

## Mortality risk factor analysis in colonic perforation: would retroperitoneal contamination increase mortality in colonic perforation?

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**Purpose:** Colonic perforation is a lethal condition presenting high morbidity and mortality in spite of urgent surgical treatment. This study investigated the surgical outcome of patients with colonic perforation associated with retroperitoneal contamination.

**Methods:** Retrospective analysis was performed for 30 patients diagnosed with colonic perforation caused by either inflammation or ischemia who underwent urgent surgical treatment in our facility from January 2005 to December 2014. Patient characteristics were analyzed to find risk factors correlated with increased postoperative mortality. Using the Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) audit system, the mortality and morbidity rates were estimated to verify the surgical outcomes. Patients with retroperitoneal contamination, defined by the presence of retroperitoneal air in the preoperative abdominopelvic CT, were compared to those without retroperitoneal contamination.

**Results:** Eight out of 30 patients (26.7%) with colonic perforation had died after urgent surgical treatment. Factors associated with mortality included age, American Society of Anesthesiologists (ASA) physical status classification, and the ischemic cause of colonic perforation. Three out of 6 patients (50%) who presented retroperitoneal contamination were deceased. Although the patients with retroperitoneal contamination did not show significant increase in the mortality rate, they showed significantly higher ASA physical status classification than those without retroperitoneal contamination. The mortality rate predicted from Portsmouth POSSUM was higher in the patients with retroperitoneal contamination.

**Conclusion:** Patients presenting colonic perforation along with retroperitoneal contamination demonstrated severe comorbidity. However, retroperitoneal contamination was not found to be correlated with the mortality rate.

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**Key Words:** Retroperitoneal space, Intestinal perforations, Postoperative complications, Sepsis, Mortality

### INTRODUCTION

Colonic perforation is a major cause of severe sepsis and septic shock in patients, requiring urgent surgical treatment. The prognosis of patients with colonic perforation appears to be determined by their septic status, regardless the cause of colonic perforation and the types of surgical treatment given

[1]. In spite of immediate surgical interventions and aggressive postoperative management following the evidence-based guidelines for severe sepsis and septic shock, postoperative sepsis-related mortality in the patients with colonic perforation is still exceedingly high [2-4].

Previously, several studies have attempted to identify risk factors of mortality in patients with colonic perforation, including

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the patient's age, presence of organ failure, and American Society of Anesthesiologists (ASA) physical status classification III or IV [1,5,6]. However, the degree of peritonitis, even fecal peritonitis, observed during the operation apparently does not influence the clinical prognosis [1,5]. Rather, it is the septic status that strongly determines the surgical outcome.

In an attempt to characterize the determinant value of septic status in patients with colonic perforation, the researchers hypothesized that patients with retroperitoneal contamination would have a higher mortality rate than those without retroperitoneal contamination. Because retroperitoneal contamination would influence septic status due to the abundant lymphatic channels in the retroperitoneum, it allows the septic focus to infiltrate systemic circulation easily. To the researchers' knowledge, not a single study investigating the relationship of retroperitoneal contamination to the mortality rate among patients with colonic perforation has been carried out. Therefore, this study compared the mortality rate among patients with colonic perforation along with retroperitoneal contamination to the rate among patients without retroperitoneal contamination. In addition, to verify the observed result of the mortality rate, the researchers applied the Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM) audit system [7].

## METHODS

Following approval by the Institutional Review Board of St. Vincent Hospital at the Catholic University of Korea (VC15RISI0196) with the waiver of informed consent, a retrospective review was performed for patients who were diagnosed with colonic perforation caused by either benign inflammation (specifically diverticulitis) or ischemia and underwent urgent surgical treatment from January 2005 to December 2014 in the institution. The patients with iatrogenic or traumatic colonic perforation or with colonic perforation due to malignancy were not included.

Patient characteristics were analyzed to find risk factors related to increased postoperative mortality. Analyzed factors included: age, sex, body mass index (BMI; kg/m<sup>2</sup>), ASA physical status classification, types of operative procedure performed, cause of colonic perforation, perforation site of colonic segment, colostomy formation, attempts at colostomy reversal, and 30-day mortality. The operation record was reviewed to assess the type of operative procedure, site of perforation, and colostomy formation. The degree of peritonitis, categorized either a diffuse or localized, was assessed from the operation record. To document the cause of colonic perforation, the pathology report was used.

An abdominopelvic CT scan of each patient was reviewed to identify the location of free air. Retroperitoneal contamination

was defined by the presence of air in the retromesenteric plane in the preoperative abdominopelvic CT scan [8]. Each patient was classified into 1 of 2 groups: one with retroperitoneal free air and another without retroperitoneal free air.

In order to estimate the mortality and morbidity risk of all subjects, the POSSUM audit system was applied, calculating the physiological and operative scores; mortality and morbidity rates were estimated to verify the surgical outcome. In fact, to improve the predicted values, Portsmouth POSSUM (P-POSSUM) as well as Colorectal POSSUM (Cr-POSSUM) scores were used to obtain predicted mortality rates.

The P-POSSUM scoring system uses 2 parameters: one is physiological, and the other is operative. The variables used to calculate the physiological score include age, systolic blood pressure (mmHg), pulse rate (beats/min), level of plasma hemoglobin (g/dL) and white blood cell count ( $\times 10^{12}/L$ ), and levels of plasma urea (mmol/L), sodium (mEq/L), and potassium (mEq/L). Symptoms and signs of cardiac failure as well as respiratory failure are considered as scoring variables. Chest X-ray results are also taken into consideration as a variable. Finally, electrocardiogram and Glasgow Coma Scale results were also considered in the analysis. The operative variables include the operation type identified by the level of predicament, number of procedures, amount of blood loss during the operation, level of peritoneal contamination, presence of malignancy, and timing of the operation. For each patient, P-POSSUM scores and mortality risk were calculated using the P-POSSUM calculator on the Risk Prediction in Surgery website [9].

The Cr-POSSUM scoring system is similar to the P-POSSUM in that it employs 2 parameters: physiological and operative. However, the variables are different; the physiological parameters include age, symptoms and signs of cardiac failure, systolic blood pressure (mmHg), pulse rate (beats/min), level of plasma hemoglobin (g/dL), and level of plasma urea (mmol/L). The operative parameters include the operation type, level of peritoneal contamination, status of malignancy, and timing of the operation. The Cr-POSSUM calculator on the Risk Prediction in Surgery website was also used to calculate the Cr-POSSUM scores and mortality risk [9].

Risk factor analysis was performed via comparing the patients who died within 30 days with those who survived. Furthermore, investigating the impact of the retroperitoneal contamination to the mortality, the patients with retroperitoneal contamination were compared to those without retroperitoneal contamination.

Statistical analysis was performed by using SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were compared using the Pearson chi-square test or Fisher exact test, and continuous variables were compared using the Student t-test. A one-way analysis of variance test was performed to compare the variables in 2 groups: the patient group with 30-day mortality

versus patients without 30-day mortality, as well as the patient group with retroperitoneal contamination versus patients without retroperitoneal contamination.

## RESULTS

A total of 30 patients were diagnosed with colonic perforation due to acute inflammation, such as diverticulitis or ischemia, and underwent urgent surgical treatment. Eight out of 30 patients (26.7%) with colonic perforation had died within 30 days. Two patients were diagnosed with cecal perforation due to ischemic colitis, and 2 other patients presented sigmoid colon perforation caused by ischemia as well. The remaining four patients exhibited sigmoid colon perforation due to diverticular perforation. Three out of 8 patients showed sigmoid colon perforation with retroperitoneal contamination. The reason for colonic perforation for them was ischemic colitis. The mortality risk factor analysis, shown in Table 1, indicated that the deceased patients were older, suffered from underlying comorbidities, and were more likely to develop colonic perforation due to ischemia. The average age of the deceased patients was  $80.4 \pm 6.8$ , whereas the age of the survivors was  $71.0 \pm 12.1$  ( $P = 0.049$ ). Also, the deceased patients belonged to a higher ASA physical status classification than the survivors. Seven out of 8 deceased patients were classified in ASA physical status classification III or IV. In contrast, 15 patients out of 22 survivors were in classification I or II ( $P = 0.012$ ). Moreover, the patients with colonic perforation due to ischemia showed a higher risk of mortality rate than those whose perforation was caused by acute diverticular perforation. However, sex, BMI, perforation site in the colonic segment, degree of fecal peritonitis, and type of operative procedure did not show any correlation with mortality. Mortality seen in the patients with retroperitoneal contamination itself was higher than the patients without the retroperitoneal contamination, although this correlation did not demonstrate statistical significance (62.5% vs. 37.5%,  $P = 0.3$ ) (Table 2). Calculating the P-POSSUM and Cr-POSSUM scores, P-POSSUM physiological scores as well as operative scores were significantly higher in the deceased than in the survivors. The predicted mortality values from the P-POSSUM and Cr-POSSUM were also significantly higher in the deceased.

Comparing the patients with retroperitoneal contamination to those without retroperitoneal contamination, demonstrated in Table 2, the mortality rate was not significantly different. Other factors, such as age, BMI, and sex, were not different in two groups. Furthermore, the 2 groups did not demonstrate statistically significant differences in terms of perforation site, degree of fecal peritonitis, cause of colon perforation, type of operative procedure, and colostomy reversal rate. Interestingly, the colonic perforation site only occurred in the left side of the colon. Patients with retroperitoneal contamination showed

**Table 1.** Univariate analysis for the mortality

Variable	Mortality (-) (n = 22)	Mortality (+) (n = 8)	P-value
Age (yr)	71.0 ± 12.1	80.4 ± 6.8	0.049
Body mass index (kg/m <sup>2</sup> )	23.5 ± 3.1	23.4 ± 6.1	0.943
Sex			>0.999
Male	6 (75.0)	2 (25.0)	
Female	16 (72.7)	6 (27.3)	
ASA PS classification			0.012
I/II	15 (93.8)	1 (6.3)	
III/IV	7 (50.0)	7 (50.0)	
Perforation site of colonic segment			0.645
Right	4 (66.7)	2 (33.3)	
Left	18 (75.0)	6 (25.0)	
Degree of fecal peritonitis			0.210
Localized	15 (83.3)	3 (16.7)	
Diffuse	7 (58.3)	5 (41.7)	
Retroperitoneal contamination			0.300
(-)	19 (79.2)	5 (20.8)	
(+)	3 (50.0)	3 (50.0)	
Cause of colon perforation			0.003
Inflammation	22 (84.6)	4 (15.4)	
Ischemia	0 (0)	4 (100)	
Operative procedure			0.721
Hartmann's operation	15 (68.2)	7 (31.8)	
Resection and anastomosis	5 (83.3)	1 (16.7)	
Loop colostomy	1 (100)	0 (0)	
Primary repair	1 (100)	0 (0)	
P-POSSUM			
Physiological score	31.9 ± 7.1	39.5 ± 5.6	0.011
Operative score	21.3 ± 2.0	24.6 ± 2.2	0.001
Morbidity (%)	90.4 ± 18.3	99.1 ± 0.7	0.192
Mortality (%)	45 ± 25.3	77.3 ± 14.5	0.002
Cr-POSSUM			
Physiological score	12.2 ± 2.9	14.4 ± 2.2	0.064
Operative score	15.5 ± 0.6	15.9 ± 0.4	0.154
Mortality (%)	43.7 ± 21.0	62.5 ± 15.6	0.029

Values are presented as mean ± standard deviation or number (%). ASA PS, American Society of Anesthesiologists physical status; POSSUM, Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity; P-POSSUM, portsmouth POSSUM (P-POSSUM); Cr-POSSUM, colorectal POSSUM.

significantly higher ASA physical status classification than those without retroperitoneal contamination. Six out of 7 patients presenting with retroperitoneal contamination belonged to ASA physical status classification III or IV, whereas 15 out of 24 patients without retroperitoneal contamination were grouped in classification I or II. Calculating the P-POSSUM and Cr-POSSUM scores, P-POSSUM physiological and operative scores were higher in the patients with retroperitoneal contamination. The predicted mortality value from P-POSSUM only, not Cr-POSSUM, was significantly higher in the patients with retroperitoneal contamination.

**Table 2.** Univariate analysis for retroperitoneal contamination

Variable	Retroperitoneum (-)	Retroperitoneum (+)	P-value
Age (yr)	72.4 ± 12.6	78.3 ± 3.6	0.273
Body mass index (kg/m <sup>2</sup> )	23.0 ± 3.9	21.9 ± 4.2	0.285
Sex			>0.999
Male	7 (87.5)	1 (12.5)	
Female	17 (77.3)	5 (22.7)	
ASA PS classification			0.044
I/II	15 (93.8)	1 (6.3)	
III/IV	9 (64.3)	5 (35.7)	
Perforation site of colonic segment			0.645
Right	6 (100)	0 (0)	
Left	18 (75.0)	6 (25.0)	
Degree of fecal peritonitis			0.660
Localized	15 (83.3)	3 (16.7)	
Diffuse	9 (75.0)	3 (25.0)	
Mortality			0.300
(-)	19 (86.4)	3 (13.6)	
(+)	5 (62.5)	3 (37.5)	
Cause of colon perforation			0.169
Inflammation	22 (84.6)	4 (15.4)	
Ischemia	2 (50.0)	2 (50.0)	
Operative procedure			0.436
Hartmann's operation	16 (72.7)	6 (27.3)	
Resection and anastomosis	6 (100)	0 (0)	
Loop colostomy	1 (100)	0 (0)	
Primary repair	1 (100)	0 (0)	
Colostomy reversal			0.633
(-)	9 (90.0)	1 (10.0)	
(+)	15 (78.0)	5 (25.0)	
P-POSSUM			
Physiological score	32.5 ± 7.4	39.3 ± 5.6	0.045
Operative score	21.7 ± 2.0	24.3 ± 3.2	0.016
Morbidity (%)	91.2 ± 17.6	99.1 ± 0.6	0.288
Mortality (%)	48.2 ± 26.9	75.3 ± 13.1	0.025
Cr-POSSUM			
Physiological score	12.5 ± 2.9	13.8 ± 2.8	0.320
Operative score	15.5 ± 0.59	16.0 ± 0.0	0.070
Mortality (%)	46.4 ± 21.6	58.3 ± 18.1	0.225

Values are presented as mean ± standard deviation or number (%). ASA PS, American Society of Anesthesiologists physical status; POSSUM, Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity; P-POSSUM, portsmouth POSSUM (P-POSSUM); Cr-POSSUM, colorectal POSSUM.

## DISCUSSION

In a vigorous effort to manage severe sepsis and septic shock by means of various research studies, the overall mortality rate for sepsis has been falling over the last few decades [10-14]. However, considering the site of infection as an independent prognostic factor in sepsis, intra-abdominal contamination is recognized as a predominant cause of mortality in surgical intensive care units [12]. Unfortunately, the prognosis for sepsis

still remains dreadful, yielding mortality rates as high as 60% [2,3,15]. Intestinal perforation, especially colonic perforation, is a common cause of intra-abdominal contamination. In patients suffering from sepsis caused by intra-abdominal contamination due to colonic perforation, age and comorbidity are consistently reported as the major factors correlated with increased mortality rate [1,16,17]. In this study, the result was consistent with previous findings.

Moreover, the study result has indicated that the ischemic cause of colonic perforation is a factor that significantly increases mortality. A comparable result was shown in examining the prognostic factors for patients with left colonic peritonitis; ischemic colitis was found to increase septic-related mortality [18]. It is not unexpected to learn that elderly individuals with high ASA physical status classification are vulnerable to ischemic insult perioperatively. Many retrospective and prospective studies on sepsis have demonstrated that early intervention to restore global tissue perfusion along with simultaneous control of septic focus is the key to the survival; thus, the current guidelines and protocols for managing severe sepsis and septic shock suggest various approaches to reestablish appropriate tissue perfusion [10,11,19]. However, shown in the result, in which all three deceased patients with retroperitoneal contamination presented ischemia for the cause of colonic perforation, the elderly individuals with high ASA physical status classification may exhibit impaired or decreased capacity for tissue perfusion. Therefore, they may not respond to optimal management, resulting in death.

Contemplating the correlation between retroperitoneal contamination and mortality for patients with colonic perforation, the researchers anticipated that, since the retroperitoneal space does not have a physiological barrier, exposing an abundant amount of lymphatic channel, the retroperitoneal contamination by feces would provoke rapid progression of septic status [20]. In this study, three out of six patients with retroperitoneal contamination died, a 50% mortality rate, although this figure is lacking statistical significance. The sample size may not have been large enough to demonstrate statistical significance. As a matter of fact, collecting and analyzing data for a longer period of time and at multiple hospitals is necessary.

Considering age and comorbidity are the major factors determining postoperative prognosis in colonic perforation, the P-POSSUM and Cr-POSSUM audit systems incorporate those 2 factors as the determinant variables for predicted values. The predicted values from both the P- and Cr-POSSUM audit systems indicated higher mortality rate in the deceased patients in this study, consistently shown in the results. In patients with retroperitoneal contamination, the predicted mortality risk from the P-POSSUM score was statistically significant. Although the observed cases in this study failed to show statistical significance, it is imprudent to neglect the significance of the pre-

dicted mortality risk.

In this study, colonic perforation from trauma or medical mishap, colonoscopy especially, was excluded due to the different nature of disease progression. Diagnosis of iatrogenic colonic perforation can be made by direct visualization of intraperitoneal fat by an endoscopist during the procedure. It can also be made based on suspicion regarding the development of symptoms and signs of patient following a diagnostic or therapeutic colonoscopy. Regardless of how the diagnosis is made, vigilant surveillance and immediate management are usually given to a patient suspected of having colonic perforation under such circumstances. Also, bowel preparation before colonoscopy reduces the degree of intraperitoneal and retroperitoneal contamination. Thus, patients presenting colonic perforation caused by iatrogenicity are apt to receive immediate treatment with a diminished amount of contaminant, which is different from patients with colonic perforation caused by ordinary inflammation or ischemia. Several studies on mortality due to colonoscopic perforation have demonstrated nearly 1/6 to 1/2 of the mortality rate compared to colonic perforation in general, reporting 10%–25.6% of mortality rate after surgery [21,22]. Further study on patients demonstrating retroperitoneal contamination after colonoscopy, either diagnostic or therapeutic, may help clarify the effect of retro-

peritoneal contamination.

Limitation in this study sprouts from the retrospective nature. Selection bias is a great concern, regarding the patient group presenting colonic perforation only with ischemia and inflammatory causes. In the future study, it is necessary to investigate the mortality rate in patients with retroperitoneal contamination by biliary or gastric spillage, or even cancer perforation. A small sample size is another obstacle in verifying the validity of this study. Over a decade, only six patients with colonic perforation were identified with retroperitoneal contamination, reflecting its scarcity. A larger sample gathered from multiple centers may help to address this issue.

In conclusion, the patients presenting with colonic perforation along with retroperitoneal contamination tended to be older and suffering from underlying comorbidity. However, in contrast to this study's hypothesis, retroperitoneal contamination did not demonstrate significant correlation with mortality rate. The POSSUM audit system is a valuable method of predicting mortality rate in patients with colonic perforation.

## CONFLICTS OF INTEREST

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

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