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ORIGINAL ARTICLE

Diagnostic effectiveness of preoperative water-soluble contrast enema in colorectal perforation

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Colorectal perforation;
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Summary *Objective:* To evaluate the diagnostic usefulness of performing a preoperative water-soluble contrast enema (WSCE) before emergency surgery for colorectal perforation.
Methods: We retrospectively reviewed 68 consecutive patients who underwent a preoperative WSCE before emergency surgery for colorectal perforation during the period from January 2011 to December 2017. Clinical characteristics and inflammatory biomarkers were compared between patients with Hinchey I–II versus those with Hinchey III–IV.
Results: WSCE leakage occurred in 27 of 68 patients (39.7%). Univariate analysis showed that the two groups (Hinchey I–II and Hinchey III–IV) significantly differed regarding age, perforation site, cause of perforation, American Society of Anesthesiologists grade, presence or absence of WSCE leakage, and white blood cell count. Multivariable analysis revealed that WSCE leakage was a predictor of Hinchey III–IV, with an odds ratio of greater than 24 ($P = 0.002$). The sensitivity and specificity of WSCE leakage for differentiating those with Hinchey III–IV from those with Hinchey I–II were 76.5% and 97.1%, respectively.
Conclusions: This retrospective study indicates that preoperative WSCE before emergency surgery is a useful tool for predicting the presence of Hinchey III–IV in patients with colorectal perforation.
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1. Introduction

Colorectal perforation is a common cause of acute abdomen that may require emergency surgery. The major causes of colorectal perforation are diverticulitis and malignant neoplasm, followed by spontaneous stercoral perforation, trauma, ischemia, distant inflammatory lesions, and iatrogenic injury.[1]

Computed tomography (CT) is the main imaging method for diagnosing colorectal perforation. CT can determine the site and cause of perforation with an accuracy of 86%.[2] However, CT does not have a high degree of accuracy in predicting the severity of colorectal perforation, such as the Hinchey classification.[3]

Water-soluble contrast enema (WSCE) is an effective radiological procedure for identifying colorectal perforation, especially anastomotic leakage prior to restoration of a diverting stoma.[4,5] However, there has been no report about the usefulness of WSCE for assessing colorectal perforation before emergency surgery. Our hypothesis was that the additional information obtained via WSCE would improve the preoperative diagnosis of colorectal perforation. The present study aimed to evaluate the usefulness of preoperative WSCE before emergency surgery for colorectal perforation.

2. Methods

2.1. Study design and setting

The present single-center, retrospective, case-control study was performed in Minoh City Hospital in Japan. The study was performed in compliance with the Helsinki Declaration, and was approved by the Ethics Committee of Minoh City Hospital (approval no. H29-B35).

2.2. Patients

From January 2011 to December 2017, a total of 68 consecutive patients had a preoperative WSCE performed within 24 h before emergency surgery for colorectal perforation. The preoperative diagnosis of colorectal perforation requiring surgical treatment was based on CT findings combined with physical findings in 64 cases, and based on WSCE findings combined with physical findings in four cases. Perforation was definitively diagnosed in all 68 patients via pathological findings as determined by a pathologist postoperatively or via macroscopically apparent perforation (exploratory laparotomy was performed in one case). All blood tests were performed within 24 h before emergency surgery. The white blood cell (WBC) count, C-reactive protein (CRP) concentration, WBC-to-neutrophil ratio (WNR), and WBC-to-lymphocyte ratio (WLR) were measured as inflammatory biomarkers.

2.3. Enema procedure

The enema procedure was performed by an experienced radiologist or an experienced colorectal surgeon under fluoroscopic guidance. WSCE was performed using a Y-tube double-balloon rectal catheter (Create Medic, Yokohama, Japan) per anum with inflation of both balloons in 66 non-anastomotic leakage cases, and was performed using a 14 or 16 Fr Nelaton tube without a balloon (Terumo, Tokyo, Japan) per anum in two anastomotic leakage cases.[6] The catheter was slowly inserted and used to introduce a sufficient amount of water-soluble contrast medium (Gastrografin; Bayer AG, Berlin, Germany).

2.4. Surgery and postoperative clinical outcomes

All surgical procedures were performed or supervised by experienced colorectal surgeons. All of these surgeons were members of the Japanese Society of Coloproctology and the Japanese Society of Gastroenterological Surgery. All of the procedures were performed via open surgery. The severity of intra-abdominal pathology was intraoperatively graded using the Hinchey classification.[7] Postoperative complications were graded using the Clavien-Dindo classification.[8] Medical records were reviewed, and clinical data were retrospectively obtained.

2.5. Statistical analysis

Statistical analyses were performed using JMP Pro 11 software (SAS Institute, Cary, NC, USA). In the univariate analysis, categorical variables were compared using Fisher's test. Continuous data are reported as the average $\pm$ standard error. Comparisons of continuous variables were done using the Wilcoxon rank test. Statistical significance was defined as $P < 0.05$. Variables with a P value of <0.05 in the univariate analysis were entered into the multivariate analysis with logistic regression.

3. Results

3.1. Patient characteristics

The patients' characteristics are shown in Table 1. Of the 68 patients, 27 had WSCE leakage, while 41 did not have WSCE leakage. The rate of WSCE leakage-positivity was significantly higher in females ($P = 0.013$), older patients ($P = 0.002$), patients with perforation of the sigmoid colon and rectum ($P = 0.008$), patients with a higher American Society of Anesthesiologists (ASA) grade ($P < 0.001$), patients with Hinchey III–IV ($P < 0.001$), and patients with non-diverticulitis or primary colorectal cancer ($P = 0.002$). Regarding the biomarkers, patients with WSCE leakage had a significantly greater WLR ($P = 0.044$) and a significantly lower WBC count ($P = 0.002$) than those without WSCE leakage (Table 1).

3.2. Surgical and postoperative clinical outcomes

The surgical and postoperative clinical outcomes are shown in Table 2. Compared with WSCE leakage-negative patients, WSCE leakage-positive patients had more blood loss ($P = 0.002$), longer operation time ($P = 0.003$), and longer postoperative hospital stay ($P < 0.001$). Stoma creation was performed significantly more frequently in WSCE

Table 1 Characteristics of patients with and without WSCE leakage.

	WSCE (+) (n = 27)	WSCE (−) (n = 41)	P value
Sex			
Male	7	24	0.013
Female	20	17	
Age (y)			
18−39	0	4	0.002
40−59	6	24	
60−79	13	8	
80+	8	5	
Site of perforation			
Right-sided colon	0	8	0.008
Transverse colon	1	5	
Descending colon	1	5	
Sigmoid colon and rectum	25	23	
Cause of perforation			
Diverticulitis	13	35	0.002
Primary colorectal cancer	2	2	
Others (constipation, iatrogenic, etc.)	12	4	
ASA			
1	2	10	<0.001
2	4	24	
3	18	7	
4	3	0	
Hinchey classification			
I−II	1	33	<0.001
III−IV	26	8	
WBC count (/μl)			
0−9000	15	7	0.002
9001−13000	3	16	
13000+	9	18	
WLR			
0−10	12	19	0.044
10−20	4	15	
20+	11	7	
WNR			
1.0−1.1	9	6	0.34
1.1−1.2	9	17	
1.2−1.3	6	10	
1.3−1.4	3	8	
NLR			
−5	3	7	0.80
5−10	11	17	
10+	13	17	
CRP levels (mg/dl)			
0−9.99	10	17	0.48
10−19.99	7	15	
20−29.99	8	6	
30+	2	3	

WSCE, water soluble contrast enema; ASA, American Society of Anesthesiologists; WBC, white blood cell; WLR, white blood cell-to-lymphocyte ratio; WNR, white blood cell-to-neutrophil ratio; NLR, neutrophil-to-lymphocyte ratio; CRP, C-reactive protein.

leakage-positive patients than in WSCE leakage-negative patients (P = 0.022). Although there was no significant association between WSCE leakage and the incidence of postoperative complications, those with WSCE leakage tended to have a higher rate of postoperative complications than those without WSCE leakage (P = 0.073).

3.3. Predictive markers for Hinchey I−II and Hinchey III−IV as determined by univariate analysis

The univariate associations between Hinchey classification and clinical and inflammatory markers are shown in Table 3. Of the 68 patients, 34 had Hinchey I−II, while 34 had Hinchey III−IV. The incidence of Hinchey III−IV was significantly higher in older patients (P = 0.003), WSCE leakage-positive patients (P < 0.001), patients with perforation of the sigmoid colon and rectum (P = 0.011), patients with higher ASA grades (P < 0.001), and patients with non-diverticulitis or primary colorectal cancer (P < 0.001). Regarding the biomarkers, patients with Hinchey III−IV had a significantly lower WBC count than those with Hinchey I−II (P < 0.001; Table 3).

3.4. Predictive markers for Hinchey I−II and Hinchey III−IV as determined by multivariate analysis

Multivariate logistic regression analysis was performed using the following variables: age, location of the perforation, reason for the perforation, ASA grade, WSCE leakage, and WBC count (Table 4). WSCE leakage was the only independent significant predictive marker of Hinchey III−IV (P = 0.002); the adjusted association was strong, with an odds ratio of greater than 24 (Table 4).

3.5. Diagnostic performance of WSCE for differentiating patients with Hinchey III−IV from those with Hinchey I−II

The diagnostic performance of WSCE for differentiating patients with Hinchey III−IV from those with Hinchey I−II is shown in Table 5. The sensitivity, specificity, positive predictive value, and negative predictive value were 76.5%, 97.1%, 96.3%, and 80.4%, respectively.

4. Discussion

In colorectal perforation, it is desirable to precisely predict the intra-abdominal pathology preoperatively. However, it is sometimes difficult to definitively and precisely diagnose colorectal perforation preoperatively. The present study evaluated whether preoperative WSCE could provide additional information for diagnosing colorectal perforation before emergency surgery. There was a low incidence of WSCE leakage in patients with colorectal perforation (39.7%, 27/68); thus, WSCE was not useful as an indicator of the presence of colorectal perforation. However, WSCE leakage was significantly associated with worse surgical and postoperative clinical outcomes. Furthermore, there was a significant association between WSCE leakage and the severity of intra-abdominal pathology as assessed via the Hinchey classification, which suggests that the worse surgical and postoperative clinical outcomes of WSCE leakage-

Table 2 Surgical and postoperative clinical outcomes in patients with and without WSCE leakage.

	WSCE (+) (n = 27)	WSCE (−) (n = 41)	P value
Operation time (min; average ± SE)	239.67 ± 14.35	188.49 ± 11.64	0.003
Blood loss (ml; average ± SE)	675.88 ± 98.01	316.85 ± 75.92	0.002
Postoperative hospital stay (days; average ± SE)	40.04 ± 4.17	12.19 ± 3.38	<0.001
Stoma creation			
Present	11	6	0.022
Absent	16	35	
Complocations (Clavien-Dindo classification)			
II	8	0	0.073
IIIa	4	2	
IIIb	1	0	
IVa	2	0	
IVb	1	0	
V	1	1	

WSCE, water soluble contrast enema; SE, standard error.

positive patients were due to the worse intra-abdominal pathology present in those with WSCE leakage compared with those without WSCE leakage.

In 1978, Hinchey et al published their classification for acute diverticulitis.[7] Traditionally Hinchey classification is a classification for diverticulitis.[7] However, this classification is also used for colorectal perforation due to other causes.[9–11] The Hinchey classification has been used internationally to distinguish four stages of perforated disease: grade I (localized debris or pus), grade II (abdominal or pelvic abscess), grade III (purulent peritonitis), and grade IV (fecal peritonitis).[9–11] We divided the present patients into two groups: those with Hinchey I–II (without diffuse peritonitis) and those with Hinchey III–IV (with diffuse peritonitis). While the risk of death is less than 5% for most patients with Hinchey I–II, this risk is approximately 13% for those with Hinchey III, and 43% for those with Hinchey IV.[12] The therapeutic strategy varies in accordance with the Hinchey grade.[12] Surgical intervention is needed for patients with Hinchey III–IV, while it is not necessarily needed for those with Hinchey I–II.[12] Hence, we consider it clinically important to differentiate between Hinchey III–IV and Hinchey I–II.

CT is the main imaging method used for diagnosing colorectal perforation. In fact, in all of our cases, perforation was suspected based on CT findings before WSCE. However, CT does not have a high accuracy in predicting the severity of colorectal perforation (the Hinchey grade), and there is a tendency to underestimate the Hinchey grade when the severity is assessed using CT.[3] In addition, CT is not always interpreted by experienced radiologists before emergency surgery, especially during the night shift.[3]

Biomarkers are reportedly useful for predicting the severity of colorectal perforation. Inflammatory markers such as the CRP concentration and the WLR are widely used, and are useful in assessing the severity of acute diverticulitis, and in distinguishing between uncomplicated and complicated diverticulitis.[13] As expected, the WBC count was the most useful of the inflammatory markers; however, unexpectedly, the CRP concentration was not useful. In general, the CRP concentration is the most widely used objective indicator of disease activity in peritonitis.[14] The concentration of CRP, a plasma protein, rises dramatically as a result of cytokine-mediated responses to most forms of infection, inflammation, and tissue injury.[15] This rise in CRP concentration may be delayed, and the serum CRP concentration might actually peak 24–36 h after perforation occurs.[16] CRP concentration can be used as an indicator of the presence of complications in cases of acute diverticulitis,[17] although a low CRP concentration does not definitively exclude complicated diverticulitis.[18,19] In our study, CRP concentration had low diagnostic power to differentiate between Hinchey III–IV and Hinchey I–II.

Multivariate analysis showed that WSCE leakage was the only variable that was a strong predictor of whether each patient had Hinchey III–IV versus Hinchey I–II. We hypothesize that inflammatory biomarkers rise in patients with Hinchey I–II, and that at the time of emergency surgery after perforation, the duration of inflammation varies and so there is a wide range in the concentrations of inflammatory biomarkers. WSCE leakage had a high negative predictive value and sensitivity, and a high positive predictive value and specificity. Only one patient with Hinchey I–II was WSCE leakage-positive, while 97% (33/34) were WSCE leakage-negative. We speculate that WSCE did not extravasate outside of the bowel because of the high internal pressure of abscesses in patients with Hinchey I–II. We also consider that WSCE was only able to detect perforation resulting from Hinchey III–IV, but was not able to detect small perforations, such as pinhole perforation. In patients with Hinchey III–IV, false negative results of WSCE leakage were observed in patients whose perforated site was packed by organs, such as the small intestine and bladder.

There are some limitations to the present study. First, this was a small, retrospective, non-randomized study, and the results may have been affected by its retrospective design. However, to reduce possible biases, we investigated all consecutive patients who underwent emergency surgery and preoperative WSCE for pathologically confirmed colorectal perforation. Furthermore, the Hinchey classification of our study population was similar to a previous report.[3] Second, although unlikely, it is

Table 3 Univariate analysis of the characteristics of patients with Hinchey I–II versus those with Hinchey III–IV.

	Hinchey III–IV (n = 34)	Hinchey I–II (n = 34)	P value
Sex			
Male	11	20	0.051
Female	23	14	
Age (y)			
18–39	1	3	0.003
40–59	9	21	
60–79	13	8	
80+	11	2	
Site of perforation			
Right-sided colon	1	7	0.011
Transverse colon	1	5	
Descending colon	2	4	
Sigmoid colon and rectum	30	18	
Cause of perforation			
Diverticulitis	17	31	<0.001
Primary colorectal cancer	3	1	
Others (constipation, iatrogenic)	14	2	
ASA			
1	2	10	<0.001
2	9	19	
3	20	5	
4	3	0	
WSCE leakage			
Positive	26	1	<0.001
Negative	8	33	
WBC count (/μl)			
0–9000	18	4	<0.001
9001–13000	4	15	
13000+	12	15	
WLR			
0–10	16	15	0.12
10–20	6	13	
20+	12	6	
WNR			
1.0–1.1	12	3	0.054
1.1–1.2	10	16	
1.2–1.3	8	8	
1.3–1.4	4	7	
NLR			
−5	4	6	0.85
5–10	14	14	
10+	16	14	
CRP levels (mg/dl)			
0–9.99	12	15	0.66
10–19.99	10	12	
20–29.99	9	5	
30+	3	2	

ASA, American Society of Anesthesiologists; WSCE, water soluble contrast enema; WBC, white blood cell; WLR, white blood cell-to-lymphocyte ratio; WNR, white blood cell-to-neutrophil ratio; NLR, neutrophil-to-lymphocyte ratio; CRP, C-reactive protein.

possible that WSCE might have increased the luminal pressure and therefore widened the perforating hole. Although we consider it unlikely that a WSCE performed just before surgery could have caused the intraabdominal findings, the WSCE might have acted as a kind of burst pressure test. Third, WSCE might have detected both actual Hinchey III–IV and potential Hinchey III–IV in the present study. However, this problem is present in all

Table 4 Multivariate model evaluating the risk factors for Hinchey III–IV.

Predictor	Odds ratio	95% Confidence interval	P value
Age >80 y	3.893	0.4655–41.228	0.21
Location of perforation: left-sided colon and rectum	3.094	0.4165–35.001	0.28
Reasons of perforation: Non-diverticulitis	5.131	0.6536–50.239	0.12
ASA 3–4	3.721	0.4719–28.628	0.20
WSCE leakage-positive	24.267	2.9018–548.853	0.002
WBC count (/μl) < 9000	4.654	0.5912–42.2541	0.14

ASA, American Society of Anesthesiologists; WSCE, water soluble contrast enema; WBC, white blood cell.

Table 5 Diagnostic performance of WSCE for the differentiation of Hinchey III–IV from Hinchey I–II.

	Sensitivity, %	Specificity, %	PPV, %	NPV, %
WSCE	76.5	97.1	96.3	80.4

WSCE, water soluble contrast enema; PPV, positive predictive value; NPV, negative predictive value.

enema studies. Fourth, we excluded patients who did not undergo laparotomy. However, some patients avoided laparotomy because the WSCE excluded the diagnosis of perforation. In fact, there were some cases in which perforation was suspected based on CT findings, but was denied based on negative WSCE findings, resulting in the avoidance of laparotomy. In particular, WSCE was useful for the diagnosis of perforation in patients who had undergone gynecologic and urologic surgery, for whom the interpretation of intraabdominal air and abdominal pain is difficult. Lastly, we performed laparotomy in patients with Hinchey I–II, which can potentially be treated without laparotomy. However, this enabled the definitive confirmation of intra-abdominal pathology, which could not otherwise have been definitively diagnosed. Our results might be helpful in developing future treatment strategies.

In conclusion, this retrospective study indicates that preoperative WSCE does not provide additional information about the presence of colorectal perforation before emergency surgery. However, preoperative WSCE is a useful tool for predicting the severity of colorectal perforation, which is associated with surgical and postoperative clinical outcomes. These findings might provide useful information for the selection of therapeutic strategies. However, a direct association between therapeutic strategies and WSCE findings still needs to be elucidated. Our results should be confirmed by a larger prospective study.

Declarations of interest

None.

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