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# Risk Factors for Severe Complications After Laparoscopic Surgery for T3 or T4 Rectal Cancer for Chinese Patients: Experience from a Single Center

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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**Background:** Patients with rectal cancer are usually at advanced stage with or beyond serosa invasion in China. Severe complications after laparoscopic rectal surgery leads to prolonged hospitalization and high medical cost. This study aimed to explore risk factors for severe complications after laparoscopic surgery of T3 or T4 rectal cancer.

**Material/Methods:** A total of 287 patients diagnosed with T3 or T4 rectal cancer were enrolled from the Department of Gastrointestinal Surgery of Anhui Provincial Hospital from February 2012 to February 2017. Univariate analysis and multivariable logistic regression model were used to analyze the risk factors for severe complications (Clavien-Dindo grade ≥III) after laparoscopic surgery.

**Results:** Eighteen patients (6.25%) had severe complications; 15 patients were categorized as Clavien-Dindo grade III, and 3 patients were categorized as Clavien-Dindo grade IV. Univariate analysis showed that male gender, high preoperative white blood cells (WBC), diabetes mellitus, pulmonary dysfunction, and tumor distance from anus were associated with increased risk of severe complications after laparoscopic surgery for rectal cancer. Multivariate analysis showed that preoperative WBC ≥6.9×10$^9$/L (OR=5.54 (1.58–19.45), *P*=0.008), diabetes mellitus (OR=13.07 (3.31–51.67), *P*=0.000) and pulmonary dysfunction (OR=7.75 (1.69–35.63), *P*=0.008) were independent risk factors for postoperative severe complications.

**Conclusions:** Preoperative high white blood cells, diabetes mellitus and pulmonary dysfunction were independent risk factors for severe complications after laparoscopic surgery for T3 or T4 rectal cancer.

**MeSH Keywords:** Laparoscopes • Postoperative Complications • Rectal Neoplasms • Risk Factors

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## Background

Epidemiological studies have showed that incidence and mortality of rectal cancer are increasing year by year in China, and it seriously threatens the lives of Chinese people [1]. Besides, most rectal cancers at diagnosis are at a locally advanced stage with or beyond serosal invasion (T3 or T4 stage). Surgery along with chemoradiotherapy and immunotherapy remains the main treatments for these patients.

With the rapid development of laparoscopic instruments and techniques, laparoscopic rectal surgery (LRS) has been widely used for treating rectal cancer with minimal trauma and rapid recovery [2]. Clear surgical field and full exposure of anatomical structure enables LRS to achieve curative resection for rectal cancer, to reduce surgical trauma and improve quality of life after surgery [3]. Despite these advantages, complications after LRS are still inevitable. Previous studies have reported that the incidence rate of postoperative complications is 20% to 30% for rectal cancer, incidence rate of serious complications is 5% to 12%, and the mortality is about 2% [4,5]. Besides, some situations including obesity, male gender, low location of tumor, and advanced stage of cancer likely impose increased difficulty for LRS for rectal cancer, which leads to prolonged operative time, more blood loss, and increased risk of postoperative complications. Yasui et al. reported that 25.9% of patients had postoperative complications after LRS, and that tumor size (≥4 cm) and tumor stage (T4) were independent risk factors for postoperative complications, which suggests that it is very important to select appropriate patients for LRS [6].

Clavien-Dindo system has been widely used to classify postoperative complications. Clavien-Dindo III/IV complications that require re-operation, endoscopic or radiological intervention are defined as severe complications [7] that always lead to disastrous outcomes like organ failure or even death as well as significantly high medical costs. In this study, we summarized the clinical data of the patients with T3 or T4 rectal cancer who underwent LRS for rectal cancer. In addition, we also explored potential risk factors for postoperative severe complications to ensuring safety of LRS for T3 or T4 rectal cancer patients.

## Material and Methods

### Patients

From February 2012 to February 2017, clinical data from 287 patients who were diagnosed as T3 or T4 rectal cancer and underwent LRS in the First Affiliated Hospital of Chinese University of Science and Technology (Anhui Provincial Hospital) were retrospectively collected. According to the 8th TNM staging system (American Joint Committee on cancer, AJCC), T3 or T4 rectal cancer is defined as tumor penetrates into or beyond serosal layer of rectum. This study was approved by our ethics committee, and the study complied with the Helsinki declaration.

Inclusion criteria of patients were as follows: 1) patients were pathologically diagnosed with rectal cancer, and tumor lesion was within 15 cm from the anus; 2) preoperative magnetic resonance imaging (MRI) examination indicated that TNM stage of rectal cancer were T3N0–2M0, or T4N0–2M0, which was further confirmed by postoperative pathological examination; 3) patients underwent radical LRS for rectal cancer, including Dixon, Miles, or Hartmann procedure; 4) clinical records were complete and available. Exclusion criteria of this study included: 1) clinical data was missing and incomplete; 2) patients had a history of malignant tumors; 3) emergency surgery due to massive bleeding, obstruction, or perforation.

### Perioperative assessment and management

*Perioperative assessment*

All patients underwent a preoperative evaluation to determine whether they could successfully undergo surgery, including physical examination, colonoscopy with tumor biopsy, MRI, and thoraco-abdominopelvic computed tomography (CT) scan. The following clinical data were collected: 1) perioperative data, including age, gender, American Society Anesthesiologist (ASA) score, distance from the low verge of tumor to anus, cardiovascular disease, respiratory disease, cerebrovascular disease, hypertension, diabetes, previous abdominal surgery, neoadjuvant radiochemotherapy. 2) Preoperative laboratory parameters, including white blood cell count (WBC; $10^9$/L), neutrophil count ($10^9$/L), albumin (g/L), and hemoglobin (Hb; g/L). 3) Intraoperative parameters, including operative time, estimated blood loss, types of operations (Dixon, Miles, Hartmann), stoma (yes or no), and combined organ resection (yes or no). 4) Postoperative data, including pathological assessment using 8th TNM system (AJCC), and postoperative hospital stay defined as period from surgery to discharge and severe complication.

*Perioperative management*

Mechanical bowel preparation with oral antibiotics was routinely conducted for patients without obstruction. Prophylactic antibiotics were administrated within 30 minutes via intravenous perfusion before surgery, and stopped within 48 hours after surgery. Patients were required to walk (get out of bed) at day 2 and allowed liquid diet at day 3 after surgery. All patients were given intravenous nutrition until resumption of semiliquid diet.





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**Table 1.** Clavien-Dindo scale for definition of severe complication.

| Clavien-Dindo classification | |
|---|---|
| Grade I | Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Appropriate treatments are allowed: antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physical therapy. Wound infections that are open at the bed are also part of this class |
| Grade II | Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Including need for blood transfusions and total parenteral nutrition |
| Grade III | Requires surgery, endoscopy or radiological intervention |
| Grade IIIa | Intervention not under general anesthesia |
| Grade IIIb | Intervention under general anesthesia |
| Grade IV | Life-threatening complication (including CNS complications) and requiring IC/ICU-management |
| Grade IVa | Single organ dysfunction (including dialysis) |
| Grade IVb | Multiple organ dysfunction |
| Grade V | Death |

### Surgical technique

Surgical procedures for LAR have been described in a previous study [8]. In brief, after success of general anesthesia, 5 trocars were inserted into abdominal cavity. Laparoscopic exploration was conducted to determine whether there was intraperitoneal metastasis. A standardized surgical technique termed total anatomical dissection was adopted. The rectum along with its fascial layers was dissected in the bloodless plane. The splenic flexure was mobilized if necessary. The inferior mesenteric vein was ligated at the lower border of the pancreas, and inferior mesenteric artery was ligated at initial part. A total mesorectal excision (TME) was performed in patients with middle- and lower-third tumor; whereas the perirectal fat was divided and ligated 5 cm below the tumor for patients with upper-third tumor. Prophylactic ileum stoma was created in patients with tumor under peritoneal reflection.

### Definition of postoperative severe complications

Severity of postoperative complications within 30 days after surgery was evaluated using the Clavien-Dindo scale (Table 1). Clavien-Dindo III/IV complications requiring surgical, endoscopic or radiological interventions were defined as severe complications.

### Statistical analysis

All statistical analyses were performed using SPSS® version 20.0 software (SPSS, IBM). Categorical variables were present as percentage, whereas continuous variables were transformed into categorical variables using 75% quartile of interquartile ranges as cut-value, and then all categorical data were compared using chi-square test. Multivariate logistic regression was conducted based on the variables in the univariate analysis ($P$<0.10) and on the factors clinically related to the sever complications after surgery. $P$-value <0.05 was considered statistically significant.

## Results

### Characteristics of patients

A total of 287 patients were enrolled in this study, including 170 males (59.2%) and 117 females (40.8%); basic information for these patients is listed in Table 2. Among these patients, 211 patients (73.5%) were <71 years old, and 76 patients (26.5%) were ≥71 years old; 86.8% of all study patients (249 patients) were classified as ASA I/II and 13.2% (38 patients) were classified as ASA III. A total of 12 patients received neoadjuvant radiochemotherapy. Proportions of patients with upper, middle, and lower rectal tumors were 19.5%,43.2%, and 37.3%, respectively.

### Intraoperative and pathological outcomes

Intraoperative parameters are shown in Table 3. Operative time, intraoperative blood loss, proportions of surgical procedures were not statistically different between 2 group. We noted that, although no statistical significance, patients with severe complications had lower proportion of stoma than patients without severe complications ($P$=0.09).

Information for pathological outcomes and postoperative recovery are shown in Table 4. There were no statistical significances





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**Table 2.** Basic characteristics of patients.

| Variables | Total (n, %) | Group A (n, %)* | Group B (n, %)* | Test value | *P* value |
|---|---|---|---|---|---|
| Total patients | 287 | 269 | 18 | | |
| Gender | | | | $\chi^2$=4.62 | 0.045 |
| Male | 170 (59.2) | 155 (57.6) | 15 (83.3) | | |
| Female | 117 (40.8) | 114 (42.4) | 3 (16.7) | | |
| Age (years) | | | | $\chi^2$=0.18 | 0.80 |
| <71 | 211 (73.5) | 197 (73.2) | 14 (77.8) | | |
| ≥71 | 76 (26.5) | 72 (26.8) | 4 (22.2) | | |
| Preoperative WBC ($10^9$/L) | | | | $\chi^2$=6.11 | 0.02 |
| <6.9 | 214 (74.6) | 205 (76.2) | 9 (50.0) | | |
| ≥6.9 | 73 (25.4) | 64 (23.8) | 9 (50.0) | | |
| Preoperative neutrophil ($10^9$/L) | | | | $\chi^2$=2.07 | 0.15 |
| <4.41 | 216 (75.3) | 205 (76.2) | 11 (61.1) | | |
| ≥4.41 | 71 (24.7) | 64 (23.8) | 7 (38.9) | | |
| Preoperative hemoglobin (g/L) | | | | $\chi^2$=0.01 | 1.00 |
| <138 | 210 (73.2) | 197 (73.2) | 13 (72.2) | | |
| ≥138 | 77 (26.8) | 72 (26.8) | 5 (27.8) | | |
| Preoperative albumin (g/L) | | | | $\chi^2$=0.63 | 0.41 |
| <43.4 | 214 (74.6) | 202 (75.1) | 12 (66.7) | | |
| ≥43.4 | 73 (25.4) | 67 (24.9) | 6 (33.3) | | |
| ASA classification | | | | $\chi^2$=0.08 | 1.00 |
| 1–2 | 249 (86.8) | 233 (86.6) | 16 (88.9) | | |
| 3 | 38 (13.2) | 36 (13.4) | 2 (11.1) | | |
| Distance from the anus (cm) | | | | $\chi^2$=6.05 | 0.049 |
| >10 (high) | 56 (19.5) | 52 (19.4) | 4 (22.2) | | |
| 5–10 (middle) | 124 (43.2) | 112 (41.6) | 12 (66.7) | | |
| ≤5 (low) | 107 (37.3) | 105 (39.0) | 2 (11.1) | | |
| Comorbidities | | | | | |
| Hypertension | 71 (24.7) | 65 (24.2) | 6 (33.3) | $\chi^2$=0.76 | 0.40 |
| Diabetes | 29 (10.1) | 22 (8.2) | 7 (38.9) | $\chi^2$=17.52 | 0.001 |
| Pulmonary dysfunction | 15 (5.2) | 11 (4.1) | 4 (22.2) | $\chi^2$=11.20 | 0.01 |
| Heart dysfunction | 27 (9.4) | 25 (9.3) | 2 (11.1) | $\chi^2$=0.07 | 0.68 |
| Cerebral diseases | 12 (4.2) | 11 (4.1) | 1 (5.6) | $\chi^2$=0.09 | 0.55 |
| Previous abdominal surgery | 39 (13.6) | 36 (13.4) | 3 (16.7) | $\chi^2$=0.16 | 0.72 |
| Neoadjuvant radiochemotherapy | 12 (4.2) | 11 (4.1) | 1 (5.6) | $\chi^2$=0.09 | 0.55 |

* Group A was patients with non-severe complications, whereas Group B was patients with severe complications.





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**Table 3.** Intraoperative outcomes.

| Variables | Total (n, %) | Group A (n, %)* | Group B (n, %)* | Test value | *P* value |
|---|---|---|---|---|---|
| Total patients | 287 | 269 | 18 | | |
| Surgical procedures | | | | $\chi^2$=3.78 | 0.15 |
| Dixon | 199 (69.3) | 183 (68.0) | 16 (88.9) | | |
| Miles | 68 (23.7) | 67 (24.9) | 1 (5.55) | | |
| Hartmann | 20 (7.0) | 19 (7.1) | 1 (5.55) | | |
| Stoma | 152 (53.0) | 146 (54.2) | 6 (33.3) | $\chi^2$=2.97 | 0.09 |
| Combined organ resection | 6 (2.1) | 6 (2.2) | 0 (0.0) | $\chi^2$=0.41 | 1.00 |
| Operative time | | | | $\chi^2$=0.70 | 0.41 |
| <221 min | 215 (74.9) | 203 (75.5) | 12 (66.7) | | |
| ≥221 min | 72 (25.1) | 66 (24.5) | 6 (33.3) | | |
| Estimated blood loss | | | | $\chi^2$=2.52 | 0.14 |
| <100 mL | 109 (38.0) | 99 (36.8) | 10 (55.6) | | |
| ≥100 mL | 178 (62.0) | 170 (63.2) | 8 (44.4) | | |

* Group A was patients with non-severe complications, whereas Group B was patients with severe complications.

**Table 4.** Pathological outcomes and postoperative recovery.

| Variables | Total (n, %) | Group A (n, %)* | Group B (n, %)* | Test value | *P* value |
|---|---|---|---|---|---|
| Total patients | 287 | 269 | 18 | | |
| Number of lymph node | | | | $\chi^2$=0.00 | 1.00 |
| <11 | 207 (72.1) | 194 (72.1) | 13 (72.2) | | |
| ≥11 | 80 (27.9) | 75 (27.9) | 5 (27.8) | | |
| Number of metastatic lymph node | | | | $\chi^2$=0.38 | 0.79 |
| <3 | 205 (71.4) | 191 (71.0) | 14 (77.8) | | |
| ≥3 | 82 (28.6) | 78 (29.0) | 4 (22.2) | | |
| Tumor size (cm) | | | | $\chi^2$=0.18 | 0.79 |
| <5 | 204 (71.1) | 192 (71.4) | 12 (66.7) | | |
| ≥5 | 83 (28.9) | 77 (28.0) | 6 (33.3) | | |
| Differentiation | | | | $\chi^2$=0.08 | 1.00 |
| Moderate/high | 215 (74.9) | 201 (74.7) | 14 (77.8) | | |
| Low | 72 (25.1) | 68 (25.1) | 4 (22.2) | | |
| TNM stage, n (%) | | | | $\chi^2$=2.76 | 0.14 |
| II | 153 (53.3) | 140 (52.0) | 13 (72.2) | | |
| III | 134 (46.7) | 129 (48.0) | 5 (27.8) | | |
| Postoperative feeding time (days, mean±SD) | 4.14±2.27 | 3.94±1.73 | 7.11±5.41 | t=73.43 | 0.00 |
| Postoperative hospital stay (days, mean±SD) | 11.21±6.41 | 9.93±3.00 | 30.22±11.96 | t=140.62 | 0.00 |

* Group A was patients with non-severe complications, whereas Group B was patients with severe complications. SD – standard deviation.





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**Table 5.** Multivariate logistic regression analysis of severe complications after laparoscopic surgery for T3 or T4 rectal cancer.

| Variates | Regression coefficient | Standard error | Wald values | OR value | *P* value |
|---|---|---|---|---|---|
| Gender (Male *vs.* Female) | 1.13 | 0.71 | 2.54 | 3.10 (0.77–12.45) | 0.11 |
| Preoperative WBC (≥6.9 *vs.* <6.9, $10^9$/L) | 1.71 | 0.64 | 7.14 | 5.54 (1.58–19.45) | 0.008 |
| Diabetes (yes *vs.* no) | 2.57 | 0.70 | 13.44 | 13.07 (3.31–51.67) | 0.000 |
| Pulmonary dysfunction (yes *vs.* no) | 2.05 | 0.78 | 6.93 | 7.75 (1.69–35.63) | 0.008 |
| Surgical procedures | | | | | |
| Dixon | | | 1.20 | 1 | 0.55 |
| Miles | –0.59 | 1.41 | 0.18 | 0.56 (0.04–8.72) | 0.68 |
| Hartmann | –1.42 | 1.35 | 1.11 | 0.24 (0.02–3.39) | 0.29 |
| Diverting stoma (yes *vs.* no) | –0.03 | 0.69 | 0.002 | 0.97 (0.25–3.74) | 0.96 |
| Estimated blood loss (≥100 *vs.* <100 mL) | –0.49 | 0.59 | 0.70 | 0.61 (0.19–1.95) | 0.40 |
| Tumor distance (cm) | | | | | |
| >10 | | | 1.41 | 1 | 0.50 |
| 5–10 | 0.73 | 0.72 | 1.04 | 2.07 (0.51–8.43) | 0.31 |
| ≤5 | –0.08 | 1.18 | 0.004 | 0.93 (0.09–9.25) | 0.95 |
| TNM stage (III *vs.* II) | –0.76 | 0.61 | 1.58 | 0.47 (0.14–1.53) | 0.21 |

of number of lymph node harvested, positive lymph node, tumor size, or TNM stage between patients with or without severe complications. As expected, patients with severe complications had prolonged postoperative feeding and hospital time than patients without severe complication.

### Severe complications

A total of 18 patients (6.25%) had severe complications. According to the Clavien-Dindo staging scale, 15 patients were classified as grade III and 3 cases were grade IV. Detail information of severe complications for these patients is shown in Supplementary Table 1. There was no death in all patients.

### Univariate analysis of severe complications and Postoperative situation

Univariate analysis showed that male patients, high preoperative WBC, diabetes, pulmonary dysfunction, and the distance of tumor to anal verge were associated with severe complications after LRS ($P<0.05$); whereas prophylactic stoma likely contributed to the decreased risk of severe complications, although it did not reach statistical significance ($P=0.09$). In contrast, other variates including age, hypertension, cardiac dysfunction, cerebral disease, ASA classification, TNM stage, etc, were not statistically significant ($P>0.05$). The details are shown in Table 2–4.

### Multivariate logistic regression analysis of severe complications

Multivariate logistic regression analysis was performed to analyze the factors that were associated with postoperative severe complications in the univariate analysis ($P<0.1$) and preoperative white blood cells (OR=6.11, $P=0.02$), diabetes (OR=17.52, $P=0.001$) and pulmonary dysfunction (OR=11.20, $P=0.01$) were independent risk factors for severe complications after laparoscopic surgery for rectal cancer (Table 5).

## Discussion

Surgery is the most effective approach for treatment of rectal cancer. However, postoperative complication still remains a problem that surgeons have to face. Published studies have reported that the incidence of postoperative complications ranged from 20% to 30%, of which the incidence of severe complications ranged from 5% to 12% [4,5]. In this study, univariate analysis of clinical data from 287 patients with T3 or T4 rectal cancer showed that male gender, high WBC, diabetes, pulmonary dysfunction, and low site of cancer contributed





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to the increased risk of severe postoperative complications. Multivariate logistic regression analysis further indicated that preoperative high WBC, diabetes, and pulmonary dysfunction were independent risk factors for postoperative severe complications for these patients.

In China, most patients diagnosed as T3 or T4 rectal cancer [9], which is characterized by large tumor size and involvement of rectal fascial layers, and which leads to significantly difficult dissection in the bloodless plane as well as more technically challenging for laparoscopic surgery than early rectal cancer. The rate for severe complication after laparoscopic surgery for advanced-stage rectal cancer has been reported to be 22.5%, whereas the rate for early-stage rectal cancer was 2% [10,11], which suggested that risk factors of severe complications for advanced rectal cancer is different from that for early-staged rectal cancer after laparoscopic surgery.

There were several important observations of this study. Firstly, we found that male patients were at higher risk of severe complications after laparoscopic surgery for T3 or T4 rectal cancer than female patients, which was in line with previous studies [12–14]. Saadat et al. reported that male gender and chronic pulmonary diseases contributed to reoperation after surgery for rectal cancer [15]. Another study conducted by Kang et al. suggested that male gender was an independent risk factor for postoperative complication after robotic rectal cancer surgery [16]. In addition, male gender was also identified as a risk factor for postoperative complication for transanal total mesorectal excision (TaTME) for rectal cancer [17]. These evidences indicated that male status increases postoperative complication of rectal cancer surgery regardless of surgical approach. This may be related to pelvic stenosis in males, which leads to small surgical space, difficulties in surgical separation, dissection, and anastomosis. Increased difficulty of surgical manipulation also causes the damage of blood vessels surrounding rectum, which leads to disrupted blood supply to anastomosis and increase the risk of postoperative anastomotic leakage [18].

The second important finding of this study was that diabetes was an independent risk factor for laparoscopic surgery after rectal cancer. Diabetes is one of the most common chronic and metabolic diseases that not only causes neurological and vascular diseases, but it is also closely related to occurrence and prognosis of cancer [19,20]. In this study, all diabetic patients were monitored for blood glucose pre- and post-surgery. Endocrinologist consulted to control blood glucose between 8 and 10 mmol/L before and after surgery. However, not every patient is tested for HbA1C level before surgery. Both univariate analysis and multivariate logistic regression analysis suggested that diabetes was an independent risk factor for severe complications after laparoscopic rectal surgery, which was consistent with the results reported by Penna et al. [17]. Previous studies have reported that hyperglycemia caused by diabetes significantly increased risk of postoperative complications in patients with rectal cancer [21,22]. This may be related to poor tissue healing ability of diabetic patients [23]. In addition, diabetic patients are prone to arteriosclerosis, which causes poor blood supply to the anastomosis and affects healing of the anastomosis. Meanwhile, the risk of incision infection in diabetic patients far exceeds that of non-diabetics.

The third important finding of this study was that pulmonary dysfunction was an independent risk factor for postoperative severe complications after laparoscopic rectal surgery, which was in line with the report by Alves et al. [24]. In laparoscopic surgery, it is necessary to maintain a certain carbon dioxide pneumoperitoneum. However, blood gas analysis is performed only when the patient's vital signs are not stable, so blood gas monitoring is not performed for all patients. The main consideration is the effect of carbon-dioxide pneumoperitoneum on the respiratory system during laparoscopic surgery which induces systemic oxidative stress. In addition, hypercarbia and acidosis can occur because of ventilation-perfusion mismatch caused by impaired gas exchange due to increased intra-abdominal pressure or absorption of insufflated $CO_2$, which promotes the produce of serum oxidative stress markers and leads to altered hemodynamics[25–27]. In our research, of the 15 patients (5.2%) with preoperative pulmonary dysfunction, 4 patients developed severe complications after surgery. The difference was statistically significant ($P$=0.008). The difference may be due to decrease in tolerance to pneumoperitoneum and surgery in patients with preoperative pulmonary dysfunction. Therefore, sufficient preoperative assessment and active control of preoperative comorbidity are important to reduce the occurrence of surgical complications.

At last, both univariate and multivariate analysis showed that high preoperative white blood cell (WBC) count was associated with increased risk of postoperative severe complication after laparoscopic rectal cancer surgery in our study. WBC count is a non-specific marker for inflammatory reaction, and high preoperative WBC count indicates that the body is in an inflammatory and immune stress state, and will have poor resistance to surgical trauma and infection. Preoperative inflammation is not only associated with high risk of postoperative complication, but also with poor prognosis [28–30]. Moyes et al. reported that elevated preoperative white cell count ($P$<0.05) were independently associated with increased risk of developing a postoperative infection [31]. Another recent study showed that increased preoperative WBC count was independently associated with anastomotic leak after esophagectomy [32]. In aforementioned analysis, the authors estimate that for every 3000/μL increase in the preoperative WBC count, the associated risk increased by 32% [32].





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Some limitations should be acknowledged here. First, clinical data used in this study were retrospectively collected, which might cause bias. To avoid this bias, the data were inter-checked by 2 authors (LL and DL). Second, neoadjuvant chemoradiotherapy is currently the standard treatment for locally advanced rectal cancer and has been recommended by guidelines [33,34]. Although previous studies have reported that neoadjuvant chemoradiotherapy increased the risk of severe complications [13,35–37], we could get reach this conclusion, because few patients received neoadjuvant chemoradiotherapy.

## Conclusions

In summary, this study suggested that preoperative high WBC count (≥6.9×10$^9$/L), diabetes, and pulmonary dysfunction were independent risk factors for severe complications after laparoscopic surgery for T3 or T4 rectal cancer. Prospective high-quality studies are required to confirm our findings in the future.

### Conflicts of interest

None.

## Supplementary Data

**Supplementary Table 1.** Details of severe postoperative complications for 18 patients.

| No of patients | Age | Gender | Details of complications | Tumor location | Treatment |
|---|---|---|---|---|---|
| Patient 1 | 54 | Male | Anastomotic leakage | Middle | Reoperation; transverse colostomy |
| Patient 2 | 57 | Male | Anastomotic leakage | Middle | Reoperation; transverse colostomy |
| Patient 3 | 59 | Male | Anastomotic leakage | Middle | Conservative treatment; drainage and irrigation |
| Patient 4 | 60 | Female | Cerebral infarction | Low | Conservative treatment |
| Patient 5 | 60 | Male | Anastomotic leakage | High | Conservative treatment; drainage and irrigation |
| Patient 6 | 41 | Male | Anastomotic leakage | Low | Conservative treatment; drainage and irrigation |
| Patient 7 | 55 | Female | Postoperative Bleeding | Middle | Conservative treatment |
| Patient 8 | 69 | Male | Ileus and renal dysfunction | Middle | Conservative treatment |
| Patient 9 | 76 | Male | Postoperative bleeding | Middle | Reoperation; hemostasis |
| Patient 10 | 64 | Male | anastomotic leakage | High | Reoperation and ileostomy |
| Patient 11 | 70 | Male | Wound infection | High | Secondary incision |
| Patient 12 | 55 | Male | Anastomotic leakage | Middle | Conservative treatment; drainage and irrigation |
| Patient 13 | 78 | Male | Abdominal infection and pulmonary dysfunction | High | Conservative treatment; drainage and irrigation |
| Patient 14 | 73 | Male | Postoperative bleeding | Middle | Conservative treatment |
| Patient 15 | 68 | Male | Anastomotic leakage | Middle | Reoperation and ileostomy |
| Patient 16 | 66 | Male | Intestinal obstruction | Middle | Reoperation and small intestine resection |
| Patient 17 | 78 | Female | Anastomotic leakage | Middle | Reoperation and ileostomy |
| Patient 18 | 51 | Male | Postoperative bleeding | Middle | Reoperation; hemostasis |





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