



Is laparoscopic lavage safe in purulent diverticulitis versus colonic resection? A systematic review and meta-analysis



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ARTICLE INFO

Keywords:

Purulent diverticulitis
Hinchey classification
Laparoscopic lavage
Colonic resection
Meta-analysis

ABSTRACT

Background: Diverticulitis is one of the most common gastrointestinal diseases in western population. Colonic resection is recommended by international guidelines as a routinely used technique for purulent diverticulitis. Laparoscopic lavage was introduced as a non-resection alternative. The studies available so far have shown contradictory results. This meta-analysis aims to compare laparoscopic lavage versus colonic resection in patients with Hinchey III-IV diverticulitis.

Methods: We did a systematic review of articles published before March 20, 2019, with no language restriction by searching PubMed, Cochrane library, EMBASE databases, clinicaltrials.gov, and Google Scholar databases. We included all RCTs and cohort studies comparing outcomes between patients with Hinchey III-IV diverticulitis undergoing laparoscopic lavage versus colonic resection. Important outcomes were mortality, complications, length of stay, readmission and reoperation rates. We combined data to assess the outcomes using DerSimonian and Laird random-effects model.

Results: A total of 569 patients with diverticulitis of which more than 80% were Hinchey III were enrolled from 3 RCTs and 5 cohort studies. Laparoscopic lavage was associated with shorter operative time (WMD -78.9, 95%CI -100.58 to -57.11, $P < 0.0001$) and total postoperative hospital stay (WMD -7.62, 95%CI -11.60 to -3.63, $P = 0.0002$) but a higher rate of intra-abdominal abscess (OR 2.69, 95%CI 1.39 to 5.21, $P = 0.0032$) and secondary peritonitis (OR 5.30, 95%CI 1.91 to 14.73, $P = 0.0014$).

Conclusion: Laparoscopic lavage for patients with Hinchey III to IV diverticulitis does provide similar mortality, shorter operative time and hospital stay. However, the evidence so far suggests that it might be inadequate for sepsis control and may result in more unplanned reoperations. Further studies are needed to standardize the formal indication for laparoscopic lavage.

1. Introduction

Diverticulitis is one of the most common gastrointestinal diseases in western world. The annual admission rate in Europe is estimated to be 209/100,000 adults [1]. Many complications can arise from diverticulitis, and one of the more serious complications of this is perforation of the bowel. Diffuse diverticular peritonitis (Hinchey III-IV) is traditionally treated by the colonic resection (CR) surgery [2] including the Hartmann procedure or primary resection with high rates of complications resulting in frequent hospital readmissions [3].

Non-resection alternatives to perforated diverticulitis have been increasingly used. Laparoscopic lavage (LL) was introduced in 1996 by O'Sullivan [4] and has been reported in several consecutive series of LL patients [5]. A retrospective population study from Ireland found that

17% (427/2555) patients were treated only with laparoscopic lavage for diverticulitis between 1995 and 2008. Compared with patients undergoing open resection, these patients had lower mortality (4.0% vs 10.4%, $p < 0.001$), shorter hospital stays (10 days vs 20 days, $p < 0.001$) and a lower incidence of complications (14.1% vs 25.0%, $p < 0.001$) [6]. However, a recently published multicenter cohort study conducted in Dutch reported long-term (46 months) follow-up data on patient outcomes. Re-intervention and readmission rates after laparoscopic lavage were high, 32% (12/38) patients underwent surgical re-interventions while 39% (15/38) patients had at least one readmissions [7].

In this meta-analysis, we aimed to examine the available evidence to date and investigated the effectiveness of laparoscopic lavage and bowel resection concerning post-procedure mortality and complications

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<https://doi.org/10.1016/j.ijisu.2019.10.007>

Received 30 July 2019; Received in revised form 17 September 2019; Accepted 5 October 2019

Available online 11 October 2019

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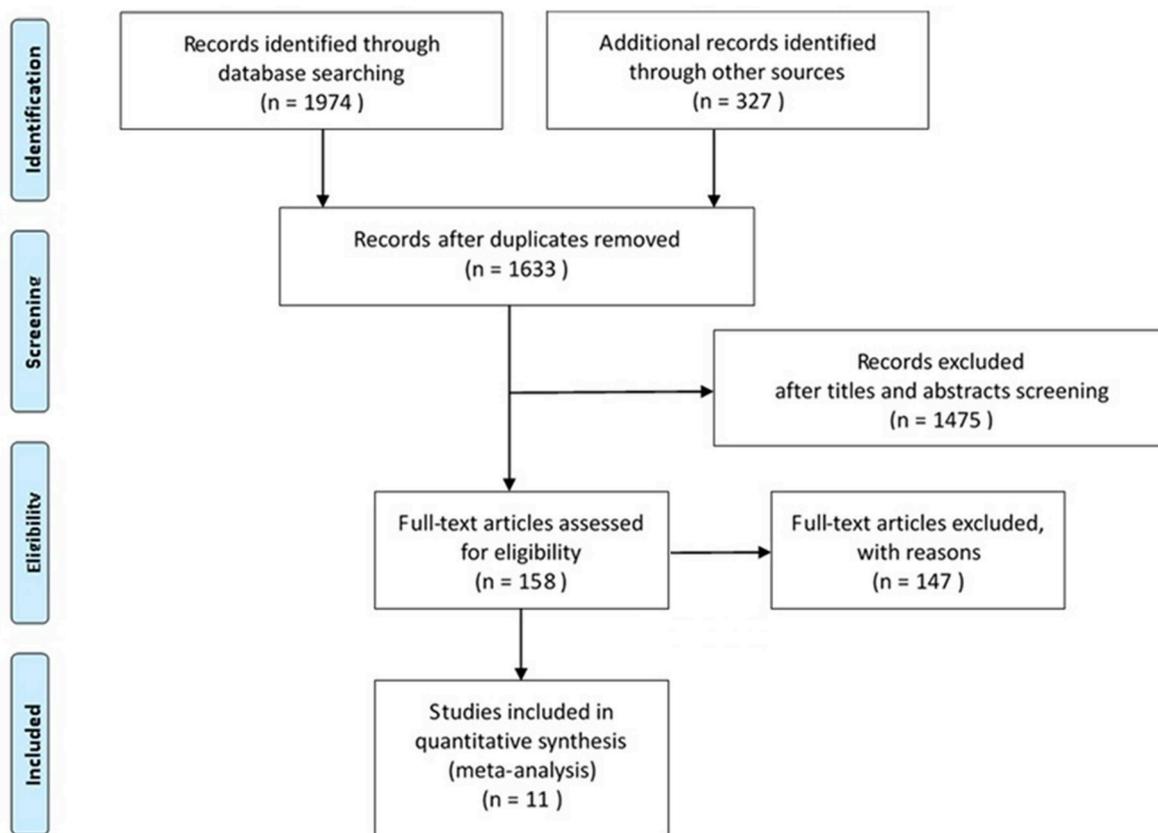


Fig. 1. Preferred Reporting items for systematic reviews and meta-analysis (PRISMA) flow diagram for the literature search.

along with long-term outcomes as rates of reoperations, hospital stay and quality of life.

2. Method

This systematic review and meta-analysis was conducted following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8] and the Assessing the methodological quality of systematic reviews (AMSTAR) [31] guidelines. The protocol for this meta-analysis is available in PROSPERO (CRD42019123995).

2.1. Search strategy and selection criteria

We searched the PubMed, Cochrane library, EMBASE databases and clinicaltrials.gov from the inception dates to March 20, 2019, with no language restrictions, using the keywords "diverticulosis" OR "diverticulitis" AND "laparoscopic lavage" OR "lavage" AND "Hartmann's" OR "colonic resection" to identify studies comparing LL with CR for diverticulitis. Reference lists of relevant studies were searched manually and the "related articles" function in PubMed was used. A search of Google Scholar databases was also performed. Trials were included if they were RCTs, and observational studies enrolling patients categorized by Hinchey classification and comparing LL with CR. We excluded noncomparative trials and studies not including an LL or CR group.

The methodological quality assessment for the included trials was conducted independently by 2 researchers (Z.P., Z.H.P.). RCTs included were appraised using a modified Cochrane Risk of Bias assessment tool [9]. Seven items were used to evaluate bias in each trial included the randomization sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Observational studies were assessed according to the Newcastle–Ottawa Scale

(NOS) [30]. Studies were ranked with a maximum of 9 stars, assessing the methodological quality concerning "selection of patients", "comparability" and "outcome of study participants." Any disagreement between reviewers was resolved by a third reviewer (Y.X.X.) if consensus could not be reached.

2.2. Data analysis

Z.P. extracted the following data from included trials: study details; patient demographics; intervention detail; and major operative and postoperative outcome. These were checked by Z.H.P., and disagreement was solved by consensus. If data could not be obtained from the manuscript, we contacted the original author to supply the required information. Nonresponders received contact up to 2 times.

After entering data into a computerized spreadsheet, we performed meta-analysis using R studio (version 1.0.136) with 'meta' package. For dichotomous variables, we calculated the odds ratios (OR) with 95% CI. Weighted mean difference (WMD) with 95% CI was calculated for the effect size on continuous variables. Heterogeneity was assessed using Cochran's Q and I^2 statistics. An $I^2 > 50\%$ and a P-value of < 0.1 was defined as statistically significant and meaningful heterogeneity. Summary measures were pooled using DerSimonian and Laird random-effects models [10]. A P value of < 0.05 was considered statistically significant for each pooled effect. A funnel plot was used to test for potential publication biases for each outcome. Subgroup analyses were conducted based on the type of study design.

3. Result

3.1. Search results

We identified 1633 records through the electronic database searching. After screening of titles and abstracts, we found 158

Table 1
Study characteristics.

Study	Year	Design	Funding	Trial Name	Number of Recruiting Centers	Number of Patients Enrolled in Outcome Analysis		Operative Strategy for Colonic Resection	Follow-up
						LL	CR		
						Kohl	2018		
Angenete	2016								
Thornell	2016								
Schultz	2017	RCT	ALF and Sahlgrenska University Hospital, Gothenburg.	SCANDIV	21	74	70	Laparoscopic or open, Hartmann's	12 months
Vennix	2015	RCT	Netherlands Organisation for Health Research and Development.	LADIES-IOLA	42	46	42	Laparoscopic or open, Hartmann's or primary anastomosis	12 months
Karoui	2009	Cohort (Prospective for LL, retrospective for CR)		-	3	35	24	Open primary anastomosis	86 months
Liang	2012	Prospective Cohort		-	1	47	41	Laparoscopic Hartmann's	-
Gentile	2014	Retrospective Cohort		-	1	14	16	Open Hartmann's	-
Gatry	2016	Prospective Cohort		-	2	15	25	Laparoscopic or open primary anastomosis with	-
Desai	2017	Prospective Cohort		-	1	2	35	Primary resection and anastomosis with stoma or PRA without stoma	3 months

publications that met the inclusion criteria. We obtained 11 studies for inclusion by full-text screening the included reviews. Fig. 1 shows the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram for the literature search. Of these 11 studies [11–21], 5 studies (3 for DILALA, 2 for SCANDIV) reported the outcomes from the DILALA (Diverticulitis-Laparoscopic LAvege vs resection [12,16,17]) and the SCANDIV(Scandinavian Diverticulitis [15,19]) at different follow-up time points. Table 1 outlines the main characteristics and established outcomes of the included studies, which included 3 RCTs and 5 observational studies.

3.2. Methodological quality

After the assessment of 3 RCTs, we found the study by Angenete [12,16,17] did not report random sequence generation resulting in the risk of selection bias remained unclear. Blinding of participants might be difficult while blinding of outcome assessment was not performed in all 3 studies, therefore the risk of distortion of the measured effect by performance bias remained unclear and the effect by detection bias is high. Three of all five clinical cohort studies [18,20,21] were considered as low or moderate quality (NOS score < 6). All studies did not demonstrate that the outcome of interest was not present at the start of the study. Two multicenter study was detected [13,18]. Three studies are lacking detailed information on follow-up [18,20,21]. The result of risk of bias assessment is shown in Fig. 2 and Table 2. Publication bias was not assessed statistically due to the insufficient number of studies [9] while the funnel plot (Supplement Figure S1) showing potential publication bias.

3.3. Patient characteristics

As highlighted in Table 3, a total of 569 patients were included for outcomes measurement of which 85% as Hinchey III. 276 patients received LL and 283 underwent CR. Meta-analyses of patient demographics found no significant difference between the two groups in sex ratio, proportion of Hinchey III, previous occurrence of diverticulitis and previous surgery in abdomen. Notably, results for age, BMI and American Society of Anesthesiologists (ASA) grade I-II showed statistical difference between groups. Patients who underwent LL were younger, heavier and had higher ASA grade.

3.4. Postoperative outcomes

Meta-analysis of the primary clinical complications revealed that patients who underwent LL and CR had no difference in mortality rates within 90 days (OR 1.06, 95%CI 0.41 to 2.78, P = 0.90) or 24 months (OR 0.70, 95%CI 0.38 to 1.31, P = 0.26). Rates of wound infection, heart complications, pneumonia or venous thromboembolism were not significantly different between two groups. However LL group had significantly more patients developing intra-abdominal abscess (Fig. 3) (OR 2.69, 95%CI 1.39 to 5.21, P = 0.003) and secondary peritonitis (Fig. 4) (OR 5.30, 95%CI 1.91 to 14.73, P = 0.001) compared to CR group. Also, patients who underwent LL needed more reoperations (stoma reversal included) within 90 days (OR 2.52, 95%CI 1.10 to 5.74, P = 0.028) while no difference was found at 12 months. Overall the LL group had significantly shorter operative time (Fig. 5) (WMD -78.85, 95%CI -100.58 to -57.11, P < 0.0001) and length of hospital stay (Fig. 6) after the procedure (WMD -7.62, 95%CI -11.60 to -3.63, P = 0.0002). 3 RCTs [11,12,15] reported outcomes of quality of life measured in different instruments and showed no difference between groups (Table 4).

We performed subgroup analyses by including only outcomes from the 3 RCTs which showed generally identical results with pooled analysis. However, in contrast to the pooled analysis, the LL group showed no significant increase in the risk of reoperations at both 30 days (OR 2.13, 95%CI 0.80 to 6.31, P = 0.17) and 90 days (OR 2.42, 95%CI 0.75

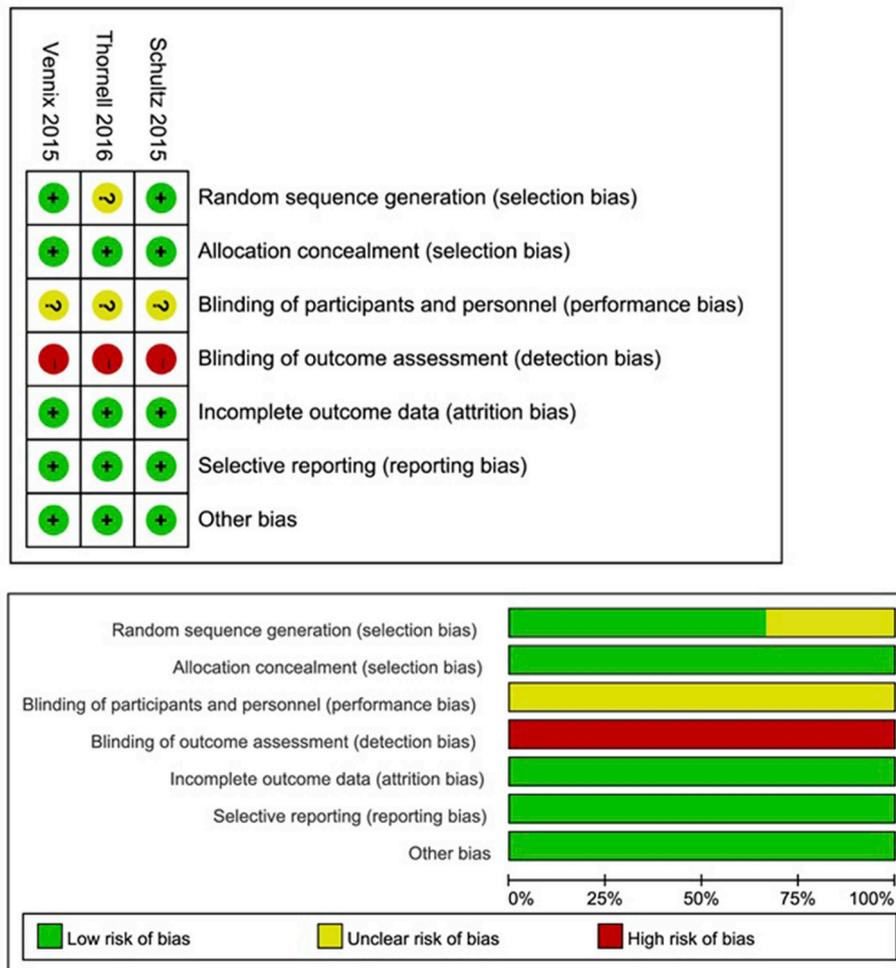


Fig. 2. Result of the Cochrane Collaboration's tool for assessing risk of bias in the included randomized controlled trials.

to 7.80, P = 0.14).

4. Discussion

In this meta-analysis, laparoscopic lavage shows a similar mortality and morbidity rate when compared to colonic resection and may not yet be recommended as a safer alternative in the management of purulent perforated acute diverticulitis (Hinchey III). 3 published multicenter RCTs and 5 cohort studies including 569 patients were identified to investigate whether LL is superior to CR. In general, LL provided significantly shorter operative time and total postoperative hospital stay, and improved mortality rates in 24 months, wound infection, heart complications, and venous thromboembolism risks, although these improvements did not reach statistical significance. In contrast, the rate of intra-abdominal abscess and secondary peritonitis is in favor of the CR group. Additionally, LL significantly increased the

rate of reoperations within 90 days from the presentation whereas, no difference was found at 12 months. However no significant difference was found in the subgroup analysis, which is consistent with previous meta-analyses [22,23]. The LADIES-LOLA trial [11] reported this outcome after exclusion of stoma reversal procedures for the rates of reoperation while most other studies did not. And the DILALA trial [12,16,17] considered stoma reversal as an reoperation while did not include percutaneous drainage of an abscess. These difference might caused great heterogeneity regarding the result of analysis. Although subgroup analysis confirmed there was an increased rate of abscess or peritonitis, only a few patients underwent surgical reoperation for these complications. In the SCANDIV trial [15,19], three of sixteen patients have intra-abdominal abscess in the LL group and none of seven in the CR group underwent reoperation. In the DILALA trial [12,16,17], reoperation for the abscess control was even less, two in the LL group and one in the CR group. Most patients present with these complications

Table 2
Methodological assessment of cohort studies.

Reference	Selection			Comparability		Outcome		Total Points	
	Representativeness	Selection	Ascertainment	Conflicted Interest	Comparability	Assessment	Follow-up Length		Adequacy of Follow-up
Karoui	+	+	+	-	++	+	+	+	8
Liang	-	+	+	-	++	+	-	-	5
Gentile	-	+	+	-	++	+	-	-	5
Catry	+	+	+	-	+	+	-	-	5
Desai	-	+	+	-	+	+	+	+	6

Table 3
Patient demographics.

	LL	CR	Pooled Result	95% CI	p	I ²	Cochran Q	P
Age,mean	63.27	64.37	-3.72	-5.61, -1.84	< 0.0001	0.73	25.47	0.006
Gender, mean	0.51	0.56	0.88	0.63, 1.25	0.48	0.00	4.30	0.74
BMI,mean	28.05	26.60	1.67	0.14, 3.19	0.03	0.86	35.53	< 0.0001
ASAI-II,%	0.74	0.62	1.54	0.93, 2.55	0.09	0.31	8.71	0.19
HincheyIII,%	0.91	0.80	1.63	0.82, 3.21	0.16	0.00	3.00	0.39
Previous diverticulitis episode, %	0.26	0.27	0.92	0.53, 1.58	0.75	0.36	9.36	0.15
Previous abdominal surgery, %	0.35	0.39	0.88	0.53, 1.47	0.62	0.21	7.57	0.27

were treated with antibiotics or other interventions that were not considered as surgical reoperation such as drainage. After further investigating the data from 3 RCTs, one previous meta-analysis did demonstrate an preference to colonic resection in the reoperation for sepsis control [24].

We noted all the included studies varied in trial methodology, operation performance, outcomes assessment and timing of publication, which causes potential interstudy heterogeneity. For example, there was no guideline or expert consensus for the standardization of operation performance and different exclusion criteria of patients was observed among the selected studies. According to the results of this meta-analysis, patients who are younger, heavier are more likely to be included in the LL group which is also confirmed in the subgroup analysis. Comparing to the patients with lower BMI, those who are higher might present with less emergent situation and have better post-operational prognosis which might explained for the preference to LL in studies considering the unclear post procedure outcomes. And older patients who usually presented with other comorbidities including chronic kidney diseases and rheumatological diseases are more likely to be included in the traditional CR group in real life [6]. Those have more previous abdominal surgery with higher ASA scores tended to be excluded. Thus a potential selection bias within this groups was provided. Otherwise, the volume of fluid used being reported in studies was ranging from 4 to 25 L [11–21]. Surgeons were not limited to the gastrointestinal filed. Thus, the risk of performance bias may be present. Additionally, in most cohort studies, it's up to surgeons to decide whether patients should be included in the LL group based on individual characteristics, previous comorbidities history, and clinical presentation. Hence, the different opinions of surgeons might introduce confounding. The various timing of outcome publications was also selected for different studies, which resulted in insufficient information in different time frames. In the DILALA trial [12,16,17], a long-term endpoint was selected within 24 months and reported outcomes separately in 90 days, one year and two years. Whereas in the LADIES-LOLA study [11], a primary endpoint of morbidity and mortality was selected within 12 months, however due to the significantly higher reoperation rate in the LL group, the trial was early terminated. And the SCANDIV

trial [15,19] have an endpoint in 12 months. The other 5 cohort studies lack detailed description for follow-up. The different endpoint selected for each trials reflected the unclear and contradictory views towards this procedure. In our opinion, we suggest to set an endpoint within least 12 months so that potential risks as well as benefit can generally presents.

Undeniably, laparoscopic lavage shows great feasibility and requires no expensive equipment [25], however, it does need experienced surgeons with advanced laparoscopic skills [26] therefore it is still not available in some proportions of low-volume regional units [6]. Thus, we can not simply apply these findings to the community and the difficult learning curve should be considered. From a practical point of view, not all the patients with purulent diverticulitis have the same intraoperative findings, and the significant heterogeneity generally presents within individual patients. In our real-world experience, we found the use of LL was currently limited due to the fact that most of patients admitted with a less severe condition and do not require an emergency operation. Thus we normally tend to choose a traditional colonic resection surgery as a Hartmann's procedure which is commonly considered safer and easier. On the other hand, we inevitable prefer to perform LL in patients with better condition due to the lack of guidelines with the risk of losing control of septic condition and other issues. Therefore a so-called 'case-by-case' basis is caused. Surgeons must make decisions based on individual situation. It is possible to introduce LL to the future management of Hinchey III diverticulitis for widespread use only after a few problems are settled: how to evaluate the risk of missing diagnosis including persistent perforation and sigmoid carcinoma as stated by Gervaz [27]; how to decide a proper indication for performing LL. Is Hinchey classification accurate enough as purulent peritonitis can present with various clinical symptoms? We suggest that future studies should combine it with Acute Physiology and Chronic Health Evaluation (APACHEII) score [28] as inclusion criteria.

Several limitations must be considered in our study. Five of eight included studies were not randomized. We hence performed a subgroup analysis by excluding the cohort studies. We also found moderate interstudy heterogeneity in the comparison and our funnel plot analysis showed a potential publication bias (Supplement Figure S1) which is

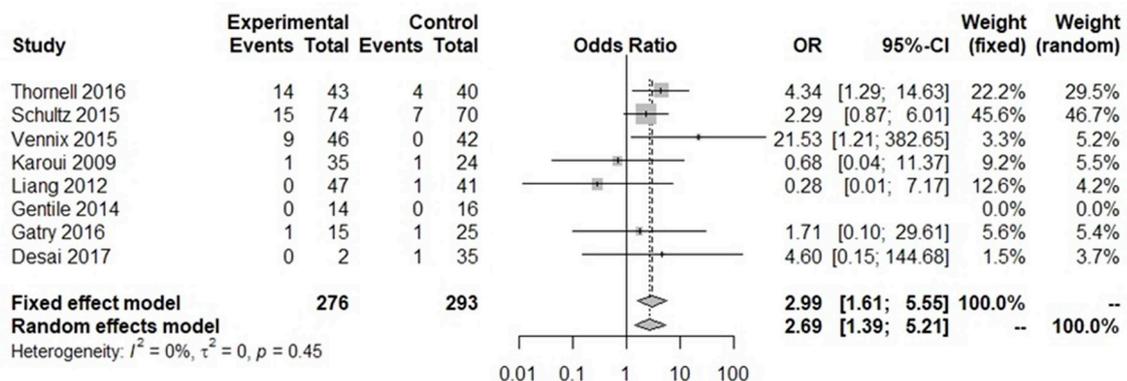


Fig. 3. Intra-abdominal abscess.

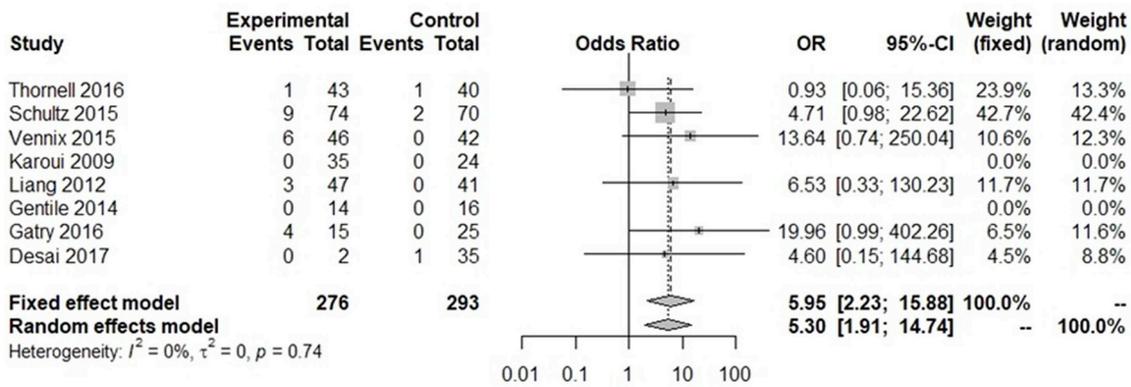


Fig. 4. Secondary peritonitis.

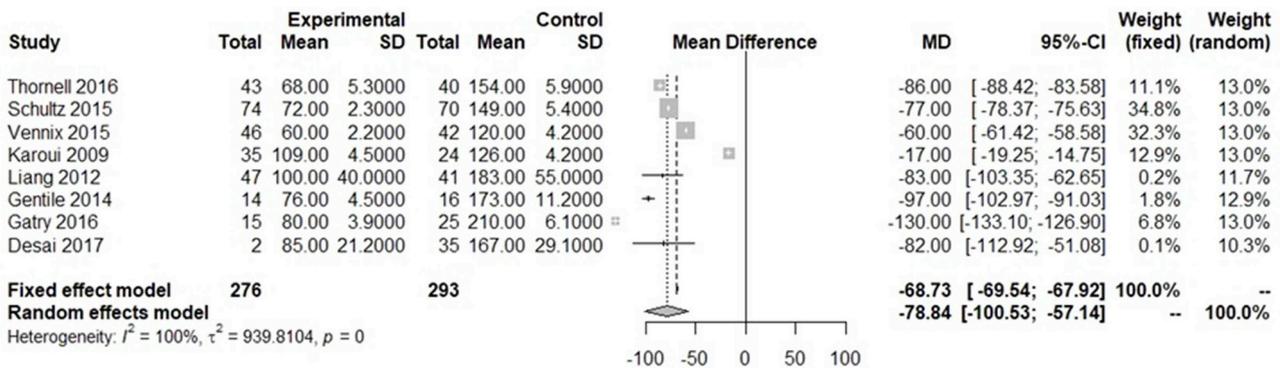


Fig. 5. Operative time.

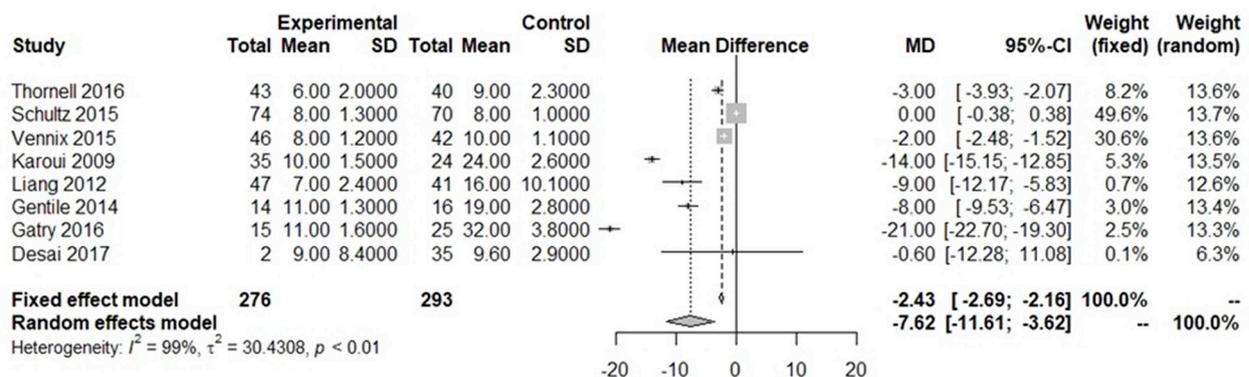


Fig. 6. Length of hospital stay after procedure

tough to quantify with a small number of studies. We had no individual patient data, thus individual patient data meta-analysis can not be done. Finally, the limited amount of patients enrolled may still be underpowered to detect minor prognostic differences between laparoscopic lavage and colonic resection.

In conclusion, laparoscopic lavage for patients with purulent perforated acute diverticulitis does provide similar mortality with colonic resection, shorter operative time and hospital stay. However, based on our systematic review, the evidence so far suggests that it might be inadequate for sepsis control and may result in more unplanned re-operations. Our result do not support that laparoscopic lavage is superior to a traditional colonic resection. More high-quality trials are needed to assess carefully the inclusion criteria and surgical quality. We believe the ongoing LapLand study [29] in Ireland will certainly benefit

our decision. Till then, surgeons may prefer standardized colonic resection procedure, but it is necessary to consider LL as an effective alternative based on the individual situation.

Ethical approval

N/A for this kind of research.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Table 4
Outcomes.

	Pooled Result	95% CI	P	I ²	Cochrane Q	P
Mortality,						
30 days	1.06	0.41, 2.78	0.90	0.27	8.20	0.22
12 months	0.70	0.38, 1.31	0.26	0	3.67	0.72
Severe complications						
Wound infect	0.45	0.13, 1.52	0.20	0.51	12.22	0.57
Intra-abdominal abscess	2.69	1.39, 5.21	0.0032	0	5.77	0.45
Peritonitis	5.30	1.91, 14.73	0.0014	0	2.73	0.74
Heart complications	0.65	0.15, 2.90	0.58	0.63	8.16	0.04
Pneumonia	1.12	0.49, 2.56	0.79	0	4.73	0.45
VTE	0.62	0.12, 3.27	0.57	0	1.31	0.52
Reoperation						
30 days	2.75	1.06, 7.12	0.037	0.44	10.81	0.094
90 days	2.76	1.01, 7.53	0.047	0.02	3.07	0.38
12 months	0.96	0.32, 2.82	0.94	0.77	8.54	0.014
Operative time	−78.85	−100.58, −57.11	< 0.0001	0.998	4104.75	< 0.0001
Hospital stay	−7.62	−11.60, −3.63	0.0002	0.994	1078.88	< 0.0001

Author contribution

Zhe Pan: study design and writing.
 Ze-Hao Pan: data collections and data analysis.
 Rui-Zhi Pan: data collections and data analysis.
 Yu-Xuan Xie: data analysis and writing.
 Gunjan Desai: data collections and writing.

Conflict of interests

None.

Research registration number (UIN)

1. Name of the registry:
 PROSPERO.
 2. Unique Identifying number or registration ID:
 CRD42019123995.
 3. Hyperlink to the registration (must be publicly accessible):https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=123995.

Guarantor

Zhe Pan(pz929675410@gmail.com).

Data statement

This is a systematic review of the literature; all the data presented are available and cited in the references section.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijso.2019.10.007>.

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