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ORIGINAL ARTICLE

High-pressure CO_2 insufflation is a risk factor for postoperative ileus in patients undergoing TaTME

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Abstract

The aim of this study is to evaluate the influence of high-pressure CO_2 insufflation during TaTME on the occurrence of postoperative ileus. All patients undergoing elective transanal total mesorectal excision (TaTME) between April 2015 and March 2019 were included in a prospective database. Eligible patients were adults with mid and low-level rectal cancer undergoing elective TaTME with colorectal anastomosis and diverting ileostomy, following a standardized ERAS pathway. Patients were divided into a low-pressure (LP) group, where surgery was performed with an intrabdominal CO_2 pressure of 12 mmHg, and a high-pressure (HP) group, where the intrabdominal pressure reached 15 mmHg of CO_2 once the two surgical fields were connected. Of 98 patients undergoing TaTME in the observed period, 74 met the inclusion criteria and were included in this study. There was no significant difference in postoperative complications between the LP and HP groups, except for postoperative ileus, which occurred in seven patients (13.2%) in the LP group and seven patients (33.3%) in the HP group (*p* value 0.046). The logistic multivariate analysis showed that a high intraabdominal CO_2 pressure (OR 7040, 95% CI 1591–31,164, *p* value 0.01) and male sex (OR 10,343, 95% CI 1078–99,256, *p* value 0.043) were significantly associated with postoperative ileus after TaTME. Intraabdominal CO_2 pressure should be carefully set, as it may represent a risk factor for postoperative ileus in patients undergoing TaTME.

Keywords Rectal cancer · TaTME · Colorectal surgery · Minimally invasive surgery · Complications

Introduction

Rectal resection with total mesorectal excision (TME) is considered the gold standard for the treatment of rectal cancer. This approach has strongly improved the oncological outcomes of rectal resection for 30 years [1, 2]. Minimally invasive TME techniques have been introduced since the early 1990s, demonstrating equivalent outcomes when compared with open techniques, both in terms of the quality of oncological resections and long-term survival [3, 4]. During minimally invasive rectal resection, a high body mass index (BMI) and a low tumor location have been recognized as risk factors for conversion to open surgery [5]. Moreover, a narrow pelvis, male sex, a high BMI and small tumors that are difficult to locate have been advocated as factors that increase the technical difficulty of minimally invasive approaches [6, 7]. Transanal total mesorectal excision (TaTME) was developed in 2010 to overcome some of the challenges associated with minimally invasive TME [8, 9]. Since then, it has been proven to be a safe and efficient technique for the treatment of rectal cancer [1]. However, as with any new surgical technique, new complications and new issues related to this technique are routinely described in the center [2].

At Fondazione Policlinico Universitario A. Gemelli (Rome—Italy), double-team TaTME has been routinely used to treat mid-low-levels of rectal cancer since 2015 [3]. During the double-team approach, the connection between the abdominal and transanal surgical fields may cause problems in managing the pressure of a unique chamber with two insufflators. In particular, the transanal team may be disadvantaged in terms of smoke evacuation and visibility within the surgical field. For this reason, at a certain point

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in our experience, we started to perform TaTME without equalizing the intraabdominal (12 mmHg) and transanal (15 mmHg) pressures when the two fields were connected to create a gradient favoring smoke evacuation from the transanal field. However, during an internal audit, we noticed an increase in the occurrence of postoperative ileus.

For this reason, we performed this study to evaluate the influence of the non-equalization of the abdominal and transanal pressures during TaTME, resulting in high-pressure CO_2 insufflation from the transanal field, on postoperative ileus (PI).

Methods

Patient selection

Ninety-eight patients underwent elective TaTME between 30 April 2015 and 15 March 2019 at Fondazione Policlinico Universitario A. Gemelli IRCCS—Rome, Italy. All patients were included in a prospectively recorded institutional database that was retrospectively analyzed for the purposes of this study. Patients considered eligible for this study were adults with mid and low-level rectal cancer undergoing elective double-team TaTME with colorectal anastomosis and diverting ileostomy. The exclusion criteria were conversion to open surgery, ASA class IV, benign disease, synchronous tumors, procedures with terminal stoma/no colorectal anastomosis and multivisceral resection.

Data collection

Data were retrospectively collected from the institutional database. The collected data included demographic and clinical features (sex, age, BMI, preoperative hemoglobin level, previous abdominal surgery, ASA score, preoperative tumor stage, preoperative neoadjuvant treatment and operative time) and postoperative outcomes (time to first flatus, time to first stool, time to oral feeding, time to autonomous mobilization, postoperative blood transfusions, 30-day morbidity, 30-day mortality, reoperation, discharge day and readmission).

Postoperative ileus (PI) was defined as a temporary delay in gastrointestinal motility, with an ileostomy output < 200 cc in the first 48 h after surgery, accompanied by nausea, vomiting or necessity to insert a nasogastric tube. Postoperative morbidity was defined and classified according to the Clavien–Dindo classification, and severe postoperative morbidity was defined as any complication graded 3 or 4 [4]. Tumor stage was determined according to the Tumor–Node–Metastasis (TNM) classification (American Joint Committee on Cancer, 8th edition, 2017) [5].

Surgical technique and perioperative management

All patients received preoperative antimicrobial and antithrombotic prophylaxis. Antimicrobial prophylaxis consisted of a single-dose intravenous administration of 2 gr cefazoline and 500 mg metronidazole 30 min prior to the skin incision. A urinary catheter was placed at the beginning of each surgery and removed on postoperative day 2.

All patients followed a standardized perioperative enhanced recovery after surgery (ERAS) protocol [6]. All patients received mechanical bowel preparation before surgery with 280 mg of polyethylene glycol macrogol diluted in 4 L of water, divided over 2 days: 2 L 2 days before surgery and 2 L 1 day before surgery. Nasogastric or orogastric tubes that were eventually placed during surgery were removed before the end of every surgical procedure. Intravenous infusions consisted of an isotonic solution administered at a velocity of 1 ml/kg/h for the first 24 h. On postoperative day 1, patients were mobilized and started oral feeding. All patients underwent morphine-free pain-control management.

All surgical procedures consisted of a synchronous double-team approach performed by the same abdominal and transanal surgeons. The abdominal procedure was performed as a standard laparoscopic rectal resection: a 3 or 4 trocar technique including central vascular ligation, medial-to-lateral mesocolic mobilization, mobilization of the splenic flexure and incision of the peritoneal reflection. CO_2 insufflation in the abdominal surgical field was performed with a standard laparoscopic insufflator. The CO_2 pressure was set at 12 mmHg.

The transanal time started after mobilization of the splenic flexure and was performed as described by Lacy et al. [7]. CO_2 insufflation in the transanal surgical field was performed with the iFS Airseal® (Conmed Corporation), with the initial CO_2 pressure set at 15 mmHg. After the connection between the abdominal and transanal surgical fields, the dissection was completed, and colorectal anastomosis was performed within a unique field. During the first 71 cases, the transanal pressure was decreased to 12 mmHg after the connection of the abdominal and transanal fields. Starting from case number 72, the transanal pressure was left at 15 mmHg, the abdominal pressure was left at 12 mmHg, and one transabdominal trocar was left partially open to create air flow from the pelvis to the abdomen.

All the specimens were extracted through a Pfannenstiel incision with the use of a wound protector.

Oncologic management

Initial tumor staging was performed using a thoracoabdominal CT scan and pelvic MRI or endoscopic ultrasonography (EUS). Patients with locally advanced rectal cancer (cT3–T4, nodal involvement) were treated with neoadjuvant chemoradiotherapy. After neoadjuvant therapy, patients were locally restaged according to the MRI or EUS results. Patients with T4 tumors at the time of restaging were not considered eligible for TaTME. Surgery was performed a minimum of 8 weeks after the end of radiotherapy. After surgery, according to the pathological staging, patients received a postoperative evaluation with a contingent indication for the administration of postoperative chemotherapy.

Study design and outcomes

In this cohort study, patients were divided into two groups: a low-pressure (LP) group, which included patients who received 12 mmHg of intrabdominal pressure throughout the procedure, and a high-pressure (HP) group, which included patients who received 15 mmHg of intrabdominal pressure during the second part of the procedure.

The primary outcome of this study was the comparison of the clinical outcomes between the two groups. The secondary outcome was the identification of possible risk factors associated with PI in the entire population.

Statistical analysis

Quantitative data were reported as either the mean ± standard deviation (range) or median ± range. Normally distributed quantitative data were analyzed with Student's t tests. Qualitative data were reported as the number of patients (percentage of patients) and were compared with the Pearson χ^2 test. Univariate and multivariate logistic regression analyses for factors associated with postoperative ileus were conducted on patients without anastomotic leakage or abdominal abscesses. Variables with a p value < 0.1 in the univariate analysis were entered in the multivariate analysis. All analyses were performed using IBM SPSS, version 23 (IBM Co., Armonk, NY, USA). All tests were two-sided, with the significance level set at 0.05.

Results

Study population and clinicopathological data

Ninety-eight patients underwent TaTME at Fondazione Policlinico Universitario A. Gemelli IRCCS in the observed period. The first eight cases were excluded from the database due to the performance of a noncomplete standardized double-team surgical technique. According to the remaining inclusion and exclusion criteria, 74 patients were selected for

Table 1 Clinicopathologic features ($n = 74$ patients)

	LP ($n = 53$)	HP ($n = 21$)	p-value
Sex (n, %)			0.300*
Male	37 (70%)	12 (57%)	
Female	16 (30%)	9 (43%)	
Age, years (mean ± SD, range)	68.7 ± 10.6 (47–87)	72.4 ± 9.6 (44–88)	0.172**
BMI, kg/m^2 (mean ± SD, range)	26.5 ± 4.1 (19.5–41.3)	23.7 ± 3.6 (14.3–28.5)	0.007**
Preoperative Hb, g/dl (mean ± SD, range)	12.5 ± 2.2 (8.5–16.6)	12.6 ± 2.1 (8.6–16.2)	0.858**
ASA classification (n, %)			0.515*
ASA I	2 (3.8%)	2 (9.5%)	
ASA II	46 (86.8%)	18 (85.7%)	
ASA III	5 (9.4%)	1 (4.8%)	
Previous abdominal surgery (n, %)	16 (30%)	9 (43%)	0.310*
Operative time, min (mean ± SD, range)	286 ± 56 (180–427)	288 ± 44 (216–420)	0.848**
Neoadjuvant therapy (n, %)	31 (58.5%)	13 (61.9%)	0.787*
Tumor stage (n, %)			0.842*
0	11 (20.7%)	4 (19%)	
I	18 (34%)	5 (23.8%)	
II	13 (24.5%)	7 (33.3%)	
III	10 (18.9%)	4 (19%)	
IV	1 (1.9%)	1 (4.8%)	

*χ^2 test

**Student's t test

this study. Patients were divided into 2 groups: 53 patients in the LP group and 21 patients in the HP group.

The clinicopathological features are reported in Table 1. There were no significant differences in terms of clinicopathologic features except for the mean BMI, which was greater in the LP group than in the HP group (26.5 ± 4.1 kg/m^2 vs. 23.7 ± 3.6 kg/m^2, $p = 0.007$). The mean operating times were 286 ± 56 min in the LP group (180–427) and 288 ± 44 min in the HP group ($p = 0.848$). Neoadjuvant treatment was administered to 31 (58.5%) patients in the LP group and 13 patients (61.9%) in the HP group ($p = 0.787$).

Postoperative outcomes

The postoperative outcomes are reported in Table 2. Both the LP and HP groups displayed a similar mean time to first flatus, time to first stool and time to tolerate oral feeding with fluids. The time to tolerate oral feeding with solid foods was longer in the HP group than in the HP group (1.68 ± 1.75 days in the LP group and 2.86 ± 3.05 days in the HP group, $p = 0.041$).

The rate of postoperative complications was similar between the two groups, with no significant differences except for the rate of postoperative ileus, which occurred in seven patients (13.2%) in the LP group and seven patients (33.3%) in the HP group ($p = 0.046$). The mortality rate (1.9% in the LP group vs. 0% in the HP group), the reoperation rate (3.8% in the LP group vs. 0% in the HP group) and the readmission rate (5.7% in the LP group vs. 0% in the HP group) were not significantly different between the two groups. The mean day of discharge (6.11 ± 3.42 in the LP group and 7.10 ± 4.29 in the HP group, $p = 0.304$) did not show any significant difference between the two groups.

Univariate and multivariate logistic regression analyses

A univariate analysis was performed across the entire population to analyze the possible risk factors associated with PI. Patients presenting with PI and contemporary anastomotic leakage or intraabdominal abscess (one patient) were excluded from the analysis. The following risk factors were considered: sex, age, BMI, ASA score, previous abdominal surgery, neoadjuvant therapy, tumor stage, operative time, CO_2 insufflation pressure and pathologic stage. According to the univariable analysis, sex, operative time and CO_2 insufflation pressure obtained a p value < 0.1 and were included in the multivariate analysis. The multivariate analysis demonstrated that a high CO_2 insufflation pressure (OR 7.040, 95% CI 1591–31,164, p value 0.01) and male sex (OR 10,343, 95% CI 1078–99,256, p value 0.043) were significantly associated with PI, while the operative time did not reach statistical significance ($p = 0.083$). These results are reported in detail in Table 3.

Table 2 Postoperative outcomes after TaTME ($n = 74$ patients)

	LP ($n = 53$)	HP ($n = 21$)	p value
Time to first flatus, days (mean ± SD, range)	1.62 ± 0.86 (1–5)	1.71 ± 1.1 (1–5)	0.705**
Time to first stool, days (mean ± SD, range)	1.87 ± 1.04 (1–6)	2.14 ± 1.52 (1–6)	0.375**
Time to oral feeding (FLUIDS), days (mean ± SD, range)	1.25 ± 1.63 (1–10)	2.03 ± 3.14 (1–12)	0.190**
Time to oral feeding (SOLIDS), days (mean ± SD, range)	1.68 ± 1.75 (1–10)	2.86 ± 3.05 (1–12)	0.041**
Postoperative blood transfusions (n, %)	1 (1.9%)	0	0.526*
Postoperative complications (n, %)	24 (45.3%)	8 (38.1%)	
Anastomotic leakage	5 (9.4%)	0	0.145*
Intrabdominal abscess	1 (1.9%)	0	0.524*
Cardiopulmonary complications	4 (7.5%)	0	0.160*
Wound infections	0	0	
Bleeding	0	0	
Urinary tract infection	2 (3.8%)	1 (4.8%)	0.846*
Postoperative ileus	7 (13.2%)	7 (33.3%)	0.046*
Other	5 (9.4%)	0	0.145*
Reoperations (n, %)	2 (3.8%)	0	0.367*
Postoperative mortality (n, %)	1 (1.9%)	0	0.526*
Discharge, days (mean ± SD, range)	6.11 ± 3.42 (3–17)	7.10 ± 4.29 (3–19)	0.304**
Readmission within 30 days, days (n, %)	3 (5.7%)	0	0.266*

*χ^2 test

**Student's t test

Table 3 Univariate and multivariate logistic regression analyses (*n* = 73 patients)

Univariate analysis			
Factor	OR	95% CI	*p* value*
Age	1.024	0.964–1.088	0.446
Sex (male vs female)	8.000	0.975–66.615	**0.053**
CO_2 pressure (HP vs LP)	3.833	1.105–13.296	**0.034**
BMI	0.999	0.997–1.001	0.182
Preoperative hemoglobin	1.010	0.980–1.040	0.534
Previous abdominal surgery	0.557	0.138–2.248	0.411
ASA score < 3 vs = 3	–	–	1
Neoadjuvant therapy	0.496	0.148–1.665	0.256
Operative length	1.012	1.001–1.024	**0.039**
p/yp stage 0 (ref)			0.659
p/yp stage I	1.667	0.277–10.034	0.577
p/yp stage II	0.667	0.082–5.399	0.704
p/yp stage III	1.636	0.229–11.703	0.624
p/yp stage IV	6.000	0.257–140.045	0.265
Multivariate analysis			
Factor	OR	95% CI	*P* value*
CO_2 pressure (HP vs LP)	7.040	1.591–31,164	**0.010**
Sex (male vs female)	10.343	1.078–99.256	**0.043**
Operative time	1.013	0.998–1.027	0.083

*Wald test

OR Odd ratio, *CI* Confidence interval

Discussion

In this study, a high CO_2 insufflation pressure creating a gradient from the transanal to the transabdominal surgical field during TaTME was investigated as a possible risk factor for PI. The results of this study identified high CO_2 insufflation from the transanal field and male sex as independent risk factors for postoperative ileus. In patients in the HP group, there was a significant delay in the postoperative intake of solid foods, and the discharge date was delayed by one full day, even though this difference did not reach statistical significance.

During minimally invasive surgery, an intra-abdominal pressure between 12 and 15 mmHg is considered safe and effective to guarantee the visualization and manipulation of instruments [8]. However, excessive abdominal pressure is well known to cause hemodynamic changes, decreased pulmonary compliance, altered blood gas parameters, decreased kidney and liver perfusion, decreased venous blood return from the lower extremities, and even increased risk of arrhythmias and cardiac events [9–12]. Additionally, a high CO_2 pressure may be responsible for postoperative pain, making postoperative recovery less comfortable [13]. The association between pneumoperitoneum and PI is controversial. Previous animal studies did not demonstrate a significant association between prolonged pneumoperitoneum and PI [14, 15]. Instead, a recent study by Rohloff et al. documented a reduced rate of PI in patients undergoing robotic rectal resection when the pneumoperitoneal pressure was 12 mmHg instead of 15 mmHg [16]. Moreover, a 2016 study from Christensen et al., investigating the effect of low pneumoperitoneal pressure during robotic prostatectomy, reported a reduced rate of postoperative ileus in patients in the low-pressure group [17].

Postoperative ileus is one of the most frequent postoperative complications after abdominal surgery. The development of PI lengthens patient recovery time and delays resumption of oral feeding and postoperative discharge, therefore, increasing the cost of hospitalization. PI is well known to be associated with other postoperative complications [18, 19]. Among patients who developed PI in this study, only one had a contemporary intra-abdominal complication (anastomotic leakage). Considering PI as a possible consequence of anastomotic leakage, patients with other intraoperative complications were excluded from the logistic analysis in this study. Currently, the most common cause of postoperative paralytic ileus is the inflammatory response resulting from intestinal manipulation and trauma. Other possible causes are alterations in the physiology of neural reflexes and neurohumoral peptides. Most recently, PI after colorectal surgery has been associated with alterations in the composition of bowel microbiota [18, 20, 21]. The risk for PI has also been linked to other conditions that adversely affect gastrointestinal motility, including diabetes and chronic obstructive pulmonary disease [22]. Sex has been significantly associated with PI in many other studies, with male sex being consistently reported to be most affected. This association has been attributed to underlying confounders, such as specific medical comorbidities or anatomical characteristics of the male sex that may affect the difficulty of surgical procedures (i.e., narrow pelvis) [23, 24].

This is the first study reporting a possible role of high CO2 insufflation pressure in the occurrence of postoperative ileus after TaTME. The main advantage of this study is its homogeneous population, consisting of patients managed with the same protocol and operated on with a standard technique by the same surgeons. Moreover, to exclude possible confounders, univariate and multivariate logistic regression analyses for factors associated with postoperative ileus were conducted on patients without anastomotic leakage or abdominal abscesses. This study has some limitations, the main one being its relatively small sample size, which may have reduced its power. Another possible limitation is the slight significant differences between the two groups in terms of BMI (greater in the LP group than in the HP group). However, this difference may actually strengthen the results of this study. Indeed, patients with a higher BMI may be considered more at risk of PI, as they often need additional small bowel manipulation due to the technical challenges of operating within a reduced surgical field [6]. Consistently, these patients have been reported to be more subject to PI in previous studies [25]. In our study, BMI was assessed in the logistic analysis without detecting a significant association with PI. For these reasons, we believe that this difference does not compromise the results of the analysis. To further support our results, the potential adverse effects of high-pressure insufflation during mini-invasive rectal resections could be investigated with different study methodologies (i.e., prospective studies, propensity score matching).

The results of this study have some relevant implications. First, they prompt the cautious management of the gradient between the transanal and abdominal CO_2 insufflation pressures to ameliorate the postoperative outcomes after TaTME. Second, they stimulate the debate on the causes of postoperative ileus, which remains one of the poorly understood complications occurring after colorectal surgery.

Conclusions

Transanal total mesorectal excision is a relatively novel technique that still needs complete standardization to minimize the occurrence of postoperative complications strictly related to the surgical technique. In this study, the occurrence of postoperative ileus after TaTME was significantly associated with a high CO_2 insufflation pressure. According to these results, the CO_2 insufflation pressure during TaTME should be carefully set and equalized once the abdominal and transanal surgical fields are in communication.

Authors' contribution RP, MG and AB designed the study, performed most of the surgery and revised the manuscript. MG, FT, AA and PS collected data, analyzed data, and wrote the manuscript. All authors agreed on the final version of the manuscript and are accountable for all the aspect of the work. All authors will ensure that question related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

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Data availability The dataset generated during the current study are available from the corresponding author on reasonable request.

Code availability BM SPSS, version 23 (IBM Co., Armonk, NY, USA).

Declarations

Conflict of interests Dr. Michele Grieco, Dr. Flavio Tirelli, Dr. Annamaria Agnes, Dr. Pietro Santocchi, Dr. Alberto Biondi and Prof. Roberto Persiani have no conflicts of interest to declare that are relevant to the content of this article.

Ethical approval This study follows the ethical standards and was approved by the institutional Ethics Committee and conducted according to the declaration of Helsinki.

Consent to participate Informed consent was obtained from all patients.

Consent for publication Informed consent was obtained from all patients.

Research involving human participants All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript. The authors have no financial or proprietary interests in any material discussed in this article.

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