Journal of Surgery
[Jurnalul de Chirurgie]
Research Article Open Access

Non-Elective Surgery for Acute Complicated Diverticulitis. Primary Resection-Anastomosis or Hartmann's Procedure? A Systematic Review and Meta-Analysis

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Abstract

Background: The use of Primary Resection-Anastomosis with or without protective ileostomy

(PRA) or Hartmann's Procedure (HP) in the surgery of complicated acute diverticulitis is still an open question. The latest published meta-analyses were limited to the most severe stages (Hinchey III and IV). Our systematic review aimed to compare PRA with the HP in all non-elective surgical patients with complicated acute diverticulitis (perforation or obstruction).

Methods: A computerized literature search was performed on Medline databases until July 2014. The studies included in the meta-analysis were 24 with a total of 4,062 patients. Study outcomes included postoperative surgical complications, reintervention, 30-day mortality, overall mortality as well as the length of stay as secondary outcome. The pooled effects were estimated using a fixed effect model or random effect model based on the heterogeneity test. Results were expressed as odds ratio (OR) and 95% confidence interval (CI) for dichotomous outcomes and as mean difference (MD) with 95% CI for continuous outcomes. Subgroup analyses by study type were performed.

Results: The PRA group had a lower rate of postoperative surgical complications (OR=0.525, 95% CI 0.387-0.713), reintervention (OR=0.688, 95% CI 0.525-0.902), 30-day mortality (OR=0.389, 95% CI 0.259-0.586), overall mortality (OR=0.467, 95% CI 0.272-0.803) and length of stay (MD=9.129, 95% CI 2.391-15.867) compared to the HP group.

Conclusion: Our meta-analysis shows that the PRA technique is better than HP for all considered outcomes. Due to the high variability of the included studies, further randomized controlled trials would be required to confirm these results.

Keywords: Acute complicated diverticulitis; Primary resection-anastomosis; Hartmann's procedure

Introduction

Colonic diverticulosis is a common condition in the Western world and its incidence increases substantially with age. It was estimated that in patients older than age 60 years, 50% have diverticulosis [1,2]. Surgeons' interest for this disease is related to the treatment of the complications of diverticulitis (perforation, occlusion, bleeding). About 25% of patients hospitalized for diverticulitis will require a non-elective surgical intervention, in most cases for perforation [3,4]. The surgical management of emergencies for diverticulitis progressed over the past years. The three stage procedure (stoma without resection of the diseased segment as first stage) only maintains a historical value. The two stage procedure, better known as Hartmann's procedure (HP), includes the resection of the perforated or stenotic segment with terminal colostomy (first stage) and the subsequent restoration of the bowel continuity (second stage). Most recently a one stage surgical approach was proposed including resection of involved colon and primary anastomosis realized in the same setting, with or without protective ileostomy (PRA). Many studies demonstrated no differences between HP and PRA in terms of morbidity and mortality [5,6]. Nevertheless, most surgeons still prefer HP in the emergency setting to treat perforation or obstruction from acute colonic diverticulitis [3,7,8]. Most retrospective studies and the only two prospective trials [6,9] are focused only on patients operated for perforated diverticulitis and peritonitis (Hinchey stage III and IV). Our systematic review aimed to evaluate the literature comparing PRA (with or without protective ileostomy) with HP in all non-elective surgical patients with complicated acute diverticulitis (perforation or obstruction) to assess the effectiveness and safety of the one-stage technique.

Methods

Data sources and search strategy

A comprehensive computerized literature search was performed until July 2014 on Medline databases using the following search terms: "Hartmann", "primary anastomosis", "perforated diverticulitis", and "acute diverticulitis". Only papers published in English were considered while no publication date restrictions were applied. The computer search was supplemented with a manual search of reference lists for all available review articles and meta-analyses to identify further relevant works not found by the computer search. We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses.

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Received June 19, 2016; **Accepted** June 21, 2016; **Published** June 27, 2016

Citation: Lorusso D, Giliberti A, Bianco M, Gioacchino. Non-Elective Surgery for Acute Complicated Diverticulitis. Primary Resection-Anastomosis or Hartmann's Procedure? A Systematic Review and Meta-Analysis. Journal of Surgery [Jurnalul de chirurgie]. 2016; 12(2): 43-49 DOI:10.7438/1584-9341-12-2-1

Eligibility criteria

Eligible studies were those comparing PRA (with or without protective ileostomy) with HP in non-elective surgical patients with acute diverticulitis complicated by peritonitis or bowel obstruction. The laparoscopic techniques were not considered in the present review. Peritonitis and bowel obstructions caused by inflammatory bowel diseases or cancer were also excluded. Surgical interventions on acute colonic diverticulitis meeting the above criteria had also to include at least one of the following primary outcomes: (i) postoperative surgical complications, (ii) reintervention, (iii) 30-day mortality and (iv) overall mortality. Postoperative surgical complications included wound infection, wound dehiscence, intra-abdominal infection/abscess, rectal stump dehiscence, sepsis, multiorgan failure, stoma complications, bowel occlusion and intra-abdominal hemorrhage. The number of events for each study was obtained by summing all postoperative surgical complications occurred while the number of possible complications was calculated multiplying the number of patients by 9, which expressed the number of complications. This method was applied to estimate the postoperative complications occurred after the first intervention as well as to sum the complications occurred after the first and the second intervention, when the restoration of the bowel continuity was indicated. Reintervention was defined as any surgical procedure required in a postoperative patient within a few days/weeks following the initial surgical procedure and related to the initial surgery. The 30-day mortality expressed the number of deaths from any cause within 30 days from the first hospital admission for non-elective surgery in patients with complicated diverticular disease. Overall mortality recorded the number of deaths occurred after both the first intervention and the second intervention of recanalization. The overall mortality coincided with 30-day mortality, for patients who underwent PRA without diverting loop ileostomy. Secondary outcome considered the length of stay (LOS) in days for first admission in both groups. Randomized controlled trials (RCT), prospective non randomized trials (PNR) and retrospective studies (R) were included in this study.

Data extraction

Original articles were reviewed and the variables of interest were abstracted, where reported. When discrepancies occurred between reviewers, the reasons were identified and a final decision was made based on the reviewers' agreement. Quality score was assigned to each study by the Jadad scale assessing 3 major criteria: reporting and handling of randomization and blinding and handling of withdrawals. The maximum possible score was 5 while studies with extensive flaws were those with a ≤ 2 score. The validity assessment was performed by the same two reviewers who extracted data from the full text articles.

Statistical analysis

For dichotomous outcomes formal statistical tests for heterogeneity of the odds ratios (ORs) were performed with the Cochrane Q test, heterogeneity being assumed with a p value ≤ 0.05. When a Q test indicated substantial heterogeneity, a random-effects model weighted by the DerSimonian-Laird method was used. A fixed-effects model weighted by the Mantel-Haenszel method was used for pooling the ORs. Results were expressed as OR and 95% confidence interval (95% CI). For continuous outcomes, the mean difference (MD) with 95% CI was calculated. The pooled effects were estimated using a fixed effect model or random effect model based on the heterogeneity test.

We performed subgroup analyses to assess the effect of the study type (RCT, PNR or R) on the association between surgical technique and outcomes.

All meta-analytical data were analyzed according to intention-to treat analyses. All procedures and calculations used in the meta-analyses were made following the methodology reported elsewhere [10].

Results

A total of 372 potentially eligible studies were identified, as reported in Figure 1. Study titles and abstracts were screened for inclusion. 307 were excluded and the remaining 65 possibly relevant studies were retrieved as full text articles. Based on the full text assessment, 41 studies were excluded for the following reasons: elective surgery (n=9), outcomes not reported or not available (n=25), other surgical technique (n=1), data included in previous or more complete studies (n=4), Italian language (n=2). The USA national survey conducted by Masoomi et al. [11] was excluded to avoid a selection bias because the authors compared 56,866 HP patients with 3,361 patients treated

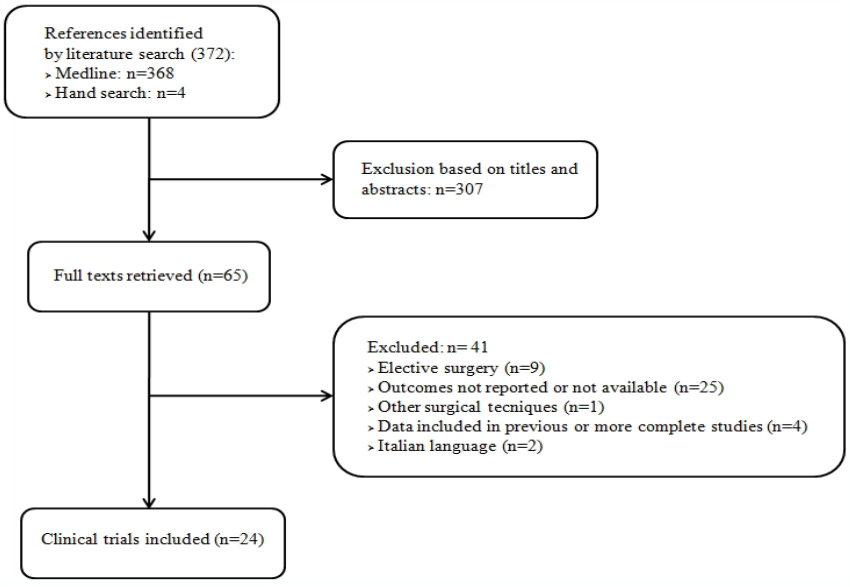

Figure 1: Systematic review PRISMA flow diagram.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model

with PRA and proximal diversion, excluding from the analysis 39,032 patients treated with PRA without diversion. A total of 24 studies met our eligibility criteria and were included in the meta-analysis, yielding a total of 4,062 non-elective surgical patients with acute complicated diverticulitis. 1,184 patients underwent PRA (with or without protective ileostomy) while 2,878 patients were submitted to HP. The selected study characteristics are summarized in Table 1 [12-33]. Two randomized controlled trials [6,9] were included in the meta-analysis and ranked as high quality studies with a Jadad's score of 3, while four were prospective non randomized studies and eighteen followed a retrospective design. The inherent lower methodological quality of retrospective and prospective non randomized designs suggested us to perform subgroup analyses by study type (Figures 2-6).

Postoperative surgical complications

Patients who underwent to PRA had a substantial lower risk to develop postoperative surgical complications compared to HP (OR=0.525, 95% CI 0.387-0.713; heterogeneity: Q value=49.364; P<0.0001). The observed heterogeneity is mainly due to the retrospective studies in which, however, the average effect went in the same direction of the other two groups that, instead, did not show heterogeneity. For this reason we considered the random effect model used strong enough.

The PRA group also showed lower postoperative surgical complications in all study types analyzed (R, PNR and RCT) (Figure 2). Although few studies [6,9,17-25] reported the complications occurred after the second intervention planned to restore the bowel continuity, the same results were found considering the sum of the complications occurred after the first and the second intervention (OR=0.490; 95% CI 0.361-0.664; heterogeneity: Q value=50.716; P<0.0001) (data not shown). The previous considerations about heterogeneity could also be applied in this case.

Reintervention

HP patients showed a higher risk to be submitted to reintervention compared to PRA (OR=0.688, 95% CI 0.525-0.902; heterogeneity: Q value=33.027; P=1.000). Such result was confirmed in the R and PNR subgroups but not in the only RCT considered (Figure 3). Despite the absence of heterogeneity, in our opinion this result should be interpreted with caution and further studies would be required to confirm it. The complications that led to perform a reintervention were reported only by six studies and amounted to 18.0% for HP and 9.7% for PRA. In the HP group, the main causes of reintervention were related to wound complications (41.8%), stoma complications (27.3%) and intraabdominal abscess (14.5%) while patients submitted to PRA were reoperated for anastomotic leak (57.9%), wound complications (21.1%) and resuturation of abdominal incisions (21.1%).

30-day mortality

Statistical heterogeneity was present among the 24 studies considered (Q value=50.548; P= 0.001). By using a random effect model, pooled analysis showed a statistically significant advantage in the PRA group in terms of lower 30-day mortality rate (OR=0.389, 95% CI 0.259-0.586), which was confirmed in the three subgroups considered (Figure 4).

Overall mortality

The overall mortality rate was 8.5% (19/224) in the PRA group and 16.9% (50/295) in the HP group, respectively (Figure 5). Data were pooled from 8 studies and demonstrated a significant lower overall mortality risk in the PRA group (OR=0.467, 95% CI 0.272-0.803), which was confirmed in the three subgroups considered. Heterogeneity among the studies was no significant (Q value=6.247; P=0.511), allowing us to use a fixed effect model.

Length of hospital stay

The trend was in favor of the PRA technique with a pooled MD of 9.129 (95% CI 2.391-15.867), in spite of the presence of significant heterogeneity among the 4 considered studies (Q value= 25.730; P<0.0001). The quantitative aspect of this analysis (hospital days saved)

Table I: Characteristics of included studies.

Author	Region	Year	Study type	Number of patients	
				HP	PAR
Alanis et al. [12]	USA	1989	R	26	34
Alizai et al. [13]	Germany	2013	R	72	26
Berry et al. [14]	England	1989	R	47	27
Binda et al. [9]	Multicenter	2012	RCT	56	34
Blair et al. [15]	Canada	2002	R	64	33
Gawlick et al. [16]	USA	2012	R	1678	340
Gooszen et al. [17]	Netherlands	2001	R	28	32
Herzog et al. [18]	Germany	2011	R	19	21
Hold et al. [19]	Austria	1990	R	76	99
Kourtesis et al. [20]	USA	1988	R	10	23
Mäkelä et al. [21]	Finland	2005	R	93	64
Mueller et al. [22]	Germany	2011	R	26	47
Oberkofler et al. [6]	Switzerland	2012	RCT	30	32
Pasternak et al. [23]	Switzerland	2010	R	65	46
Regenet et al. [24]	France	2003	PNR	33	27
Richter et al. [25]	Germany	2006	R	5	36
Saccomani et al. [26]	Italy	1993	R	8	26
Schilling et al. [27]	Germany	2001	PNR	42	13
Smirniotis et al. [28]	Greece	1992	R	18	6
Stumpf et al. [29]	USA	2007	R	30	36
Tabbara et al. [30]	USA	2010	R	176	18
Trenti et al. [31]	Spain	2011	PNR	60	27
Tudor et al. [32]	England	1994	PNR	77	76
Vermeulen et al. [33]	Netherlands	2007	R	139	61

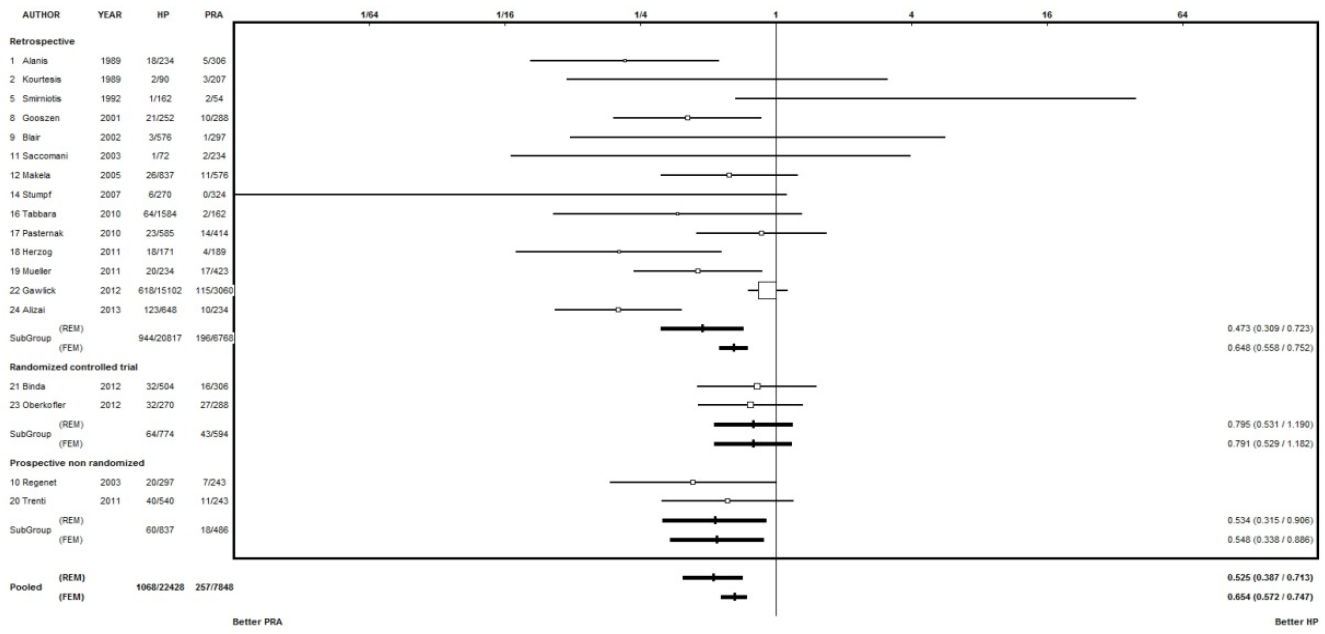

Figure 2: Forest plot for postoperative surgical complications by study type and results of meta-analysis.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model

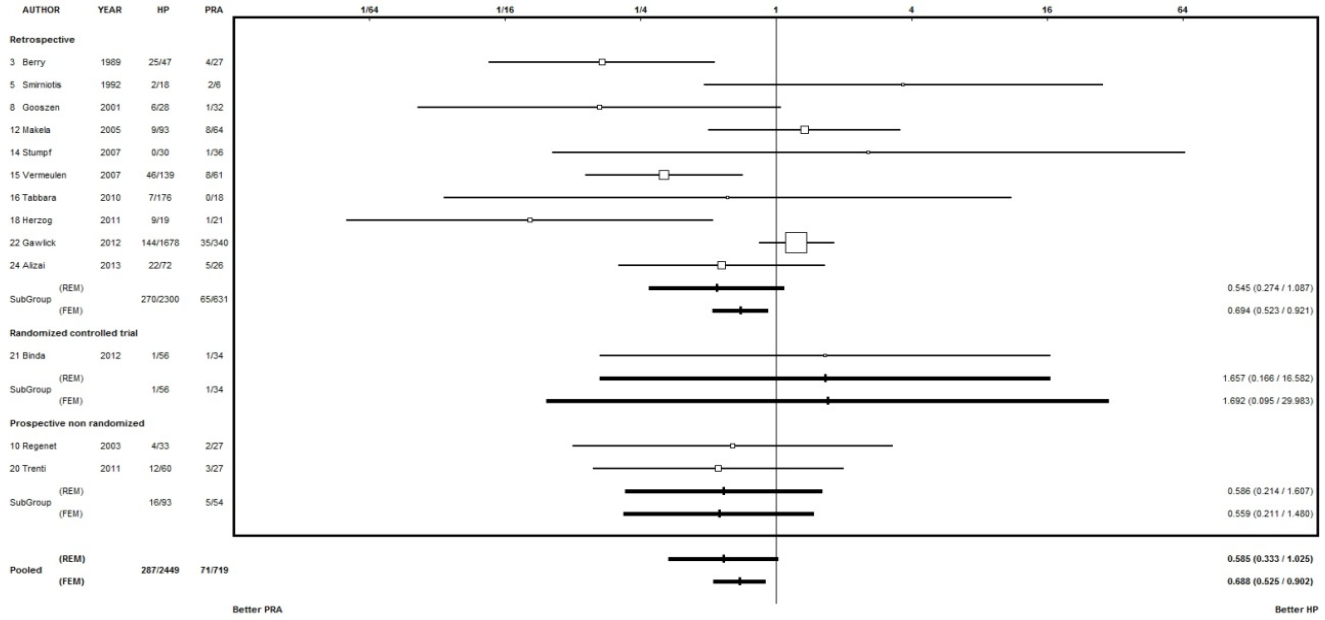

Figure 3: Forest plot for reintervention by study type and results of meta-analysis.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model.

must be interpreted with caution due to the significant heterogeneity between prospective and retrospective studies (Figure 6).

Discussion

Worldwide, HP is still the most common procedure performed in emergency surgery for complications of acute diverticulitis. This tendency was also reflected in the data collected in our meta-analysis: excluding the two RCT, out of a total of 3,910 patients 2,792 (71.4%) patients were submitted to HP while only 1,118 (28.6%) patients underwent PRA (with or without protective ileostomy). Emergency colorectal resection is an independent risk factor for anastomotic leak (relative risk 4.6, 95% CI 1.9-9.8) and the presence of peritonitis and/or bowel obstruction is also a predictive factor [34]. This is the reason why, in patients with a diffuse peritonitis or occlusion in a colon not prepared, most surgeons commonly avoid the anastomosis for the high risk of dehiscence with major complications for the patient [25,35]. However, many studies, including the only completed randomized clinical trial and four systematic reviews, have demonstrated the feasibility of anastomosis for peritonitis due to perforated diverticulitis so that nowadays the colorectal anastomosis is not absolutely contraindicated in emergency surgery for this disease [5,6,8,36,37]. In particular, the above mentioned studies showed that morbidity and mortality

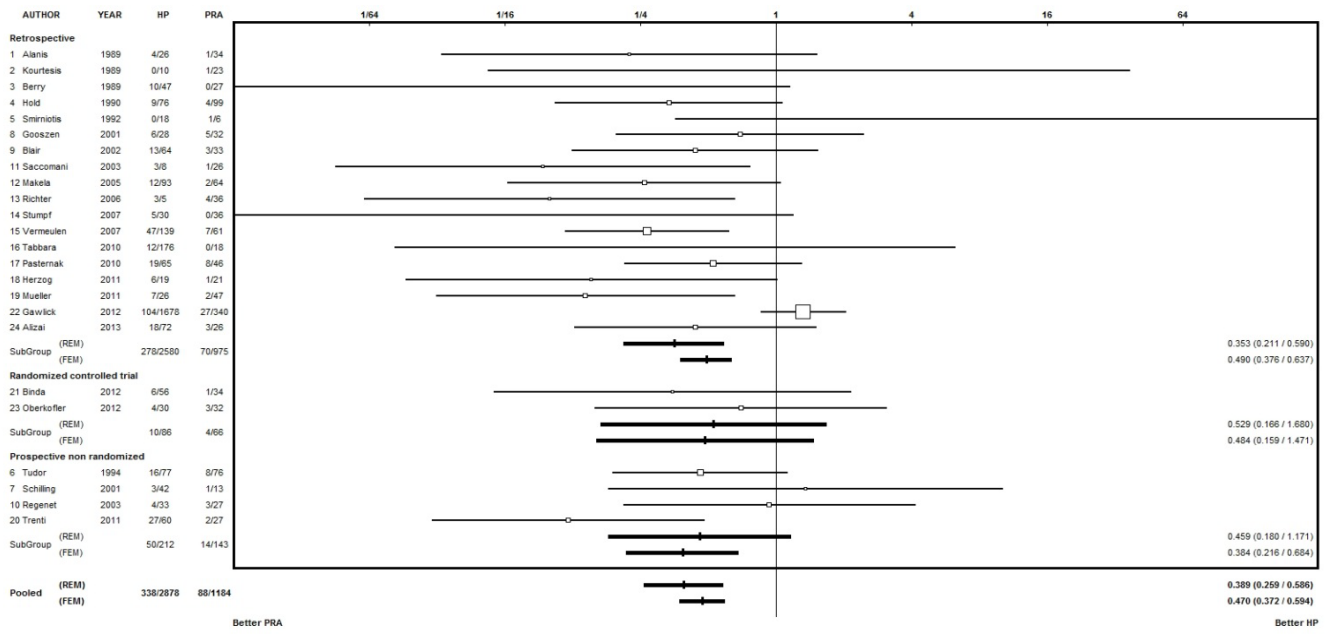

Figure 4: Forest plot for 30-day mortality by study type and results of meta-analysis.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model.

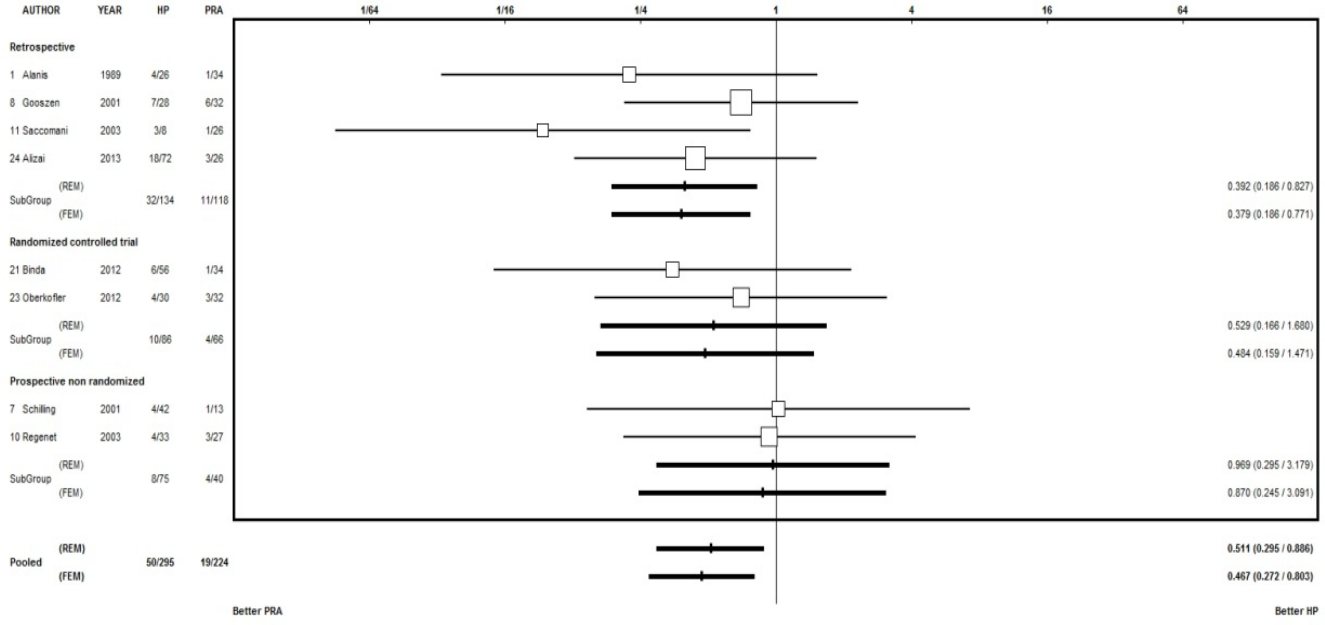

Figure 5: Forest plot for overall mortality by study type and results of meta-analysis.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model.

rates were similar for PRA and HP, but for the second intervention (recanalization) hospital costs, length of stay, operative time and the likelihood of stoma reversal all favored the PRA group [6,38]. Almost all of the studies reviewed, including the two randomized controlled trials and three out of four systematic reviews [5,8,37], considered only patients with peritonitis secondary to perforated diverticulitis (Hinchey stage III-IV). Our review, instead, together with the review performed by Constantinides et al. [36], is the only one that considered all non-elective surgical patients with complicated acute diverticulitis (perforation or bowel obstruction). Indeed, we consider common practice to perform HP also for acute intestinal obstruction secondary to diverticular sigmoid stenosis with dilated and unprepared proximal colon. Constantinides et al. [36] reported in their review a significantly decreased mortality for emergency operations with PRA vs HP (7.4% vs. 15.6%; OR=0.44). Also the incidence of wound infection and postoperative abscess or peritonitis was significantly lower in the PRA group (OR=0.42 and 0.43, respectively). The results of our review are in agreement with those of Constantinides. In fact, our meta-analysis shows that the 30-day mortality rate is significantly lower in the PRA group vs. the HP group. Also the overall mortality (number of deaths occurred after both the first intervention and the second intervention of recanalization, when indicated) was 8.5% in the PRA group and

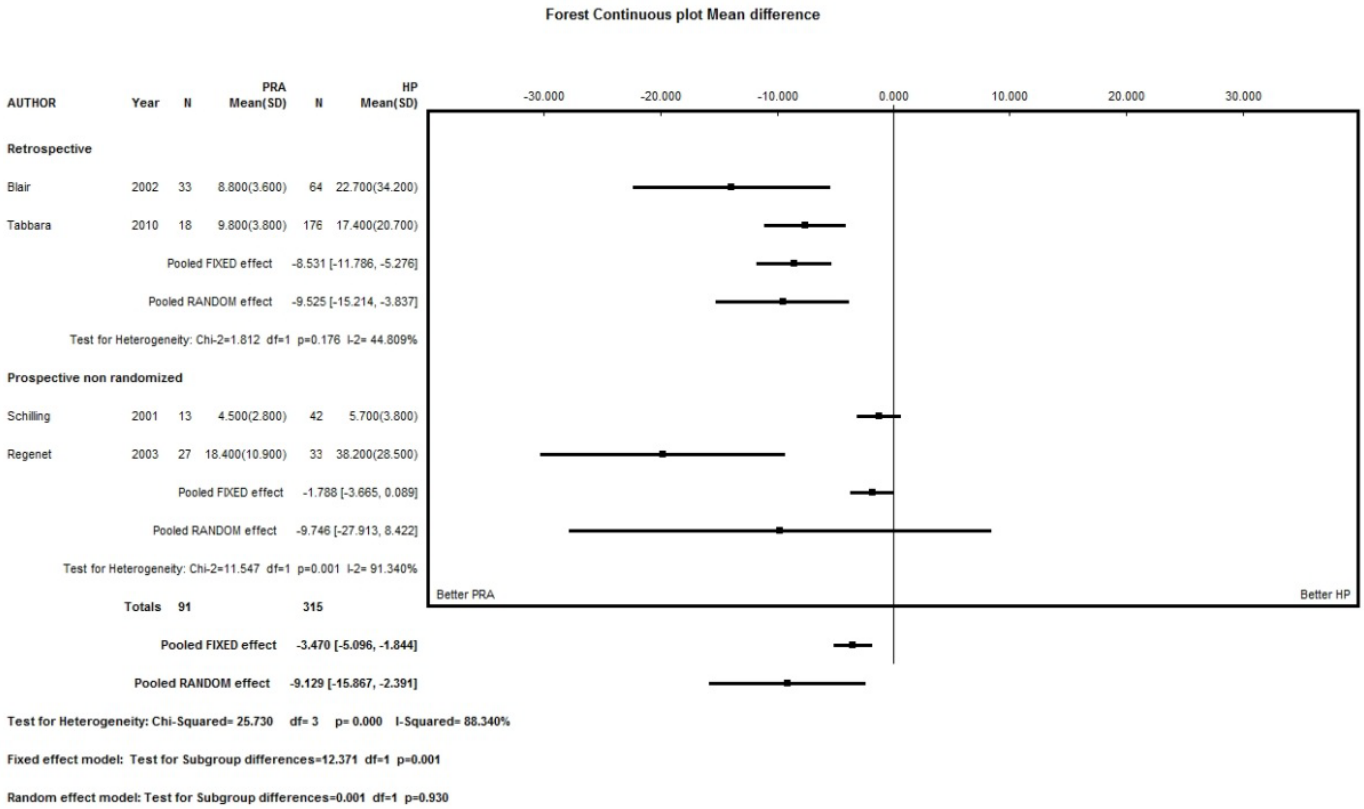

Figure 6: Forest plot for length of hospital stay (days) by study type and results of meta-analysis.

Abbreviations : HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; SD: Standard Deviation; N: Numerosity

16.9% in the HP group. Our study also shows that patients undergoing PRA have a lower risk of reintervention compared to HP group. However, it should be noted that the first cause of reintervention in the PRA group was the anastomotic leak (57.9% of reinterventions). Some of the results of our meta-analysis should be interpreted with caution for several biases related to the variability of the studies, the inclusion of only two RCT of which one was stopped early [39], the wide span of time in which the trials were conducted (1988-2014) and, above all, the patients' selection bias which definitely influenced the results. As previously highlighted, in the retrospective and prospective non randomized studies included in our meta-analysis, the PRA technique was performed only in 28.6% of cases, suggesting that surgeons followed rigorous criteria, such as most favorable clinical conditions, to define the indication to the PRA technique. This could explain the better outcomes shown in this group, in terms of both morbidity and mortality. However, the two randomized controlled trials, of which only one was, concluded [6], and the prospective studies showed average values in favor to the PRA technique, encouraging the promotion of further studies to confirm the hypothesis that the PRA technique is more effective and safer in emergency setting for acute complicated diverticulitis. Furthermore, based on the results of our review, we can assert that the HP is not the only technique to perform in non-elective surgical patients with acute complicated diverticulitis and that, in selected cases; PRA can be executed without increased morbidity and mortality, even obtaining in some cases better results. The surgeon will choose, case by case, the most appropriate technique, taking into account his own experience in colorectal surgery [40] and considering that the anastomotic leak risk is based on the patient's risk factors (severe comorbidities, significant intraoperative hemorrhage, shock, sepsis) [34].

Highlights

- Best surgical technique for complicated acute diverticulitis is an open question.
- Included studies didn't provide strong evidence to define the best surgical technique.
- Primary Anastomosis was better than Hartmann's procedure for all included outcomes.
- Further well-designed studies should be performed to confirm our evidences.

Conclusion

The available studies do not provide strong evidence to define the best surgical technique in non-elective patients with complicated acute diverticulitis (perforation or obstruction). However, in selected cases, the PRA technique may be preferred to HP for the lower morbidity and postoperative mortality. Further randomized controlled trials are required to assess if the PRA technique could be routinely executed, leaving the Hartmann's procedure for particularly severe cases.

Conflicts of interest

Authors have no conflict of interest to disclose.

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