Hartmann's procedure versus sigmoidectomy with primary anastomosis for perforated diverticulitis with purulent or fecal peritonitis

LADIES Trial Collaborators; Edomskis, Pim P.; Hoek, Vincent T.; Stark, Pieter W.; Lambrichts, Daniël P.V.; Draaisma, Werner A.; Consten, Esther C.J.; Bemelman, Willem A.; Lange, Johan F.

Published in:
International Journal of Surgery

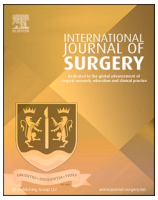
DOI:
10.1016/j.ijsu.2021.106221

International Journal of Surgery 98 (2022) 106221

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu



Randomised Controlled Trial

Hartmann's procedure versus sigmoidectomy with primary anastomosis for perforated diverticulitis with purulent or fecal peritonitis: Three-year follow-up of a randomised controlled trial

Pim P. Edomskis [a,*,1], Vincent T. Hoek [a,1], Pieter W. Stark [a], Daniël P.V. Lambrichts [a], Werner A. Draaisma [b], Esther C.J. Consten [c,d], Willem A. Bemelman [f], Johan F. Lange [a,e], on behalf of the LADIES trial collaborators

[a] Department of Surgery, Erasmus University Medical Center, Rotterdam, the Netherlands
[b] Department of Surgery, Jeroen Bosch Hospital, Den Bosch, the Netherlands
[c] Department of Surgery, Meander Medical Center, Amersfoort, the Netherlands
[d] Department of Surgery, University Medical Center Groningen, Groningen, the Netherlands
[e] Department of Surgery, IJsselland Hospital, Capelle aan den IJssel, the Netherlands
[f] Department of Surgery, Amsterdam University Medical Center, University of Amsterdam, the Netherlands

ARTICLE INFO

Keywords:
Complicated diverticulitis
Hartmann's procedure
Primary anastomosis
Stoma free rate
Surgery
long-term;therapy

ABSTRACT

Background: The aim of the present study is to present the three years follow-up a randomised controlled trial that compared Hartmann's Procedure (HP) with sigmoidectomy with primary anastomosis (with or without defunctioning ileostomy) (PA) in a randomised design to determine the optimal treatment strategy for perforated diverticulitis with purulent or fecal peritonitis.

Methods: Data were prospectively gathered for the first 12 months after randomization and retrospectively collected up to 36 months. The primary long-term endpoint was stoma free rate 36 months after the index procedure. Secondary outcomes were patients with a stoma at 36 months, percentage of stoma reversals, related reinterventions, parastomal/incisional hernia rates, total in hospital days including all readmissions regardless their relation to the intervention, overall morbidity and mortality.

Results: Three years follow-up was completed in 119 of the originally 130 included patients, with 57 (48%) in the PA-group and 62 (52%) patients in the HP-group. 36 months stoma free rate was significantly better for patients undergoing PA compared with HP (PA 92% vs HP 81%, hazard ratio 2.326 [95% CI 1.538–3.517]; log-rank $p < 0{\cdot}0001$). Stoma reversal rates did not significantly differ (PA 31/40(78%) versus HP 45/61(74%), $p = 0.814$). Overall cumulative morbidity (PA 21/57(36%) versus HP 30/62(48%), $p = 0.266$) and mortality (PA 6/57(11%) versus HP 7/62 (11%), $p = 1.000$) did not differ between groups. However, more parastomal hernias occurred in the HP-group (HP 10/62(16%) vs PA 1/57(2%), $p = 0.009$) and the mean total in hospital days after three years follow-up was significantly lower in the PA-group compared to the HP-group (PA 14 days (IQR 9.5–22.5) versus HP 17 days (IQR 12.5–27.5)), $p = 0.025$).

Conclusion: Long-term results showed that in haemodynamically stable, immunocompetent patients primary anastomosis is superior to Hartmann's procedure as treatment for perforated diverticulitis with respect to long-term stoma free rate, overall hospitalization and parastomal hernias.

1. Introduction

In western countries colonic diverticulosis develops in the majority of individuals and its incidence increases with age [1–3]. Often diverticulosis remains asymptomatic, but acute colonic diverticulitis will occur in an estimated 4–7% of these patients [4–6]. Moreover, the

; HP, Hartmann's procedure; PA, primary anastomosis.

* Corresponding author. Department of Surgery, Erasmus University Medical Center, Wytemaweg 80, 3015 CN Rotterdam, Room Ee-173, the Netherlands.
E-mail address: p.edomskis@erasmusmc.nl (P.P. Edomskis).

[1] Both these authors contributed equally and should both be considered as joint first authors.

https://doi.org/10.1016/j.ijsu.2021.106221
Received 25 November 2021; Received in revised form 28 December 2021; Accepted 29 December 2021
Available online 10 January 2022

incidence of diverticulitis seems to increase over time, especially in younger people [7]. Of these patients, 0–15% suffer from complicated diverticulitis, defined as diverticular inflammation with free perforation, abscess, fistula, obstruction and/or stricture, requiring further treatment in the form of close observation, antibiotics, percutaneous drainage or surgery [8,9].

Despite accumulating evidence, optimal surgical treatment for perforated diverticulitis with peritonitis remains a topic of debate. The Hartmann's procedure (HP) remains a popular procedure compared to sigmoidectomy with primary anastomosis (PA) for patients presenting with perforated diverticulitis with purulent or fecal peritonitis even though the evidence points towards PA as being the most optimal treatment option, as demonstrated in the meta-analysis of the short-term results of four randomised trials by Lambrichts et al. [10–16], this is not universally accepted.

Long-term results of PA versus HP for patients with perforated diverticulitis are of importance to determine whether these benefits of PA persist on the long-term. Therefore, the aim of the present study was to assess long-term follow-up of the randomised Ladies trial.

2. Methods

2.1. Study design and participants

All patients included in the DIVA arm of the LADIES trial were found to be eligible for long-term follow-up. This study was a multicentre, randomised, open-label, superiority trial done at 34 teaching hospitals and eight academic hospitals in Belgium, Italy, and the Netherlands. Initially, the trial had a combined design to compare laparoscopic peritoneal lavage with sigmoidectomy for purulent perforated diverticulitis (LOLA arm) and HP with sigmoidectomy with PA in both purulent and fecal perforated diverticulitis (DIVA arm). After preliminary termination of the LOLA arm, patients with purulent peritonitis were no longer randomly assigned to laparoscopic lavage and enrolment of patients with both purulent or fecal peritonitis continued in the DIVA arm [16].

Participants aged between 18 and 85 years, who presented with clinical signs of general peritonitis and suspected perforated diverticulitis were eligible for inclusion if plain abdominal radiography or CT scan showed diffuse free air or fluid. Patients with Hinchey I and II diverticulitis were not eligible for inclusion. Exclusion criteria were dementia, previous sigmoidectomy, previous pelvic radiotherapy, chronic steroid treatment ($\geq$20 mg daily), and preoperative shock requiring inotropic support. The study was designed in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki and local approval for this trial was obtained in the participating hospitals. Before randomization, written informed consent was obtained from all patients. The study protocol with details on the study design, procedures, and outcome assessment was published previously, as well was the 12-month outcomes of the DIVA arm [16,17]. The trial was registered with the Netherlands Trial Register (NTR2037) and ClinicalTrials.gov (NCT01317485).

2.2. Long-term follow-up

In the present study, long-term outcomes were assessed up to 36 months after the index procedure. In the first 12 months after surgery, outcomes were collected prospectively. Additional follow-up was retrospectively collected through review of patient's medical records. All patients included in the DIVA arm were found eligible for participation. With regards to General Data Protection Regulation, patients who were still alive had to be asked for their consent to retrieve long-term outcome measurements, by means of an information letter. Patients who did not wish to participate or did not respond could not be included for long-term follow-up.

2.3. Procedures

The American Society of Colon and Rectal Surgeons guidelines were used to perform sigmoidectomy with primary anastomosis, the decision on the type of anastomosis, construction of a diverting ileostomy, and drain placement was left to the surgeon's preferences [18]. Surgical procedures including reinterventions and stoma reversals have been described previously [17].

2.4. Outcomes

The primary endpoint of the present study was the stoma free rate in 36 months after index procedure. Secondary outcomes were patients with a stoma at 36 months, percentage of stoma reversals, number of readmissions (including all readmissions with and without relation to the index procedure), total in-hospital days (index procedure, reversals and readmissions combined), sigmoid carcinomas, overall morbidity and mortality. Overall morbidity included the occurrence of any of the following conditions or events: surgical reintervention (surgical- and percutaneous interventions, excluding stoma reversal), abscess with drainage, abdominal wall complications (acute fascial dehiscence or parastomal/incisional hernia) or recurrent diverticulitis. All episodes of uncomplicated and complicated diverticulitis were included in recurrent diverticulitis. Diverticulitis with the presence of a phlegmon, abscess, stenosis, fistula or perforation was defined as complicated recurrent diverticulitis. Episodes of diverticulitis without the above mentioned complications were registered as uncomplicated diverticulitis, when described in the patient's medical records.

2.5. Statistical analysis

Patients were analysed according to the intention-to-treat principle. Categorical data were presented as numbers with percentages. For comparison, the Pearson Chi-square test was used, and if group counts were <5 the Fisher Exact test was applied. Continuous variables were presented as mean (standard deviation) or median (interquartile range) depending on distribution. If normally distributed, the *t*-test was applied to compare means. If not, the non-parametric Mann-Whitney *U* test was used to compare medians. 36-month stoma free rate was estimated with the Kaplan-Meier method. Difference in rate was analysed using the Mantel-Cox logrank test.

3. Results

3.1. Study population

A total of 130 patients were randomly assigned between July 1, 2010, the early termination of the LOLA arm on Feb 22, 2013, and trial termination of the DIVA arm June 3, 2016.

66 patients were assigned to Hartmann's procedure (HP) and 64 to sigmoidectomy with primary anastomosis (PA). Eventually, 119 patients could be included in a modified intention-to-treat analysis for a 36-month follow-up, with 62 (52%) in the HP-group and 57 (48%) in the PA-group. 11 patients could not be included in the present long-term follow-up with following reasons: not responding (n = 5), refusal to participate (n = 6). Notably, 7 of 62 (11%) patients in the HP-group and 5 of 57 (9%) in the PA-group died within the 12 months of follow-up. The trial profile is presented in Fig. 1.

3.2. Baseline characteristics

Tables 1 and 2 provides baseline- and perioperative characteristics. No major differences in (pre)operative characteristics were observed between HP and PA (Table 1).

In the HP group, 19 of 62 (31%) patients had Hinchey grade IV diverticulitis compared to 17 of 57 (30%) in the PA group (p = 1.000). In

CONSORT
TRANSPARENT REPORTING of TRIALS

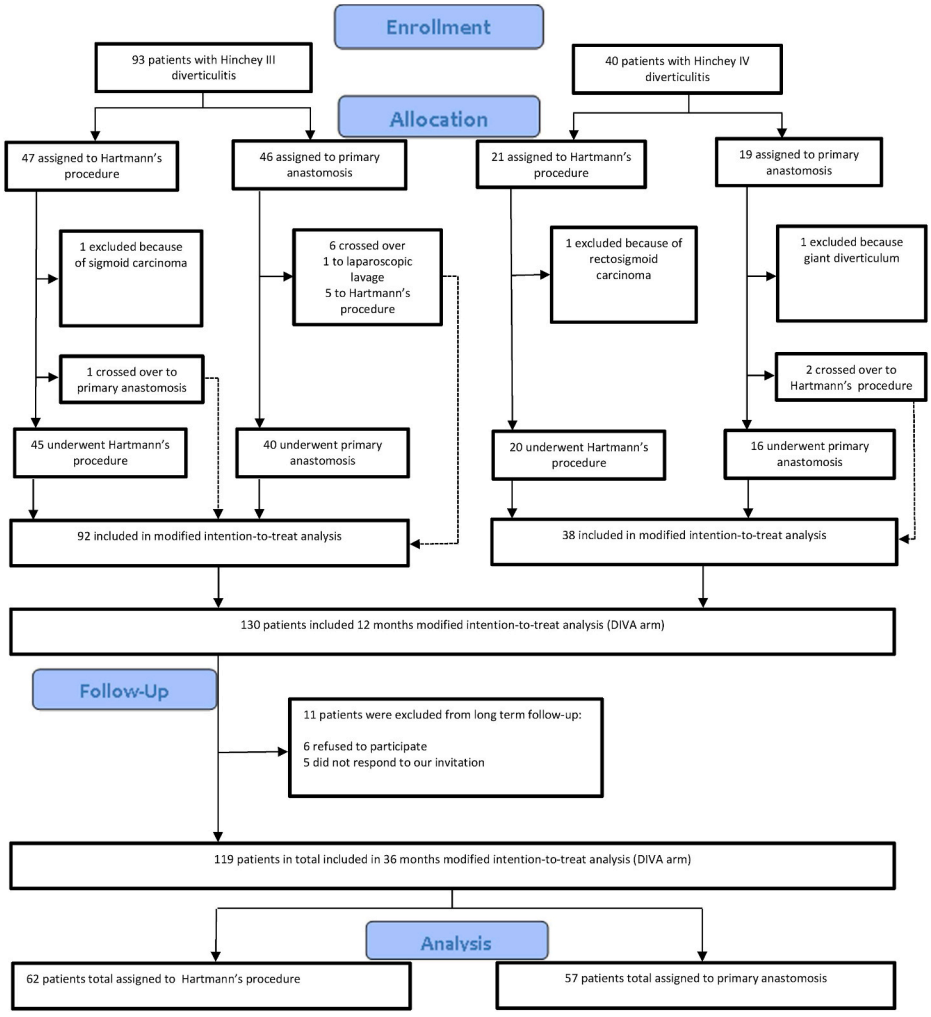


Fig. 1. Trial profile long-term follow-up.

61 of 62 (98%) patients of the HP group a colostomy was constructed. One patient crossed over from HP to PA without ileostomy. Six of 57 (11%) patients allocated to the PA-group crossed over to the HP-group and one patient crossed over to laparoscopic lavage. Reasons for cross-over are provided in Supplementary Table 1. Eventually, 33 of 57 (58%) patients received an ileostomy, 6 of 57 (11%) patients received a colostomy and 17 of 57 (30%) patients did not get a stoma and were free after time of the index procedure (Table 2). Postoperative histopathology showed a sigmoid carcinoma in two of 57 (4%) patients in the PA-group, this compared to zero patients in the HP-group.

3.3. Primary outcome

36 months stoma free rate was significantly better for patients undergoing PA compared with HP (HP 81% vs PA 92%, hazard ratio 2·326 [95% CI 1·538–3.517]; log-rank p < 0·0001). Median time to being stoma-free was 197.2 days for HP and 87.7 days for PA (Fig. 2).

3.4. Secondary outcomes and stoma reversals within 36 months

The median total in hospital days was significantly lower in the PA-group compared to the HP-group (HP 17 days (13–28) versus PA 14 days (9-20), p = 0.013). Median days in hospital for stoma reversal did not differ between both groups (HP 5 days (4–7) versus PA 5 days (3–6), p = 0.176). No differences in median number of readmissions was found (Table 3). However, a per-protocol analysis showed a shorter total duration of in hospital days per patient in favor of the PA-group (HP 17 days (12–28) vs PA 14 days (9-23), p = 0.025). Stoma reversal rates did not significantly differ (HP 45/61(74%) versus PA 31/40(78%), p = 0.814). Only four stoma reversals, being in the HP group, were performed 12 months or later after index procedure. Reasons not to reverse are provided in Table 3.

3.5. 36 months morbidity

Table 4 presents the overall morbidity and mortality after 36 months. Overall morbidity did not significantly differ between both groups (HP 30/62(48%) versus PA 21/57(36%), p = 0.266). No difference in mortality was found either (HP 7/62 (11%) versus PA 6/57(11%), p = 1.000). Supplementary Table 2 presents the morbidity during 12–36 months follow-up. Overall morbidity did not significantly differ between both groups (HP 11/55 (20%) versus PA 9/52 (17%), p = 0·807). In four patients who underwent stoma reversal after 12 months, no reversal related morbidity was observed (see Table 5).

Table 1
Baseline characteristics.

	Hartmann's procedure (n = 62)	Primary anastomosis (n = 57)	P-value
Age (years)	61.8(11.5)	62.9(12.9)	0.603
Sex			0.576
Male	37(59.7)	37(64.9)	
Female	25(40.3)	20(35.1)	
Body-mass index (kg/m2)	27.9(4.6)	26.1(5.1)	0.155
ASA			0.537
I	13(23.6)	12(22.6)	
II	28(50.9)	22(41.5)	
III	12(21.8)	18(34.0)	
IV	2(3.6)	1(1.9)	
Missing			
Previous diverticulitis	11(17.7)	11(19.3)	1.000
Previous laparotomy	3(4.8)	1(1.8)	0.621
Disease severity preoperative			
APACHE II	8.0(5.0–12.0)	8.0(5.0–10.0)	0.333
MPI score	23.0(17.0–27.0)	22.0(17.0–26.5)	0.357
POSSUM physiological score	20.0(17.8–24.3)	20.0(17.0–23.0)	0.224
POSSUM operative score	19.0(19.0–20.0)	19.0(19.0–20.0)	0.590
Interval from ER to surgery (h)	8.0(4.6–20.1)	9.4(5.5–30.5)	0.336

Data are mean (SD), n (%), or median (IQR). POSSUM=Physiological and operative severity score for the enumeration of mortality and morbidity. Occasional missing data*; The American Society of Anesthesiologists (ASA); Acute Physiology and Chronic Health Evaluation (APACHE).

Table 2
(Post)operative characteristics.

	Hartmann's procedure (n = 62)	Primary anastomosis (n = 57)	P-value
Procedure			
Sigmoidectomy			
Primary anastomosis	1	50	
Hartmann's procedure	61	6	
Laparoscopic lavage	0	1	
Stoma constructed within the first year			
Ileostomy	0	33	
Colostomy	61	7	
Stoma free after index procedure	1	17	
Hinchey grade IV	19(30.6)	17(29.8)	1.000
Operation time (min)	117.0 (93.5–134.3)	125.0 (110.0–152.0)	**0.047**
Number of patients operated on by a gastrointestinal surgeon	55(88.7)	51(89.5)	1.000
Laparoscopic approach	18(36.0)	13(28.3)	0.418
Sigmoid carcinoma	0(0.0)	2(3.5)	0.105

Data are n (%) or median (IQR).

Significantly more patients in the HP group suffered from parastomal hernias compared to the PA group (HP 10/62 (16%) versus PA 1/57 (2%), p = 0.009). Prevalence of incisional hernia did not differ between both groups (HP 13/62(21%) versus PA 10/57(18%), p = 0.651). 28 cases of incisional or parastomal hernias were found in 21 of 62 (36%) patients in the HP-group, of which eight underwent surgical repair and 20 were treated conservatively.

14 cases of incisional or parastomal hernias were found in 12 of 57 (21%) patients in the PA-group, five underwent surgical repair and nine were treated conservatively.

3.6. Hinchey III vs IV

Stoma free rate did not significantly differ for HP and PA in patients with Hinchey III (HP 32/43 (75%) versus PA 36/40 (90%), p = 0.088) and Hinchey IV (HP 11/19 (58%) versus PA 12/17 (71%), p = 0.502) disease separately (Supplementary Table 3). Neither did the proportion of patients with a stoma in situ, stoma reversal rates, overall morbidity and mortality (Supplementary Table 3).

4. Discussion

The present long-term follow-up of the DIVA arm of the Ladies trial showed a significantly better 36-month stoma free rate and less in-hospital days (including readmissions) for patients with Hinchey III or IV diverticulitis undergoing PA as compared to HP. Also more parastomal hernias occurred in the HP-group. No significant differences in 36-month mortality was found between both groups.

Long-term outcome data comparing PA with HP beyond 18 months of follow-up are scarce.

They are of great importance to fully comprehend the differences between both procedures with respect to long-term complications (e.g. abdominal wall hernia, adhesions), stoma free and recurrence rates.

In the present study seventeen patients in the PA group (30%) were stoma free immediate after index procedure. Reversal rates of colostomies and ileostomies were comparable between both groups (PA 31/40(78%) vs HP 45/61(74%)). This finding is remarkable because it was expected that the more complicated closure of a Hartmann would be reflected in a lower stoma closure rate compared to ileostomy closure. Therefore the long-term differences between the two procedures being stoma free is attributed to a lower stoma rate in the PA group at index surgery and not because of a higher stoma closure rate of ileostomies. It should be considered that all PA patients who did not undergo reversal died within 36-months with their ileostomy in situ. Follow-up of patients with stomas is apparently so well organized that reversal takes place relatively shortly after the index procedure or does not happen at all.

The long-term follow-up of the DIVERTI trial found reversal rates in favor of the PA group compared to the HP group(PA 46/50(92%) vs 33/52(63%) [19]. It should be noted that in the present study there were only a few stoma reversals after twelve months. Importantly, ileostomies were closed on average four months earlier than colostomies. This accounts for less burden for patients and is in line with a better quality of life that was found at the long-term follow-up of the DIVERTI trial [19]. Moreover, it also correlates to a more cost-effective therapy as was concluded earlier by Lambrichts et al. [20] Furthermore no differences in outcome were found between patients being diagnosed with Hinchey III or IV. Other surgical strategies such as damage control surgery with blind closure of both colonic ends after sigmoid resection [21], postponing the decision on definitive reconstruction are interesting alternatives, however confirmation from literature is warranted. Especially in the case of hemodynamic or instable patients this therapy could be further assessed.

Previous randomised clinical trials comparing PA with HP, showed that outcomes regarding short-term overall morbidity after stoma reversal were in favor for PA, as well as a shorter time to reversal and postoperative stay after reversal [13–15]. Nevertheless, a recent meta-analysis also concluded that PA patients were more likely to have their stoma reversed and be stoma free on the short-term follow up compared to the HP group [12]. The short term follow-up of this study concluded that primary anastomosis was superior to Hartmann's procedure with regard to 12-month stoma-free rate and overall morbidity after stoma reversal, with no significant differences in short-term morbidity and mortality after the index procedure [16]. The DIVERTI trial concluded that PA is associated with fewer long-term complications than HP [19].

In the present study, HP led to more parastomal hernias compared to those who underwent PA (PA 1/57(1.8%) vs HP 10/62(16.1%) which was comparable to prevalence of parastomal hernias reported in literature [22]. The number of incisional hernias was not significantly different in both groups in this study(PA 8/57(14%) vs HP 12/62(19%)).

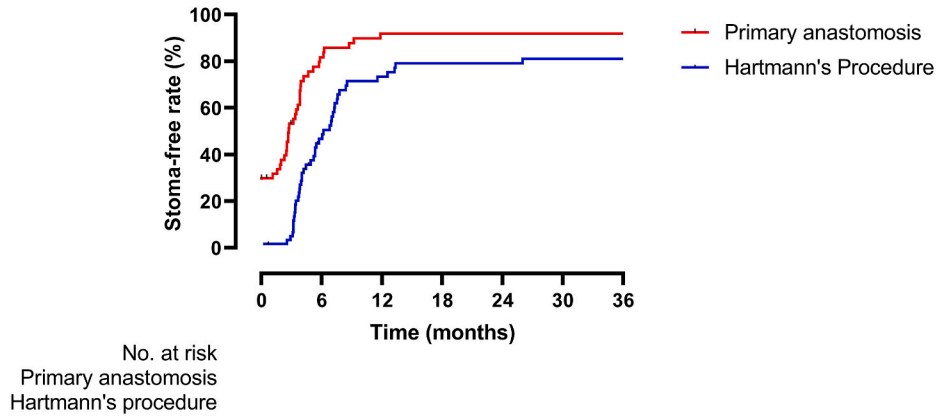


Fig. 2. 36-months Kaplan-Meier stoma-free rate. Stoma-free rate was significantly better for patients undergoing PA compared with HP.

Table 3
Stoma outcomes and admissions from 0 to 36 months after index procedure.

	Hartmann's procedure (n = 62)	Primary anastomosis (n = 57)	P-value
Intention-to-treat analyses			
Stoma reversal	45/61(73.8)	31/40(77.5)	0.814
Ileostomy reversal	0	28/34(82.4)	
Colostomy reversal	45/61(73.8)	3/6(50.0)	
Reason stoma reversal was not performed			
Patient died with colostomy in situ	7	1	
Patient died with ileostomy in situ		6[a]	
Surgeon did not support reversal	5	2	
Patient preferred to keep the stoma	3	1[a]	
Recurrent diverticulitis with colostomy construction after initial reversal	1		
Reversal was complicated by anastomotic leakage and colostomy was constructed	1		
Unknown	2		
Per-protocol analyses			
Stoma reversal	48/67(71.6)	28/34(82.4)	0.330
Total duration in hospital per patient (days)[a]	17(13–28)	14(9–23)	**0.025**
Days in hospital for stoma reversal per patient	5(4–7)	5(3–6)	0.176
Total readmissions per patient (number)	1(1.0–2.0)	1(0.0–2.0)	0.380
Readmission per patient			
0	13(21.0)	15(26.4)	
1	28(45.2)	25(43.9)	
2	13(21.0)	14(24.6)	
≥3	8(12.9)	3(5.3)	

Data are n(%), p-values are from numbers of patients, not event numbers.
[a] Patient with ileostomy preferred to keep the stoma and died within 36 months of follow-up.

Table 4
Overall morbidity and mortality.

	Hartmann's procedure (n=62)		**Primary anastomosis (n=57)**		**P-value**
	patients	Events	Patients	Events	
Overall morbidity	30(48)		21 (36.8)		0.266
Reintervention	20 (25.8)	35	13 (21.1)	20	
Surgical	15 (24.2)	23	11 (17.5)	15	
Percutaneous	9(14.5)	12	5(8.7)	5	
Abscess with drainage	8(12.9)	11	3(5.3)	3	
Others	1(1.6)[a]	1	2(3.5)[+]	2	
Abdominal wall complication	22 (35.5)	29	14 (24.6)	15	
Fascial dehiscence	1(1.6)	1	2(3.5)	2	
parastomal/incisional hernia	21 (33.9)	28	12 (21.1)	13	
Recurrence diverticulitis	1(1.6)	1	1(1.8)	1	
Mortality	7(11.2)	7	6(10.5)	6	1.000

Data are n(%), p-values are from numbers of patients, not event numbers.
[a] Percutaneous drainage because of abdominal compartment syndrome; [+]One patient underwent percutaneous intervention due to porth-a-cath placement and one patient suffered from a pneumothorax requiring a thorax drain.

Table 5
Incisional and parastomal hernia outcomes 0–36 months.

	Hartmann's procedure (n = 62)	Primary anastomosis (n = 57)	P-value
	patients	Patients	
Incisional hernia	13(21.0)	10(17.5)	0.651
Stoma site (events)	3	2	
Incisional (events)[a]	12	8	
Laparotomy	10/42(23.8)	5/42(11.9)	
Laparoscopy	2/20(10.0))	3/15(20.0)	
	10(16.1)	1(1.8)	**0.009**
Parastomal hernia			

Data are n(%), p-values are from numbers of patients.
[a] Including incisional, port site and extraction site hernia's.

This is in contrast to the DIVERTI trial that showed a difference in the number of incisional hernias in favor of the PA group (PA 11/38(29%) vs HP 21/40(52%)) [19]. Hereby, it should be mentioned that the median follow-up in the DIVERTI trial was longer compared to this study (9 years vs. 3 years), which could explain the difference in incidence rates.

In this study the decision for the construction of a diverting ileostomy in the PA group was at the surgeons' discretion, in contrast with previous studies where an ileostomy was constructed in all patients. Whether the primary anastomosis in this patient group required mitigating the consequences of an anastomotic leak, is an unanswered question. The presence of an ileostomy is associated with additional morbidity, readmission rates and longer in hospital days. An earlier study by Vermeulen et al. found no difference in complications that needed reintervention between PA patients with or without an ileostomy (respectively, 19% vs. 11%, p = 0.42) [23]. Dreifuss et al. found more morbidity, readmission rates and increased length of stay for

patients having a diverting ileostomy without reduction of mortality or anastomotic leakage rates [24]. Furthermore the DIVERTI trial found that overall morbidity and severe complications were significantly lower in their group of patients without ileostomy [19].

A limitation of this trial is that attrition bias might have been introduced due to General Data Protection Regulations. To comply, all patients had to provide approval for participation in the long-term follow-up. Nonetheless, losses to follow-up were limited and equally distributed among randomised groups. Subsequently, effects of losses to follow-up were most likely not different. In addition, the retrospective retrieval of data from patients records for the long-term follow-up could have led to information bias as patients might have visited other hospitals for further care.

Strengths of this study are the low numbers of lost to follow-up, and the high external validity of this subset of patients presenting with perforated diverticulitis in multicenter setting. In addition, it should be recognized that the present cohort is the largest cohort which such a long follow-up.

In conclusion, long-term results showed that in haemodynamically stable, immunocompetent patients sigmoidectomy and primary anastomosis is superior to Hartmann's procedure as treatment for perforated diverticulitis with respect to long-term stoma-free rate, overall hospitalization, parastomal hernias and time of having a stoma.

Data statement

If requested, deidentified data collected for the LADIES trial, the studyprotocol, and informed consent form can be made available. Please contact WAB (w.a.bemelman@amsterdamumc.nl) or JFL (j.lange@erasmusmc.nl), who will review all requests with the LADIES trial investigators. Requests should fulfil the following access criteria: research can only be conducted in collaboration with and after approval of the LADIES trial investigators, and with a signed data access and sharing agreement. The LADIES trial investigators must approve all research done with the shared data.

Please state whether ethical approval was given, by whom and the relevant Judgement's reference number

Initial ethical approval was given by the medical ethical committee of the Amsterdam Medical Centre (METC: NL28998.018.09, AMC: 2009_234).

Long term follow-up was again checked for approval by the AMC medical ethical committee (w18_055 # 18.073) and they confirmed that the Medical Research Involving Human Subjects did not apply.

Furthermore local approval of all participating centres was obtained.

Please state any sources of funding for your research

No funding was received for this long-term follow-up. However, short term follow-up was funded by the Netherlands Organisation for Health Research and Development (ZonMw).

Author contribution

PPE, DPVL, WAB, and JFL contributed to study design or coordination.

PPE, VTH, DPVL, PWS, WAB, and JFL contributed to data acquisition.

PPE, VTH and DPVL contributed to data analysis.

PPE, VTH, DPVL, WAD, ECJC, WAB, JFL contributed to data interpretation.

PPE, VTH, DPVL, WAB, and JFL drafted the report.

All authors critically revised the content and approved the final manuscript.

Research registration Unique Identifying number (UIN)

Name of the registry: The trial was registered with the Netherlands Trial Register and ClinicalTrials.gov.

Unique Identifying number or registration ID: NTR2037; NCT01317485.

Hyperlink to your specific registration (must be publicly accessible and will be checked):https://www.trialregister.nl/trial/1920

https://clinicaltrials.gov/ct2/show/NCT01317485?term=NTR2037&draw=2&rank=1.

Guarantor

Johan F. Lange.

International journal of surgery author disclosure form

The following additional information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories, then this should be stated.

CRediT authorship contribution statement

Pim P. Edomskis: Funding acquisition, Formal analysis, Writing – original draft, contributed to study design or coordination. contributed to data acquisition. contributed to data analysis. contributed to data interpretation. drafted the report. **Vincent T. Hoek:** Funding acquisition, Formal analysis, Writing – original draft, and contributed to data acquisition. contributed to data interpretation. drafted the report. **Pieter W. Stark:** contributed to data acquisition. **Daniël P.V. Lambrichts:** Funding acquisition, Formal analysis, Writing – original draft, contributed to study design or coordination. contributed to data acquisition. contributed to data analysis. drafted the report. **Werner A. Draaisma:** contributed to data interpretation. **Esther C.J. Consten:** contributed to data interpretation. **Willem A. Bemelman:** Funding acquisition, Formal analysis, Writing – original draft, contributed to data interpretation. All authors critically revised the content and approved the final manuscript, contributed to study design or coordination. contributed to data acquisition. drafted the report. **Johan F. Lange:** Funding acquisition, Formal analysis, Writing – original draft, contributed to study design or coordination. contributed to data acquisition. contributed to data interpretation. drafted the report.

Declaration of competing interest

We declare no competing interests.

Acknowledgements

We thank all patients who were willing to participate in this trial and all staff of the participating hospitals for their efforts.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2021.106221.

References

[1] L.B.O. Rustom, A.I. Sharara, The natural history of colonic diverticulosis: much ado about nothing? Inflamm Intest Dis 3 (2) (2018) 69–74.

[2] A.F. Peery, T.O. Keku, C. Addamo, A.N. McCoy, C.F. Martin, J.A. Galanko, et al., Colonic diverticula are not associated with mucosal inflammation or chronic gastrointestinal symptoms, Clin. Gastroenterol. Hepatol. 16 (6) (2018) 884–891 e1.

[3] A.F. Peery, S.D. Crockett, C.C. Murphy, J.L. Lund, E.S. Dellon, J.L. Williams, et al., Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2018, Gastroenterology 156 (1) (2019) 254, 72 e11.
[4] L.B. Ferzoco, V. Raptopoulos, W. Silen, Acute diverticulitis, N. Engl. J. Med. 338 (21) (1998) 1521–1526.
[5] K. Shahedi, G. Fuller, R. Bolus, E. Cohen, M. Vu, R. Shah, et al., Long-term risk of acute diverticulitis among patients with incidental diverticulosis found during colonoscopy, Clin. Gastroenterol. Hepatol. 11 (12) (2013) 1609–1613.
[6] R.J. Loffeld, Long-term follow-up and development of diverticulitis in patients diagnosed with diverticulosis of the colon, Int. J. Colorectal Dis. 31 (1) (2016) 15–17.
[7] A.E. Bharucha, G. Parthasarathy, I. Ditah, J.G. Fletcher, O. Ewelukwa, R. Pendlimari, et al., Temporal trends in the incidence and natural history of diverticulitis: a population-based study, Am. J. Gastroenterol. 110 (11) (2015) 1589–1596.
[8] H.E. Bolkenstein, B.J.M. van de Wall, E.C.J. Consten, I. Broeders, W.A. Draaisma, Risk factors for complicated diverticulitis: systematic review and meta-analysis, Int. J. Colorectal Dis. 32 (10) (2017) 1375–1383.
[9] N. Stollman, W. Smalley, I. Hirano, Committee AGAICG. American gastroenterological association institute guideline on the management of acute diverticulitis, Gastroenterology 149 (7) (2015) 1944–1949.
[10] L. Trenti, S. Biondo, T. Golda, M. Monica, E. Kreisler, D. Fraccalvieri, et al., Generalized peritonitis due to perforated diverticulitis: hartmann's procedure or primary anastomosis? Int. J. Colorectal Dis. 26 (3) (2011) 377–384.
[11] D. Li, N.N. Baxter, R.S. McLeod, R. Moineddin, A.S. Wilton, A.B. Nathens, Evolving practice patterns in the management of acute colonic diverticulitis: a population-based analysis, Dis. Colon Rectum 57 (12) (2014) 1397–1405.
[12] D.P. Lambrichts, P.P. Edomskis, R.D. van der Bogt, G.J. Kleinrensink, W. A. Bemelman, J.F. Lange, Sigmoid resection with primary anastomosis versus the Hartmann's procedure for perforated diverticulitis with purulent or fecal peritonitis: a systematic review and meta-analysis, Int. J. Colorectal Dis. 35 (8) (2020) 1371–1386.
[13] V. Bridoux, J.M. Regimbeau, M. Ouaissi, M. Mathonnet, F. Mauvais, E. Houivet, et al., Hartmann's procedure or primary anastomosis for generalized peritonitis due to perforated diverticulitis: a prospective multicenter randomized trial (DIVERTI), J. Am. Coll. Surg. 225 (6) (2017) 798–805.
[14] C.E. Oberkofler, A. Rickenbacher, D.A. Raptis, K. Lehmann, P. Villiger, C. Buchli, et al., A multicenter randomized clinical trial of primary anastomosis or Hartmann's procedure for perforated left colonic diverticulitis with purulent or fecal peritonitis, Ann. Surg. 256 (5) (2012) 819–826, discussion 26-7.
[15] G.A. Binda, J.R. Karas, A. Serventi, S. Sokmen, A. Amato, L. Hydo, et al., Primary anastomosis vs nonrestorative resection for perforated diverticulitis with peritonitis: a prematurely terminated randomized controlled trial, Colorectal Dis. 14 (11) (2012) 1403–1410.
[16] D.P.V. Lambrichts, S. Vennix, G.D. Musters, I.M. Mulder, H.A. Swank, A.G. M. Hoofwijk, et al., Hartmann's procedure versus sigmoidectomy with primary anastomosis for perforated diverticulitis with purulent or faecal peritonitis (LADIES): a multicentre, parallel-group, randomised, open-label, superiority trial, Lancet Gastroenterol Hepatol 4 (8) (2019) 599–610.
[17] H.A. Swank, J. Vermeulen, J.F. Lange, I.M. Mulder, J.A. van der Hoeven, L. P. Stassen, et al., The ladies trial: laparoscopic peritoneal lavage or resection for purulent peritonitis and Hartmann's procedure or resection with primary anastomosis for purulent or faecal peritonitis in perforated diverticulitis (NTR2037), BMC Surg. 10 (2010) 29.
[18] J. Rafferty, P. Shellito, N.H. Hyman, W.D. Buie, , Standards Committee of American Society of C, S. Rectal, Practice parameters for sigmoid diverticulitis, Dis. Colon Rectum 49 (7) (2006) 939–944.
[19] M. Loire, V. Bridoux, D. Mege, M. Mathonnet, F. Mauvais, C. Massonnaud, et al., Long-term outcomes of Hartmann's procedure versus primary anastomosis for generalized peritonitis due to perforated diverticulitis: follow-up of a prospective multicenter randomized trial (DIVERTI), Int. J. Colorectal Dis. 36 (10) (2021) 2159–2164.
[20] D.P.V. Lambrichts, S. van Dieren, W.A. Bemelman, J.F. Lange, Cost-effectiveness of sigmoid resection with primary anastomosis or end colostomy for perforated diverticulitis: an analysis of the randomized Ladies trial, Br. J. Surg. 107 (12) (2020) 1686–1694.
[21] M. Sohn, A. Agha, I. Iesalnieks, F. Gundling, J. Presl, A. Hochrein, et al., Damage control strategy in perforated diverticulitis with generalized peritonitis, BMC Surg. 21 (1) (2021) 135.
[22] J. Shabbir, D.C. Britton, Stoma complications: a literature overview, Colorectal Dis. 12 (10) (2010) 958–964.
[23] J. Vermeulen, G.P. Akkersdijk, M.P. Gosselink, W.C. Hop, G.H. Mannaerts, E. van der Harst, et al., Outcome after emergency surgery for acute perforated diverticulitis in 200 cases, Dig. Surg. 24 (5) (2007) 361–366.
[24] N.H. Dreifuss, C. Bras Harriott, F. Schlottmann, M.E. Bun, N.A. Rotholtz, Laparoscopic resection and primary anastomosis for perforated diverticulitis: with or without loop ileostomy? Updates Surg 73 (2) (2021) 555–560.