Organ/space infection is a common cause of high output stoma and outlet obstruction

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Abstract

Aim: The objectives of this study are to identify causes of high-output stoma (HOS) and outlet obstruction (OO), which are major complications of diverting ileostomy.

Methods: A retrospective analysis was performed in 103 patients who underwent colorectal surgery and diverting ileostomy between December 2015 and November 2018.

Results: HOS was found in 32 patients (31.1%) and OO in 19 (18.4%). Organ/space surgical site infection (SSI), anastomotic leakage and OO were independent HOS-related factors in univariate analysis, and OO (odds ratio [OR] 3.82, p=0.022) was a independent HOS-related factor in multivariate analysis. Organ/space SSI and HOS were independent OO-related factors in univariate analysis, and organ/space SSI (OR 3.69, p=0.02) was a independent OO-related factor in multivariate analysis. The white blood cell (WBC) count on postoperative day (POD) 3 was significantly higher in the HOS group compared to the non-HOS group (9765 vs. 8130 /mL, p<0.05), and the WBC count (9400 vs. 7475 /mL, p<0.05) and C-reactive protein level (6.01 vs. 2.92 mg/L, p<0.05) on POD 6 were significantly higher in the OO group compared to the non OO group.

Conclusion: Organ/space infection is involved in the common pathology of HOS and OO. Decreased intestinal absorption due to intestinal edema caused by organ/space SSI and relative stenosis at the abdominal wall-penetrating site are major causes of HOS and OO

Background

Diverting ileostomy reduces the risk of anastomotic leakage (AL) after surgery for rectal cancer, and use of diverting stoma (DS) has increased [1-3]. However, complications of ileostomy-related high output stoma (HOS) and outlet obstruction (OO) have incidences of 16-23%[4, 5] and 5.6-25.8% [4, 5], respectively. HOS cause dehydration, electrolyte imbalance and renal dysfunction, resulting in a significant decrease of QOL. Most studies
of HOS have described detection or management, but few have examined the pathology of HOS. Causes of HOS include diabetes, total proctocolectomy, intraabdominal abscess, paralytic ileus, AL and OO, but no clear pathology has been shown [6–11]. OO is defined as intestinal obstruction in an abdominal wall-penetrating site, but differs from general intestinal obstruction because symptoms are relieved by tube insertion from the stoma. Causes of OO include total proctocolectomy and the thickness of the rectus abdominis muscle, but as for HOS, the pathology remains to be elucidated [12–14]. Furthermore, no study has examined HOS and OO simultaneously and the relationship between HOS and OO is unknown. Therefore, this study was performed as a retrospective examination of patients with DS to determine the pathology and relationship of HOS and OO, and to identify related factors.

Methods

The subjects were 103 consecutive patients who underwent colorectal surgery and DS between December 2015 and November 2018. The study was performed as a retrospective analysis. The indications for DS creation were intersphincteric resection (ISR), preoperative therapy, or male patients with anastomosis just above anal canal after total mesorectal excision. Patients who underwent total proctocolectomy or emergency surgery were often considered for DS creation. The DS site was 40 cm distant from the terminal ileum in the right lower abdomen to penetrate the abdominal wall in the direction to allow lifting of the wall naturally. The aponeurosis of the rectus abdominis muscle was longitudinally incised with a two-finger width. A standardized technique was used to create the loop stoma.

Patient characteristics of age, sex, disease, body mass index (BMI), diabetes, smoking history, preoperative blood albumin (Alb), preoperative estimated glomerular filtration rate (eGFR) and thickness of the rectus abdominis muscle were examined. The thickness
of the rectus abdominis muscle was measured using a slice at the umbilical level on CT recorded immediately before surgery. A straight line was drawn orthogonally to the horizontal axis at the maximal thickness, and the thickness of the rectus abdominis muscle was determined [13]. Surgical factors, such as operative procedure, approach, lateral lymph node dissection (LLND), operative time, blood loss volume, transfusion, intraoperative fluid, anastomotic procedure were also examined. The preoperative conditions including perforation, stenosis and preoperative chemotherapy were also examined.

Postoperative complications were analyzed using the Clavien-Dindo classification. AL was defined as clinical symptoms such as fever, abdominal pain and peritoneal irritation, and based on pus-like or stool-like output draining from the pelvic floor, anastomotic dehiscence found in a digital rectal examination, extravasation of endoluminally administered water-soluble contrast enema, and fluid or gas retention surrounding the anastomotic site detected by CT. Organ/space surgical site infection (SSI) was defined as antibiotic therapy for fever, abdominal pain and peritoneal irritation without marked findings of AL.

HOS was defined as two-days continuous output of >1500 mL per day [15]. OO was defined as symptoms of intestinal obstruction, imaging of caliber changes in the abdominal wall-penetrating site in ileostomy by CT, and a condition that was improved by tube retention in the oral stoma [14, 16]. These symptoms and signs were used to confirm the diagnosis of OO. Associations of clinical factors with HOS and OO were examined by Fisher chi-square test and Mann-Whitney U test. Factors with a significant difference (p<0.05) were then evaluated by multivariate analysis. All statistical analyses were conducted using EZR [17].

Results
Background of subjects

The median age of the 103 patients was 66 years-old and the median BMI was 22.9 (16.9–38.9) kg/m². Eighty two (80%) patients were male, 16 (15.5%) patients had diabetes, 26 (25.2%) were smokers, and 6 (5.8%) were being treated with steroids. Preoperatively, the Alb level was 4.2 (2.4–5.0) g/dL, eGFR was 74.9 (20.1–135.2) mL/min/1.73 m², and the thickness of the rectus abdominis muscle was 10.25 (5.46–19.14) mm. The underlying diseases were malignant tumor in 84 (81.2%) patients, inflammatory bowel disease in 17 (16.5%), and perforation of colon in 2 (1.9%).

Surgical procedures were low anterior resection in 52 (50.5%) patients, intersphincteric resection in 31 (30.1%), total proctocolectomy in 17 (16.5%), and high anterior resection, sigmoidectomy and ileocecal resection in one subject each. Anastomotic procedures were a double stapling technique in 57 (55.3%) patients and hand-sewn anastomosis in 46 (44.7%). Approaches for intraperitoneal cavity used laparoscopy in 78 (75.7%) patients, a robot-assisted method in 15 (14.6%), and laparotomy in 10 (9.7%). LLND was performed in 28 (27.2%) patients and preoperative chemotherapy in 34 (33%). The median operative time was 319 (123–639) min, median blood loss volume was 60 (0–3550) mL, median intraoperative fluid volume was 2800 (419–8800) mL, and intraoperative transfusion was performed in 10 patients (9.7%). The postoperative complications were AL in 21 (20.4%) patients, organ/space SSI in 21 (20.4%), HOS in 32 (31.1%), and OO in 19 (18.4%). Grade IIIb and IV complications were found in 9 patients (8.7%), of whom 7 had AL (Table 1).

Analysis of HOS

The median onset time of HOS was postoperative day (POD) 4 (range POD 2–15), the median output volume was 2460 (1800–5450) mL, and the median maximum output volume on the onset day was 3005 (1800–5450) mL (Table 2). Organ/space SSI, AL, and
were significant HOS-related factors in univariate analysis, and OO (odds ratio [OR] 3.82, p = 0.022) remained as a significantly independent factor associated with HOS in multivariate analysis (Table 3). The white blood cell (WBC) count on POD 6 was significantly higher in the HOS group than in the non-HOS group (9765 vs. 8130/mL, p<0.05) (Table 4). The WBC count on POD 3 and C-reactive protein (CRP) levels on PODs 3 and 6 were also higher in the HOS group.

Analysis of OO
The median onset time of OO was POD 4 (range POD 1–14), the median output volume was 1100 (25–3600) mL, and the median maximum output volume on the onset day was 2275 (80–4700) mL (Table 2). Organ/space SSI and HOS were significant OO-related factors in univariate analysis, but thickness of the rectus abdominis muscle did not show this relationship. Organ/space SSI (OR 3.69, P = 0.02) was a significantly independent factor associated with OO in multivariate analysis (Table 5). The WBC count (9400 vs. 7475/mL, p<0.05) and CRP level (6.01 vs. 2.92 mg/L, p<0.05) on POD 6 were significantly higher in the OO group than in the non-OO group (Table 6). The WBC count and CRP level on POD 3 were also higher in the OO group.

Discussion
The criteria for the creation of DS vary among institutions. A meta-analysis of the significance of DS in rectal cancer showed that the anastomosis close to the anus was protected by DS [18]. A multicenter study in Japan showed that DS did not decrease the incidence of AL, but reduced the severity [1], and three quarters of patients with AL avoided reoperation, showing the usefulness of DS. In addition, a multicenter study confirmed that oncological safety is comparable in sphincter-preserving surgery and abdominoperineal resection of locally advanced lower rectal cancer [19]. Therefore, the DS will continue to be created in patients with rectal cancer.
Intraabdominal abscess, paralytic ileus, AL and OO have previously been identified as risk factors for HOS [6–11]. Total proctocolectomy and a history of diabetes have also been suggested to be preoperative predictors of HOS [20], but these factors were not identified as significant risk factors in this study. The reported risk factors for OO are total proctocolectomy and thickness of the rectus abdominis muscle at the stoma-penetrating site [12–14]. However, these factors also had no marked relationship with OO in this study. Infection in organ/space site was associated with the causes of HOS and OO. HOS and OO were associated with the same factor which suggested similar pathology.

WBCs and CRP were examined on PODs 1, 3 and 6 as markers that reflect infectious conditions. The HOS and OO groups both had higher WBC counts and CRP levels on PODs 3 and 6 compared to the non-HOS and non-OO groups. The WBC count on POD 1 has previously been suggested to be a predictor of HOS [21], but this relationship was not significant in this study. The high WBC counts and CRP levels on PODs 3 and 6 show a prolonged postoperative infection in organ/space site, and suggest that intestinal edema and a prolonged decrease in intestinal absorption, which may be caused by infection in organ/space site, contribute to the pathology of HOS and OO. Consequently, patients with organ/space SSI due to AL should be managed with the probability of HOS and OO kept in mind. The median onset time of HOS and OO was POD 4, but some patients experienced HOS and OO on POD 1 and 2. Therefore, HOS and OO may be useful for an early sign suggesting infection in organ/space site or AL.

In terms of output volume of OO, many patients had output volume >1000 mL on the day of clinical diagnosis of OO. It may be because of prompt tube insertion in the stoma for patients with symptoms such as abdominal distension. In this study, all subjects who developed OO were fully improved by conservative treatment such as tube insertion in the oral stoma. Therefore, the OO pathology is relative stenosis of an abdominal wall-
penetrating site of a stoma due to intestinal edema caused by organ/site SSI. Thus, OO should be differentiated from general structural intestinal obstruction. And it may better to say relative outlet stenosis.

The limitations of this study are its performance at a single-center study and lack of external validity. There is a possibility that OO was a real structural obstruction leading to HOS. However, the results of the study suggest that infection in organ-space site is the major cause of HOS and OO. Consequently, the most important countermeasure for reducing HOS and OO is to decrease the incidence of AL and infection in organ-space site. Intraoperative assessment of tissue perfusion during colorectal resection using ICG [22], insertion of an anal drain to decrease pressure in the anastomosed region [23], and stabilization of procedures using robotic-assisted surgery [24–26] may potentially improve outcomes. It is critical to treat organ-space infection with consideration of the possibility of HOS and OO onset.

Conclusions

HOS and OO were found in 31% and 18% of subjects who underwent colorectal surgery and DS, respectively. Infection in the organ-space was associated with the causes of HOS and OO. HOS and OO were associated with the same factor which suggested similar pathology.

Declarations

Ethics approval and consent to participate: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. The study was approved by the Ethics Committee of our institution (2018–1131).

Consent for publication: Not applicable
Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authors’ contributions: YH and TM analyzed and interpreted the patient data. YS, HM and HN performed surgery and patient management. YH was a major contributor in writing the manuscript. KH and TM revised the manuscript. All authors given their final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Tables

Table 1. Clinicopathological characteristics of 103 patients

| Variable                      | Value                     |
|-------------------------------|---------------------------|
| Age (year)*                   | 66 (17-82)                |
| Gender, n (%)                 |                           |
| Male                          | 82 (80)                   |
| Female                        | 21 (20)                   |
| Body mass index (kg/m²) *     | 22.9 (16.9-38.9)          |
| Diabetes, n (%)               | 16 (15.5)                 |
| Smoker, n (%)                 | 26 (25.2)                 |
| Steroid user, n (%)           | 6 (5.8)                   |
| Alb (g/dL)                    | 4.2 (2.4-5)               |
| eGFR (ml/min/1.73m²)          | 74.9 (20.1-135.2)         |
| Diameter of muscle (mm)       | 10.25 (5.46-19.14)        |
| Condition                                      | n (%)     |
|-----------------------------------------------|-----------|
| Perforation, n (%)                            | 2 (1.9)   |
| Stenosis, n (%)                               | 9 (8.7)   |
| Preoperative chemotherapy, n (%)              | 34 (33)   |
| Cause of resection, n (%)                     |           |
| Neoplasia                                     | 84 (81.2) |
| Inflammatory disease                          | 17 (16.5) |
| Benign pathologies                            | 2 (1.9)   |
| Type of resection, n (%)                      |           |
| Low anterior resection                        | 52 (50.5) |
| Intersphincteric resection                    | 31 (30.1) |
| Total proctocolectomy                        | 17 (16.5) |
| Others                                        | 3         |
| Approach, n (%)                               |           |
| Laparoscope-assisted surgery                  | 78 (75.7) |
| Robotic surgery                               | 15 (14.6) |
| Open surgery                                  | 10 (9.7)  |
| Double stapling technique, n (%)              | 57 (55.3) |
| Lateral lymph node dissection, n (%)          | 28 (27.2) |
| Operation time (min) *                        | 319 (123-639) |
| Blood loss (ml) *                             | 60 (0-3550) |
| Blood transfusion, n (%)                      | 10 (9.7)  |
| Replacement fluid volume in the operation (ml)| 2800 (419-8800) |
| Double stapling technique, n (%)              | 57 (55.3) |
| Preoperative chemotherapy, n (%)              | 34 (33)   |
| Anastomotic leakage, n (%)                   | 21 (20.4) |
| Organ/space SSI, n (%)                        | 39 (37.9) |
| High output stoma, n (%)                      | 32 (31.1) |
| Outlet obstruction, n (%)                     | 19 (18.4) |
| Complications (Clavien-Dindo), n (%)          |           |
| All (I-IV)                                    | 69 (67.0) |
| IIIa                                          | 12 (11.7) |
| IIIb                                          | 3 (2.9)   |
| IV                                            | 6 (5.8)   |
Table 2. Output volume about OO and HOS

|                               | OO          | HOS         | non-OOHOS   |
|-------------------------------|-------------|-------------|-------------|
| Onset POD of HOS or OO median (range) | 4 (1-14)    | 4 (2-15)    | -           |
| Output volume with onset day (ml) median (range) | 1100 (25-3600) | 2460 (1800-5450) | -           |
| Maximum volume of stoma output (ml) median (range) | 2275 (80-4700) | 3005 (1800-5450) | 1030 (390-3300) |

HOS; high output stoma, OO; outlet obstruction, POD; post operative day
Table 3. Univariate and multivariate analyses of clinicopathological variables on High output stoma
| Variables                          | N  | Univariate analysis | Multivariate analysis |
|-----------------------------------|----|---------------------|-----------------------|
|                                   |    | n (%)               | \(P\) value           | Odds ratio (95% CI)   | \(P\) value |
| **Age**                           |    |                     |                       |                       |             |
| ≥65                               | 40 | 15 (37.5)           | 0.670                 |                       |             |
| <65                               | 53 | 15 (28.3)           |                       |                       |             |
| **Gender**                        |    |                     |                       |                       |             |
| Female                            | 21 | 3 (14.3)            |                       |                       |             |
| Male                              | 82 | 29 (35.4)           | 0.070                 |                       |             |
| **BMI (kg/m\(^2\))**             |    |                     |                       |                       |             |
| ≥25                               | 78 | 23 (29.5)           | 0.621                 |                       |             |
| <25                               | 25 | 9 (36)              |                       |                       |             |
| **Diabetes**                      |    |                     |                       |                       |             |
| No                                | 87 | 26 (29.9)           |                       |                       |             |
| Yes                               | 16 | 6 (37.5)            | 0.565                 |                       |             |
| **Smoker**                        |    |                     |                       |                       |             |
| No                                | 77 | 21 (27.3)           |                       |                       |             |
| Yes                               | 25 | 10 (40)             | 0.317                 |                       |             |
| **Steroid user**                  |    |                     |                       |                       |             |
| No                                | 97 | 28 (28.9)           |                       |                       |             |
| Yes                               | 21 | 3 (14.3)            | 0.073                 |                       |             |
| **Alb**                           |    |                     |                       |                       |             |
| ≥4.2                              | 44 | 14 (31.8)           |                       |                       |             |
| <4.2                              | 59 | 18 (30.5)           | 1                     |                       |             |
| **eGFR**                          |    |                     |                       |                       |             |
| ≥60                               | 91 | 30 (33.0)           |                       |                       |             |
| <60                               | 12 | 2 (16.7)            | 0.333                 |                       |             |
| **Diameter of muscle (mm)**       |    |                     |                       |                       |             |
| ≥10.25                            | 42 | 12 (28.6)           |                       |                       |             |
| <10.25                            | 61 | 20 (32.8)           | 0.672                 |                       |             |
| **Neoplasia**                     |    |                     |                       |                       |             |
| No                                | 19 | 9 (47.4)            |                       |                       |             |
| Yes                               | 84 | 23 (27.4)           | 0.105                 |                       |             |
| **Perforation**                   |    |                     |                       |                       |             |
| No                                | 101| 31 (30.7)           |                       |                       |             |
| Yes                               | 2  | 1 (50)              | 0.527                 |                       |             |
| **Stenosis**                      |    |                     |                       |                       |             |
| No                                | 94 | 28 (29.8)           |                       |                       |             |
| Yes                               | 9  | 4 (44.4)            | 0.454                 |                       |             |
| **Operation time (min)**          |    |                     |                       |                       |             |
| ≥319                              | 53 | 20 (37.7)           |                       |                       |             |
| <319                              | 50 | 12 (24)             | 0.143                 |                       |             |
| **Blood loss (ml)**               |    |                     |                       |                       |             |
| ≥60                               | 50 | 19 (38)             |                       |                       |             |
| <60                               | 53 | 13 (24.5)           | 0.201                 |                       |             |
| **Total proctocolectomy**         |    |                     |                       |                       |             |
| No                                | 86 | 24 (27.9)           |                       |                       |             |
| Yes                               | 17 | 8 (47)              | 0.153                 |                       |             |
| **LLND**                          |    |                     |                       |                       |             |
| No                                | 75 | 24 (32)             |                       |                       |             |
| Yes                               | 29 | 8 (27.6)            | 0.814                 |                       |             |
| **Double stapling technique**     |    |                     |                       |                       |             |
| No                                | 43 | 17 (39.5)           |                       |                       |             |
| Yes                               | 60 | 15 (25)             | 0.134                 |                       |             |
| **Preoperative chemotherapy**     |    |                     |                       |                       |             |
| No                                | 69 | 21 (30.4)           |                       |                       |             |
| Yes                               | 34 | 11 (32.4)           | 1                     |                       |             |
| **Blood transfusion**             |    |                     |                       |                       |             |
| No                                | 93 | 28 (30.1)           |                       |                       |             |
| Yes                               | 10 | 4 (40)              | 0.497                 |                       |             |
| **Replacement fluid volume in the operation (ml)** |    |                     |                       |                       |             |
| ≥2800                             | 53 | 21 (39.6)           |                       |                       |             |
| <2800                             | 50 | 11 (22)             | 0.059                 |                       |             |
| **Anastomotic leakage**           |    |                     |                       |                       |             |
| No                                | 84 | 22 (26.2)           | 0.024                 | 2.03 (0.52-7.96)      | 0.310       |
| Yes                               | 18 | 10 (55.6)           |                       |                       |             |
| **Organ space SSI**               |    |                     |                       |                       |             |
| No                                | 64 | 13 (20.3)           | 0.044                 | 2.19 (0.69-6.98)      | 0.184       |
| Yes                               | 39 | 19 (48.7)           |                       |                       |             |
| **OO**                            |    |                     |                       |                       |             |
| No                                | 84 | 21 (25)             | 0.011                 | 3.82 (1.21-12.1)      | 0.022       |
| Yes                               | 19 | 11 (57.9)           |                       |                       |             |

BMI; body mass index, LLND; lateral lymph node dissection, SSI; surgical site infection
Table 4. 1, 3, 6 POD WBC and CRP about HOS and non-HOS

|        | HOS   | non-HOS | p-value | HOS   | non-HOS | p-value |
|--------|-------|---------|---------|-------|---------|---------|
| 1 POD  | 9670  (8200-11575) | 10170 (8750-11568) | 0.606 | 6.39 (4.35-10.30) | 6.68 (4.93-8.63) | 0.72 |
| 3 POD  | 9765 (8058-13210) | 8130 (6950-100909) | 0.015 | 13.28 (7.60-19.50) | 11.787 (7.20-14.27) | 0.22 |
| 6 POD  | 8085 (6907-9605) | 7540 (6410-8725) | 0.122 | 5.20 (1.69-10.81) | 3.01 (1.70-5.71) | 0.20 |

HOS; high output stoma, POD; post operative day, WBC; white blood cell (3300-8600),
CRP; C-reactive protein (0.00-0.14)
Table 5. Univariate and multivariate analyses of clinicopathological variables on outlet
| Variables                      | N   | Univariate analysis | Multivariate analysis |
|-------------------------------|-----|---------------------|-----------------------|
|                               |     | n (%)               | P value               | Odds ratio (95% CI) | P value |
|                               |     |                     |                       |                     |         |
| Age                           |     |                      |                       |                     |         |
| ≥65                           | 53  | 10 (18.9)            | 1                     |                     |         |
| <65                           | 50  | 9 (18)               | 1                     |                     |         |
| Gender                        |     |                      |                       |                     |         |
| Female                        | 21  | 0 (0)                | NA                    |                     |         |
| Male                          | 82  | 19 (23.2)            | 0.011                 |                     |         |
| BMI (kg/m²)                   |     |                      |                       |                     |         |
| ≥25                           | 78  | 13 (16.7)            | 0.393                 |                     |         |
| <25                           | 25  | 6 (24)               | 0.011                 |                     |         |
| Diabetes                      |     |                      |                       |                     |         |
| No                            | 87  | 15 (17)              | 0.129                 |                     |         |
| Yes                           | 16  | 4 (25)               |                       |                     |         |
| Smoker                        |     |                      |                       |                     |         |
| No                            | 25  | 5 (20)               | 1                     |                     |         |
| Yes                           | 77  | 14 (18.2)            |                       |                     |         |
| Steroid user                  |     |                      |                       |                     |         |
| No                            | 97  | 18 (18.6)            | 0.143                 |                     |         |
| Yes                           | 6   | 1 (16.7)             |                       |                     |         |
| Alb                           |     |                      |                       |                     |         |
| ≥4.2                          | 44  | 11 (25)              | 1                     |                     |         |
| <4.2                          | 59  | 8 (13.6)             |                       |                     |         |
| eGFR                           |     |                      |                       |                     |         |
| ≥60                           | 91  | 15 (16.5)            |                       |                     |         |
| <60                           | 12  | 4 (33.3)             |                       |                     |         |
| Diameter of muscle (mm)       |     |                      |                       |                     |         |
| ≥10.25                        | 42  | 8 (19.0)             | 0.227                 |                     |         |
| <10.25                        | 61  | 11 (18)              |                       |                     |         |
| Neoplasia                     |     |                      |                       |                     |         |
| No                            | 19  | 3 (15.8)             |                       |                     |         |
| Yes                           | 84  | 16 (19.0)            |                       |                     |         |
| Perforation                   |     |                      |                       |                     |         |
| No                            | 101 | 19 (18.9)            | 1                     |                     |         |
| Yes                           | 2   | 0 (0)                |                       |                     |         |
| Stenosis                      |     |                      |                       |                     |         |
| No                            | 94  | 16 (17.0)            | 1                     |                     |         |
| Yes                           | 9   | 3 (33.3)             | 0.361                 |                     |         |
| Total proctocolectomy         |     |                      |                       |                     |         |
| No                            | 86  | 16 (18.6)            | 1                     |                     |         |
| Yes                           | 17  | 3 (17.6)             |                       |                     |         |
| LLND                           |     |                      |                       |                     |         |
| No                            | 75  | 14 (18.37)           | 1                     |                     |         |
| Yes                           | 29  | 3 (10.3)             |                       |                     |         |
| Double stapling technique     |     |                      |                       |                     |         |
| No                            | 43  | 11 (25.6)            | 1                     |                     |         |
| Yes                           | 60  | 8 (13.3)             | 0.129                 |                     |         |
| Preoperative chemotherapy      |     |                      |                       |                     |         |
| No                            | 69  | 13 (18.8)            | 1                     |                     |         |
| Yes                           | 34  | 6 (17.6)             |                       |                     |         |
| Operation time (min)          |     |                      |                       |                     |         |
| ≥319                          | 53  | 10 (18.9)            | 1                     |                     |         |
| <319                          | 50  | 9 (18)               |                       |                     |         |
| Blood loss (ml)               |     |                      |                       |                     |         |
| ≥60                           | 50  | 10 (20)              | 1                     |                     |         |
| <60                           | 53  | 9 (17.0)             | 0.801                 |                     |         |
| Blood transfusion             |     |                      |                       |                     |         |
| No                            | 93  | 16 (17.2)            |                       |                     |         |
| Yes                           | 10  | 3 (30)               | 0.388                 |                     |         |
| Replacement fluid volume in the operation (ml) | | | | | |
| ≥2800                         | 53  | 9 (17.0)             |                       |                     |         |
| <2800                         | 50  | 10 (20)              | 0.801                 |                     |         |
| Anastomotic leakage           |     |                      |                       |                     |         |
| No                            | 84  | 14 (16.7)            | 0.518                 |                     |         |
| Yes                           | 18  | 4 (22.2)             |                       |                     |         |
| Organ space SSI               |     |                      |                       |                     |         |
| No                            | 64  | 6 (9.4)              |                       |                     |         |
| Yes                           | 39  | 13 (33.3)            | 0.004                 | 3.69 (1.21-11.3)    | 0.022   |
| HOS                           |     |                      |                       |                     |         |
| No                            | 71  | 8 (11.3)             | 0.011                 | 2.95 (0.99-8.8)     | 0.052   |
| Yes                           | 32  | 11 (34.4)            |                       |                     |         |

BMI; body mass index, LLND; lateral lymph node dissection, SSI; surgical site infection
Table 6. 1, 3, 6 POD WBC and CRP about OO and non-OO

|       | WBC          | CRP (mg/L)   |       |       |       |       |
|-------|--------------|--------------|-------|-------|-------|-------|
|       | OO           | non-OO       | p-value | OO    | non-OO | p-value |
| 1 POD | 10950 (8835-12900) | 10060 (8410-11500) | 0.470 | 5.52 (4.20-7.91) | 6.78 (4.92-9.91) | 0.508 |
| 3 POD | 10180 (7775-12690) | 8130 (7195-10343) | 0.068 | 14.0 (9.75-22.33) | 11.73 (7.27-15.27) | 0.099 |
| 6 POD | 9400 (7050-10007) | 7475 (6408-8810) | 0.031 | 6.01 (2.97-11.05) | 2.92 (1.50-6.49) | 0.023 |

OO; outlet obstruction, POD; post operative day, WBC; white blood cell (3300-8600), CRP; C-reactive protein (0.00-0.14)