in charge and it was based on dynamics in patients`overall condition, results of abdominal palpation, changes in CRP-level and leukocyte count and– in some cases– repeat CT scan.

Non-operative treatment

Non-operative treatment consisted of intravenous antibiotics (combinations of piperacilline and tazobactam, cefuroxime and metronidazole or ciprofloxacin and metronidazole) and analgesics. If technically feasible, abscesses were drained percutaneously, and the drainage was removed after the discharge had ceased. Oral food intake was stopped, and parenteral electrolyte solutions were only provided in cases of nausea or vomiting. In cases of severe constipation, oral laxatives or small volume enemas were given.

Definitions

“Complicated diverticular disease” was defined as the presence of extraluminal air or fluid collection/abscess on the CT scan [9, 12]. “Damage control surgery” (DCS) included two operations: sigmoidectomy with blind closure of the oral and aboral colon, and application of an abdominal negative pressure dressing in the first surgery. 48 h later, definitive reconstruction (primary anastomosis with or without ileostomy or Hartmann’s procedure) was performed within a second look surgery [13].

Rescue surgery

Rescue surgery was defined as unplanned emergency surgery in patients, who were initially scheduled for non-operative treatment due to signs of peritonitis and/or sepsis.

Radiological assessment

CT was routinely performed with a water-soluble oral and rectal contrast agent in addition to an i.v. contrast agent. The presence of extraluminal air and/or fluid collection was the study inclusion criterion. The direction of perforation was detected using four radiological signs: (1) location of extraluminal air and/or fluid collection, (2) location of the thickened colonic wall, (3) presence of thickening and contrast enhancement in the adjacent structures: small bowel, abdominal wall, pelvic wall, urogenital organs or retroperitoneum, and (4) extravasation site of the rectally applied contrast enema. Two main groups were compared: the first group consisted of patients with perforation towards the small bowel (Fig. 1), and the second group included patients with perforation in any other direction (i.e., towards the urogenital organs, abdominal wall, pelvic wall or retroperitoneum) but not towards the small bowel (Fig. 2). Since many patients had perforations including more than one structure (e.g., small bowel AND abdominal wall), all cases were divided according to the presence or absence of a contact between perforation site and the small bowel.

Furthermore, the level of perforation was differentiated between the pelvic and abdominal. For this purpose, a line between the promontorium and pubic symphysis was drawn. Perforations below that level were defined as pelvic, and perforations above that level as abdominal.

All CT scans were assessed by a radiologist (B.M.D.) specialized in intestinal imaging blinded to the treatment outcome. Additionally, two colorectal surgeons (S.M. and I.I.) reviewed all CT scans independently. Assessments of all investigators were compared to each other. In case of disagreement, CT scans were assessed and discussed by all three investigators together to achieve a consensus.

Clinical outcome parameters

A retrospective chart review of all included patients was conducted. The following variables were recorded: patient demographics, history of diverticular disease, intake of steroids or non-steroidal antirheumatics (NSARs), leukocyte count, glomerular filtration rate, fever at admission, C-reactive protein (CRP) level at the time of admission, difference between the first and second assessment of CRP level, presence and diameter of abscess, direction of perforation on CT scan, level of perforation on CT scan, and

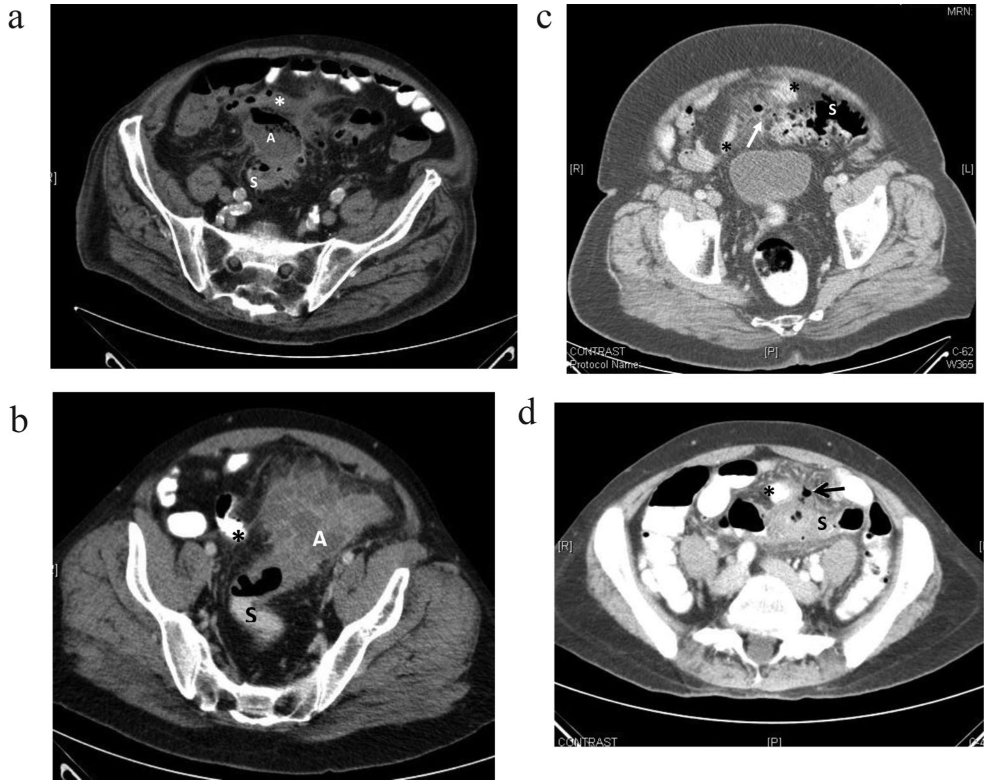

Fig. 1 **a-d.** CT scans of patients with a diverticular perforation directed towards the small bowel who did not respond to non-operative treatment and underwent rescue sigmoidectomy. asterisk– small bowel, arrow– site of perforation, A– abscess, S-sigmoid

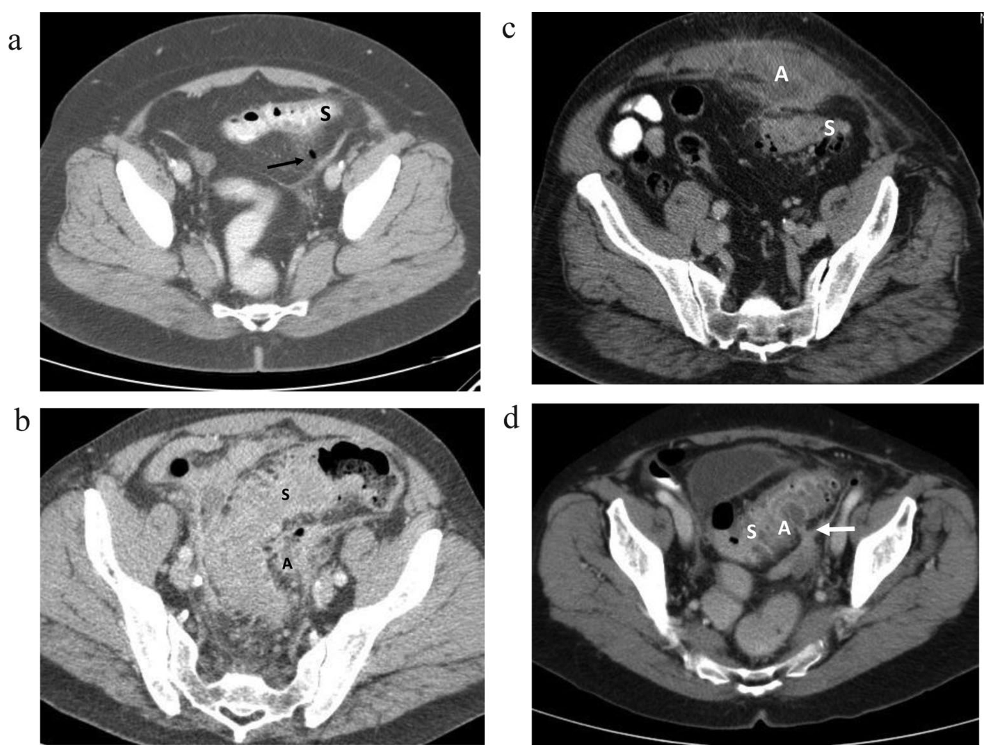

Fig. 2 **a-d**. CT scans of patients with diverticular perforations directed towards structures other than the small bowel. **a**– perforation towards the retroperitoneum, **b**– perforation with an abscess towards the pelvic wall, **c**– perforation with a large abscess directed towards the abdominal wall and bladder (not seen in picture), **d** - perforation with an abscess towards the lateral pelvic wall. S– sigmoid, A– abscess, arrow– site of perforation

postoperative morbidity. Follow-up information was also collected, including data regarding elective sigmoid resection after successful non-operative treatment and stoma reversal, if needed.

Statistical analysis

Descriptive statistics were calculated for each variable measured and are reported as means, medians or proportions. The Mann-Whitney U test was used for non-normally distributed continuous variables. In the case of normally distributed continuous variables, Student's t-test was used. Comparisons of categorial variables between patient groups were performed using Fisher's exact test. Statistical analysis was performed with SPSS software version 20.0 (IBM, Chicago, IL, United States). Factors identified by the univariate analysis to be associated with an increased risk for non-operative treatment failure at a significance level of $p < 0.05$ were included in the multivariate logistic regression analysis using backward elimination. The results were considered statistically significant at the two-sided p-level of < 0.05.

Ethics approval and informed consent

The study protocol was in accordance with the declarations of Helsinki and approved by the local ethical board (http://ethikkommission.blaek.de). Report identification number: 2016−143. Due to the retrospective character of the analysis and the lack of any parameters which potentially lead to an identification of individuals, informed consent was waived.

Results

Between October 2009 and November 2015, 140 patients (77 M: 63 F) were admitted to the hospital for non-operative treatment of acute complicated colonic diverticulitis. The mean age at the time of hospitalization was 60.5 years (range, 27–91 years). Of these patients, 25 patients ("non-responders", 18%) underwent rescue surgery after they failed initial non-operative management.

Only two of 25 non-responders had a history of in-hospital treatment for diverticular disease (8%). In contrast, 36 out of 116 patients who responded to the initial conservative treatment had reported previous episodes of left-sided diverticulitis (31%, $p = 0.023$). The leukocyte count at the time of hospital admission was significantly higher in non-responders than in responders (14.9/nl vs. 11.5/nl, $p = 0.019$). The initial CRP level did not differ significantly between the two groups (156.8 mg/l in non-responders vs. 114.9 mg/l in responders, $p = 0.066$). Additionally, the difference in CRP levels between the first and second assessments was similar between the two groups (mean increase by +10.4 mg/l in responders and by +29.9 mg/l in non-responders, $p = 0.34$).

A CT scan was performed at the initial presentation or on the next day for all patients. A second CT scan was performed due to worsening symptoms or an increase in CRP level or leukocyte count for 9 of 25 non-responders (36%) and 15 of 115 responders (13%, $p = 0.015$). The first or second CT scan revealed an intra-abdominal abscess in 19 of 25 non-responders (76%) and 38 of 115 responders (33%, $p < 0.001$). The mean size of the abscess was 4.5 cm (range, 1–12 cm), without a significant difference between groups. A CT-guided abscess drain was placed in 15 of 57 patients with an intra-abdominal abscess (26%), without a significant difference between groups.

On CT, diverticular perforation towards the small bowel was found in 28 patients (20%, Fig. 1). Nineteen of those 28 patients did not respond to the initial non-operative treatment and had to undergo emergent rescue surgery (68%). Eleven of these 19 patients were found to have diffuse peritonitis during surgery. A total of 112 patients had perforations directed to structures other than the small bowel– most frequently to the lateral abdominal or pelvic wall and retroperitoneum (Fig. 2). Six of these patients did not respond to conservative treatment (5%, $p < 0.001$). None of the six patients were found to have peritonitis during emergency surgery. Five had abscesses, of which two were feculent. One patient underwent surgery because of a colonic obstruction.

Table 1 depicts the results of the univariate analysis for factors predicting the failure of non-operative management. In multivariate analysis (Table 2), the presence of an intra-abdominal abscess and diverticular perforation towards the small bowel on CT were associated with a statistically significantly increased risk for non-operative management failure. The direction of perforation was associated with the highest risk of treatment failure (hazard ratio 75.0, 95% CI 13.7–409.7, $p < 0.001$). Of the 15 patients with perforation towards the small bowel and a concomitant abscess (Fig. 1a and b), fourteen (93%) did not respond to conservative treatment (Table 3).

Table 4 demonstrates the intraoperative findings and postoperative outcomes of 25 non-responders to conservative treatment. The median interval between hospital admission and rescue surgery in non-responders was 4 days (range, 1 to 17 days). Intraoperatively, 21 of 25 patients (83%) presented with peritonitis and/or abscess, and five were feculent. Six patients underwent Hartmann's procedure, and 6 underwent ileostomy in addition to primary anastomosis. The postoperative morbidity rate was 33% ($n = 8$), there was one anastomotic leakage treated by Hartmann's procedure, and no deaths occurred. The interval between hospital admission and rescue surgery in non-responders was significantly prolonged when CT-guided abscess drainage had been attempted (13 days vs. 4 days, $p = 0.048$).

After successful non-operative treatment, an additional 62 of 115 patients underwent elective sigmoidectomy. The only factor that was associated with an increased probability of undergoing elective surgery was a history of diverticulitis prior to current hospital admission (72% vs. 46%, $p = 0.009$). There was no correlation between the direction

Table 1 Univariate analysis of factors associated with an increased risk for the failure of non-surgical treatment of complicated diverticular disease

Variable	Condition	Proportion of patients who did not respond to non-operative treatment (%)	*p*
Age > 65	Yes	7 of 55 (13%)	0.26
	No	18 of 85 (21%)	
Sex	Male	16 of 77 (21%)	0.38
	Female	9 of 63 (14%)	
Use of NSAR	Yes	1 of 22 (4%)	0.17
	No	24 of 117 (20%)	
Fever at time of admission	Yes	4 of 9 (44%)	0.053
	No	18 of 114 (16%)	
GFR < 60 at time of admission	Yes	9 of 29 (31%)	0.055
	No	16 of 111 (14%)	
Leucocyte count at admission	> 20/nl	6 of 12 (50%)	0.008
	< 20/nl	19 of 127 (15%)	
Increase in CRP level between the 1st and 2nd assessment	Yes	13 of 64 (20%)	0.66
	No	12 of 73 (16%)	
CRP level > 200 mg/l at admission	Yes	7 of 25 (28%)	0.16
	No	18 of 114 (16%)	
History of diverticular disease	Yes	2 of 38 (5%)	0.023
	No	23 of 102 (22%)	
History of malignancy	Yes	2 of 6 (33%)	0.29
	No	22 of 134 (16%)	
Evidence of intra-abdominal abscess	Yes	19 of 57 (33%)	< 0.001
	No	6 of 83 (7%)	
CT-guided abscess drainage	Yes	4 of 15 (27%)	0.75
	No	15 of 43 (35%)	
Additional CT scan performed because of clinical impairment	Yes	9 of 24 (37%)	0.015
	No	16 of 116 (14%)	
Diverticular perforation towards the small bowel	Yes	19 of 28 (68%)	< 0.001
	No	6 of 112 (5%)	
Level of perforation	Abdominal	21 of 109 (19%)	0.60
	Pelvic	4 of 31 (13%)	

GFR - glomerular filtration rate, CRP - C-reactive protein, NSAR - non-steroidal antirheumatic, CT - computed tomography

Table 3 Failure rate according to the direction of perforation and presence of abscess in patients with acute left-sided diverticulitis

	Abscess	No abscess
Perforation towards the small bowel	93% (14 of 15)	38.5% (5 of 13)
Perforation towards other structures	12% (5 of 42)	1.4% (1 of 70)

Table 2 Multivariate analysis of factors associated with an increased risk for undergoing emergent surgery for failed medical treatment of acute complicated diverticular disease

Variable	Hazard ratio (HR)	95% Confidence interval	*p*
No history of diverticular disease	7.2	0.85–60.6	0.071
Intra-abdominal abscess	17.7	3.1–100.2	0.001
Diverticular perforation towards the small bowel on CT	75.0	13.7–409.7	< 0.001
Leukocyte count > 20/nl at hospital admission	3.5	0.60–20.26	0.16
Need for second CT scan	2.3	0.53–9.81	0.27

Table 4 Intraoperative findings and perioperative outcomes of patients undergoing rescue surgery for failed non-operative treatment of sigmoid diverticulitis ($n = 25$)

Findings	*N* (%)
Intraoperative findings*	11 (44%)
- peritonitis	17 (68%)
- abscess	14 (56%)
- inflammatory mass	1 (4%)
- colonic obstruction	
Operative procedures	5 (20%)
- Hartmann's procedure	5 (20%)
- primary anastomosis with ileostomy	8 (32%)
- primary anastomosis without ileostomy	6 (24%)
- damage control surgery	5 (20%)
* primary anastomosis without ileostomy	1 (4%)
* Hartmann's procedure	1 (4%)
- transversal colostomy	
Laparoscopy	10 (40%)
- conversion to open surgery	2
Postoperative complications*	8 (32%)
- anastomotic leakage	1
- bleeding	2
- wound infections	3
- cardiac decompensation	1
- ostomy ischaemia	1
- small bowel perforation	1
Length of postoperative stay, mean days (range)	18.0 (6–67)
Stoma reversal during the follow-up period	10 of 13

* - more than one finding/complication in one patient was possible

of perforation and elective surgery after successful non-operative treatment of acute diverticulitis.

Discussion

Most patients suffering from acute complicated diverticulitis of the left colon can be successfully treated non-operatively. After patients` recovery, decisions on further management– observational vs. surgical– can be made based on the estimated risk of recurrent flares or persistent symptoms and patient preferences. Currently, elective surgery is recommended only in patients who had had larger abscesses

(> 3–5 cm) since the risk of unfavourable outcome might be increases in that particular population [1–6]. Unfortunately, 10–30% of patients [9, 10, 14–16] do not respond to conservative treatment and require emergent sigmoidectomy. During the time between hospital admission and rescue surgery, the patients' condition worsens, and progressive disease develops, which is characterized by intraoperative findings such as abscesses, inflammatory masses, severe colonic phlegmon and peritonitis, leading to increased postoperative morbidity, mortality and an increased ostomy rate [14, 17, 18]. Surgery was delayed by a median of 4 days (range, 1 to 17) in our study in patients who necessitated rescue surgery; 44% of non-responders received an ostomy, and 33% of patients developed postoperative complications. The ostomy was not closed during the follow-up period in 3 non-responders (12%). Thus, the recognition of the factors that are associated with an increased risk of failed non-operative treatment should help to provide surgical treatment earlier to appropriate patients.

Numerous recent studies have sought to identify the predictors of failed conservative treatment. The presence of an intra-abdominal abscess has been found to be associated with an increased risk for emergent surgery in many studies, including ours. Some 20 to 30% [8] of patients with abscesses fail conservative treatment. Severe comorbidity and feculent discharge from the drainage but not abscess size seem to be associated with treatment failure. However, abscesses are a very common finding in patients with acute diverticulitis; therefore, this feature is not specific enough to decide whether to proceed with surgery, and more factors are needed to predict treatment failure. The presence of distant intraperitoneal air [10, 15, 16] has been found to be associated with a high risk of non-operative treatment failure. However, a significant proportion of patients presenting with distant free air also have generalized peritonitis and are treated by immediate surgery [14, 16, 18]. These patients were beyond the scope of the present study.

Some authors have suggested that the location of the perforation might have an impact on treatment outcome. Pelvic abscesses or fluid were found to be associated with a worse prognosis than paracolic perforations in some studies [9–11]; however, other studies did not confirm these results. Additionally, in our study, similar proportions of patients with pelvic and abdominal perforations responded to non-operative treatment.

In a significant proportion of patients undergoing rescue sigmoidectomy for failed non-operative treatment, unsuspected peritonitis is found during surgery (44% in our study). This leads to the suggestion that in some patients, diverticular perforations are not contained by the surrounding structures, leading to worsening clinical conditions and the development of sepsis. In their recent systemic review, Chua et al. [14] named this particular condition a "persistent perforation". We suspected that diverticular perforations might be better sealed by immobile structures such as the abdominal and pelvic wall, bladder and retroperitoneum than by the mobile small bowel. Thus, perforations directed towards the small bowel were expected to be associated with an increased risk of peritonitis and poorly controlled abscesses ("persistent perforation"). Indeed, our study demonstrated that perforation directed towards the small bowel was strongly associated with failed non-operative treatment. Nineteen out of 28 patients with this type of perforation underwent rescue surgery. Seventeen of these 19 patients were revealed to have an abscess or peritonitis at the time of surgery.

Currently, there is still a lack of evidence that percutaneous abscess drainage (PAD) can diminish the risk of treatment failure [8]. In fact, Elagili et al. [17] demonstrated similar success rates between PAD and antibiotics alone, even in patients with abscesses larger than 3 cm, in a study including 146 patients. However, patients who failed antibiotic treatment had less severe postoperative complications according to the Clavien-Dindo classification than patients who failed PAD. All 3 postoperative deaths occurred in the PAD group. Additionally, there was a significant delay in surgery in the PAD group. Our study also demonstrated a significantly prolonged interval between hospital admission and rescue sigmoidectomy in patients treated with PAD (13 vs. 4 days), although this delay did not lead to increased postoperative morbidity or an increased ostomy rate in a relatively small group of patients. In our study, the risk of treatment failure was highest (93%, Table 3; Fig. 1a and b) when patients presented with an abscess *and* small bowel involvement. In this particular group, the indication for PAD should be weighed very carefully against the risk of delaying surgery in case of treatment failure.

Comorbidities may be expected to be a significant predictor of failed non-operative treatment [14]. Unfortunately, any comorbidity score or index was difficult to obtain in a retrospective manner; thus, we could not draw any definitive conclusions on this very important matter. A significant comorbidity might be an important predictor of mortality and adverse outcomes of surgery but not necessarily of a failure to respond to non-operative treatment for diverticulitis. However, few studies have demonstrated an increased risk of percutaneous abscess drainage failure in elderly patients with comorbidities [17, 19].

Limitations

Although the direction of perforation is easy to classify in most cases (Figs. 1 and 2), it may be occasionally difficult to determine (Fig. 3). Additionally, abscesses found on CT

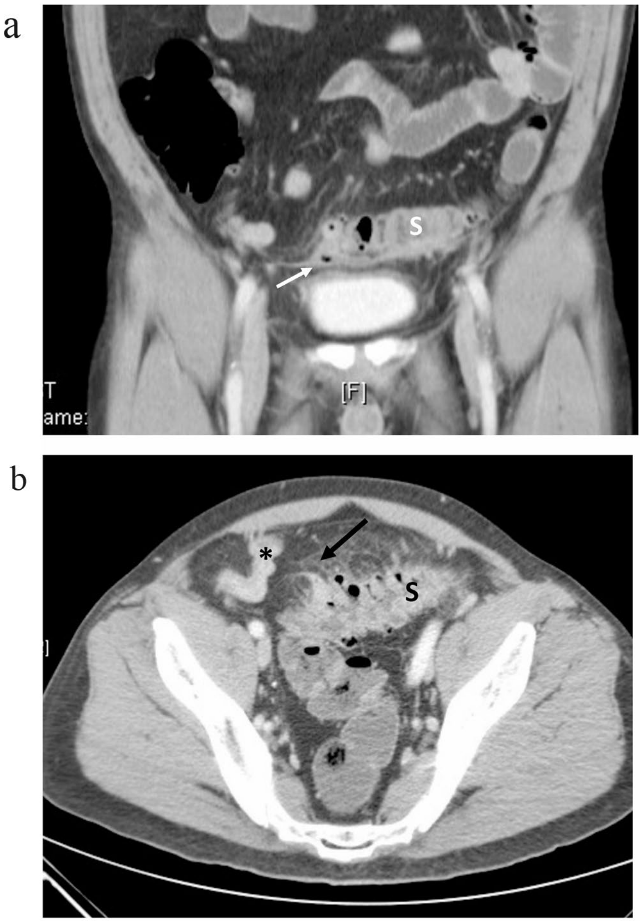

Fig. 3 a-b. A case of acute complicated diverticulitis in which the direction of perforation was difficult to determine. **a**– small extraluminal air bubble directed towards the bladder in this projection, **b**– the same patient. Contrast enhancement of the pericolic fat seems to be directed towards the small bowel. This patient was classified as having a perforation directed towards the small bowel. She responded to conservative treatment. S– sigmoid, arrow– site of perforation, asterisk– small bowel

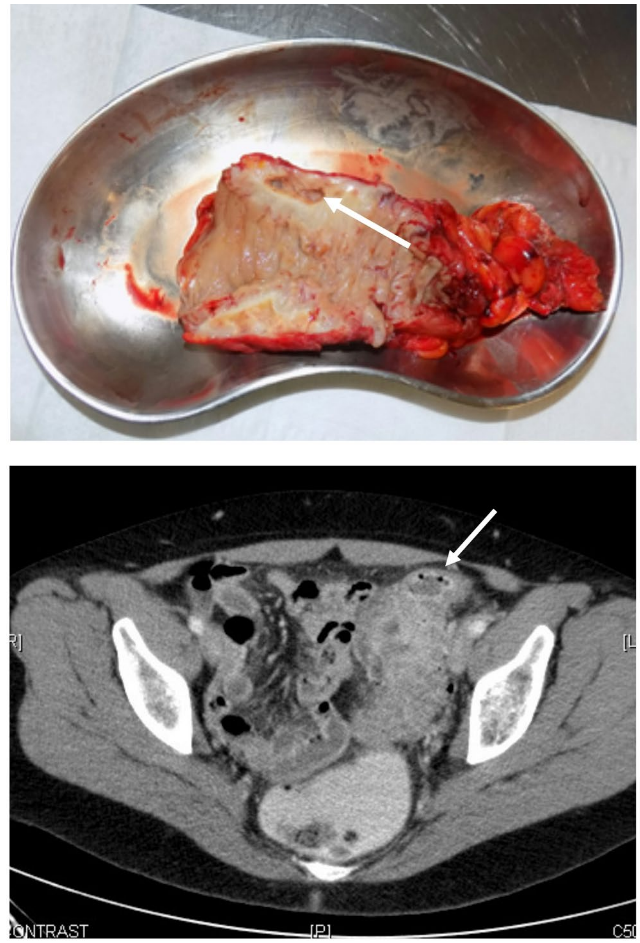

Fig. 4 Patient with an intramural abscess (arrow) that was found to have no contact with the structures surrounding the sigmoid colon during surgery

scans could actually be located intramurally without any contact with the surrounding structures (Fig. 4) - these cases might be difficult to classify correctly.

The retrospective nature limits the quality of the present study. Moreover, the number of patients who did not respond to non-operative treatment was low. Therefore, the results could potentially be biased. A larger and prospectively designed observational study could eventually clarify this matter.

Conclusion

Diverticular perforation directed towards the small bowel is associated with poor containment of the perforation site and a considerably increased risk of non-operative treatment failure because of poorly controlled abscesses and peritonitis. This type of perforation warrants very close clinical attention to avoid significant delays in surgery, which can lead to further morbidity and an increased ostomy rate.

Author contributions I.I. wrote and revised the manuscript, performed the statistical analysis, and reviewed radiological findingsM.B. analyzed all radiologic findings, constructed figures, and reviewed the manuscriptA.A. supervised the project, reviewed the manuscript, constructed tablesD.H. did chart review, constructed tables, and reviewed the manuscript M.S. wrote and reviewed the manuscript, constructed tables, and reviewed all radiological findings.

Data availability Data are available from the corresponding author on reasonable request.

Declarations

Competing interests The authors declare no competing interests.

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