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Patient outcomes and prognostic factors associated with colonic perforation surgery: a retrospective study

Do-bin Lee, Seonhui Shin, Chun-Seok Yang

Department of Surgery, Daegu Catholic University Medical Center, Daegu Catholic University School of Medicine, Daegu, Korea

Background: Despite advances in surgery and intensive perioperative care, fecal peritonitis secondary to colonic perforation is associated with high rates of morbidity and mortality. This study was performed to review the outcomes of patients who underwent colonic perforation surgery and to evaluate the prognostic factors associated with mortality.

Methods: A retrospective analysis was performed on 224 consecutive patients who underwent emergency colonic perforation surgery between January 2008 and May 2019. We divided the patients into survivor and non-survivor groups and compared their surgical outcomes.

Results: The most common cause of colon perforation was malignancy in 54 patients (24.1%), followed by iatrogenic perforation in 41 (18.3%), stercoral perforation in 39 (17.4%), and diverticulitis in 37 (16.5%). The sigmoid colon (n=124, 55.4%) was the most common location of perforation, followed by the ascending colon, rectum, and cecum. Forty-five patients (20.1%) died within 1 month after surgery. Comparing the 179 survivors with the 45 non-survivors, the patient characteristics associated with mortality were advanced age, low systolic blood pressure, tachycardia, organ failure, high C-reactive protein, high creatinine, prolonged prothrombin time, and high lactate level. The presence of free or feculent fluid, diffuse peritonitis, and right-sided perforation were associated with mortality. In multivariate analysis, advanced age, organ failure, right-sided perforation, and diffuse peritonitis independently predicted mortality within 1 month after surgery.

Conclusion: Age and organ failure were prognostic factors for mortality associated with colon perforation. Furthermore, right-sided perforation and diffuse peritonitis demonstrated a significant association with patient mortality.

Keywords: Intestinal perforation; Peritonitis; Postoperative complication; Surgical stomas

Introduction

Fecal peritonitis secondary to colonic perforation is a life-threatening condition, and emergency surgical management is associated with high morbidity and mortality rates. Despite advances in surgical techniques and perioperative management, surgical outcomes after colonic perforation have not improved [1-4]. It is important to preoperatively evaluate the severity of peritonitis and identify the associated risk factors for mortality because patients with severe peritonitis require immediate surgical management and high-quality intensive care. Additionally, the severity of the peritonitis, potential predictors, and the likelihood of mortality should be included in the information provided to patients and their families.

Several studies have investigated the prognostic factors associated with the mortality and morbidity of patients with fecal peritonitis; consequently, several scoring systems are available [1,5-7].

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Corresponding author: Chun-Seok Yang, MD
Department of Surgery, Daegu Catholic University Medical Center, Daegu Catholic University School of Medicine, 33 Duryugongwon-ro 17-gil, Nam-gu, Daegu 42472, Korea
Tel: +82-53-650-4065 • Fax: +82-53-624-7185 • E-mail: gsyangcs@gmail.com

However, these risk factors and scoring systems have only been validated in small-population studies and are not clinically prevalent. Nonetheless, many studies are ongoing to determine other risk factors associated with mortality in patients who undergo colonic perforation.

Hartmann's procedure is the standard surgical procedure for treating left colonic perforation [8,9]. Hartmann's procedure is associated with low quality of life because of the colostomy care required [10], and restoration of intestinal continuity is associated with morbidity and mortality [11]. The reversal rate of Hartmann's procedure tends to be lower than 50% in most reported articles [12]. However, it is inconclusive whether primary resection and anastomosis without fecal diversion is safer than Hartmann's procedure for left colonic perforation.

Thus, the aim of this observational retrospective study was to review the outcomes of patients who underwent emergency surgery for fecal peritonitis secondary to colonic perforation. The primary objective was to compare various factors between survivors and non-survivors. Accordingly, we aimed to predict outcomes based on patient conditions before and during surgery. The secondary objective was to evaluate the necessity of fecal diversion in patients with left colonic perforation without prognostic factors.

Methods

Ethical statements: The study protocol was approved by the Institutional Review Board (IRB) of Daegu Catholic University Hospital (IRB No: CR-21-069), which waived the need for informed consent due to the retrospective design of the study.

1. Study design and population

For this retrospective study, we selected 224 consecutive patients who underwent emergency surgery for fecal peritonitis secondary to colon perforation between January 2008 and May 2019 at Daegu Catholic University Hospital in Korea. Patients with perforations from other gastrointestinal conditions were excluded.

2. Data collection

Patient clinical and management data were collected from medical chart reviews. This included patient demographics such as sex, age, height, weight, body mass index, comorbidities, time from symptom onset to surgery, American Society of Anesthesiologists (ASA) physical status (PS) classification, initial vital signs, white blood cell count, hemoglobin, prothrombin time, activated partial thromboplastin time, serum protein levels, albumin, lactate, C-reactive protein (CRP), creatinine, and blood urea nitrogen at the time of admission. The surgical and pathological reports were reviewed to obtain data regarding the extent of peritoneal contamination, the types of surgery performed, and the sites and causes of perforation. In addition, the length of operation, perioperative complications, mortality, and length of hospital stay were reviewed. Patients were divided into survivors and non-survivors, and clinical data were compared between the groups.

We defined advanced age as > 70 years. Organ failure was defined as follows: (1) renal failure with creatinine levels of > 1.4 mg/dL, (2) circulatory failure with systolic arterial pressure of < 90 mmHg requiring inotropes, and (3) respiratory failure with partial pressure of oxygen < 60 mmHg. Free fluid was defined as the presence of hypodense fluid within the pelvic cavity, subphrenic space, paracolic gutters, or other intraperitoneal spaces on computed tomography (CT) scan. Feculent fluid was defined as the presence of feces protruding through the perforation site with spillage to the adjacent peritoneal cavity on CT scan. Free perforation was defined as air bubbles or air collection within the abdominal cavity, with a distance greater than 5 cm of the affected bowel segment. Diffuse peritonitis was defined as contamination or exudate in the four quadrants during surgery.

The left colon was defined as the descending colon to the rectum. Perioperative mortality was defined as death occurring within 1 month of surgery. Complications were graded according to the Clavien-Dindo classification [13].

3. Operative parameters

We reported postoperative morbidity and mortality, fecal diversion, specialty of the attending surgeon, and rate of bowel reconstruction. The operation results (Hartmann's procedure, primary resection and anastomosis with or without fecal diversion, anastomotic dehiscence, or stoma closure) were also recorded.

4. Subgroup analysis

In accordance with our second objective, we evaluated the necessity of fecal diversion in patients with left colonic perforation without prognostic factors. Thus, to compare the surgical outcomes with or without fecal diversion, we excluded 106 patients who had diffuse peritonitis from the 165 patients with left colonic perforation because diffuse peritonitis was an independent surgical prognostic factor. Thus, the sub-analysis included a group of patients with left colonic perforation at low risk of mortality. Accordingly, 59 patients were included in the sub-analysis.

5. Statistical methods

Comparisons between groups were performed using the chi-

square test or Student *t*-test. We used two-way contingency tables to compare discrete variables and implemented Fisher exact test when low expected values were present. Univariate and multivariate analyses were performed. The variables were analyzed for various outcomes using simple logistic regression, and odds ratios and 95% confidence intervals were reported. For multivariate analysis, a multiple logistic regression model was used. The Mann-Whitney *U*-test was used to analyze the differences in non-categorical variables among the subgroups. All analyses were performed using IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA) and all *p*-values were two-sided; *p*-values of < 0.05 were considered statistically significant.

Results

Two hundred and twenty-four patients were included in this study. The patient characteristics are presented in Table 1. The mean patient age was 67.5 ± 15.3 years (102 male, 122 female). The most common perforation site was the sigmoid colon in 124 patients (55.4%); 59 patients (26.3%) had perforations on the right side and 165 (73.7%) had perforations on the left side. Resection and anastomosis (50.0%) were the most frequently performed surgeries, followed by Hartmann's procedure (27.7%). Malignancy was the most common cause of perforation in both groups, but stercoral and ischemic colitis were more common in the non-survivors.

A comparison of the factors associated with survivors and non-survivors indicated that age (66 ± 15.5 years vs. 73.4 ± 13.2 years, $p = 0.004$), organ failure (19.6% vs. 53.3%, $p < 0.001$), systolic blood pressure (117.7 ± 22 mmHg vs. 105.4 ± 30.3 mmHg, $p = 0.003$), and heart rate (87.5 ± 16.1 beats/min vs. 94.5 ± 20.6 beats/min, $p = 0.041$) were significantly different (Table 2). Analysis of laboratory values indicated that CRP, creatinine, prothrombin time, and lactate levels were significantly different between the groups. Analysis of the factors associated with characteristics of peritonitis indicated that free fluid (50.6% vs. 76.7%, $p = 0.003$), feculent fluid (36% vs. 55.6%, $p = 0.027$), diffuse peritonitis (52.6% vs. 82.2%, $p = 0.001$), and right-sided perforation (22.9% vs. 40%, $p = 0.033$) were significantly different. The operative outcomes are summarized in Table 3. There were 89 patients (39.7%) with Clavien-Dindo classification ≥ III, of whom 45 (20.1%) died within 1 month after surgery. Of the total, 120 patients (53.6%) underwent fecal diversions, such as Hartmann's procedure, ileostomy, or colostomy, and 64 (72.7%) of the 88 surviving patients underwent stoma closure.

The univariate and multivariate regression analyses are presented in Table 4. Age of > 70 years, ≥ 2 comorbidities, organ failure, renal failure, prolonged prothrombin time, free fluid, feculent fluid, diffuse peritonitis, and right-sided perforation were associated with mortality. When multivariate analysis was performed to determine whether the aforementioned factors were prognostic, only advanced age, organ failure, right-sided perforation, and diffuse peritonitis were statistically significant.

Sub-analysis between the group that underwent fecal diversion (n = 30) and the group that underwent surgical methods without fecal diversion (n = 29) revealed that there was no significant difference between the groups in terms of preoperative and intraoperative findings such as age and comorbidities. This suggests that there were no preoperative differences in other risk factors for mortality. Moreover, there were nine patients (30.0%) whose stoma could not be reversed. Nonetheless, there was no significant difference in mortality and morbidity between the groups (Table 5).

Discussion

Colonic perforation causes widespread dissemination of bacteria and feces into the intraperitoneal space and can lead to peritonitis, septic shock, and multiple organ failure. The mortality rate associated with colon perforation reportedly ranges from 6.2% to 33.3% [1,5-7,14-17]. Similarly, the mortality rate in our study was 20.1%. Our results also showed that old age, organ failure, right-sided perforation, and diffuse peritonitis were associated with mortality. In addition, in the absence of diffuse peritonitis, even patients with left colon perforations showed comparable surgical outcomes with or without fecal diversion. Thus, considering that there are several complications associated with stoma reversal and that many patients have a permanent stoma, a stoma can be omitted if there are no associated risk factors.

Fecal peritonitis due to colonic perforation is largely associated with mortality due to factors such as patient characteristics (including age, ASA PS classification, concurrent medical disease, immunosuppression, and performance status), peritonitis severity, or an interaction between them. Factors such as organ failure and various deteriorations of the blood represent an interaction between patient characteristics and peritonitis severity. Moreover, there are reports of worsening prognosis in patients with lactic acidosis, leukopenia, and bleeding tendency [9,18,19].

In a large cohort of patients with fecal peritonitis, the strongest independent risk factors for mortality were increased age, renal dysfunction, hypothermia, and low hematocrit levels [20]. Furthermore, Tan et al. [21] showed that there was a significant association between mortality and morbidity rates and ASA PS classification, as well as the acute physiology component of the Acute Physiology and Chronic Health Evaluation II score in patients

Table 1. Characteristics of the study population and comparison between the survivors and non-survivors

Characteristic	Overall	Survivor	Non-survivor	*p*-value
No. of patients	224	179	45	
Sex				>0.999
Male	102 (45.5)	82 (45.8)	20 (44.4)	
Female	122 (54.5)	97 (54.2)	25 (55.6)	
Age (yr)	67.5±15.3	66.0 ± 15.5	73.4 ± 13.2	0.004
ASA PS classification				0.118
I	52 (23.2)	47 (26.3)	5 (11.1)	
II	119 (53.1)	94 (52.5)	25 (55.6)	
III	49 (21.9)	35 (19.6)	14 (31.1)	
IV	4 (1.8)	3 (1.7)	1 (2.2)	
Location				0.160
Cecum	18 (8.0)	14 (7.8)	4 (8.9)	
Ascending colon	22 (9.8)	16 (8.9)	6 (13.3)	
Hepatic flexure colon	3 (1.3)	2 (1.1)	1 (2.2)	
Transverse colon	16 (7.1)	8 (4.5)	7 (15.6)	
Splenic flexure colon	5 (2.2)	4 (2.2)	2 (4.4)	
Descending colon	15 (6.7)	12 (6.7)	3 (6.7)	
Sigmoid colon	124 (55.4)	105 (58.7)	19 (42.2)	
Rectum	21 (9.4)	18 (10.1)	3 (6.7)	
Sidedness				0.033
Right location	59 (26.3)	41 (22.9)	18 (40.0)	
Left location	165 (73.7)	138 (77.1)	27 (60.0)	
Types of surgery				0.004
Hartmann's operation	62 (27.7)	41 (22.9)	21 (46.7)	
Resection and anastomosis	112 (50)	93 (52)	19 (42.2)	
Primary closure	35 (15.6)	33 (18.4)	2 (4.4)	
Stoma only	11 (4.9)	10 (5.6)	1 (2.2)	
Drainage only	4 (1.8)	2 (1.1)	2 (4.4)	
Stoma creation	120 (53.6)	88 (49.2)	32 (71.1)	0.013
No stoma creation	104 (46.4)	91 (50.8)	13 (28.9)	
Causes of perforation				0.023
Malignancy	54 (24.1)	41 (22.9)	13 (28.9)	
Diverticulitis	37 (16.5)	30 (16.8)	7 (15.6)	
Iatrogenic	41 (18.3)	39 (21.8)	2 (4.4)	
Ischemic colitis	16 (7.1)	9 (5.0)	7 (15.6)	
Stercoral	39 (17.4)	28 (15.6)	11 (24.4)	
Trauma	24 (10.7)	21 (11.7)	3 (6.7)	
Unknown	13 (5.8)	11 (6.1)	2 (4.4)	

Values are presented as number only, number (%), or mean±standard deviation.
ASA, American Society of Anesthesiologists; PS, physical status.

with colon cancer perforation. These findings are further supported by those of Yoo et al. [22]. Thus, a scoring system is useful for objectively describing patient conditions, thereby aiding surgical decisions for patients with fecal peritonitis [5].

While the predictive value of factors that reflect the severity of peritonitis has been previously studied, it is difficult to quantitatively measure the degree of peritonitis. Until now, only a scoring system based on the peritonitis scope and spillage content has been developed. Nevertheless, these studies emphasize the importance of diffuse peritonitis. There are reports that the spread of ascites on a preoperative CT scan is significant for predicting mortality [18]. Similarly, we showed that prognosis was not affected by the degree of contamination of the ascites, but rather the extent to which it had spread. These results support the speculation that the

Table 2. Comparison of perioperative factors between the survivors and non-survivors

Characteristic	Survivor (n = 179)	Non-survivor (n = 45)	*p*-value
Time from symptom onset to surgery (day)	1.6 ± 2.7	2.2 ± 3.6	0.251
Organ failure	35 (19.6)	24 (53.3)	< 0.001
Systolic blood pressure (mmHg)	117.7 ± 22	105.4 ± 30.3	0.003
Heart rate (beats/min)	87.5 ± 16.1	94.5 ± 20.6	0.041
White blood cell count (10^3/μL)			0.178
< 4.0	30 (16.8)	13 (28.9)	
≥ 4.0, < 10.0	73 (40.8)	15 (33.3)	
≥ 10.0	76 (42.5)	17 (37.8)	
C-reactive protein (mg/L)	89.7 ± 104.4	135.2 ± 119.1	0.029
Creatinine (mg/dL)	1.1 ± 1.1	1.4 ± 0.9	0.037
Prothrombin time (sec)	14.4 ± 1.4	16.3 ± 3.1	< 0.001
Lactate (mmol/L)	2.8 ± 1.9	5.5 ± 2.4	0.001
Free perforation	142 (81.1)	40 (88.9)	0.315
Free fluid	88 (50.6)	33 (76.7)	0.003
Feculent fluid	63 (36.0)	25 (55.6)	0.027
Abscess	23 (13.1)	4 (9.3)	0.670
Diffuse peritonitis	92 (52.6)	37 (82.2)	0.001
Retroperitoneal perforation	25 (14.3)	7 (15.9)	0.973

Values are presented as mean ± standard deviation or number (%).

Table 3. Comparison of operative outcomes between the survivors and non-survivors

Characteristic	Survivor (n = 179)	Non-survivor (n = 45)	*p*-value
Colorectal surgeon	137 (76.5)	30 (66.7)	0.243
Operative time (min)	169.5 ± 67.1	186.2 ± 131.1	0.235
Intraoperative lavage	14 (7.8)	2 (4.4)	0.745
Stoma reversal	64 (72.7)[a]		NA
Complication			
Surgical site infection	47 (26.3)	10 (22.2)	0.716
Intraabdominal abscess	36 (20.1)	8 (17.8)	0.887
Septic shock	9 (5.0)	40 (88.9)	< 0.001
Pneumonia	19 (10.6)	8 (17.8)	0.288
Cardiovascular events	3 (1.7)	13 (28.9)	< 0.001
Paralytic ileus	8 (4.5)	0 (0)	0.363
Anastomosis leakage	2 (1.1)	6 (13.3)	0.001
Multiorgan failure	1 (0.6)	39 (86.7)	< 0.001
Clavien-Dindo classification			NA
I	19 (10.6)		
II	58 (32.4)		
III	38 (21.2)		
IV	6 (3.4)		

Values are presented as number (%) or mean ± standard deviation.
NA, not applicable.
[a]The stoma reversal rate was based on 88 survivors among patients with stoma creation.

spread of ascites indicates the severity of peritonitis or the duration from the onset of perforation. While mortality rates have been shown to increase with the interval length between the time of hollow organ perforation and the time of surgery [23], our results did not reveal interval length as a prognostic factor for mortality.

Furthermore, our result that diffuse peritonitis is an important prognostic factor is similar to results from studies on colorectal cancer obstruction. When perforation occurs proximal to the ob-

Table 4. Analysis of mortality

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*p*-value	Odds ratio (95% CI)	*p*-value
Age (yr)				
≤70	1			
>70	3.496 (1.667–7.331)	0.001	2.993 (1.254–7.139)	0.013
Comorbidity, ≥2	3.032 (1.549–5.934)	0.001	1.738 (0.767–3.938)	0.185
Organ failure	4.702 (2.353–9.397)	<0.001	4.207 (1.326–13.347)	0.015
Renal failure	3.568 (1.663–7.658)	0.001	0.606 (0.168–2.189)	0.445
Prolonged prothrombin time (>15 sec)	3.225 (1.646–6.319)	0.001	1.899 (0.855–4.219)	0.115
Free fluid	3.225 (1.497–6.947)	0.003	1.404 (0.542–3.633)	0.485
Feculent fluid	2.222 (1.144–4.317)	0.018	0.935 (0.39–2.245)	0.881
Diffuse peritonitis	4.173 (1.838–9.472)	0.001	3.184 (1.208–8.397)	0.019
Sidedness				
Right location	2.244 (1.125–4.477)	0.022	2.348 (1.026–5.373)	0.043
Left location	1			

CI, confidence interval.

Table 5. Subgroup analysis of patients with left-sided colon perforation and low risk factors

Characteristic	Without fecal diversion (n=29)	With fecal diversion (n=30)	*p*-value
Sex			0.908
Male	13 (44.8)	13 (43.3)	
Female	16 (55.2)	17 (56.7)	
Age (yr)	62.5±16.3	65.4±16.3	0.299
Systolic blood pressure (mmHg)	124.7±14.5	119.2±19.2	0.114
Heart rate (beats/min)	85.6±14.4	88.5±12.4	0.346
C-reactive protein (mg/L)	51.9±71.2	85.2±88.7	0.115
Creatinine (mg/dL)	0.7±0.2	0.8±0.3	0.169
Prothrombin time (s)	13.7±0.8	14.1±1.1	0.179
Lactate (mmol/L)	2.2±1.0	1.7±0.6	0.402
Free perforation	22 (78.6)	19 (65.5)	0.273
Free fluid	10 (35.7)	9 (31.0)	0.708
Feculent fluid	6 (21.4)	8 (27.6)	0.589
Abscess	6 (21.4)	5 (17.2)	0.689
Retroperitoneal perforation	6 (21.4)	4 (13.8)	0.504[a]
Operative time (min)	166.2±59.5	185.1±63.6	0.180
Hospital stay (day)	13.9±6.1	20.1±12.1	0.050
Clavien-Dindo classification			0.543
I	1 (3.4)	3 (10.0)	
II	10 (34.5)	7 (23.3)	
III	10 (34.5)	7 (23.3)	
IV	5 (17.2)	7 (23.3)	
Mortality	2 (6.9)	2 (6.7)	>0.999[a]

Values are presented as number (%) or mean±standard deviation.
[a]Statistical significance was assessed by Fisher exact test.

structing tumor, it tends to be severe due to intestinal distension, and peritoneal contamination is diffuse and fecal. This leads to severe septic shock, which increases the risk of perioperative mortality. In contrast, when perforation occurs at the cancer site, the contamination is usually localized, typically leading to purulent collection and resulting in a lower risk of severe peritonitis [24]. In our

study, this is also the reason that peritonitis on the right side had a worse prognosis than that on the left side. In cases of perforation on the right side, more diffuse peritonitis occurred, which led to a worse prognosis.

The optimal surgical treatment for colonic perforation remains controversial, and the treatment strategy depends on the patient's general condition and the experience of the primary surgeon. Despite advancements in surgical techniques, Hartmann's procedure is still frequently performed to treat left colonic perforation [8,9]. The literature that primary anastomosis has comparable surgical outcomes to Hartmann's procedure has mainly been studied in patients with diverticular perforation [25]. Primary anastomosis without fecal diversion has a longer operative time, and Hartmann's procedure is a safer option for patients with severe medical illness. Therefore, it is important to determine the patient's overall condition and account for risk factors and conditions that are associated with mortality prior to surgery. In the absence of diffuse peritonitis, primary anastomosis and stoma omission had similar operative outcomes to Hartmann's procedure even in patients with left colon perforation.

Our study has some limitations. First, this was a single-center study, and we could not proceed with the validation process. Second, our study had a retrospective design; thus, we could not obtain some patient information, such as CRP and lactate levels. Third, because this study included patients who underwent surgery, there may be limitations in the clinical course of fecal peritonitis. Finally, the surgeries were performed by 10 different surgeons, which may have led to inconsistent quality. However, there was no significant difference in the postoperative outcomes based on the surgeon's specialty.

In conclusion, advanced age, organ failure, right-sided perforation, and diffuse peritonitis were found to be prognostic factors for colon perforation accompanied by fecal peritonitis. Thus, these findings demonstrate that it is important to determine the type of surgery, extent of resection, and whether fecal diversion should be performed.

Notes

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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Author contributions

Conceptualization, Data curation: all authors; Investigation: DL, SS; Formal analysis, Project administration, Software, Supervision, Validation: CSY; Methodology: SS, CSY; Writing-original draft: DL; Writing-review & editing: CSY.

ORCID

Do-bin Lee, https://orcid.org/0000-0002-7249-7074
Seonhui Shin, https://orcid.org/0000-0003-4676-9037
Chun-Seok Yang, https://orcid.org/0000-0002-5527-6819

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