

Original Article

Study of the prognostic factor of the colon perforation case with the pan-peritonitis that needed emergency surgery: a single-center observational study

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Aim: We divided patients treated with emergency surgery for pan-peritonitis caused by colon perforation into the survival group and the death group based on outcome at postoperative day 30 and examined the prognostic factors for colon perforation.

Methods: The prognostic factors for colon perforation in 76 consecutive patients who underwent emergency surgery at Kansai Medical University Hospital (Hirakata, Japan) from April 2011 to March 2017 were investigated based on outcome at postoperative day 30.

Results: The average age of the 76 patients (41 men/35 women) was 73 years, and the causative disease of colon perforation was malignant/benign in 18/58 cases, with ileocecal perforation site in 8 cases, ascending colon in 6, transverse colon in 2, descending colon in 4, sigmoid colon in 49, and rectum in 7. All patients received laparotomy with irrigation drainage, and 9 patients (11.8%) were dead at 30 days. Upon comparing the 67 survivors with the 9 dead patients, we recognized a significant difference on preoperative spread of ascites on computed tomography (CT) ($P = 0.002$) in univariate analysis and on acute disseminated intravascular coagulation (DIC) score (odds ratio 2.289; 95% confidence interval, 1.188–4.410; $P = 0.013$) in multivariate analysis.

Conclusion: In our hospital, the preoperative acute DIC score was found to be a prognostic factor for colon perforation accompanied by pan-peritonitis. Appropriate evaluation of the spread of ascites on the preoperative CT might also help predict patient prognosis.

Key words: Acute DIC score, colon perforation, extensive spread of ascites on CT, preoperative CT, prognostic factor

INTRODUCTION

COLON PERFORATION CAN cause severe sepsis and multiple organ dysfunction, not only at its onset but also postoperatively, and if it is severe, the mortality rate is high and the prognosis is poor. Therefore, it is important to predict the postoperative course by evaluating patients before surgery. In 2014, Sumi *et al.* reported that the prognostic factors for colon perforation included the Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) score and Sequential

Organ Failure Assessment (SOFA) score, and the prognosis could be predicted by age, serum creatinine value, pulse rate, and the degree of peritonitis.¹ Here, we report the results of our investigation of the prognostic factors for colon perforation in patients requiring emergency surgery to predict prognosis based on the patient's condition before or during surgery.

METHODS

FROM APRIL 2011 to March 2017, 76 consecutive patients with colon perforation and pan-peritonitis who underwent emergency surgery at the Kansai Medical University Hospital Critical Care and Emergency Center (Hirakata, Japan) were the subjects of this retrospective cohort study (Table 1). Patients with perforation of the appendix or the colon due to trauma were excluded.

At 30 days after surgery, 67 of the 76 patients had survived and 9 had died (Table 1). To study the prognostic

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Table 1. Characteristics of patients treated with emergency surgery for pan-peritonitis caused by colon perforation

	<i>n</i> = 76
Age, years	73 (39–96)
Male sex	41 (53.9)
Malignant/benign	18 (23.7)/58 (76.3)
Survival/death	67 (88.2)/9 (11.8)
Cause of disease	
Diverticulitis	45 (59.2)
Malignant tumor	17 (22.4)
Ischemic bowel disease	6 (7.9)
Iatrogenic	4 (5.3)
Other	4 (5.3)
Site of perforation	
Cecum	8 (10.5)
Ascending colon	6 (7.9)
Transverse colon	2 (2.6)
Descending colon	4 (5.3)
Sigmoid colon	49 (64.5)
Rectum	7 (9.2)

Data are expressed as median (interquartile range) or *n* (%).

factors, the patients were divided into two groups, the survival group and the death group, and the two groups were compared.

The prognostic factors were divided into patient background factors, disease factors, and intraoperative factors. Patient background factors of age (years), sex (male/female), body mass index (kg/m²), surgical history, history of dialysis, oral treatment with steroids, serum lactic acid value (mmol/L), POSSUM score, SOFA score, Acute Physiology And Chronic Health Evaluation II (APACHE II) score, and preoperative acute Disseminated Intravascular Coagulation (DIC) score were assessed.

Disease factors compared included the disease (malignant/benign), spread of ascites on preoperative computed tomography (CT) (extensive/localized), spread of contaminated ascites (extensive/localized) during surgery, perforation type (free abdominal/mesenteric), intraperitoneal fecal contamination, and the Mannheim Peritonitis Index (MPI) score. To assess the spread of ascites on the preoperative CT, we defined the spread of ascites. “Extensive” was defined as existence of ascites in both subphrenic space and Douglas’ pouch despite of the location of perforation. “Localized” was every other case (Fig. 1).

The intraoperative factors compared included the range of resection (total excision/partial), presence or absence of anastomosis, operation time (min), bleeding volume (mL), intraoperative washing volume (mL), and blood transfusion.

When diagnosing intraoperative colon perforation in our department, the surgical procedure undertaken in all cases was wash drainage and lesion resection (partial excision or total ablation). If the perforation site was in the left-side colon or rectum or if the patient’s general condition required a pressor agent during surgery, a colostomy was carried out, and according to the patient’s current state, the operation was ended with open abdominal management (OAM). If the puncture site was in the right-side colon or if circulatory dynamics did not require a pressor agent during surgery, an anastomosis was carried out. In OAM, only the puncture site was resected in the intestinal tract, intraperitoneal lavage was then undertaken, and no closed surgery or colostomy was carried out. We completed the surgery in a short time and managed the patient in intensive care. We then undertook a second-look surgery within 24 to 48 h and selected a surgical procedure such as anastomotic closure or additional resection, if necessary.

As anti-DIC therapy during perioperative treatment, a thrombomodulin alpha preparation was given when the patient’s acute DIC score was ≥ 4 points, and an antithrombin III preparation was given if the antithrombin III level was $< 70\%$. Polymyxin B-direct hemoperfusion was used when circulatory dynamics remained unstable even after the use of vasopressor or fluid replacement loading when the patient was returned to the intensive care unit after surgery. Continuous hemodiafiltration was used when the urine volume was ≤ 0.5 mL/kg/h and metabolic acidosis had progressed even after a large amount of fluid replacement. A steroid was used when the vasopressor was given and it was not possible to reverse shock even with fluid replacement. Antibiotics were started with carbapenem antibiotics, were de-escalated as a result of susceptibility testing of blood cultures or ascites cultures, and terminated when the patient’s C-reactive protein level was < 5 mg/dL.

Statistical methods included univariate analysis, the χ^2 -test, and the Mann–Whitney *U*-test. Multivariate analysis was undertaken using binomial logistic regression analysis with covariates being the study items with $P < 0.05$ in the univariate analysis. A significant difference was determined when $P < 0.05$. Statistical analysis was carried out with IBM SPSS version 22 (Armonk, NY, USA). This study was undertaken with the approval of the ethics committee of our hospital (No. 2017209).

RESULTS

PROGNOSTIC FACTORS IN the survival group ($n = 67$) and death group ($n = 9$) at 30 days after surgery can be compared in Table 1. There were no significant differences in patient background factors of age, sex, body

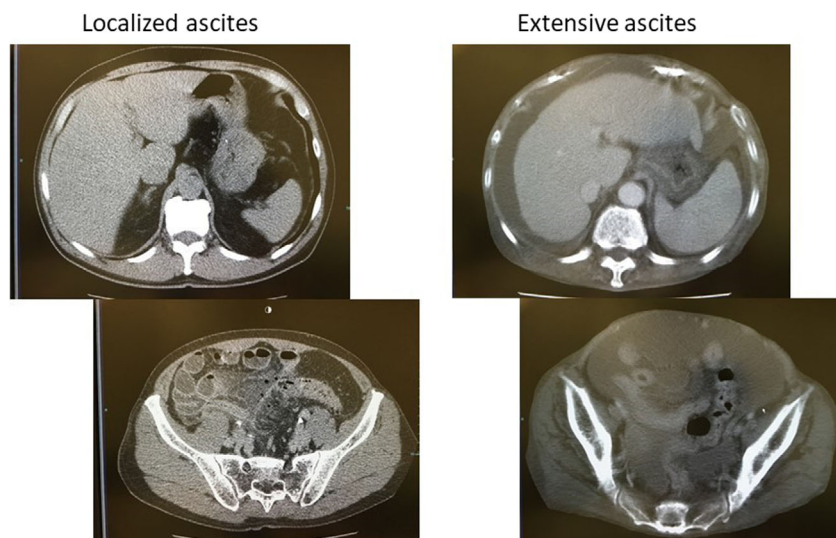


Fig. 1. Range of ascites on preoperative computed tomography in patients treated with emergency surgery for pan-peritonitis caused by colon perforation.

Table 2. Characteristics of patients at discharge following treatment with emergency surgery for pan-peritonitis caused by colon perforation

	Survival (n = 67)	Death (n = 9)	P-value
Age, years	72 (39–90)	77 (55–96)	0.2880
Male	37 (55)	4 (44)	0.7250
BMI, kg/m ²	23.4	23.0	0.8200
History of laparotomy	10 (15)	0 (0)	0.1910
Dialysis history	2 (3)	5 (56)	0.1910
Taking antithrombotic drug	16 (24)	1 (11)	0.6740
Taking steroids drug	6 (9)	1 (11)	0.2390
Serum lactate level, mmol/L	3.1 (0.8–19.9)	4.7 (1.3–10.8)	0.3290
DIC score [†]	2 (0–5)	5 (1–8)	0.0054
SOFA score	3 (0–13)	7 (0–14)	0.0230
POSSUM score	29 (16–53)	38 (27–48)	0.0110
APACHE II score	13 (2–42)	20 (5–35)	0.0530

Data are expressed as median (interquartile range) or n (%).

[†]Disseminated intravascular coagulation (DIC) diagnostic criteria established by the Japanese Association for Acute Medicine.

APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; POSSUM, Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity; SOFA, Sequential Organ Failure Assessment.

mass index, history of open surgery, history of dialysis, treatment with oral anticoagulants or steroids, or serum lactic acid value. However, the POSSUM, SOFA, and preoperative acute DIC scores were significantly higher in the death group than the survival group (Table 2).

There were no significant differences in factors of disease (malignant/benign), extent of contaminated ascites during surgery (extensive/localized), perforation type (free abdominal cavity/mesenteric membrane), fecal contamination, or

MPI score. However, a significant difference was observed in the spread of ascites (extensive/localized) on preoperative CT between the two groups (Table 3).

Intraoperative therapeutic factors showed no significant differences in the range of resection (total excision/part), anastomosis, amount of bleeding (mL), or washing volume during surgery (mL), but a significant difference was observed in the length of operation time between the two groups (Table 4).

Table 3. Disease factors of discharge outcome in patients treated with emergency surgery for pan-peritonitis caused by colon perforation

	Survival (<i>n</i> = 67)	Death (<i>n</i> = 9)	<i>P</i> -value
Malignant/benign	16 (24)/51 (76)	2 (22)/7 (78)	1.000
Range of ascites on preoperative CT, extensive/localized	31 (46)/36 (54)	9 (100)/0 (0)	0.002
Range of contamination of ascites at laparotomy, extensive/localized	47 (70)/20 (30)	9 (100)/0 (0)	0.102
Type of perforation, free intraperitoneal/in the mesentery	47 (70)/20 (30)	8 (89)/1 (11)	0.430
Fecal contamination in the peritoneal cavity	32 (48)	5 (56)	0.733
MPI score	29 (14–55)	34 (21–47)	0.158

Data are expressed as *n* (%) or median (interquartile range).
CT, computed tomography; MPI, Mannheim Peritonitis Index.

Table 4. Intraoperative therapeutic factors of discharge outcome in patients treated with emergency surgery for pan-peritonitis caused by colon perforation

	Survival (<i>n</i> = 67)	Death (<i>n</i> = 9)	<i>P</i> -value
Resection range, overall/partial	4 (6)/63 (94)	2 (22)/7 (78)	0.349
With anastomosis	5 (7)	0 (0)	1.000
Operation time, min	175 (33–280)	133 (44–221)	0.027
Amount of bleeding, mL	805 (0–3,951)	1,052 (50–3,892)	0.539
Washing volume during surgery, mL	8,694 (3,000–12,000)	7,778 (2,000–10,000)	0.407
With blood transfusion	30 (45)	8 (89)	0.028

Data are expressed as *n* (%) or median (interquartile range).

In addition, when multivariate analysis was carried out on the statistically significant prognostic factors, a significant difference was found only for the preoperative acute DIC score (odds ratio 2.289; 95% confidence interval, 1.188–4.410; *P* = 0.013) (Table 5).

Table 5. Multivariate analysis of patient characteristics for discharge outcome in those treated with emergency surgery for pan-peritonitis caused by colon perforation

	Odds ratio	<i>P</i> -value
DIC score	2.289 (1.188–4.410)	0.013
SOFA score	0.949 (0.686–1.314)	0.754
POSSUM score	1.036 (0.920–1.166)	0.562

Values in parentheses represent the 95% confidence interval.
DIC, disseminated intravascular coagulation; POSSUM, Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity; SOFA, Sequential Organ Failure Assessment.

DISCUSSION

WITH ITS MORTALITY rate said to range from 11% to 33.3%,^{2–4} colon perforation requires intensive postoperative care. As a tertiary emergency medical institution, our hospital is equipped with an intensive care unit and can manage such treatments as artificial respiration, postoperative OAM, polymyxin B-direct hemoperfusion, continuous hemodiafiltration, and others. Thanks to our postoperative management, the postoperative 30-day mortality rate of the patients with colon perforation treated at our hospital was 11.8%.

The results of the present study showed the acute DIC score to be a significant prognostic factor for the preoperative evaluation of patients with colon perforation. So far, it has been reported that the APACHE II, SOFA, and POSSUM scores are useful as prognostic factors for colon perforation,^{5–7} and differences in the SOFA and POSSUM scores were also observed in this study. To our knowledge, however, there are no reports of the acute DIC score as a prognostic factor for colon perforation. The acute DIC score is a score used in the emergency intensive care field for

diagnosing DIC, and the mortality rate of patients diagnosed as having DIC according to the acute-phase DIC diagnostic criteria, and not only in those with colon perforation, was approximately 20–21% and was 34.7% when the DIC was caused by sepsis.^{8–11} The high value of the acute DIC score in the case of colon perforation leads to the diagnosis of DIC caused by intraperitoneal infection, so it was easy to understand that the acute DIC score would be high in the death group and would be useful as a prognostic factor. The present study in fact showed the acute DIC score to be a prognostic factor for colon perforation.

In addition, the present study showed that the preoperative CT was not only useful for diagnosing perforating peritonitis but might also be a prognostic factor. There were reports that the severity of peritonitis was useful as a prognostic factor and that the POSSUM score (operative severity score) and the MPI were also useful.^{1,12} However, our results showed no difference in the MPI between the survival group and the death group. Sumi *et al.* showed differences in ascitic properties to be a prognostic factor, but our results showed that approximately half of both the survival group and the death group had fecal contamination, and there was no difference in the properties of the ascites during surgery. In addition, the POSSUM and MPI require evaluation during surgery and postoperatively. The spread of ascites on the preoperative CT, which was considered useful in the present study, can be evaluated before surgery. Additionally, the current study showed that prognosis was not affected by degree of contamination of the ascites but how far it has spread. The result could support the speculation that the spread of ascites indicates the severity of peritonitis, or the duration from the onset of perforation.

In contrast, with regard to intraoperative factors, the operation time was short in the death group, and the amount of blood transfusion was small. We tried to perform the surgery time as short as possible in a severe case, therefore this might influence the difference in the duration of the surgery. The transfusion volume was expected to increase in severe cases, but we targeted only the intraoperative blood transfusion volume in this study and considered the short operation time to have an influence on the volume transfused.

The limitations of this study are that it was undertaken at a single center, the number of cases was small, and the introduction of OAM was carried out for severe cases. In the future, we would like to increase the number of cases and participating institutions and undertake an additional investigation.

CONCLUSION

IN OUR HOSPITAL, the preoperative acute DIC score was found to be a prognostic factor for colon perforation

accompanied by pan-peritonitis. Appropriate evaluation of the spread of ascites on the preoperative CT might also help to predict patient prognosis.

DISCLOSURE

Approval of the research protocol: This study was approved by the institutional review board of Kansai Medical University (approval no. 2017209).

Informed consent: N/A.

Registry and the registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None declared.

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