Retrospective Cohort Study

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Management of acute diverticulitis with pericolic free gas (ADIFAS): an international multicenter observational study

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Background: There are no specific recommendations regarding the optimal management of this group of patients. The World Society of Emergency Surgery suggested a nonoperative strategy with antibiotic therapy, but this was a weak recommendation. This study aims to identify the optimal management of patients with acute diverticulitis (AD) presenting with pericolic free air with or without pericolic fluid.
Methods: A multicenter, prospective, international study of patients diagnosed with AD and pericolic-free air with or without pericolic free fluid at a computed tomography (CT) scan between May 2020 and June 2021 was included. Patients were excluded if they had intra-abdominal distant free air, an abscess, generalized peritonitis, or less than a 1-year follow-up. The primary outcome was the rate of failure of nonoperative management within the index admission. Secondary outcomes included the rate of failure of nonoperative management within the first year and risk factors for failure.
Results: A total of 810 patients were recruited across 69 European and South American centers; 744 patients (92%) were treated nonoperatively, and 66 (8%) underwent immediate surgery. Baseline characteristics were similar between groups. Hinchey II–IV on diagnostic imaging was the only independent risk factor for surgical intervention during index admission (odds ratios: 12.5, 95% CI: 2.4–64, $P=0.003$). Among patients treated nonoperatively, at index admission, 697 (94%) patients were discharged without any complications, 35 (4.7%) required emergency surgery, and 12 (1.6%) percutaneous drainage. Free pericolic fluid on CT scan was associated with a higher risk of failure of nonoperative management (odds ratios: 4.9, 95% CI: 1.2–19.9, $P=0.023$), with 88% of success compared to 96% without free fluid ($P<0.001$). The rate of treatment failure with nonoperative management during the first year of follow-up was 16.5%.
Conclusion: Patients with AD presenting with pericolic free gas can be successfully managed nonoperatively in the vast majority of cases. Patients with both free pericolic gas and free pericolic fluid on a CT scan are at a higher risk of failing nonoperative management and require closer observation.

Keywords: complication, diverticular disease, diverticulitis, diverticulosis, nonoperative management

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Introduction

Diverticular disease of the colon is a common disease that encompasses diverticulosis and diverticulitis. Most patients with diverticulosis remain asymptomatic; however, ~15–20% will develop acute diverticulitis (AD)[1]. AD is an inflammatory condition affecting at least one colonic diverticula, often associated with pericolic inflammation and/or perforation[2]. The extent of the perforation determines the clinical severity, and several clinical guidelines provide guidance and recommendations on the management of AD based on clinical severity.

Computed tomography (CT) represents the gold standard in the diagnosis of diverticulitis. Its sensitivity ranges from 85 to 97%[3,4] and it is highly accurate in identifying colonic perforation, which impacts treatment recommendations. The severity of diverticulitis is usually graded using the modified Hinchey's classification on CT imaging. It distinguishes four Hinchey stages of acute complicated diverticulitis, but its accuracy is poor for differentiating these stages[5,6] and is the main limitation of its clinical usefulness. Another important drawback of Hinchey's classification is that some patients do not fit in any of the groups, such as patients with distant retroperitoneal air or pericolic air, who represent ~15% of patients traditionally (mis)classified as Hinchey Ia[7,8]. Several modifications and alternative classifications have been proposed, and new subcategories have been added that take various radiological findings into account[9].

The World Society of Emergency Surgery (WSES) developed a new classification[10], dividing AD into two groups: uncomplicated (stage 0) and complicated. The latter includes stages 1a–4, with 1a ascribed to the presence of pericolic air bubbles or a small amount of pericolic fluid without abscess (within 5 cm from the inflamed bowel segment) (Fig. 1). Based on this new classification, the WSES updated its guidelines on the management of AD in 2020[11]. However, there were no definitive recommendations concerning patients classified as stage 1a (with pericolic gas but no distant air or abscess in the abdomen). They suggested a nonoperative strategy with antibiotic therapy, but this was a weak recommendation based on low-quality evidence (2C)[11] that requires further investigation. More recently, a systematic review that included more than 400 cases of AD with isolated pericolic air stage 1A suggested that conservative management is safe, but the authors noted that the quality of the studies included was poor with heterogeneous study populations, and all but one lacked a comparison cohort[12]. Therefore, the management of AD with pericolic gas and no clinical signs of sepsis varies widely and mostly depends on the surgeons' preferences.

The current study aimed to identify the optimal management for stage 1a AD and identify predictors of failure of nonoperative management.

Methods

The 'Management of Acute Diverticulitis with pericolic Free gas (ADiFas)' study was an international, multicenter, observational, prospective study performed on consecutive patients diagnosed with AD with pericolic free gas with or without a small amount of pericolic fluid without abscess (within 5 cm from the inflamed bowel segment) in the emergency setting (Fig. 2). The study was designed and presented according to the STROCSS, Supplemental Digital Content 1, http://links.lww.com/JS9/A37 criteria[13], in collaboration with the 'European Association of Endoscopic Surgery (EAES) Research Talent Academy'. The study was conducted between 20 May 2020 and 1 June 2021.

> **HIGHLIGHTS**
>
> - Patients presenting with acute diverticulitis and pericolic free gas can be successfully and safely managed conservatively in the majority of cases.
> - The finding of free fluid in addition to pericolic free gas on the computed tomography scan may indicate a higher risk of failure of nonoperative management.
> - The benefits of nonoperative management in this particular population remain stable at 1-year follow-up.

Inclusion and exclusion criteria

Patients were deemed eligible for study participation if they were older than 18 years old and if they presented with AD confirmed at CT scan with findings of pericolic free air with or without pericolic free fluid, located less than 5 cm from the affected segment of colon.

Exclusion criteria included: intra-abdominal distant free air (air > 5 cm from the affected segment); intra-abdominal abscess; generalized peritonitis; or less than 1-year follow-up.

A quality assurance process was implemented where all CT scans were independently reviewed by two reviewers to confirm the diagnosis. Cases that met the inclusion criteria after the reviewers' quality assurance but were misclassified as Hinchey greater than or equal to 2 at the site read were kept for further analysis.

Study aims

The primary objective was to analyze the rate of treatment failure in nonoperative management within the index admission. Secondary aims included determining the rate of failure of nonoperative management within the first year of follow-up and identifying risk factors for failure of nonoperative management.

Definitions and data of interest

In line with previous published studies, pericolic air or the presence of free fluid was defined as air with or without fluid located less than 5 cm from the affected segment of colon[14–19]. Extraluminal air greater than 5 cm from the affected segment was considered to be distant air. The study population was divided into two groups based on the initial management: nonoperative versus operative management.

Uncomplicated
0 Diverticula, thickening of the wall, increased density of the pericolic fat
Complicated
1A Pericolic air bubbles or small amount of pericolic fluid without abscess (within 5 cm from the inflamed bowel segment)
1B Abscess ≤ 4 cm
2A Abscess > 4 cm
2B Distant gas (> 5 cm from the inflamed bowel segment)
3 Diffuse fluid without distant free gas
4 Diffuse fluid with distant free gas

Figure 1. World Society of Emergency Surgery classification for acute diverticulitis.

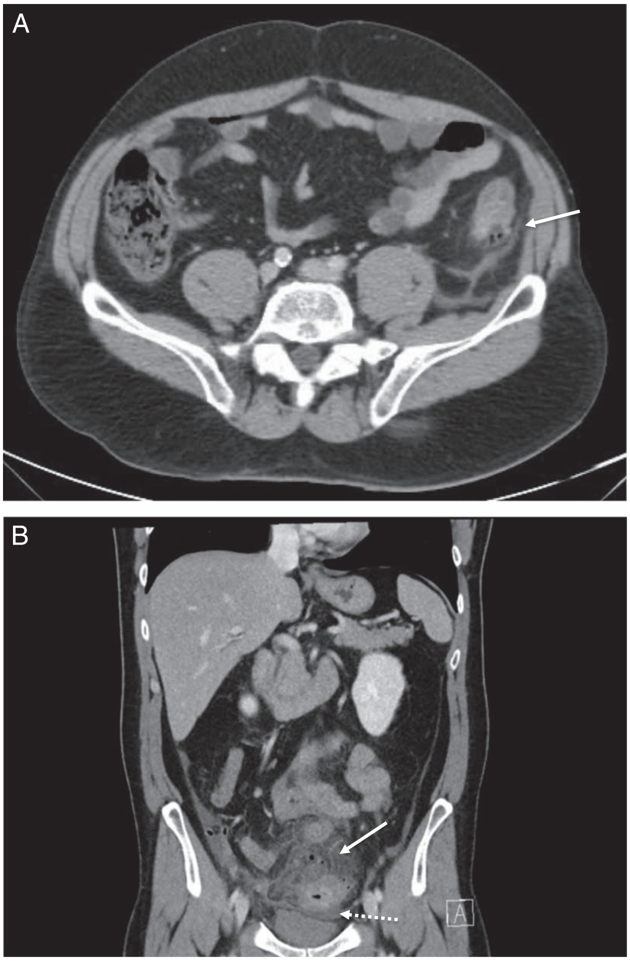

Figure 2. Computed tomography scan at index admission. (a) Patient presenting with only pericolic free gas (arrow). (b) Patient presenting with pericolic free gas (arrow) and pericolic fluid (dotted arrow).

Treatment failure has been defined as readmission, rescue operative strategy, and/or any interventional procedure performed (including percutaneous drainage).

The data collected included patient demographics (age, gender, and BMI), comorbidities, previous episodes of diverticulitis, blood test parameters, Hincheys' classification[20] based on CT imaging, and type and duration of antibiotic treatment. Short-term and long-term outcomes during and following index admission were also collected. This included the presentation of another episode of AD, perforation (with purulent or fecal peritonitis), fistula, symptomatic colonic stricture, intra-abdominal abscess, stoma formation, percutaneous drainage, emergency surgery or reoperation, and perioperative and postoperative complications graded as minor versus major categories using the Clavien–Dindo classification[21]. The length of hospital stay from the index admission was also documented. Follow-up data was collected in all patients at ~6 months and 1 year after the index admission, including data on subsequent admissions and operative and nonoperative interventions and outcomes.

Data was collected and managed using CASTOR EDC, electronic data capture tools hosted in Amsterdam, Netherlands[22]. CASTOR EDC is a secure, web-based software platform designed to support data capture for research studies. The database was in English and remained open from 20 May 2020 to 1 June 2021. All CT scans were uploaded and reviewed by two independent blinded reviewers (P.T. and C.P.).

Ethical considerations

The study was initiated after obtaining approval from the ethical committee of the organizing center (HCDGU 8/20). All centers were required to obtain approval from their ethical committees before starting enrollment. The study has been registered at clinicaltrials.gov, registration number NCT04311385. Informed consent was obtained from all participants.

Statistical analysis

Descriptive statistics are reported with mean ± SD or median with interquartile range for quantitative variables, depending on the distribution of the data. Categorical variables are reported as absolute numbers with percentages. The comparison of the differences between group means was carried out using analysis of variance for variables with normal distribution, and the Mann–Whitney *U*-test for quantitative variables with nonparametric distribution (group medians). χ^2 analysis was used for categorical variables and Fisher's exact test when any value observed in the contingency table was less than five. A logistic regression was performed to identify risk factors for treatment failure, including in the model those variables that showed a P value less than 0.05 in the univariate analysis. Results are expressed as odds ratios (OR) and 95% CI.

Sample size calculation: accepting an alpha risk of 0.05 and a beta risk of 0.8 in a two-sided test indicated 485 participants deemed necessary in the nonoperative group to recognize a difference in treatment failure greater than or equal to 0.05 units. A proportion of failure in the reference group has been estimated at 0.05. A drop-out rate of 30% was anticipated.

All statistical analyses were conducted using SPSS version 22 software (SPSS Inc., Chicago, Illinois, USA) and P values less than 0.05 were considered statistically significant.

Results

A total of 1099 patients were initially recruited over a 1-year period, but 289 did not meet the inclusion criteria. Due to a limited follow-up (< 1 year), 151 patients were excluded, and after reviewing CT imaging, another 138 were also excluded due to the presence of distant air or intra-abdominal abscess, leaving a total of 810 patients for analysis (the flow chart is presented in Fig. 3). Patients were collected from 69 centers from Europe and South America (heatmap is shown in Fig. 4). The median age was 54 (46–66) years and 475 (59%) patients were men, with a median BMI of 27 (25–29) kg/m^2. Nearly 20% of patients had prior episodes of diverticulitis ($n = 157$). The majority of patients were classified as Hinchey I (85%), while 15% were misclassified at the site as Hinchey II (12%), III (2%), and IV (1%). A total of 283 out of 810 (35%) patients with free pericolic air also presented with free fluid

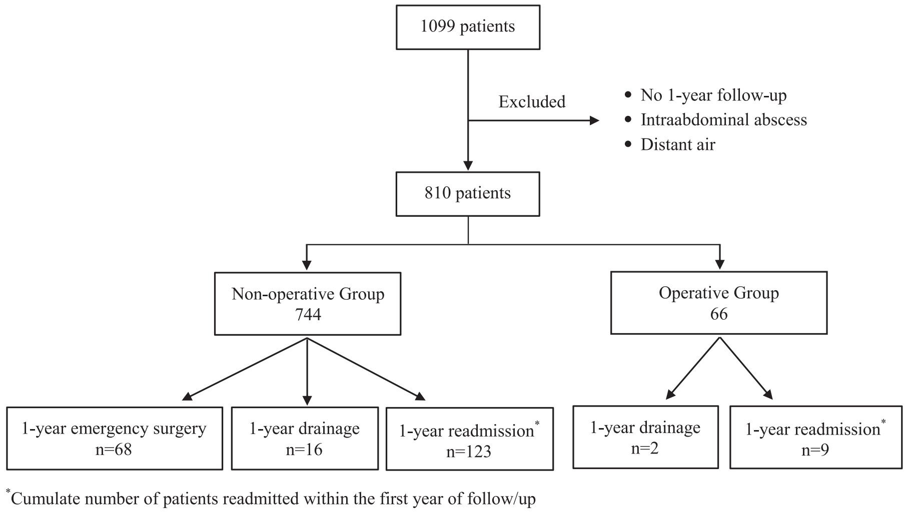

Figure 3. Flowchart.

on the CT scan, mainly located in the left pericolic (15%) or pelvis (11%). Patients' characteristics are summarized in Table 1.

Baseline characteristics

Among the 810 patients presenting with pericolic gas, 66 underwent immediate surgery; an intervention was mainly performed based on clinical deterioration ($n=36$, 55%), purely based on the CT scan findings (the presence of pericolic free air with or without free fluid, $n=19$, 29%), or for other nonspecified reasons ($n=11$, 16%). The most common procedure performed was resection and primary anastomosis ($n=28$, 42%), followed by Hartmann's procedure (HP) ($n=21$, 32%), abdominal lavage ($n=16$, 24%), and diverting the stoma only ($n=1$, 2%). Procedures were performed open in 58%, laparoscopically in 34%, and robotically in 8%.

A nonoperative approach was attempted in 744 (92%) patients, 692/744 (93%) were admitted and treated with antibiotics, while 52/744 (7%) were treated in the outpatient setting. Antibiotic therapy included oral co-amoxiclavulanic acid (27%), intravenous tazocin (27%), combinations with intravenous metronidazole (24%) and other antibiotics (22%). The median duration of antibiotic therapy was 8 (6–10) days.

A comparison of both groups' baseline characteristics is shown in Table 1. The median age in the nonoperative group was 54 (46–64) years compared to 60 (48–73) in the operative group ($P=0.014$). There were no differences in gender or BMI between

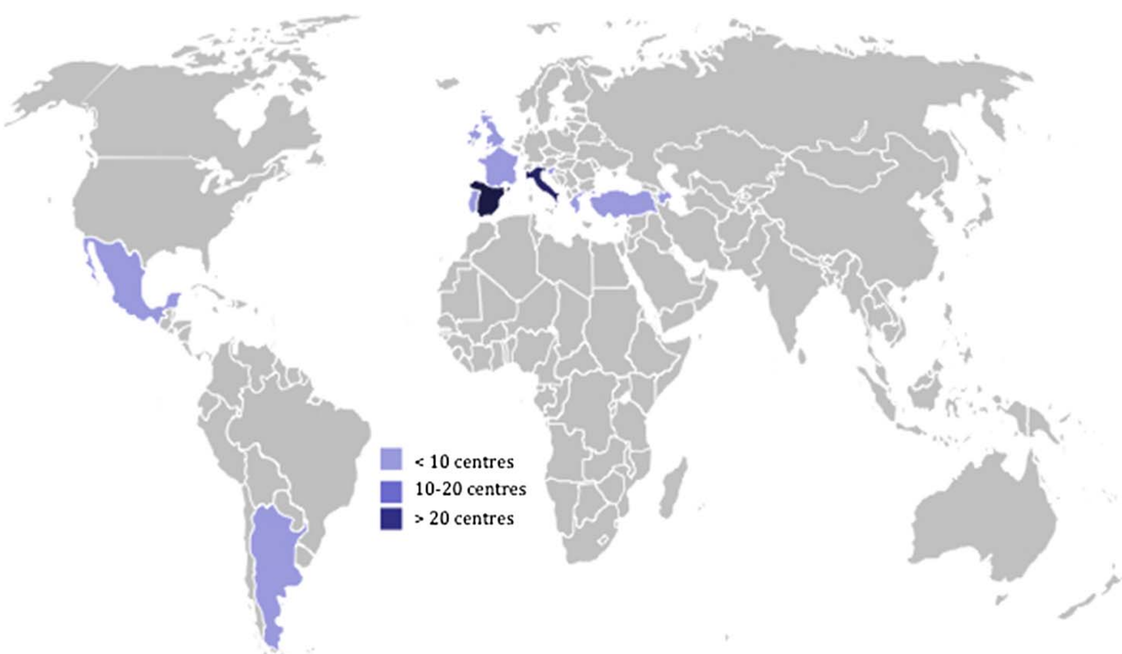

Figure 4. Heatmap of collaborating centers.

Table 1

Demographic characteristics at index admission.

	All patients ($n=810$)	Nonoperative group ($n=744$)	Operative group ($n=66$)	P value
Age (median, IQR) (y)	54 (46–66)	54 (46–64)	60 (48–73)	**0.014**
Sex (male : female) (%)	59 : 41	60 : 40	49 : 51	0.075
BMI (median, IQR) (kg/m^2)	27 (25–29)	27 (25–30)	26 (23–28)	0.011
Morbidities (%)				
Cardiovascular disease	28	27	41	**0.043**
Diabetes	10	10	11	0.880
Smoking	16	21	15	0.353
AKI	4	4	6	0.660
Previous abdominal surgery	34	35	53%	**0.005**
Previous diverticulitis of diverticulitis	19	18	35	**0.001**
Blood test				
WBC (median, IQR) ($\times 10^9$/l)	13.7 (11.3–16.5)	13.6 (11.2–16.5)	14.6 (13–17.4)	**0.018**
CRP (median, IQR) (mg/l)	94 (40–160)	94.1 (41–160)	73 (24.5–172)	0.700
INR (median, IQR)	1.1 (1–1.2)	1.1 (1–1.2)	1.1 (1–1.3)	0.983
Creatinine (median, IQR) (mg/dl)	0.9 (0.8–1.2)	0.9 (0.76–1.15)	1 (0.85–2.1)	**0.004**
Lactate (median, IQR) (mmol/l)	1.2 (1–2)	1.2 (1–2)	1.3 (0.85–2.6)	0.789
Procalcitonin (median, IQR) (ng/ml)	0.16 (0.07–0.72)	0.13 (0.1–0.52)	1.2 (0.46–10)	**0.000**
CT scan (%)				**0.000**
Hinchey I	85	90	45	
Hinchey II	12	9	37	
Hinchey III	2	1	17	
Hinchey IV	1	0	2	
Free fluid	35	33	56	**0.000**

Statistical significance $P<0.05$ values are in bold.

AKI, acute kidney injury; CRP, C-reactive protein; CT, computed tomography; INR, international normalized ratio; WBC, white blood cells.

groups; however, 53% of patients in the operative group had prior abdominal surgery, and 35% had presented with previous episodes of diverticulitis, compared to 35% and 18% in the nonoperative group, respectively (both $P<0.05$).

Laboratory blood test done at admission showed differences between groups with respect to white blood cells count, creatinine, and procalcitonin (all $P<0.05$), as shown in Table 1.

CT scan on presentation showed free fluid in 56% of patients from the operative group versus 33% in the nonoperative group ($P<0.001$), with 45% of patients classified as Hinchey I in the operative group versus 90% in nonoperative group ($P<0.001$). Patients classified as Hinchey's II–IV at diagnosis were at higher risk of having immediate surgery, with an OR 12.5 (95% CI: 2.4–64; $P=0.003$) (Table 2).

Primary aim: failure of nonoperative management during index admission

Within the operative group, 32% underwent HP, 42% a resection with primary anastomosis and 24% a laparoscopic lavage ($P=0.339$). A minimally invasive approach was performed in 42% of cases, with 14% of conversion rate. Postoperative mortality was 3% with 45% morbidity, including 21 minor and 11 major complications (Table 3). Within the nonoperative group, 12 (2%) patients required percutaneous drainage of an abscess

Table 2

Multivariate analysis – independent risks factors for operative management at index admission

				Multivariate analysis	
	Nonoperative group [n (%)]	Operative group [n (%)]	Univariate P value	OR (95% CI)	P value
Age	54 (46–64)	60 (48–73)	**0.014**	1 (0.9–1.1)	0.789
Male gender	441 (93)	32 (7)	0.075	–	
BMI (median, IQR) (kg/m^2)	27 (24.7–29.9)	26 (23–28)	**0.011**	1.1 (0.8–1.5)	0.462
WBC (median, IQR) (*10^9/l)	13.6 (11.2–16.5)	14.6 (13–17.4)	**0.018**	0.9 (0.8–1.1)	0.593
CRP (median, IQR) (mg/l)	94 (41–160)	73 (24.5–172)	0.700	–	
Creatinine (median, IQR) (mg/dl)	0.9 (0.76–1.1)	1 (0.8–2.1)	**0.004**	1 (0.8–1.3)	0.853
Procalcitonine (median, IQR) (ng/ml)	0.1 (0.1–0.5)	1.2 (0.5–10)	**0.000**	1 (0.9–1)	0.375
Previous abdominal surgery	248 (88)	33 (12)	**0.005**	3.5 (0.8–16.2)	0.109
Previous episode of diverticulitis	134 (85)	23 (15)	**0.001**	4.3 (0.9–20.2)	0.058
Hinchey II–IV	62 (65%)	33 (35%)	**0.000**	12.5 (2.4–64)	**0.003**
Free fluid CT scan	243 (87%)	37 (13%)	**0.000**	3.2 (0.7–14.7)	0.131

Statistical significance $P<0.05$ values are in bold.

CRP, C-reactive protein; CT, computed tomography; IQR, interquartile range; OR, odds ratio; WBC, white blood cells.

Table 3

Comparison of patients undergoing immediate surgery versus emergency surgery due to failure of nonoperative management within the index admission

	Emergency surgery (due to treatment failure) ($n=35$) [n (%)]	Immediate surgery ($n=66$) [n (%)]	P value
Blood test			
WBC (median, IQR) ($\times 10^9$/l)	14 (12–17)	14.6 (13–17)	0.209
CRP (median, IQR) (mg/l)	123 (20–185)	73 (25–172)	0.921
Creatinine (median, IQR) (mg/dl)	1 (0–7–1.4)	1 (0.8–2)	0.284
Procalcitonine (median, IQR) (ng/ml)	0.12 (0.1–0.4)	1.2 (0.5–10)	0.329
Surgical procedure			0.339
Primary anastomosis	10 (29)	28 (42)	
Hartmanns' resection	17 (49)	21 (32)	
Lavage	8 (23)	16 (24)	
Diverting stoma	0	1 (2)	
Approach			0.309
Open surgery	17 (49)	37 (56)	
Minimally invasive surgery	18 (51)	28 (42)	
Missing data	–	1 (2)	
Conversion	5 (28)	4 (14)	0.224
Postoperative complications (Dindo–Clavien)			0.917
Minor (I–II)	10 (29)	21 (32)	
Major (III–IV)	5 (13)	9 (14)	
Exitus	2 (6)	2 (3)	
LOS (median, IQR) (days)	14 (9–22)	11 (7–17)	0.133
1-year readmission (patients[a])	1 (3)	9 (14)	0.078
Antibiotics	1 (3)	9 (14)	
Drainage	1 (3)	0	0.725

[a]Cumulative number of patients re admitted within the first year follow-up.
CRP, C-reactive protein; LOS, length of stay; WBC, white blood cell.

(compared to none in the surgical group, $P=0.320$), and 35 failed nonoperative management and underwent emergency surgery at a median of 4.5 (2–9) days following index presentation/admission. Among patients requiring interval surgery, 49% underwent HP and 29% underwent primary anastomosis. The rate of laparoscopic surgery was 51%, with 28% conversion. Baseline characteristics were similar between patients who underwent immediate versus interval surgery (Table 3). Within the interval surgery group, postoperative mortality was 6% and postoperative morbidity was 43%, including 10 minor and 5 major complications. The remaining 697 patients (94%) were discharged with no complications. Length of hospital stay was higher in those cases that needed emergency surgery due to a failure of nonoperative management [14 (9–22) days], compared to the operative group [11 (7–17) days, $P<0.001$].

Secondary aims

A multivariate analysis was performed to identify risk factors for failure of nonoperative management during the index admission (Table 4); only the presence of free fluid on CT was a predictor for failure of nonoperative management, with an OR 4.9 (95% CI: 1.2–19.9) ($P=0.023$). The rate of success of nonoperative treatment in these patients was 88.5%, compared to 96.4% in patients without free fluid ($P<0.001$); six (2.5%) patients out of 241 who presented with free fluid required percutaneous drainage (vs. 1.2% in cases without free fluid, $P=0.170$), whereas 22 (9.1%) required emergency surgery at the index admission ($P<0.001$).

The first follow-up was recorded at a median of 43 (27–75) days after the index admission. The rate of readmission during this period was similar for both groups (7% nonoperative group vs. 8% operative group, $P=0.622$). No patients required any intervention or drainage in the operative group, only antibiotic treatment (8%); however, in the nonoperative group four patients (0.5%) underwent percutaneous abscess drainage, and 16 (2%) required emergency surgery. In most cases, resection with primary anastomosis was performed (86%). The cumulative failure rate 6 months after the index admission was similar between groups (16 vs. 11%, $P=0.058$).

Second follow-up was recorded at a median of 11 (7–13) months. The cumulative rate of readmission did not differ between groups (14% operative group vs. 16.5% nonoperative group, $P=0.272$). In the nonoperative group, a total of 16 patients (2%) required a percutaneous drainage and the overall number of patients who ultimately required emergency surgery was 68 (9%), including the index admission and the first-year follow-up. The rate of treatment failure in the nonoperative group was 16.5% at 1-year follow-up, including emergency surgery, readmissions, and percutaneous drainage (Table 5).

Elective resections during follow-up

Within the first year of follow-up, a total of 42 (5.7%) patients in the nonoperative group underwent elective resection. This included 41 patients who had a resection and primary anastomosis and one patient that had emergency surgery due to failure of nonoperative management, who during follow-up underwent a reversal of HP. In the operative group, nine (13.6%) patients underwent elective surgery including stoma reversal in three patients and resection with primary anastomosis in six patients.

Discussion

The ADiFas study demonstrated that the vast majority of clinically stable patients presenting with AD and pericolic extraluminal air can be safely managed conservatively, with a rate of failure of 6.3% during the index admission, and 16.5% within the first-year follow-up. However, in patients presenting with pericolic free air and also free fluid at CT scan, the rate of failure within the index admission is 11.5%.

Optimal classification of patients with AD is essential, as it has a great impact on their management. Additionally, and in order to enhance the reliability of staging patients in this study, a quality assurance process was implemented where all CT scans were independently reviewed to confirm the diagnosis and ensure that patients were assigned to the appropriate grade of AD. The severity of diverticulitis is usually graded with the use of modified Hinchey's criteria[20] and patients with pericolic extraluminal air represents ~15% of patients traditionally classified as Hinchey's Ia[7,8]. Some authors consider extraluminal air to be a sign of diffuse peritonitis, as shown in the current study with 3% of the patients misclassified as Hinchey III–IV, which represents itself a criterion for emergency surgery[1,5]. Although in our univariate analysis a number of clinical and radiological factors were significant, Hinchey's classification reported by the CT scan was the only independent predictor of decision making at multivariate analysis (OR: 12.5). Due to the difficulties for an accurate staging with the Hinchey's classification, the WSES has recently proposed a simple classification system based on CT scan findings[10], dividing them into two groups (Appendix 1, Supplemental Digital Content 2, http://links.lww.com/JS9/A38): uncomplicated (stage 0) and complicated (stages 1–4) diverticulitis. With this classification, 1a only includes patients with pericolic air bubbles or small amount of fluid without abscess, which is the goal of this project. According to this proposed classification, the updated WSES guidelines recommended a nonoperative treatment with antibiotic therapy for patients with this condition[11].

Most prior research on this topic was weak due to a modest sample size, a heterogeneous study population and/or its retrospective nature. This may explain the lack of clear guidance on how to manage this condition. Although WSES 2015 recommended conservative treatment, previous guidelines published by the American College of Surgeons and the Danish Surgical Society in 2012 supported emergency surgery in such cases with AD and free air[23,24].

Although our results are consistent with previous research, it is difficult to draw definite conclusions from the literature regarding the optimal management of this condition, as studies often compared patients with a different Hinchey's stage. Meyer *et al.*[8] were the first to compare outcomes of these patients with a similar group of patients staged as Hinchey Ia, but without air. Both groups of patients were considered to have a 'contained perforation' with conservative management recommended as the preferred option, but the authors concluded that the presence of pericolic air was a marker for potential clinical deterioration. On the other hand, most other published studies on this topic compared patients with pericolic air with patients with distant air[15–18], a condition that cannot be considered a 'contained perforation'. For this reason, subgroup analyses were conducted for this particular group of patients with pericolic air, where the success of conservative management ranges from 90 to 99%, in line with the results of the current study. This variation in outcomes largely depends on how failure is defined, as some of them only include surgery, while others include surgery or the need for percutaneous drainage, as done in the current ADiFas study.

Table 5

Evolution of patients within the first-year follow-up.

	Nonoperative group (*n* = 744) [*n* (%)]	Operative group (*n* = 66) [*n* (%)]	*P* value
Index admission			
Percutaneous drainage	12 (1.6)	2 (3)	0.685
Emergency Surgery	35 (4.7)	0	0.049
Failure rate (%)	6.3	3	0.218
At 6 months follow-up			
Readmission with antibiotics[a]	50 (6.7)	5 (7.6)	0.622
Percutaneous drainage	4 (0.5)	0	0.711
Emergency surgery	16 (2.2)	0	0.451
Elective surgery	10 (1.3)	3 (4.5)	0.401
Cumulative failure rate at 6 months (%)	15.7	10.6	0.058
At 1-year follow-up			
Readmission with antibiotics[a]	52 (6.9)	6 (9.1)	0.326
Percutaneous drainage	0	0	–
Emergency surgery	17 (2.3)	0	0.106
Elective surgery	32 (4.3)	6 (9.1)	**0.012**
Cumulative number at 1-year			
Readmission with antibiotics[a]	123 (16.5)	9 (13.6)	0.309
Percutaneous drainage	16 (2.2)	2 (3)	0.439
Emergency surgery	68 (9.1)	0	0.057
Elective surgery	42 (5.7)	9 (13.6)	**0.012**
Cumulative failure rate at 1-year follow-up (%)	16.5	13.6	0.272

[a]All patients readmitted underwent one or more intervention.
Statistical significance $P < 0.05$ values are in bold.

One important factor that underpins failure is the presence of free fluid. The current study included 283 patients (35%) with free fluid at CT scan, and found a higher failure rate when this was observed (12 vs. 4% in patients without free fluid). These patients may not be suitable for conservative treatment and need closer observation. This is consistent with the finding by Dharmarajan *et al.*[17], who analyzed the presence of free fluid as

Table 4

Multivariate analysis – independent risks factors for failure of conservative management within the index admission

				Multivariate analysis	
	Treatment success (n = 692)	Treatment failure (n = 46)	Univariate *P* value	OR (95% CI)	*P* value
Age <65 (years)	53 (45–64)	58 (51.5–74)	**0.014**	1 (0.9–1)	0.401
Male gender [*n* (%)]	415 (94)	26 (6)	0.644	–	
BMI (median, IQR) (kg/m^2)	27.3 (24.7–29.9)	26.6 (24–29)	0.476	–	
WBC (median, IQR) ($\times 10^9$/l)	13.5 (11.1–16.3)	15 (11.8–17)	0.113	–	
CRP (median, IQR) (mg/l)	93 (42–157)	128 (19–190)	0.383	–	
INR	1.1 (1–1.2)	1.2 (1.1–1.3)	**0.015**	0.9 (0.2–4.6)	0.851
Creatinine (median, IQR) (mg/dl)	0.9 (0.8–1.1)	1 (0.8–1.3)	0.314	–	
Lactate (median, IQR) (mmol/l)	1.2 (0.9–2)	1.9 (1.3–2.4)	0.063	–	
Procalcitonine (median, IQR) (ng/ml)	0.12 (0.06–0.4)	0.6 (0.2–10)	**0.012**	1 (0.9–1)	0.593
Previous abdominal surgery [*n* (%)]	229 (92)	19 (8)	0.263	–	
Previous episode of diverticulitis [*n* (%)]	120 (90)	14 (10)	**0.024**	1.4 (0.3–7.5)	0.703
Free fluid CT scan [*n* (%)]	215 (88.5)	28 (11.5)	**0.000**	4.9 (1.2–19.9)	**0.023**

Statistical significance $P < 0.05$ values are in bold.
CRP, C-reactive protein; CT, computed tomography; OR, odds ratio; WBC, white blood cell.

a risk factor for failure, suggesting that these patients may need emergency surgery; unfortunately, the sample size was too small to identify clinically significant differences.

In cases in which nonoperative management fails, the risk of undergoing a HP is similar to those who have immediate surgery (49 vs. 32%, $P=0.33$), and postoperative morbidity is also similar. Therefore, in the absence of hemodynamic instability, immediate surgery should be avoided, especially given the high stoma and morbidity rates.

In this study, each group was followed-up for up to 1 year. This was important to investigate the impact of each treatment modality and/or rescue strategies in case of failure. The reported recurrence for noncomplicated AD ranges between 5 and 15%[25], and it is even higher after complicated diverticulitis[26]. Our results are in concordance with previous studies, with a 16.5% rate of disease recurrence within the first year, which is considered failure of conservative management. However, the majority of patients with recurrence were successfully managed conservatively ($n=92$, 66%).

Study limitations

This study has some limitations that deserve to be mentioned. This was a multicenter and observational study, where some missing data was observed, which lead to the exclusion of 289 patients from the original sample size (1099). Patients in which the presence of pericolic free air was not mentioned in the initial CT report were not included in the study; leading to some patients not being included. As this study was not a randomized-control trial, selection biases cannot be excluded.

Despite a thorough quality assurance process for patient inclusion with blinded review of all CT scans centrally, there is still a risk of misclassification of Hinchey stage upon review of CT scans.

Conclusions

Patients presenting with AD and pericolic free gas can be successfully and safely managed conservatively in the majority of cases. Immediate surgery should be avoided, when possible, as it may lead to overtreatment of patients with high morbidity and stoma rates. The finding of free fluid in addition to pericolic free gas on CT scan may indicate a higher risk of failure of nonoperative management.

The benefits of nonoperative management in this particular population remains stable at 1-year follow-up.

Ethical approval

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Author's contribution

P.T.: data analysis and writing the manuscript. C.P.: data analysis and review of the final manuscript. G.P., P.S., and N.F.: editing the manuscript and review of the final version. All the authors critically revised the paper for important intellectual content. All authors have contributed to the work and agreed on the final version.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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