



Comparison Between Primary Resection Anastomosis and Hartmann Procedure for the Treatment of Hinchey III and IV Acute Diverticulitis in the Emergency Setting

Acil Durumda Hinchey III ve IV Akut Divertikülit Tedavisi için Primer Rezeksiyon Anastomozu ve Hartmann Prosedürü Arasında Karşılaştırma

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ABSTRACT

Aim: The surgical management of perforated sigmoid diverticulitis and generalised peritonitis is challenging. We aimed to evaluate the safety and efficacy of primary anastomosis reducing end-stoma rate and to identify the appropriate surgical timing in the emergency setting for Hinchey III and IV acute diverticulitis.

Method: Pertinent data of all patients who underwent Hartmann or primary resection anastomosis (PRA) for Hinchey III and IV diverticulitis, performed between January 2014 and April 2019, were entered in a prospectively maintained database. A retrospective analysis was conducted.

Results: During the study period 365 patients underwent emergency surgery for colorectal diseases, 84 for acute left-sided colonic diverticulitis. Patients with Hinchey Stage IIb, stenosis and diverticular hemorrhage were excluded. After selection, a total of 36 Hinchey III and Hinchey IV patients, comparing 19 primary resections anastomosis and 17 Hartmann procedures, were finally enrolled in this study. Patient characteristics were equivalent between groups. The primary anastomosis group showed a reduction in reoperation rate for postoperative complications (5.3%, 1/19 vs 23.55%, 4/17; $p=0.335$) compared with the Hartmann group. Mortality was 10.5% (2/19) vs 29.4% (5/17) for the primary anastomosis versus Hartmann resection groups ($p=0.256$). Among patients, there was a statistically significant increase in reversal rate for the primary anastomosis group (42.1% vs 0%; $p=0.002$).

Conclusion: PRA and protective ileostomy approaches for Hinchey III and IV acute diverticulitis may be safe and feasible, resulting in satisfactory perioperative outcomes, postoperative complications and reversal rate. The study is ongoing to confirm these results with increased sample size and confidence.

Keywords: Acute diverticulitis, Hinchey III and IV, generalized peritonitis, primary anastomosis, Hartmann procedure

ÖZ

Amaç: Perfore sigmoid divertikülit ve jeneralize peritonitin cerrahi tedavisi zordur. Bu çalışmada; Hinchey III ve IV akut divertikülitin acil koşullardaki tedavisinde primer anastomozun end-stoma oranını azaltmada güvenlik ve etkinliğini değerlendirmeyi ve cerrahi için uygun zamanlamayı belirlemeyi amaçladık.

Yöntem: Ocak 2014 ile Nisan 2019 arasında Hinchey III ve IV divertikülit için Hartmann prosedürü veya primer rezeksiyon anastomozu (PRA) uygulanan tüm hastaların ilgili verileri prospektif bir veri tabanına girildi. Retrospektif bir analiz yapıldı.

Bulgular: Çalışma süresince 365 hasta kolorektal hastalıklar için acil ameliyata alındı. Bunların 84'ü akut sol kolon divertikülit için opere edildi. Hinchey Evre IIb hastalığı, darlığı ve divertiküler kanaması olan hastalar çalışma dışı bırakıldı. Geriye kalan ve 19'una PRA, 17'sine Hartmann prosedürü uygulanan toplam 36 Hinchey evre III ve Hinchey evre IV hasta bu çalışmaya dahil edildi. Hasta özellikleri gruplar arasında benzer dağılmaktaydı. PRA grubunun, Hartmann grubuna kıyasla postoperatif komplikasyonlar için tekrar ameliyat edilme oranı daha düşüktü (%5,3 ve 1/19'a karşı %23,55 ve 4/17; $p=0,335$). Mortalite, PRA grubunda %10,5 (2/19) iken Hartmann rezeksiyon grubunda %29,4 (5/17) idi ($p=0,256$). PRA grubundaki hastalarda geri dönüş oranı istatistiksel olarak anlamlı derecede yüksekti (%42,1'e karşı %0; $p=0,002$).



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Sonuç: Hinchey III ve IV akut divertikülit tedavisinde PRA ve koruyucu ileostomi yaklaşımları; tatmin edici perioperatif sonuç, postoperatif komplikasyon ve geri dönüş oranları ile güvenli ve uygulanabilir gibi görünmektedir. Bu sonuçları daha fazla hasta ile daha tatmin edici şekilde doğrulamak için çalışma devam etmektedir.

Anahtar Kelimeler: Akut divertikülit, Hinchey III ve IV, jeneralize peritonit, primer anastomoz, Hartmann prosedürü

Introduction

The most recent consensus conferences on acute diverticulitis updated clinicians on the current evidence that can guide surgery management practice in an emergency setting.^{1,2,3} Perforated diverticulitis with peritonitis is a life-threatening complication that has been reported to account for more than half of emergency operations, with an increasing prevalence in developed countries from 2.4/100,000 in 1986 to 3.8/100,000 in 2000.⁴ Surgical management of Hinchey III and IV diverticulitis utilizes either Hartmann's procedure (HP) or primary resection anastomosis (PRA) with or without fecal diversion, for patients with and without comorbidities.⁵ The HP was the most commonly performed emergency operation, accounting for 72% of resections.³ In recent years, some authors have reported the role of PRA with or without a diverting stoma, in the treatment of acute diverticulitis, even in the presence of diffuse peritonitis.³ Studies comparing mortality and morbidity of the HP versus primary anastomosis did not show any significant differences and, despite what is reported in the literature, Hartmann currently remains the choice of surgeons in the emergency setting.^{6,7} The optimal procedure is still a matter of debate. We aim to evaluate the safety and efficacy of primary anastomosis versus HP in reducing the end-stoma rate and to identify the appropriate surgical timing in the emergency setting for the treatment of Hinchey III and IV acute diverticulitis.

Materials and Methods

The present study was conducted at the Emergency Department of Policlinico Umberto I of Rome. A retrospective analysis of our database of prospectively collected data was conducted. A total of 365 patients underwent emergency surgery from January 2014 to April 2019 for colorectal diseases, 84 for acute left-sided colonic diverticulitis. Surgical procedures performed include: 49 surgical resection and anastomosis with or without stoma (24 with diverting stoma and 25 without stoma) and 22 HR. Patients with Hinchey Stage IIb, stenosis and diverticular hemorrhage were excluded. Finally, a total of 36 Hinchey III and Hinchey IV patients, comparing 19 PRA and 17 HP, were enrolled in this study (Figure 1).

Surgical Characteristics

Choice of surgical approach was based on the decision of the individual operator experienced in emergency surgery. Hartmann resection was performed in all cases using open technique. The left colectomy with primary anastomosis was performed, in relation to the specific case, by means of a minimally invasive laparoscopic or open technique. Routinely, in benign colon and rectal diseases we preserve the left colic artery, in order to avoid the need of a central ligation of inferior mesenteric vessels, resulting in increased blood supply for anastomosis, especially in the most severe cases of sepsis. Knight-Griffen was preferred, although manual anastomoses have also been performed in end-to-end or end-to-side fashion. Intraoperative colonic irrigation was routinely performed, primarily in high-risk patients (Figures 2, 3, 4).

Measurements

Patients demographics included age, sex, American Society of Anesthesiology (ASA) score, comorbidity and history of prior abdominal surgery. Perioperative outcomes included

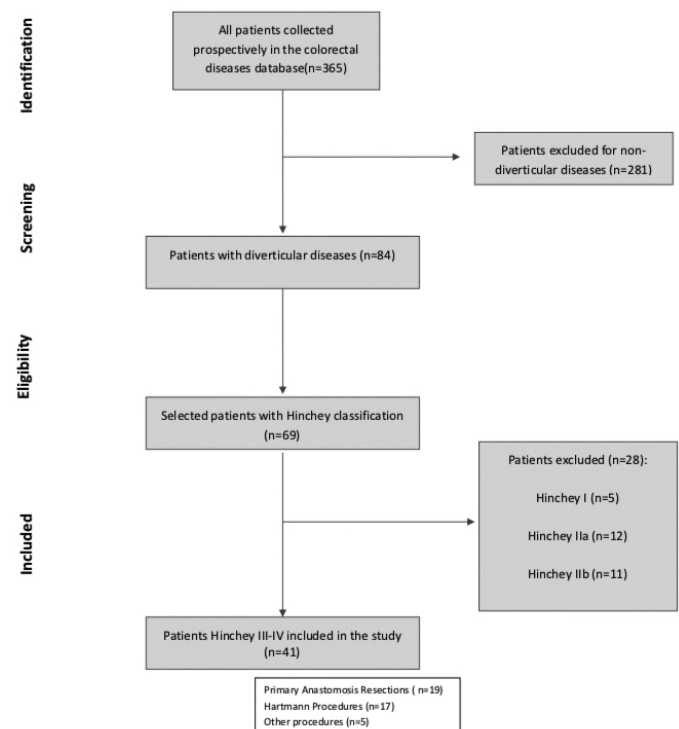


Figure 1. Patient selection flow-chart

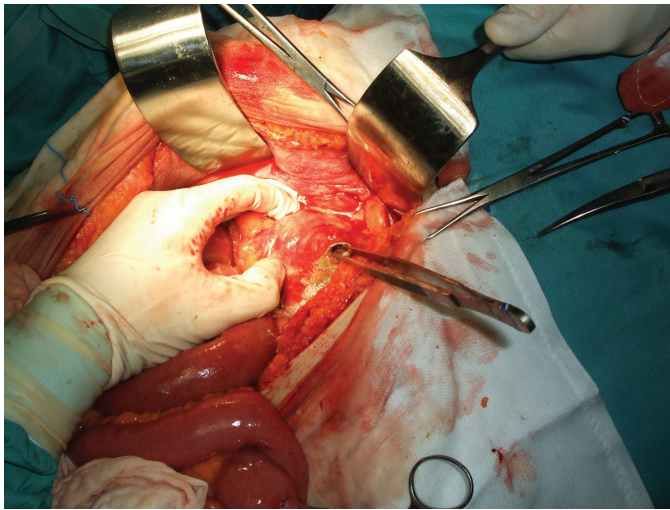


Figure 2. Sigmoid diverticular perforation

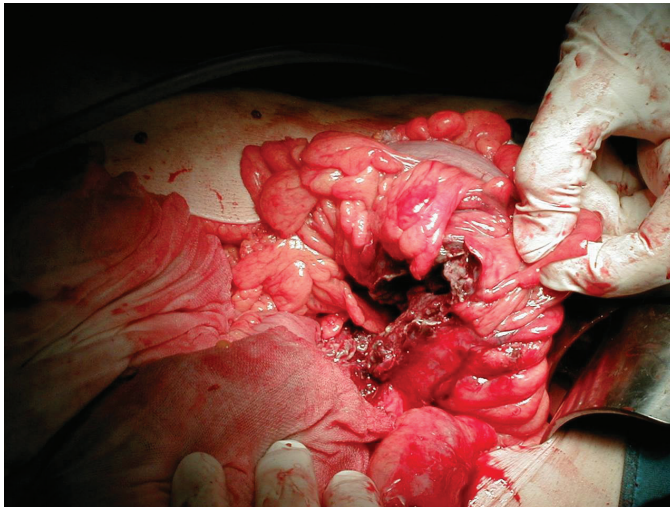


Figure 3. View before PRA in a Hinchey IV patient with acute diverticulitis
PRA: Primary resection anastomosis

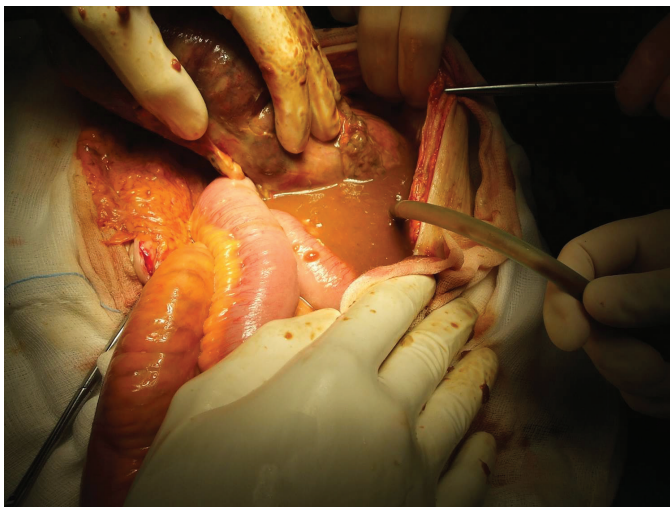


Figure 4. View of generalized fecal peritonitis following emergency laparotomy in a Hinchey IV patient

preoperative waiting time (minutes), operating room time (skin-incision to skin-closure, minutes), length of stay (days), postoperative complications (according to Clavien-Dindo classification scale), and re-operation and reversal rate.

Statistical Analysis

The patient data were collected using Microsoft Excel 2019 from an internal database. A comparative analysis was performed. Descriptive statistics are presented as mean \pm standard deviation and ranges for numeric variables and as proportions for categorical variables. Pearson's chi-squared and Fisher's exact tests were employed for categorical variables. Student's t-test was used for continuous variables. Mean difference (MD) and risk difference with confidence intervals of 95% were calculated for numeric variables and categorical variables, respectively, if a statistically significant p value was observed. A level of $p < 0.05$ was set as the criterion for statistical significance. The statistical analyses were performed using IBM SPSS (IBM Inc., Armonk, NY, USA).

Results

The demographic data are compiled in Table 1, and perioperative outcomes are listed in Table 2. In the PRA group, mean age was 63.9 ± 13.4 years and 57.9% were male. In the HP group, mean age was 70.8 ± 13.8 years and 58.8% were female. No statistically significant differences were found in age and sex but a slight difference was found in ASA score between the two groups (PRA group 10/19, 52.6% ASA 2 vs. HP group 8/17, 47% ASA 3; $p = 0.065$). Therefore, although not significant, the difference in ASA score is evident, probably influenced by the small sample of patients, and this could justify Hartmann's resection in critical settings. However, a non-significant difference was found in Hinchey staging between the two procedures (PRA group 14/19, 73.7% vs HP group 9/17, 53% in Hinchey III pts; PRA group 5/19, 26.3% vs HP group 8/17, 47% in Hinchey IV pts; $p = 0.172$). No statistically significant differences were found in operating room time ($p = 0.850$) and length of stay ($p = 0.990$) between the groups. The mean operating room time was the same in the PRA and HP group (211.7 vs 207.2 minimum; $p = 0.850$) and a MD of 4.5 min was observed. According to these preliminary data, there does not appear to be a major difference in terms of surgical time when performing an HP or a PRA in an emergency setting in our center. There was no significant correlation between preoperative waiting time ($p = 0.739$) and operating room time ($p = 0.946$) with postoperative complications in both groups. However, a statistically significant correlation was found between length of stay and postoperative complications ($p = 0.005$).

Table 1. Patient characteristics

	PRA (19 pts)	HP (17 pts)	p value
Age (yr)			
Mean (SD)	63.9 (13.4)	70.8 (13.8)	0.135
Sex n (%)			
Female	8 (42.1)	10 (58.8)	0.317
Male	11 (57.9)	7 (41.2)	
ASA score n (%)			0.065
1	3 (15.8)	2 (11.8)	
2	10 (52.6)	2 (11.8)	
3	3 (15.8)	8 (47)	
4	3 (15.8)	4 (23.5)	
5	0 (0)	1 (5.9)	
Total	19	17	

Value are expressed as mean (SD: Standard deviation) or n (%)

PRA: Primary resection anastomosis, HP: Hartmann procedure, ASA: American Society of Anesthesiologists, pts: Patients

Table 2. Perioperative outcomes

	PRA (19 pts)	HP (17 pts)	p value
Preoperative waiting time (minutes)			
Mean (SD)	2360.3 (4887)	2649.2 (3996.5)	0.853
Operating room time (min)			
Mean (SD)	211.7 (65.5)	207.2 (71.5)	0.850
Length of stay			
Mean (SD)	17.5 (17.9)	17.4 (21.7)	0.990
Reversal rate n (%)	8 (42.1)	0 (0)	0.002
Hinchey staging n (%)			0.172
III	14 (73.7)	9 (53)	
IV	5 (26.3)	8 (47)	
Total	19	17	

Value are expressed as mean (SD: Standard deviation) or n (%)

PRA: Primary resection anastomosis, HP: Hartmann procedure, pts: Patients

No intraoperative complications occurred in the PRA or the HP series. Medical complications (Clavien Dindo grade I-II) represented the most frequent cause of overall postoperative complications (19.4%; $p=0.256$). No abscess (Clavien Dindo grade I-II) was observed in either group. Surgical site infection occurred in one patient (1/19) in the PRA group and in two patients (2/17) in the HP group. No prolonged postoperative ileus or bowel occlusion was observed in either group. Two patients in the PRA group required intervention not under general anesthesia (Clavien Dindo grade IIIa) for anastomotic leak ($n=1$) and abscess ($n=1$). Postoperative complications are reported in Table 3 and Figure 5.

Symptomatic anastomotic leakage (Clavien Dindo grade IIIb) occurred in one patient (1/19) in the PRA group, requiring open revision with an end-colostomy. This event occurred in a patient who underwent PRA without diverting ileostomy. In the HP group, one patient suffered from massive hemoperitoneum from a rectal stump vessel and so required open surgery on postoperative day 12, and three patients required reoperation for a stoma complication ($n=1$), an abscess collection ($n=1$) and a wound dehiscence ($n=1$). Therefore, the overall re-operation rate was 5.3% (1/19) in the PRA group and 23.5% (4/17) in the HP group. Mortality was 29.4% (5/17 patients) in the HP group while

Table 3. Postoperative complications

	PRA (19 pts)	HP (17 pts)	p value
No complications (Dindo grade 0) n (%)	8 (42.1)	5 (29.4)	0.256
Complications (Dindo grade I-II) n (%)	4 (21)	3 (17.6)	0.256
Medical complications	3	1	
Surgical Site infection	1	2	
Abscess	0	0	
Complications (Dindo grade III-IV) n (%)	4 (21)	4 (23.5)	0.256
Anastomotic leak	2	-	
Massive bleeding	0	1	
Stoma complication	0	1	
Bowel occlusion	0	0	
Abscess	1	1	
Wound dehiscence	0	1	
Acute kidney failure	1	0	
Acute respiratory failure	0	0	
Acute myocardial infarction	0	0	
Ischaemic stroke	0	0	
Mortality (Dindo grade V) n (%)	2 (10.5)	5 (29.4)	0.256
Total	19	17	

Value are expressed as n (%), PRA: Primary resection anastomosis, HP: Hartmann procedure, pts: Patients

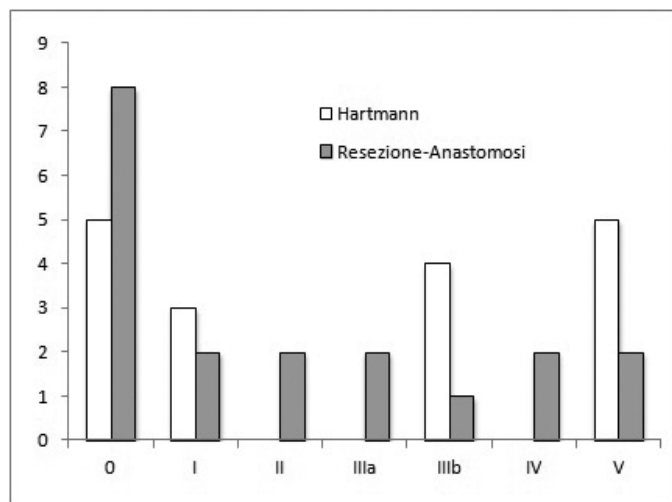


Figure 5. Relationship between treatment and postoperative complications (according to Clavien Dindo classification scale)

there were two deaths (10.5%, 2/19) in the PRA group. No statistically significant differences in postoperative complications were found in ASA ($p=0.675$) and sex ($p=0.314$) but a statistically significant correlation was found between age and postoperative complications in the two groups ($p=0.039$) (Figure 6).

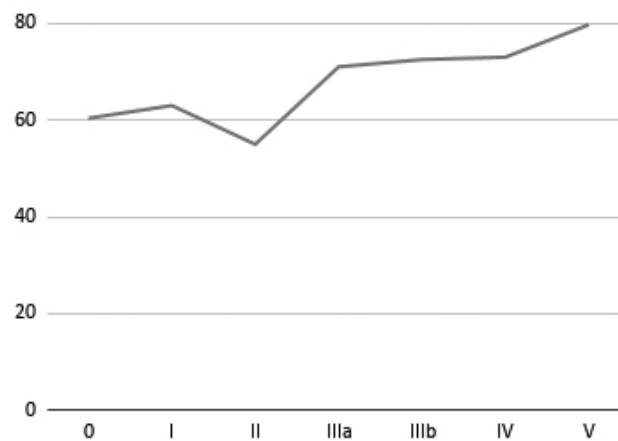


Figure 6. Postoperative complications increase with the age of patients

Furthermore, a slight difference was found by analyzing patient comorbidities and possible pre-operative predictors of the risk of postoperative complications. Among the four patients with cardiovascular disease, three underwent reoperation and one died; among the seven patients with no comorbidity, three had no complications (Clavien Dindo grade 0) and three had minor complications (Clavien Dindo grade I-II). An almost significant correlation was

found between the increase in pre-operative lactates (Lac) and postoperative complications ($p=0.077$). Finally, among Hinchey stage III-IV patients, there was a significant difference in reversal rate for the PRA group (42.1%, 8/19 vs 0%, 0/17); $p=0.002$).

Discussion

In this study, we reported our emergency surgery department experience on the feasibility and efficacy of PRA with protective ileostomy in Hinchey III and IV diverticulitis in a selected cohort of patients (Table 4). Perforated left-sided diverticulitis with generalized peritonitis, Hinchey III and IV is a well defined, life-threatening, clinical situation, which occurs frequently in every surgical emergency department.⁸ We reported reasonable operating room time, low morbidity, and an increase in reversal rate. By performing the protective ileostomy, we did not see any cases of AL or other major complications. The PRA-approach resulted in no difference in operative times, which also decreased with surgical experience. The primary anastomosis provided a technical advantage, as evidenced by the lower re-operation rate. We reported an equivalent length of stay for HP compared with primary anastomosis. In our experience, performing a technically correct and safe colorectal anastomosis did not increase length of stay of patients compared to those undergoing to end-colostomy. Although not statistically significant in this analysis, post-operative major complication rates in the HP series appeared to be higher than in the PRA series. We did observe significant differences in reversal rate, probably because an end-colostomy was performed in high-risk patients or unfit for surgery. We suggest that ileostomy closure is not a surgical procedure that is comparable to Hartmann reversal, in which there is a high risk of postoperative morbidity and mortality. Hartmann reversal represents a major complex procedure for surgeons at the time of second-stage. The pitfalls can be multiple, from adhesions formed by previous surgery, to problems in preparing the rectum for the anastomosis, which is sometimes difficult to manipulate, adhering to loco-regional structures, such as the sacrum, and with the risk of performing unsafe anastomoses and consequently undergoing further postoperative pitfalls. In

Table 4. Our experience

	PRA	HP
Preoperative timing	?	?
Operating room time	=	=
Length of stay	=	=
Morbidity	-	+
Reversal rate	+	-

PRA: Primary resection anastomosis, HP: Hartmann procedure

contrast, the ileostomy closure procedure requires a mini peri-stomal surgical access, a simple preparation of the loops of the small bowel, and therefore often a rapid postoperative recovery of the patient.

Consistent with literature reports², we had no significant data on timing of surgery. EAES and SAGES collaborative consensus conference aimed to summarize recent evidence and draw up guidelines for comprehensive acute diverticulitis management. Patients with perforated diverticulitis and peritonitis should be evaluated early for operative intervention to control infection. There is little data to inform the timing of operative intervention, but the clinical status of the patient should guide urgency of surgical intervention.² Patient comorbidities can represent possible pre-operative predictors of postoperative complications, as described by Richter et al.⁹, reporting that patients with previous transplantation or complex cardiovascular procedures have a significantly increased risk of dying after sigmoid resection for perforated diverticulitis. Four studies reported on C-reactive protein level as a risk factor for complicated diverticulitis^{10,11,12,13}, and four studies reported on white blood cell count as risk factor.^{10,12,14,15}

Fears of inadequate control of the source of sepsis prompted the implementation of the resection of the affected segment of colon with formation of a colostomy (HP) in the 1970's. Future development of treatment strategies was driven by the recognition of high morbidity and mortality associated with HP and the low Hartmann's reversal rates and this led to the wider use of resection with PRA during the 1990's.¹⁶ In a Nationwide Analysis of 2,729 Emergency Surgery Patients¹⁷ it was reported that primary anastomosis with a diverting loop ileostomy appears to be at least as safe an alternative to HP. Nevertheless, several studies^{6,7} that compare the numbers of HP and PRA performed show how Hartmann currently remains the choice of surgeons in the emergency setting. The first multicenter randomized clinical trial (RCT)¹⁸ to promote primary anastomosis with ileostomy compared to HP in patients with perforated diverticulitis was published in 2012. In the DIVERTI trial¹⁹, although mortality was similar in both procedures, the reversal rate of the stoma is significantly higher after primary anastomosis ($p=0.0001$). The international, multicentre, randomised controlled LADIES trial²⁰ aimed to compare HP with primary anastomosis (with or without defunctioning ileostomy) to determine the optimal strategy for perforated diverticulitis with purulent or faecal peritonitis. Results of this trial showed significantly better 12-month stoma-free survival for patients in the primary anastomosis group, a significantly lower short-term overall morbidity after stoma reversal for primary anastomosis and a significantly

shorter median time to reversal and post-operative stay after reversal. This is the first trial to report on 12-month stoma-free survival and this is the largest randomised trial that prefers primary anastomosis to HP for the treatment of perforated diverticulitis. Moreover, the role of laparoscopy in the treatment of complicated diverticulitis is an important area of research.²¹ Recent data suggest that resection with primary anastomosis can be performed in Hinchey III in expert hands, whereas trials specifically assessing Hinchey IV diverticulitis are still lacking.²² In the systematic review and meta-analysis on perforated diverticulitis by Shaban et al.²³, primary anastomosis had a statistically significant lower mortality (10.6%) and morbidity (41.8%) compared to the Hartmann's group (20.7% and 51.2%) ($p=0.0003$). In addition, a systematic review of the existing literature was performed by Halim et al.⁵, involving 3,546 patients, of whom 2,868 underwent HP and 860 underwent PRA. The overall mortality in the HP group was 10.8% across the observational studies and 9.4% in the RCTs. The mortality rates in the PRA group, at 8.2% in observational studies and 4.3% in the RCTs, were lower than those in the HP group. Many surgeons favour a Hartmann's resection where there is no risk of an anastomosis leak in the setting of peritonitis and where the reversal is done when the pelvic inflammation settles, usually around six months later.²³ A recent systematic review of literature²⁴ analyzed and reported risk factors for anastomosis leakage following colorectal resections, such as male sex, elevated BMI, preoperative nutritional status, postoperative hypoalbuminemia, post operative diarrhea, low level of anastomosis, diverting stoma, operative time, left colic artery ligation, and perioperative events. Prolonged operative time can be associated with leakage, with a reported threshold varying from 220 to 300 minutes.²⁴ In this systematic review the role of left colic artery preservation was reported, resulting in increased blood supply for anastomosis and subsequently improved anastomotic healing. The laterality may be relevant during left colectomy for acute diverticulitis. In fact, in benign disease there is no need for a central vascular ligation and lymphadenectomy with complete mesocolic excision, as there is in the setting of colorectal malignancies.²⁵ Furthermore, bleeding during surgery may predispose to leakage due to hemodynamic alterations at the anastomotic site. Kawada et al.²⁶ found that intraoperative bleeding at more than 100 mL was associated with significantly increased incidence of leakage ($p=0.037$). Currently, there is much research into the role of new technologies introduced in clinical practice to evaluate organ perfusion in several conditions. Indocyanine green (ICG) fluorescence angiography (FA) was introduced to

provide real-time, intra-operative evaluation of the vascular supply of anastomosis.²⁷ The rationale behind FA is that the fluorescent dye, upon systemic injection, should reach and highlight only vascularized areas.²⁸ Meyer et al.²⁹ describe pre-operative and operative measures to reduce anastomotic leakage, encouraging the implementation of FA, which leads to significant intra-operative changes in surgical strategies. In recent years, several authors published the application of this innovative technique with safe results and with no additional time-consumption during colorectal resections in the elective setting.^{30,31}

Keller et al.³² presented the first report of ICG FA imaging in emergency surgery, showing that this was safe, feasible, and effective. Nonetheless, the ease, the low cost, and the rare side effects of the procedure make FA a promising tool whose actual role in colonic resection should be studied further.³⁰ The role of ICG-FA may already represent the beginning of a new ethos in emergency colorectal resections, challenging old dogmas, increasing primary anastomosis and drastically reducing end-stoma rate.

Study Limitations

Overall, the present study demonstrated a (non-significant) improvement in postoperative complications and re-operations for Hinchey III and IV patients with acute diverticulitis when treated with primary anastomosis surgery in comparison to HP. Limitations of this study include its retrospective nature, although the data was collected prospectively, with its inherent risk-of-bias and the number of patients enrolled. Strengths of the study include the highly selected category of enrolled patients. We also provide detail of the types and severity of all complications using standardized classification criteria.

Conclusion

Based on our emergency surgery department experience, PRA and protective ileostomy safely performed may be feasible, with satisfactory perioperative outcomes, postoperative complication rates and a significant reversal rate in Hinchey III and IV patients with acute diverticulitis. Hartmann's resection should be considered as a life-saving surgery, limiting end-colostomy only to elderly patients combined with an ASA score that predicts a bad prognosis. Future randomized studies will be needed to define the correct timing of surgery to improve outcomes of complicated acute diverticulitis. The present study is ongoing to confirm these results with increased sample size and greater confidence.

Ethics

Ethics Committee Approval: Not applicable.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: M.A., G.M., S.S., G.B., E.M., P.B., D.R., F.C., Concept: M.A., G.M., F.C., Design: M.A., G.M., F.C., Data Collection or Processing: G.M., G.B., E.M., P.B., Analysis or Interpretation: G.M., G.B., E.M., P.B., Literature Search: G.M., Writing: M.A., G.M., F.C.

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