



Abordagem “wait and see” a longo prazo na diverticulite com abscesso – Será segura?

Long term wait and see approach for diverticulitis with abscess – How safe is it?

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RESUMO

Introdução: Na diverticulite aguda complicada (CAD) com abscesso, apesar do tratamento conservador já se ter tornado o *gold-standard*, a necessidade de cirurgia eletiva ainda não está esclarecida.

Objetivos: Propusemo-nos a avaliar o risco de recidiva e necessidade de cirurgia urgente numa atitude expectante após tratamento conservador eficaz da CAD com abscesso num hospital terciário.

Métodos: Efetuamos um estudo retrospectivo de todos os doentes que não foram submetidos a cirurgia eletiva após tratamento conservador eficaz de um primeiro episódio de CAD com abscesso, entre 2001 e 2016.

Resultados: Dos 79 pacientes (69,6% de Hinchey I, 19% de Hinchey IIA e 11,4% de Hinchey IIB), 11 (13,9%) tinham drenagem prévia de abscesso, percutânea ou cirúrgica. A taxa de recidiva foi de 26,6% num tempo mediano de 7 meses. 12,6% dos doentes tiveram uma recidiva complicada, embora com necessidade infrequente de cirurgia urgente (2,5%). Na análise multivariada, os doentes com diabetes (OR 2,4; IC 95% 1,2-5; $p = 0,025$) e abscesso maior que 6 cm (OR 3,1; IC 95% 1,2-8,3 $p = 0,030$) tiveram maior risco de recidiva, enquanto o risco de recidiva complicada aumentou significativamente nos doentes com proteína C-reativa (CRP) >150 mg/L no primeiro episódio (OR 2,5; IC 95% 1,1- 5,6; $p = 0,040$).

Conclusões: Com base nos nossos dados, a abordagem conservadora a longo-prazo da CAD parece segura. A diabetes, abscesso >6 cm e CRP >150 mg/L no episódio inicial são fatores preditivos de recidiva ou de complicações, devendo ser considerados na ponderação para cirurgia eletiva.

ABSTRACT

Background: Initial conservative management for complicated acute diverticulitis (CAD) with abscess has become standard procedure, however, the need for elective resection remains unclear.

Objectives: To assess the risk of recurrence and need of emergency of a wait and see approach after successful conservative management of an index episode of CAD with abscess in a single tertiary hospital.

Methods: We performed a retrospective study of all patients submitted to wait and see approach after an index episode of CAD with abscess between 2001 and 2016 in a tertiary hospital.

Results: Of the 79 patients (69,6% Hinchey I, 19% Hinchey IIA and 11,4 % Hinchey IIB), 11 (13,9%) had previous percutaneous or surgical abscess drainage. The overall recurrence rate was 26,6% in a median time of 7 months. Complicated recurrence occurred in 12,6% of the patients with rare need of emergency surgery (2,5%). On multivariate analysis, patients with diabetes (OR 2,4; 95% CI 1,2-5; $p = 0,025$) and an abscess size larger than 6 cm (OR 3,1; 95% CI 1,2-8,3; $p = 0,030$) were at higher risk of recurrence whereas C-reactive protein (CRP) over 150 mg/L during the first episode significantly increased the risk of complicated recurrence (OR 2,5; 95% CI 1,1-5,6; $p = 0,040$).

Conclusions: In our data, a wait and see approach after conservative management of an index episode of CAD with abscess seems safe, although diabetes, abscess size >6 cm and CRP >150 mg/L at first episode should be considered before recommending long-term non-operative management.

INTRODUCTION

Acute diverticulitis (AD) is a common disease with increasing incidence, high morbidity and socio-economic costs.¹⁻³ In particular, complicated acute diverticulitis with abscess (CAD) accounts for 15-20%^{4,5} of acute cases and is associated with significant morbidity and mortality.^{6,7}

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Although initial conservative management for CAD has become the standard, with percutaneous drainage and/or antibiotics, the long-term management strategy remains unclear as the necessity of elective resection a matter of ongoing debate.^{4,8-16} Until nowadays, most modern professional guidelines, including the 2014 update from the American Society of Colon and Rectal Surgeons (ASCRS) recommend an elective sigmoid resection after a single attack of complicated diverticulitis, particularly in those with a mesocolic or pelvic abscess of ≥ 5 cm, in an attempt to prevent more severe disease in the event of a recurrence.⁹ Asymptomatic patients following an episode of CAD with abscess are managed very differently from institution to institution, and surgeon to surgeon, with some being recommended an elective operation.^{17,18}

This study aims to assess the risk of recurrence and need of emergency of a wait and see approach after successful conservative management of an index episode of CAD with abscess in a single tertiary hospital.

METHODS

We performed a retrospective study of all patients submitted to wait and see approach after an index episode of CAD with abscess between 2001 and 2016 in a tertiary hospital. Wait and see approach was defined as surveillance with non-operative management after complete resolution of first episode of CAD with abscess and included patients who were not proposed for elective surgery as well as those who waited for interval surgery and complicated in the meantime. Inclusion was based on clinical diagnosis supported by radiological evidence of abscess with ultrasound (US) and/or computed tomography (CT). We also included those patients with only extraluminal air. Exclusion criteria were insufficient data, previous episode of CAD, right colon diverticulitis, acute uncomplicated diverticulitis (UAD), phlegmon without abscess, chronic sequelae, other complications (generalized peritonitis, bleeding, stenosis/obstruction, fistula and suspected neoplasia) and elective resection after complete resolution of the first episode of CAD with abscess.

Conservative management included broad-spectrum antibiotic therapy in all patients, US or CT-guided percutaneous drainage in those with an abscess greater than 3 cm with window to the procedure and surgical drainage of large

TABLE 1 Patient's characteristics

	Patient's characteristics, n = 79
Age, y	59 $\pm$ 13,5
≤ 50 ; > 50 , y	17 (21,5%); 62 (78,5%)
Sex, men	41 (51,9%)
ACCI	2,1 $\pm$ 1,7
≥ 3	31 (39,2%)
Immunosuppression	3 (3,8%)
Obesity	10 (12,7%)
Diabetes	9 (11,4%)
CRD	0 (0%)
Previous episode of UAD	0 (0%)
Values are median $\pm$ standard deviation or n (%); ACCI: Age-adjusted Charlson index; UAD: Uncomplicated acute diverticulitis; CRD: Chronic renal disease; y: Years	

symptomatic abscess without window for percutaneous drainage.

Elective surgery was defined as interval colic resection surgery performed in a hospitalization separate from the index hospitalization.

Complicated recurrence or subsequent CAD was defined as recurrence with acute inflamed diverticula causing abscess or perforation.⁶ The severity of CAD was classified according to the modified Hinchey Classification by Sher et al.: pericolic abscesses (stage I), distant abscesses amenable for percutaneous drainage (stage IIa), complex abscesses associated with a possible fistula (stage IIb), generalized purulent peritonitis (stage III) and fecal peritonitis (stage IV).⁷ Subsequent UAD or uncomplicated recurrence was defined as recurrence with acute inflamed diverticula without abscess nor perforation.⁶

The age-adjusted Charlson index (ACCI) was used to assess comorbidity. The ACCI assigns one point each for history of myocardial infarction, heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disorder, peptic ulcer disease, mild liver disease, and diabetes mellitus (DM) without complications; two points are assigned for hemiplegia, moderate to severe renal disease, DM with complications, tumour without metastases, leukemia, lymphoma, and myeloma; three points are assigned for moderate or severe liver disease; and six points are assigned for metastatic solid tumour or acquired immunodeficiency syndrome. One ad-

TABLE 2 Characteristics of index episode of CAD and clinical outcomes

	Characteristics of index episode of CAD, n = 79
Leucocyte count ($\times 10^9/l$)	1,3 $\pm$ 4,4
C-reactive protein (mg/L)	93 $\pm$ 82,6
Abscess size, cm	3,3 $\pm$ 2,5
Abscess size > 4 cm	16 (20,2%)
Abscess size > 6 cm	8 (10,1%)
Sher classification:	
Stage I	55 (69,6%)
Stage IIA	15 (19%)
Stage IIB	9 (11,4%)
Complex abscess	9 (11,4%)
Localized extraluminal air	18 (22,8%)
Antibiotic therapy alone	67 (84,8%)
Use of percutaneous drainage	8 (10,1%)
Use of surgical drainage	4 (5,1%)
Hospital stay, days	10,1 $\pm$ 7,1
	Clinical outcomes
Recurrence	21 (26,6%)
Time for recurrence, months	6 $\pm$ 15,5
Complicated recurrence	10 (12,7%)
Need for emergency surgery in recurrence	2 (2,5%)
Elective surgery after recurrence	14 (17,7%)
Mortality	0 (0%)
Values are median $\pm$ standard deviation or n (%); CAD, complicated acute diverticulitis	

ditional point is assigned per decade of age over 49 years.⁸

For this study, the 79 patients that were submitted to a wait and see approach after successful conservative management of a first episode of CAD with abscess were separated into two groups for analysis and statistical comparison: non-recurrent and recurrent groups. The demographic characteristics, baseline clinical and radiological parameters, and outcomes of patients in these groups were summarized and compared statistically.

The primary endpoint was recurrence after successful conservative management of index CAD with abscess. Successful conservative management of CAD with abscess was defined as the complete resolution of symptoms and radiological improvement at the Hospital discharge. Recurrence

was defined as a new episode of AD after an asymptomatic period of 3 months.

Secondary endpoints were severity of the recurrent episode (UAD versus CAD) and need for emergency surgery. We also evaluated possible predictive risk factors for recurrence and complicated disease.

IBM® SPSS Statistics version 22 was used for all the statistical calculations. Pearson's χ^2 test and Fisher exact test for $n < 20$ was used for categorical variables. T test was used for continuous variables with normal distribution while Mann-Whitney was used for continuous variables without normal distribution. Multivariate analysis was performed by logistic regression modeling. Independent variables that reached significance by univariate analysis were compared with the dependent variables of recurrence and complicated disease. Results have been presented as p values, odds ratios (O.R) with 95% confidence intervals (CI) and mean $\pm$ standard deviation (SD). $p < 0.05$ was considered statistically significant.

RESULTS

Of 519 patients admitted for acute sigmoid diverticulitis between 2001 and 2016, 120 (23,1%) patients were identified as having CAD with abscess. Of these, 14 (11,7%) underwent an emergency operation on index admission for peritonitis or failure of conservative management, whereas the remaining 106 patients were managed conservatively with intravenous antibiotic therapy alone or with percutaneous or surgical drainage. Of the 106 patients with CAD who recovered after effective conservative management we excluded 22 who underwent elective surgery after the first episode and 5 who presented with persistent disease within 3 months. Thus, 79 patients (74,5%) were managed non-operatively with wait and see approach and composed the study population.

The median age was 59 years and 39,2% had ACCI ≥ 3 . Median abscess size was 3,3 (range, 0,60-10) cm. 55 (69,6%) were Hinchey I, 15 (19%) Hinchey 2A and 9 (11,4%) Hinchey 2B, of whom 8(10,1%) had undergone percutaneous and 4 (5,1%) surgical drainage of abscess. Other characteristics of patients and index episode of CAD with abscess are summarized in Table 1 and 2.

After a mean follow-up of 22 months, the overall recurrence rate was 26,6% in a median time of 7 months (95%

TABLE 3 Demographics and characteristics of index episode of CAD by recurrence

	Non-recurrence, n (%) n = 58	Recurrence, n (%) n = 21	<i>p</i> value
Demographics			
Age, y	59,2 ± 13,3	59,6 ± 14,4	0,920
≤ 50, y	13 (22,4%)	4 (19,0%)	0,748
Sex, men	32 (55,2%)	9 (42,9%)	0,333
ACCI	2,0 ± 1,7	2,5 ± 1,7	0,286
ACCI ≥ 3	21 (36,2%)	10 (47,6%)	0,359
Immunosuppression	2 (3,4%)	1 (4,8%)	0,787
Corticosteroid use	2 (3,4%)	1 (4,8%)	0,787
Diabetes	4 (6,9%)	5 (23,8%)	0,037
Obesity	9 (15,2%)	1 (4,8%)	0,204
Characteristics of index episode of CAD			
Leucocyte count (×10 ⁹ /l)	1,3 ± 4,6	1,3 ± 3,9	0,964
C-reactive protein (mg/L)	110,9 ± 77,2	129 ± 98,1	0,472
Abscess size, cm	3,8 ± 2,5	4,9 ± 2,5	0,272
Abscess size > 4 cm	12 (20,7%)	4 (19,0%)	0,651
Abscess size > 6 cm	4 (6,9%)	4 (19,0%)	0,030
Sher classification:			
Stage I	40 (69%)	15 (71,4%)	0,480
Stage IIA	10 (17,2%)	5 (23,8%)	
Stage IIB	8 (13,8%)	1 (4,8%)	
Complex abscess	8 (13,8%)	1 (4,8%)	0,432
Localized extraluminal air	15 (25,9%)	3 (14,3%)	0,278
Antibiotic therapy alone	51 (87,9%)	16 (76,2%)	0,199
Use of percutaneous drainage	4 (6,9%)	4 (19,5%)	0,199
Use of surgical drainage	3 (5,2%)	1 (4,8%)	1,000
Use of percutaneous or surgical drainage	7 (12,1%)	5 (23,8%)	0,285

Values are median ± standard deviation or n (%); ACCI: Age-adjusted Charlson index; CRD: Chronic renal disease; Y: Years; CAD: Complicated acute diverticulitis

CI 5,2-8,8). Of the 79 patients that recovered completely after conservative management from the index episode, 58 (73,4%) hadn't recurred and 21 (26,6%) were readmitted with recurrence. The comparison of the 2 groups is summarized in Table 3.

The overall complicated recurrence rate was 12,6% in a median time of 7 months. Of the 10 patients with complicated recurrence, 8 (10,1%) had an abscess initially conservatively managed. The emergency surgery rate was 2,5%: 2 patients had generalized peritonitis that required

emergency surgery with a stoma at 36 and 5 months from the index episode, with one stoma reversal. 14 (17,7%) were submitted to elective surgery after recurrence: all 8 patients with subsequent CAD with abscess and the remaining 6 with subsequent UAD. There was no mortality.

We assessed potential predictive risk factors for recurrence, namely with subsequent CAD. On multivariate analysis, patients with diabetes (OR 2,4; 95% CI 1,2-5; *p* = 0,025) and an abscess size larger than 6 cm (OR 3,1; 95% CI 1,2-8,3; *p* = 0,030) were at higher risk for recurrence whereas CRP over

TABLE 4 Demographics and characteristics of index episode of CAD by type of recurrence

	Subsequent UAD, n (%) n = 11	Subsequent CAD, n (%) n = 10	p-value
Demographics			
Age, y	55,6 ± 15,4	63,9 ± 12,4	0,195
Age > 50 y	7 (63,6%)	10 (100%)	0,034
ACCI	2,2 ± 2,0	2,8 ± 1,3	0,425
ACCI ≥ 3	4 (36,4%)	6 (60%)	0,279
Immunosuppression	0	1 (10%)	0,476
Diabetes	2 (18,2%)	3 (30%)	0,635
Obesity	1 (9,1%)	0	1,000
Characteristics of index episode of CAD			
Leucocyte count (×10 ⁹ /l)	1,3 ± 0,17	1,3 ± 0,53	0,734
C-reactive protein (mg/L)	102,3 ± 80,1	158,7 ± 112,11	0,221
C-reactive protein >150 md/dl	1 (9,1%)	5 (50%)	0,038
Abscess size, cm	5,5 ± 2,1	4,7 ± 2,8	0,533
Abscess size > 4 cm	1 (9,1%)	3 (30%)	1,000
Abscess size > 6cm	1 (9,1%)	3 (30%)	1,000
Sher classification:			
Stage I	8 (72,7%)	7 (70%)	0,543
Stage IIA	3 (27,3%)	2 (20%)	
Stage IIB	0	1 (10%)	
Complex abscess	0	1 (10%)	0,476
Localized extraluminal air	2 (18,2%)	1 (10%)	1,000
Use of percutaneous drainage	3 (27,3%)	1 (10%)	0,586
Use of surgical drainage	0	1 (10%)	0,476
Use of percutaneous or surgical drainage	3 (27,3%)	2 (20%)	1,000
Other characteristics			
Time for recurrence	7 ± 13,3	6,5±18,8	0,472
Need for emergency surgery	0	2 (20%)	0,099

Values are median ± standard deviation or n (%); ACCI: Age-adjusted Charlson index; CRD: Chronic renal disease; y: Years; CAD: Complicated acute diverticulitis; UAD: Uncomplicated acute diverticulitis

150 mg/L during the first episode significantly increased the risk for subsequent CAD (OR 2,5; 95% CI 1,1-5,6; p = 0,040).

DISCUSSION

In the last years, there has been a shift from the surgical paradigm of elective resection to continued observation after the resolution of CAD with abscess, although it remains widely accepted that these patients warrant elective

resection.^{2,4,12,14,19–22,16} Most recent updates still recommend elective surgery after CAD, successfully conservatively managed when there's a pericolic abscess of 5 cm or larger or a pelvic abscess, regardless of whether it was percutaneously or surgically drained.^{9,13}

In theory, the purpose of managing CAD with abscess with elective surgery is to avoid the high risk of future recurrence and further complications, namely emergency

surgery.^{4,23} There's a wide variety of reported recurrence rates among different studies, ranging from 3% to as high as 68%,^{4,6,8,10,13,14,20,24-31} although a recent systematic review composed by 22 studies carried out between 1986 and 2014 reported an average recurrence rate of 28% and rare need for subsequent emergency surgery (0,96%).²⁵ Gregersen et al. obtained similar results in a meta-analysis that incorporated the long-term outcomes of CAD with abscess of 21 studies with a total of 7,653 patients, where he found a recurrence rate of 25,5% and a subsequent emergency surgery rate of 4,8%.²⁶

As described in modern literature, most of the patients with CAD with abscess followed a benign course with a recurrence rate of 26.6% and need for emergency surgery in only 2,5% of the individuals.^{25,26} Additionally, in our study, the complicated recurrence was not reflected in a statistically significant emergency surgery rate ($p = 0,99$). Based on these data, we have assumed that a wait and see approach is safe after successful conservative management of CAD with abscess.

It has been described that recurrence is higher within the first year after the index episode, with a shorter recurrence-free interval after CAD with abscess.^{25,29} In our study, recurrence occurred mainly in the first year with a median recurrence time of 7 months regardless of whether this was complicated or not.

Although high-level evidence is lacking, there are several studies on predictive factors for diverticulitis recurrence. Hupfeld et al. recently published a systematic review where it is suggested that young age, comorbidities, immunosuppression, severity of index episode, abscess size and location, as prior percutaneous or surgical drainage of abscess are predictive factors for recurrence.²⁵ In this study, along with the impression that CAD with abscess at the index episode could be a risk factor for complicated recurrence, it was also noted that CRP level at primary episode could be a useful predictor for short-term recurrences.²⁵

In our study, although variables such as age, immunosuppression, severity of the first episode or previous abscess drainage were not predictive factors for recurrence, the same wasn't true for diabetes or abscess size parameters. On the other hand, subsequent CAD was more frequent in older patients and when CRP was above 150 mg/L in the index episode. In the multivariate analysis only, the CRP had

a significant effect on complicated recurrence

In fact, the multivariate analysis of our study showed that patients with diabetes and an abscess size larger than 6 cm were at higher risk for recurrence whereas CRP over 150 mg/L during the first episode significantly increased the risk of complicated recurrence.

In our analysis, 10% of the patients had an abscess size >6 cm and recurred three times more than those with smaller abscesses (OR 3,1; 95% CI 1,2-8,3; $p = 0,030$). These data are in agreement with some studies that reveal that abscess size is a predictive risk factor for recurrence.²⁵

We didn't find a higher recurrence rate among patients undergoing abscess drainage as in some studies reviewed by Gregersen et al. and Hupfeld et al. suggesting that treatment itself may not be a factor associated with recurrence.^{25,26}

We observed a higher risk of recurrence in diabetic patients (OR 2,4; 95% CI 1,2-5; $p = 0,025$), although without impact on the efficacy of conservative management in the acute setting nor on the likelihood of subsequent CAD. The role of diabetes in diverticulitis has not yet been well studied, but this result may be explained by the higher pro-inflammatory status in this group of patients.³²

There are several studies that point out CRP as the most sensitive serological marker in UAD, and recent evidence suggests that a concentration above 150-200 mg/L may be correlated with perforation.³³⁻³⁵ In our study, a raised CRP (over 150 mg/L) during the first episode was associated with complicated recurrence (OR 2,5; 95% CI 1,1-5,6; $p = 0,040$). This is in line with Buchs et al. who reported that a raised CRP (over 240mg/L) during the first episode was associated with recurrence in the first 6 months.³⁶

This study is limited by its retrospective nature. Future prospective research with extended patient follow-up evaluating the long-term consequences of non-operative management and comparing with those submitted to surgery may help to identify patients prone to recur who would benefit from prophylactic surgery after CAD. For this reason, our research group has already started a prospective study on this subject, but long-term results are needed to draw conclusions.

CONCLUSIONS

Our study shows that a wait and see approach is a safe option in patients who had a successfully treated CAD with abscess,

with a very low rate of emergency surgery.

Based on our data, diabetes, abscess size >6 cm and CRP >150 mg/L at first episode of CAD should be considered before recommending a long-term non-operative approach for CAD.

Future research is needed to better determine the criteria for elective surgery in this group of patients. ● ● ●

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