



Long-term outcomes and risk factors for diverticulitis recurrence after a successful laparoscopic peritoneal lavage in Hinchey III peritonitis

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Abstract

Purpose Recently, treatment of Hinchey III diverticulitis by laparoscopic peritoneal lavage has been questioned. Moreover, long-term outcomes have been scarcely reported. Primary outcome was to determine the recurrence rate of diverticulitis after a successful laparoscopic peritoneal lavage in Hinchey III diverticulitis. Secondary outcomes were identification of associated risk factors for recurrence and elective sigmoidectomy rate.

Methods A retrospective cohort study in a tertiary referral center was performed. Patients with Hinchey III diverticulitis who underwent a successful laparoscopic peritoneal lavage between June 2006 and December 2019 were eligible. Diverticulitis recurrence was analyzed according to the Kaplan–Meier and log-rank test, censoring for death, loss of follow-up, or elective sigmoid resection in the absence of recurrence. Risk factors for recurrence were identified using Cox regression analysis.

Results Sixty-nine patients had a successful laparoscopic peritoneal lavage (mean age: 63 years; 53.6% women). Four patients had an elective sigmoid resection without recurrences. Recurrence rate was 42% ($n=29$) after a median follow-up of 63 months. The cumulative global recurrence at 1, 3, and 5 years was 30% (95% CI, 20–43%), 37.5% (95% CI, 27–51%), and 48.9% (95% CI, 36–64%), respectively. Smoking (HR, 2.87; 95% CI, 1.22–6.5; $p=0.016$) and episodes of diverticulitis prior to laparoscopic peritoneal lavage (HR, 5.2; 95% CI, 2.11–12.81; $p<0.001$) were independently associated with an increased risk of recurrence.

Conclusions Diverticulitis recurrence after a successful laparoscopic peritoneal lavage is high, decreasing after the first year of follow-up. Smoking and previous episodes of acute diverticulitis independently increase the risk of new episodes of diverticulitis.

Keywords Laparoscopic peritoneal lavage · Acute diverticulitis · Recurrence · Risk factors

Introduction

Laparoscopic peritoneal lavage (LPL) has been proposed as an alternative therapy to resective options (Hartmann's procedure and colonic resection with primary anastomosis with or without fecal diversion) in Hinchey III perforated diverticulitis [1–3]. The rationale behind this proposal was based on its low morbidity and mortality as well as its benefits in

terms of shorter operative time, lower stoma rate, and faster postoperative recovery than standard procedures [4, 5].

During the last decade, this procedure has been submitted to a rigorous clinical evaluation in three large clinical trials [6–9]. Two of these studies found that LPL was associated with a significantly higher rate of postoperative abscess formation and a higher 30-day unplanned reoperation rate [6, 7]. These findings pushed to discourage its implementation, generating growing skepticism across the colorectal surgical community [10]. However, in all of these three studies sepsis control was highly achieved in patients who underwent LPL (70–86%). Moreover, the recently published long-term outcomes of these studies showed no differences regarding severe complications and mortality, and significantly fewer

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stoma prevalence and reoperations in patients who underwent LPL [11, 12]. This emphasizes the need to improve patient selection to reduce short-term complications after which LPL could still be a valuable treatment option.

The long-term management of the patients successfully treated with LPL has been scarcely reported. While some authors systematically advocate for elective sigmoidectomy in all cases after discharge [2, 13], others only perform it when chronic complications (fistulas or stenosis) or recurrent episodes occur [14]. Moreover, the best available evidence regarding this issue is based on a small multicenter series with short follow-up which limits its interpretation [15].

We have previously reported our initial experience with LPL as the treatment of perforated diverticulitis [16], mainly focused on the short-term postoperative outcomes. In the original study, 85% of patients managed by LPL successfully controlled sepsis avoiding major resection and stoma formation. The primary outcome of this study was to report long-term recurrence rate of diverticulitis after a successful LPL. The secondary outcomes were to investigate the associated risk factors for recurrence of diverticulitis and the sigmoidectomy rate after a successful LPL.

Methods

Population

Patients were identified from a prospectively maintained practice-specific database. Adult patients (≥ 18 years old) who underwent a successful LPL between June 2006 and December 2019 for Hinchey III diverticulitis were selected. LPL failures and patients with a postoperative diagnosis of colon cancer during immediate follow-up were excluded. This study was approved by the Institutional Review Board.

Procedures

After the initial clinical evaluation, all suspected cases of acute diverticulitis were confirmed by an abdominopelvic computed tomography (CT) scan. Patients were resuscitated with crystalloids and intravenous antibiotics (ciprofloxacin 500 mg and ornidazole 1000 mg). Emergency surgery decision was based on the clinical assessment and radiologic findings. Hemodynamically stable patients in which laparoscopic approach revealed a Hinchey III diverticulitis without evidence of perforation were offered a LPL. The surgical procedure has been previously described by our group [16] and is summarized in Fig. 1.

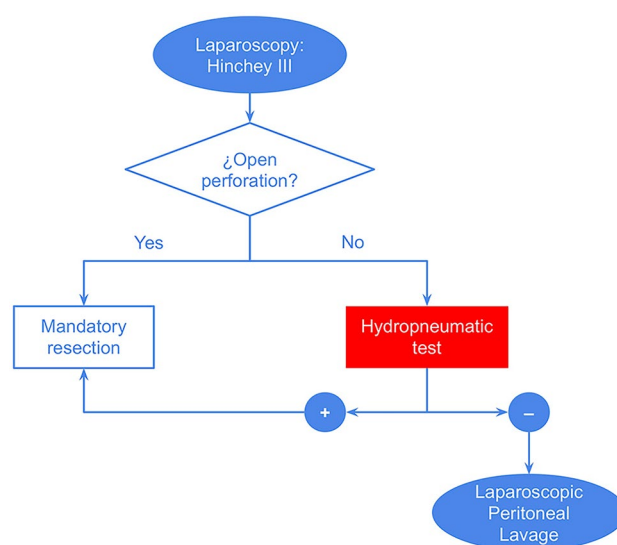


Fig. 1 Intraoperative strategy algorithm for patients with diverticular peritonitis

LPL was defined as successful if the patient was asymptomatic, colectomy-free, and alive during the first 30 postoperative days. Only successful LPL patients were included.

Patients follow-up

All patients were monitored a week and a month after discharge and, subsequently, every 6 months. In all cases, a colonoscopy or a contrast enema was performed a month after discharge. Patients with colon cancer confirmed by endoscopic biopsy performed at follow-up studies were excluded.

A CT scan was indicated if new episodes of acute diverticulitis were suspected during follow-up (see definition of recurrence of diverticulitis in the “Outcomes” section). Patients with a recurrence were managed on an outpatient basis or hospitalized according to the symptoms and the patient’s medical history. Emergency colectomy was indicated if symptoms persisted or worsen in spite of medical treatment. The type of surgery (resection and primary anastomosis with/without stoma or Hartmann’s procedure) was defined according to the hemodynamic stability of the patient and intraoperative findings. In patients with a successful nonoperative management of the recurrence, the indication for elective colectomy was individually considered [17, 18].

Outcomes

Recurrence was defined as a new episode of acute diverticulitis after a 60-day symptom-free interval after a successful LPL confirmed by a CT scan. If symptoms appeared within

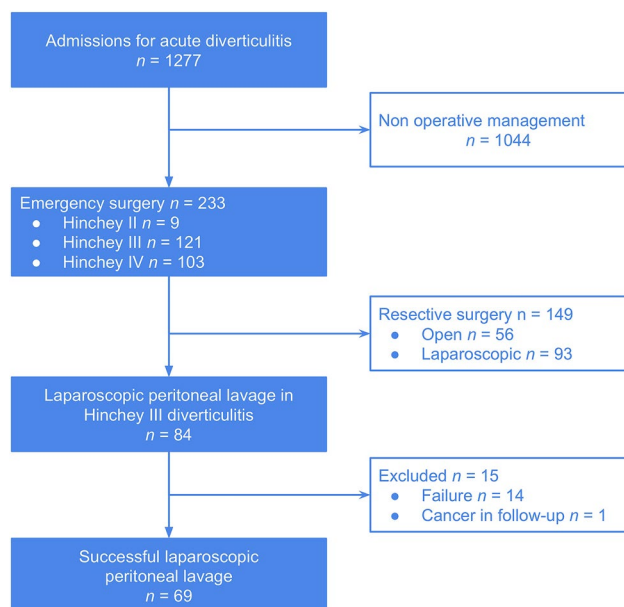


Fig. 2 Flowchart depicting the distribution of patients according to the treatment strategy

60 days after LPL, they were deemed to be part of the index episode and not as a recurrence. This definition of disease recurrence has been previously reported by other authors [19, 20]. New episodes were suspected by clinical manifestations, such as acute abdominal pain in the lower left quadrant, fever, and leukocytosis, and confirmed by previously described tomographic findings [21]. Need for hospitalization or outpatient management was recorded. Recurrences were classified as complicated or uncomplicated according to the presence of pericolic abscess, extraluminal air, or associated peritonitis. The mean time-to-recurrence was the average time between a successful LPL and first recurrence, expressed in months. The median time-to-recurrence was defined as the period of time in which half of all the included

population could develop a recurrence. Recurrence density rate was defined as the ratio between the number of new cases and the sum of risk periods of each individual at risk during follow-up. It was expressed as 100 patients-year.

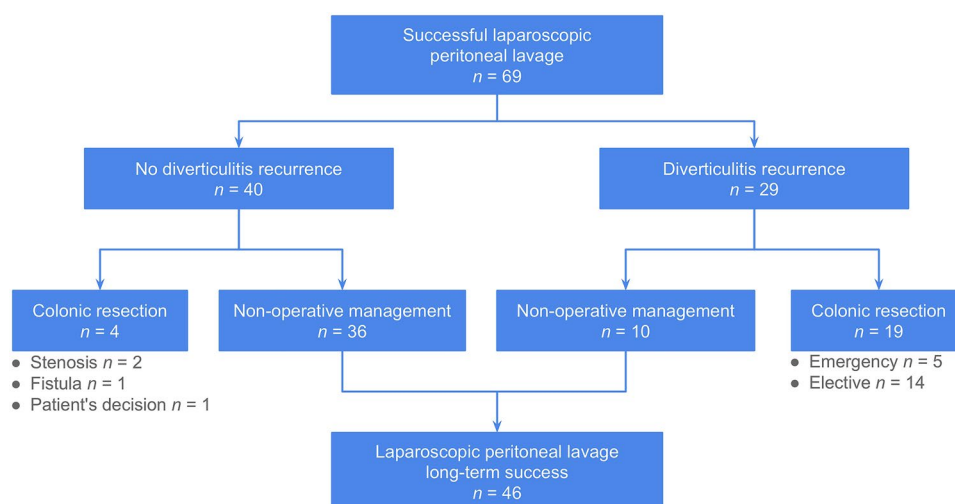
Sigmoidectomy rate was defined as the number of patients who underwent an emergency or elective colectomy after a successful LPL, divided by the total cohort. The mean time-to-colectomy was defined as the average time between a successful LPL and an elective colectomy.

Demographic variables were analyzed to determine risk factors associated with recurrence. Episodes of diverticulitis before the LPL were recorded as categorical (at least one episode of diverticulitis before the LPL) and continuous variables (number of previous episodes). Previous episodes were divided according to whether they had been managed with or without hospitalization. Clinical and imaging characteristics of the index episode were considered: Mannheim peritonitis index (MPI) [22], hospital stay, and morbidity, defined as any complications within 30 days after LPL and classified according to the Clavien-Dindo classification [23]. Tomographic findings of the index episode were classified according to the World Society of Emergency Surgery (WSES) [24].

Statistical analysis

Categorical variables were reported as proportions and continuous variables as means with their respective standard deviations or medians with their interquartile ranges, according to distribution. Recurrence was evaluated as a time-to-event variable. The Kaplan–Meier with log-rank test was used to analyze time-to-recurrence, censoring for death, loss to follow-up, or resective colonic surgery in absence of recurrence. Multivariate analyses were performed using Cox proportional hazards model adjusting for covariates included for statistical significance or clinical relevance. The proportional

Fig. 3 Study flow chart showing long-term outcomes of laparoscopic peritoneal lavage for acute Hinchey III diverticulitis



hazards assumption was verified using the Schoenfeld test and the log–log graph. All statistical tests were two-tailed and a p -value < 0.05 was considered statistically significant. STATA 13 (Stata Corp, College Station, TX, USA) was used for all the analysis.

Results

During the study period, 84 LPLs out of 121 Hinchey III diverticulitis (69%) were performed. Seventy patients had no need for further surgery after the LPL, which represents an 83.3% success rate of this procedure in the acute setting. Fourteen LPL failures and 1 patient with colon cancer detected during follow-up were excluded. All the different strategies taken in the whole population are depicted in Fig. 2.

Table 1 Demographic and preoperative characteristics of patients undergoing laparoscopic peritoneal lavage for Hinchey III diverticulitis

Laparoscopic peritoneal lavage in Hinchey III ($n = 69$)	
Age, mean (SD)	62.9 (15.4)
Female, n (%)	37 (53.6)
BMI (kg/m^2), mean (SD)	27.9 (5.4)
ASA classification, n (%)	
1	3 (4.3)
2	35 (50.7)
3	31 (44.9)
Charlson ≥ 3 , n (%)	35 (50.7)
Medical history, n (%)	
Cardiologic	37 (53.6)
Respiratory	19 (27.5)
Nephrologic	4 (5.80)
Neurologic	9 (13.0)
Diabetes	8 (11.6)
Immunosuppression	1 (1.45)
Chronic steroid intake	6 (8.70)
Smoking	21 (30.4)
Obesity ($\text{BMI} \geq 30 \text{ kg}/\text{m}^2$)	21 (30.4)
Alcoholism	6 (8.70)
Previous episodes of diverticulitis, n (%)	12 (17.4)
Requiring at least one hospitalization, n (%)	6 (8.70)
Previous episodes, median (range)	0 (0–5)
WSES classification (CT prior LPL), n (%) [*]	
1A–1B	8 (12.9)
2A–2B	5 (8.06)
3	8 (12.9)
4	41 (66.1)

SD standard deviation, BMI body mass index, ASA American Society of Anesthesiologists, WSES World Society of Emergency Surgery, CT computed tomography, LPL laparoscopic peritoneal lavage

^{*}According to 62 patients with a CT scan

A total of 69 patients (mean age 63 years, 53.6% women) were finally included (Fig. 3). Demographic and preoperative characteristics are detailed in Table 1, while intraoperative findings and postoperative outcomes are described in Table 2.

After a median follow-up of 63 months (IQR: 35–97), 29 patients had recurrences after a successful LPL, thus representing a recurrence rate of 42% (95% CI, 30.8–54.2%). Fourteen of these patients (48.3%) were admitted to hospital for treatment. The cumulative global recurrence rate at 1, 3, and 5 years was 30% (95% CI, 20–43%), 37.5% (95% CI, 27–51%), and 48.9% (95% CI, 36–64%), respectively (Fig. 4A). While the mean time-to-recurrence was 17.8 months (SD 24; range: 2–89), the median time-to-recurrence was 74 months (95% CI, 24–not reached). The recurrence density rate was 13.8 cases per 100-patients-year (95% CI, 9.6–20.4).

Five patients (17.2%) had a complicated diverticulitis recurrence that required emergency colectomy: one Hartmann's procedure, one resection with primary anastomosis, and 3 resections with primary anastomosis and diverting stoma. Fourteen patients (48.3%) underwent an elective colectomy after diverticulitis recurrence, all of them laparoscopic resections with primary anastomosis without diverting stomas. Four patients underwent elective colectomy without recurrences after the LPL: two patients had a symptomatic colonic stenosis, one presented a chronic colonic fistula requiring percutaneous drainage, and one patient opted for elective colectomy to avoid the risk of recurrent attacks. The mean time-to-colectomy in these four patients was 4.3 months (SD 2.6; range: 2–7). The overall sigmoidectomy rate was 33.3% (95% CI, 23–45%). The cumulative risk of sigmoidectomy was 27.8% (95% CI, 18–40%), 34.5% (95% CI, 24–48%), and 34.5% (95% CI, 24–48%) at 1, 3, and 5 years of follow-up, respectively (Fig. 4B).

Smoking (HR, 2.87; 95% CI, 1.22–6.5; $p = 0.016$) and previous episodes of diverticulitis (HR, 5.2; 95% CI, 2.11–12.81; $p < 0.001$) were significantly associated with

Table 2 Intraoperative findings and postoperative evolution of patients undergoing laparoscopic peritoneal lavage for Hinchey III diverticulitis

Laparoscopic peritoneal lavage in Hinchey III ($n = 69$)	
MPI, median (IQR)	22 (17–26)
Lavage volume (L), median (IQR)	3 (2.5–3.5)
Number of drainages, median (range)	2 (1–4)
Morbidity, n (%)	
Global	15 (21.7)
Major	6 (8.70)
Postoperative percutaneous drainage, n (%)	6 (8.70)
Length of hospital stay (days), median (range)	6 (3–41)
ICU admissions, n (%)	24 (34.7)

MPI Mannheim peritonitis index, IQR interquartile range, ICU intensive care unit

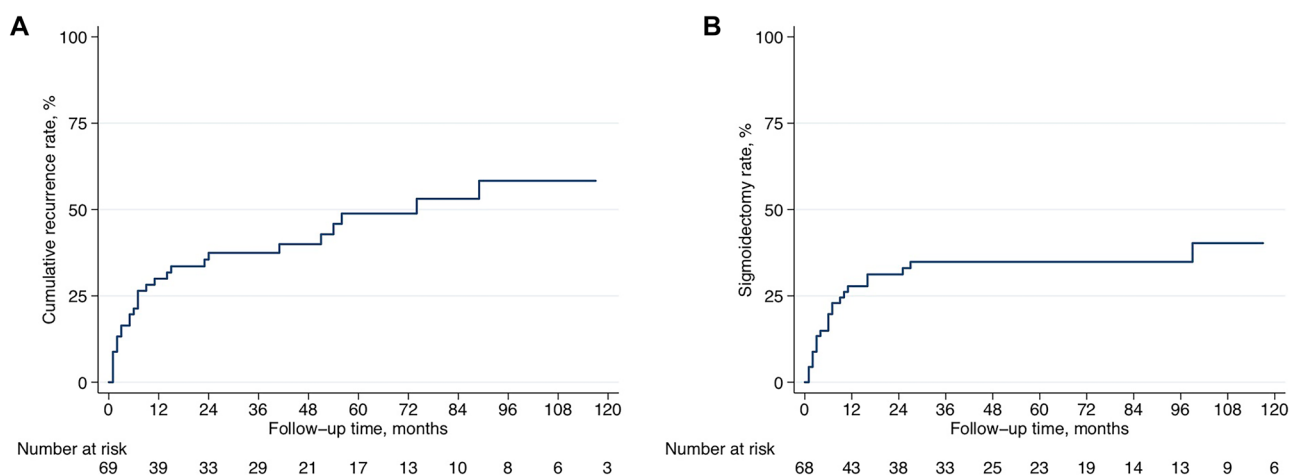


Fig. 4 Kaplan–Meier curve showing **A** the cumulative global recurrence rate and **B** colonic resection rate due to recurrence in patients who underwent a successful LPL for acute Hinchey III diverticulitis

an increased risk of recurrence regardless of other covariates (Table 3). During the first year of follow-up, 47.3% of smokers and 68.2% of patients with previous episodes had at least one episode of diverticulitis recurrence (Fig. 5).

Discussion

After a median follow-up of 63 months, 42% of the patients had at least one diverticulitis recurrence following a successful LPL. Only one-third underwent a colectomy during follow-up, and just 7.2% were emergency procedures. Previous episodes of acute diverticulitis before the LPL and smoking habits were independent risk factors for recurrence.

Few studies have reported the long-term outcomes of patients undergoing LPL for Hinchey III diverticulitis; thus, recurrence rate in these patients is scarcely known. Although small retrospective studies have reported low recurrence rates after LPL [2, 4], the long-term results of randomized controlled trials and multicenter studies have shown higher recurrence rates, which is consistent with our findings. The 2-year results of the DILALA trial [25] show that 18.6% of the patients undergoing LPL had to be readmitted for new symptoms. The LLO study [26], a multicenter study, reported a recurrence rate of 26.7% after a median follow-up of 22 months. Readmission rate for new episodes was 20.3% in our series, which is similar to that reported in these two studies. However, unlike our study, episodes managed on an outpatient basis were not considered in any of them, underestimating the real recurrence rate.

It is relevant to determine whether these new episodes are more or less serious than the index case. A population-based

study from the Netherlands evaluated long-term outcomes of 38 patients undergoing LPL at 10 university hospitals between 2008 and 2010 [15]. After a median follow-up of 46 months, 12 patients (31.6%) had a recurrence, 7 of them requiring emergency surgery for a complicated episode. This is quite higher than in our series in which only 5 patients underwent an emergency resection.

Long-term outcomes of the SCANDiV study [12] show that, after a median follow-up of 59 months, the LPL group had a lower stoma rate (8% vs 33%) and, predictably, a higher recurrence rate (21% vs 4%) than the sigmoidectomy group. However, as in our series, most of the recurrences were uncomplicated and only half of the patients with recurrences underwent a colonic resection in the long term. It is unclear whether recurrences were treated with or without hospitalization.

Recently, the 3-year follow-up results of the LOLA trial were published [11]. Although no differences were found regarding morbidity or mortality, reoperations and permanent stoma were significantly lower in the lavage group. Recurrent diverticulitis in this group was 21% and, as shown in our study, most of them were treated conservatively.

A recent Italian study including patients with Hinchey II and III diverticulitis who underwent either LPL or sigmoidectomy reported a 27% (6 of 22) recurrence rate in the LPL group after 6 months of follow-up [27]. As in our study, the recurrence rate in the first 6 months of follow-up is high, around 30%. However, after the first year of follow-up, the risk of recurrence decelerated significantly in our population, remaining stable thereafter. The subsequent years following the first two of follow-up only contributed to a 5% increased risk of diverticulitis recurrence.

Table 3 Univariate and multivariate Cox proportional hazards analysis. Proportional hazards assumption tested by Schöenfeld's global test ($p = 0.64$)

	Univariate analysis			Multivariate analysis		
	HR	95% CI	<i>p</i> -value	HR	95% CI	<i>p</i> -value
Age, every 1 year	0.99	0.96–1	0.32	0.99	0.95–1.03	0.7
Gender						
Male	1.00					
Female	0.88	0.4–1.76	0.74	0.92	0.4–2.2	0.84
ASA classification						
1	1.00					
2	0.49	0.1–2.2	0.35			
3	0.38	0.08–1.77	0.22			
Charlson index						
Charlson < 3	1.00					
Charlson ≥ 3	0.84	0.41–1.8	0.65	0.79	0.26–2.37	0.68
Medical history						
Cardiologic	0.75	0.36–1.56	0.45			
Respiratory	1.04	0.44–2.48	0.92			
Nephrologic	0.58	0.08–4.27	0.59			
Neurologic	0.55	0.17–1.83	0.33			
Diabetes	1.47	0.5–4.3	0.48			
Immunosuppression	0.00	NA	NA			
Chronic steroid intake	0.72	0.17–3	0.65			
Smoking	2.37	1.09–5.15	0.03	2.9	1.23–6.87	0.015
Obesity	1.03	0.47–2.28	0.93	0.65	0.27–1.54	0.33
Alcoholism	0.34	0.05–2.6	0.3			
Previous episodes						
Global	4.1	1.84–9.2	0.001	5.38	2.19–13.21	<0.001
Hospitalization	3.2	1.22–8.5	0.02			
WSES classification						
1A–1B	1					
2A–2B	2.6	0.56–12.1	0.22			
3	0.68	0.15–3	0.61			
4	0.76	0.25–2.28	0.63			
LOS, every 1 day	1.00	0.93–1.07	0.93			
Global morbidity	1.16	0.47–2.9	0.75			
Major morbidity	1.70	0.5–5.74	0.39			
Percutaneous drainage	1.70	0.5–5.74	0.39			

HR hazard ratio, 95% CI 95% confidence interval, ASA American Society of Anesthesiologists, WSES World Society of Emergency Surgery, LOS length of hospital stay, NA not analyzable according to the method employed

Other authors have also noticed this *plateau* in the risk of recurrence, showing that between 55 and 82% of these new episodes occur within the first year of follow-up [28–30].

Although recurrence rates can be high in patients who have had complicated diverticulitis, resective surgery may be omitted in certain situations. A retrospective study including high-risk patients treated with percutaneous drainage for diverticular abscesses [31] showed that after a follow-up period of 7 years, only 16% of the patients had uncomplicated recurrences and 13% had recurrent abscesses that were successfully treated by a

new percutaneous drainage. This study concludes that the conservative management of patients with recurrent episodes can be safe in selected cases. A more recent study [32] evaluated long-term outcomes of 107 patients who had been treated conservatively for diverticular abscesses. After a median follow-up of 110 months, 20% of these patients had recurrences, and only 4 required an emergency colectomy. A heterogeneous cohort study [33] including patients with Hinchey II–IV who underwent LPL showed that after a median follow-up of 54 months, only 7% of patients had to undergo elective

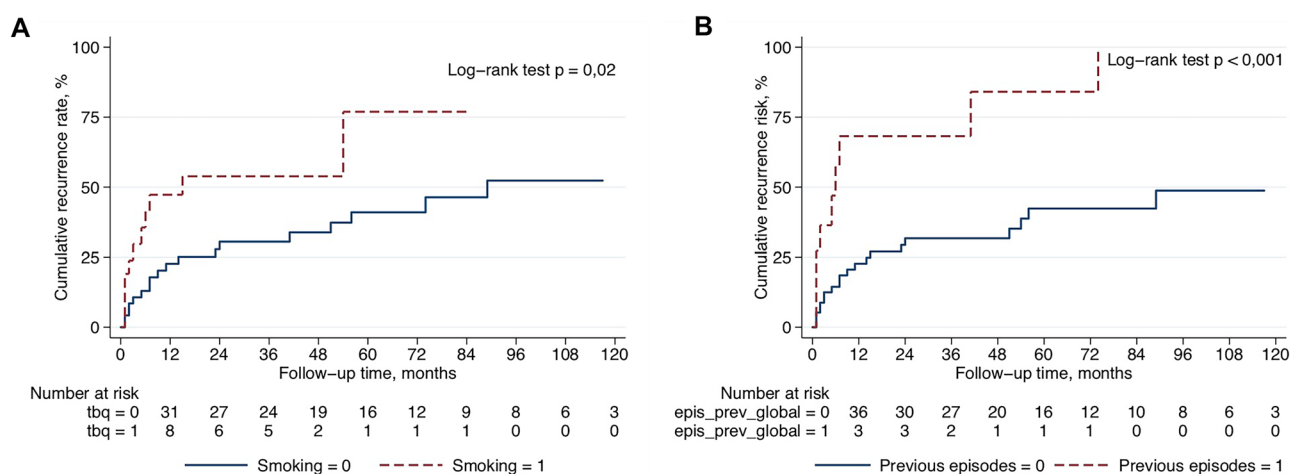


Fig. 5 Kaplan–Meier curve for cumulative recurrence in patients undergoing laparoscopic peritoneal lavage according to **A** history of smoking and **B** previous episodes of acute diverticulitis

surgery for recurrent episodes. This slightly differs from our series where 19 patients out of the 29 that had recurrences underwent a colectomy. However, this could be explained by the shorter follow-up time in the multicenter study.

A relevant question is whether it is possible to predict which patients are at a higher risk of recurrence and if conservative management should be avoided in these cases. Many factors have been previously associated with recurrences. A population-based study [34] including more than 65,000 patients treated nonoperatively showed that female gender, young age, smoking, obesity, and initial complicated diverticulitis were independently associated with recurrence and emergency surgery. The association between smoking and diverticular disease has already been described by other authors. A systematic review [35] including six prospective studies concluded that current and former smokers had an increased risk of diverticular disease and more severe episodes. Interestingly, this risk rose according to the number of daily cigarettes. The underlying mechanism could be multifactorial. Smoking is a pro-inflammatory agent that decreases collagen formation, increases intestinal motility and intraluminal pressure, alters blood flow, and increases colonic permeability [36–38]. Recent studies have shown that smoking affects colonic microbiome [39], contributing to an increased incidence of diverticulitis [40].

Previous episodes of acute diverticulitis have been associated with an increased risk of recurrence by other authors. A systematic review including 35 studies with over 390,000 patients showed a two-fold increased risk of recurrence in patients with a history of two previous episodes of diverticulitis [41]. Age, male gender, and the absence of diverticulitis episodes prior to LPL have been

proposed as protective factors for recurrences after a successful LPL [26]. The risk of uncomplicated diverticulitis recurrences increases with a greater number of previous episodes. However, these may not increase the risk of more severe events requiring emergency surgery [42]. Furthermore, the morbidity associated with new events appears to be similar among patients with multiple episodes versus those with 1 or 2 [43].

Identifying risk factors to predict recurrences is clinically relevant. Based on our findings, we could contemplate that early elective colectomy should be considered after a successful LPL in patients with clinical history of previous episodes of diverticulitis and/or smoking.

The main strengths of this study are the long follow-up period, the strict selection criteria, and the homogeneity of this Hinchey III population, since other studies have included different stages of the disease. It must be recognized that lately, LPL has been questioned as a treatment option for Hinchey III diverticulitis, mainly based on the results reported in two (LADIES and SCANDIV) out of three trials [6–9]. Accordingly, the ESCP [44] states that LPL is feasible in selected cases while the ASCRS [10] recommends colectomy in this population. However, in spite of this, the success rate of LPL reported in these trials is still high (LADIES: 76%, SCANDIV: 80%, DILALA: 87%), favoring LPL [45]. Our own success rate (83.3%) is consistent with these findings. Moreover, certain methodological issues of the LADIES and SCANDIV trials were highlighted by some authors, such as high inter-hospital and inter-operator variability and randomization performed before laparoscopy, respectively [46, 47].

The present study has some limitations. To begin with, this is a retrospective study and, as such, information bias cannot

be dismissed, especially regarding subclinical diverticulitis episodes for which patients may not have consulted. However, this population is part of a larger cohort whose data are collected prospectively in a specially dedicated database, which requires exhaustive monitoring in all cases. Secondly, despite the sample size analyzed may be considered small, it was powerful enough to demonstrate statistically significant differences. Thirdly, as our series has been performed over a long period of time, the number of participating surgeons could generate variability in the decision to LPL and may have contributed to a source of bias. Finally, this cohort was not compared with a colectomy group. However, we believe that successful LPL is not directly comparable to colectomy in Hinchey III diverticulitis since the absence of the sigmoid colon in the latter group virtually precludes any subsequent episode of inflammation, used as an important clinical endpoint here.

Conclusions

The recurrence rate of diverticulitis after a successful LPL is high, especially during the first year of follow-up. The majority of these new episodes are successfully managed with conservative treatment. Smoking and previous episodes of acute diverticulitis independently increase the risk of new episodes of diverticulitis in this clinical setting. These two variables should be considered to indicate an early elective colectomy after a successful LPL and promptly discussed with the patient after discharge.

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Author contribution Study conception and design: Campana, Rossi Acquisition of data: Campana, Gonzalez M., Gonzalez Salazar, Moya Analysis and interpretation of data: Campana, Rossi Drafting of manuscript: Campana, Rossi Critical revision of manuscript: Rossi, Mentz, Vaccaro.

Data availability The datasets generated and/or analysed during the current study are available in the Trovare Institutional Repository of the Hospital Italiano de Buenos Aires. [Available from: <http://trovare.hospitalitaliano.org.ar/greenstone/cgi-bin/library.cgi?c=tesisyr&a=d&d=D1419>]

Declarations

Competing interests The authors declare no competing interests.

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