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Effects of a multifaceted individualized pneumoperitoneum strategy in elderly patients undergoing laparoscopic colorectal surgery

A retrospective study

Liping Liu, MD, Na Lv, MD, Chunmiao Hou, MD*

Abstract

Background: Laparoscopic colorectal surgery may adversely affect respiration, circulation, and acid-base balance in elderly patients, owing to the relatively long duration of CO_2 absorption. We conducted this retrospective study to determine the safety and efficacy of warmed, humidified CO_2 pneumoperitoneum in elderly patients undergoing laparoscopic colorectal surgery.

Methods: We enrolled 245 patients between January 2016 and August 2018.

The experimental group (warming and humidification group [WH]) received warmed (37°C), humidified (98%) insufflation of CO_2, and the control group (cold, dry CO_2/control group [CD]) received standard CO_2 (19°C, 0%). All other aspects of patient care were standardized. Intraoperative hemodynamic data, arterial blood pH, and lactic acid levels were recorded. We also recorded intra-abdominal pressure, incidence of shivering 1 hour after surgery, satisfaction scores of patients and surgeons 24 hours after surgery, times to first flatus/defecation, first bowel movement, and tolerance of semiliquid food, discharge time, and incidence of vomiting, diarrhea, and surgical site infections.

Results: Compared with the WH group, heart rate and mean arterial pressure were significantly higher from T3 to T8 ($P < .05$), lactic acid levels were significantly higher from T4 to T9 ($P < .05$), and recovery time in the post-anesthesia care unit (PACU) was significantly longer in the CD group ($P < .05$). Patient and surgeon satisfaction scores were significantly higher in the WH group than the CD group ($P < .05$). In addition, the times to first flatus/defecation and bowel movement were significantly longer in the CD group ($P < .05$). No significant differences were noted between the groups in the time to tolerance of semiliquid food and time of discharge ($P > .05$). The incidence of vomiting, diarrhea, and shivering was significantly lower in the WH group ($P < .05$). The number of patients with a shivering grade of 0 was significantly higher in the WH group, whereas the number with a shivering grade of 3 was significantly higher in the CD group ($P < .05$).

Conclusion: Warmed, humidified insufflation of CO_2 in elderly patients undergoing laparoscopic colorectal surgery could stabilize hemodynamics, and reduce lactic acid levels, recovery time in the PACU, and the incidence of acute gastrointestinal injury-related symptoms.

Abbreviations: AGI = acute gastrointestinal injury, AHFI = acute hypervolemic fluid infusion, ASA = American Society of Anesthesiologists, BIS = bispectral index, CD = cold, dry CO_2/control group, GI = gastrointestinal, HR = heart rate, IAP = intra-abdominal pressure, MAP = mean arterial pressure, PACU = post-anesthesia care unit, PEEP = positive end-expiratory pressure, PTC = post-tetanic count, SSI = surgical site infections, TOF = train of 4 stimulation, WH = warming and humidification group.

Keywords: carbon dioxide, elderly patients, hypothermia, laparoscopic colorectal surgery, pneumoperitoneum

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Department of Operation Room, Liaocheng People's Hospital, Liaocheng, Shandong, China.

* Correspondence: Chunmiao Hou, Department of Operation Room, Liaocheng People's Hospital, Liaocheng, Shandong, China (e-mail: xzpdllp@163.com).

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1. Introduction

Laparoscopy has been widely used in abdominal surgery since 1987, especially in the field of gastrointestinal (GI) surgery. It has now become the main strategy for minimally invasive techniques.[1–3] However, laparoscopic colorectal surgery may produce noticeable adverse effects on respiration, circulation, and the acid-base balance of patients, owing to the relatively long duration of carbon dioxide (CO_2) absorption.[4,5] These effects seem more common among elderly patients, who usually have coexisting systemic disorders.[6–8] Guidelines for laparoscopic abdominal surgery recommend the use of the lowest possible intra-abdominal pressure (IAP) rather than a standard level of IAP, as high IAP is associated with peritoneal damage, impaired splanchnic, hepatic, and abdominal wall perfusion, decreased gastric mucosal oxygen saturation, and postoperative pain.[9–11]

Earlier data suggest that cold, dry gas can cause structural and biochemical injury to the peritoneal mesothelium, which results in a local inflammatory and cytokine response that may increase postoperative pain, and potentially contribute to adhesion formation, tumor seeding, and systemic progression.[12,13] However, more recent evidence from high quality, randomized controlled trials and a Cochrane meta-analysis have shown no difference in postoperative pain scores or opiate use with warming and humidification.[14,15] Surgical site infections (SSIs) represent up to 20% of all healthcare-associated infections.[16] Previous studies report that surgery on the colon and rectum is responsible for the highest incidence of SSIs across all surgical specialties.[17] The aim of this study was to investigate the effects of a multifaceted individualized pneumoperitoneum strategy on elderly patients undergoing laparoscopic colorectal surgery.

2. Materials and methods

2.1. Patients

The Ethics Committee of Liaocheng People's Hospital, Shandong, China approved the protocol of this study (No. 2017051). The project was also in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. This trial was also registered at chictr.org (ChiCTR-IOR-17010915). Patients were considered eligible if they: had a biopsy-proven histological diagnosis of colorectal carcinoma; were scheduled for laparoscopic colorectal surgery; were aged between 65 and 75 years; and had an American Society of Anesthesiologists (ASA) physical status of I to III. Exclusion criteria included: body mass index (BMI) $>30\,kg/m^2$; emergency or unplanned surgery; clinical evidence of metastasis; immunologic, cognitive, or neuromuscular diseases; serious cardiopulmonary, renal, or hepatic diseases; abnormal coagulation function; history of allergy to gelatin; and conversion to open surgery. Data were acquired from electronic charts and a DoCare Clinic electronic anesthesia recording system.

2.2. Standard procedures

No preoperative medication was used. A nasogastric tube was inserted before the induction of anesthesia. Once the patient was moved into the operating room, a Datex S/5 monitor was used for noninvasive blood pressure, electrocardiogram, blood oxygen saturation, and continuous neuromuscular monitoring. An intravenous infusion was established in the left forearm, and a single dose of midazolam (0.04 mg/kg) was administered. Esophageal temperature was measured as an indicator of core body temperature. Under local anesthesia, a catheter was placed in the left radial artery and blood samples were collected at different time points. Patients received an intravenous infusion of 10 mL/kg of gelatin within 30 minutes of entering the operating room. Intraoperative patient warming consisted of a forced-air warming blanket and intravenous fluid warmers. Before induction with the general anesthetic, all patients received intravenous antibiotic prophylaxis, and a repeat dose was administered if the operation was longer than 3 hours. Anesthesia was induced using propofol (1.5–2 mg/kg), fentanyl (2–4 μg/kg), and cisatracurium (0.2 mg/kg). Pure oxygen was manually delivered to the patients for 3 minutes to remove nitrogen. After tracheal intubation, mechanical ventilation was conducted with a mixed gas flow of 1.5 L/min.

During the operation, intravenous administration of propofol target-controlled infusion (2–2.6 μg/mL) and inhalation of 0.6 minimum alveolar concentration sevoflurane was combined to maintain a bispectral index between 50 and 60. Intravenous injections of fentanyl and cisatracurium were also administered to maintain a stable depth of anesthesia. Tidal volume was 6 to 8 mL/kg, positive end-expiratory pressure (PEEP) was set at 5 mm Hg, oxygen inspiratory fraction was 0.8, and respiratory rate was 12 to 15 per minute to maintain an end-tidal (ET) CO_2 of 35 to 45 mm Hg. The pressure limit was modulated so that the peak airway pressure (Ppeak) would not exceed 25 cm H_2O. Throughout the surgery, neuromuscular blockade maintained a train of 4 stimulation (TOF) of 0, and a post-tetanic count (PTC) between 1 and 5. We also adopted the modified lithotomy position during surgery to increase the anteroposterior intra-abdominal space by correcting lumbar lordosis. An electronic CO_2 gas insufflator (Endoflator, Karl Storz, Tuttlingen, Germany) was used for CO_2 insufflation into the abdominal cavity through a laparoscopic trocar, which was warmed to 37°C and humidified to 98% using a laparoscopic humidification system (Fisher & Paykel Healthcare Ltd, Auckland, New Zealand) in the experimental (warming and humidification group [WH]) group. If operating space was insufficient, surgeons who were blinded to the level of IAP could have requested an increase in IAP at any time, in 1 mm Hg steps, up until 15 mm Hg. The laparoscopic procedures were standardized and performed by an identical surgical team in all groups. A small incision, with varying size that corresponded to the resection specimen, was performed to achieve anastomosis.

Hypertension was treated with an infusion of 10 to 15 mg urapidil to maintain the systolic blood pressure <140 mm Hg and the diastolic pressure <90 mm Hg. Hypotension was treated with bolus doses of ephedrine 6 to 12 mg. For persistent bradycardia (pulse <50 bpm), atropine 0.2 to 0.4 mg was administered. If clinically significant oliguria (less than 40 mL/h) was detected, an infusion of furosemide 10 mg was administered. At the end of the operation, the neuromuscular block was antagonized with neostigmine and atropine.

2.3. Data collection

We recorded intraoperative hemodynamic data, arterial blood pH (pHa), and lactic acid levels at the following time points: at baseline (T0); before induction (T1); before pneumoperitoneum (T2); 10 (T3), 30 (T4), 60 (T5), and 90 minutes (T6) into pneumoperitoneum; and 5 (T7), 10 (T8), and 15 minutes (T9) after pneumoperitoneum. We also recorded IAP during surgery; the incidence of shivering 1 hour after surgery (on a 5-point scale as follows: 0 = no shivering; 1 = piloerection or peripheral vasoconstriction, but no visible shivering; 2 = muscular activity in only 1 muscle group; 3 = muscular activity in more than 1 muscle group, but not generalized; and 4 = shivering involving the whole body)[18]; satisfaction scores of patients and surgeons 24 hours after surgery (on a 10-point scale from 0 = poor, to 10 = excellent); time to first flatus/defecation; time to first bowel movement; time to tolerance of semiliquid food (criteria included: normothermia; no adverse reactions with liquid food; and normal defecation/free flow through stoma), the incidence of vomiting, diarrhea, SSIs (objective clinical and microbiological criteria used, according to guidance from Public Health England)[19]; and the discharge time (criteria included: normothermia; tolerance of semiliquid food for more than 24 hours; and normal defecation/free-flow through stoma).

2.4. Statistical analysis

The Kolmogorov–Smirnov test was used to assess the distribution of variables. Homogeneity of variance was determined using the Levene test. Quantitative data were expressed as mean and standard deviation or median and interquartile range. Intergroup comparisons were performed using repeated-measure analysis of variance. Bonferroni correction was used for post-hoc multiple comparisons. The nonparametric Wilcoxon—Mann—Whitney test was used for variables that were not normally distributed. Categorical data were expressed as frequency and percentage, and analyzed using the chi-squared test or Fisher exact test, when appropriate. Probability (*P*) values <.05 were considered statistically significant. Statistical analysis was performed with the SPSS for Windows (Version 22.0) software.

3. Results

3.1. Baseline characteristics

Figure 1 shows the flow diagram of patient enrollment. A total of 323 elderly patients undergoing laparoscopic colorectal surgery between January 2016 and August 2018 were enrolled in the study. Seventy-eight patients were excluded: 21 patients had a BMI >30 kg/m^2; 12 patients had emergency or unplanned surgery; 9 patients had clinical evidence of metastasis; 9 patients had immunologic, cognitive, or neuromuscular diseases; 12 patients had serious cardiopulmonary, renal, or hepatic diseases; 5 patients had abnormal coagulation function; 3 patients had a history of allergies to gelatin; and 7 patients underwent conversion to open surgery. Thus, 245 elderly patients were included and divided into 2 groups, according to the different methods of pneumoperitoneum: the WH group (intraoperative CO_2, warmed to 37°C and humidified to 98%, n=125); and the cold, dry CO_2/control group (CD) group (intraoperative cold and dry CO_2, n=120).

No significant differences were noted between the 2 groups with respect to age, BMI, gender, ASA grade, operating room temperature, intraoperative blood loss, total infused fluid, IAP, total volume CO_2 used, comorbidity, conversion to laparotomy, or the duration of anesthesia and operation (Table 1).

3.2. Perioperative characteristics

Baseline HR and MAP showed no significant differences between the 2 groups ($P>.05$, Fig. 2). Compared with the WH group, both HR and MAP in the CD group were significantly higher from T3 to T8 ($P<.05$, Fig. 2). No significant differences in pHa from T0 to T9 ($P>.05$, Fig. 3) were noted between the 2 groups. In comparison to the WH group, lactic acid levels in the CD group were significantly higher from T4 to T9 ($P<.05$, Fig. 4). Furthermore, recovery time in the post-anesthesia care unit (PACU) was significantly longer in the CD group ($P<.05$, Table 1). The satisfaction scores of both patients and surgeons were significantly higher in the WH group than in the CD group ($P<.05$, Table 2).

In compared to the WH group, both the times to first flatus/defecation and bowel movement were significantly longer in the CD group ($P<.05$, Table 3). However, no significant differences

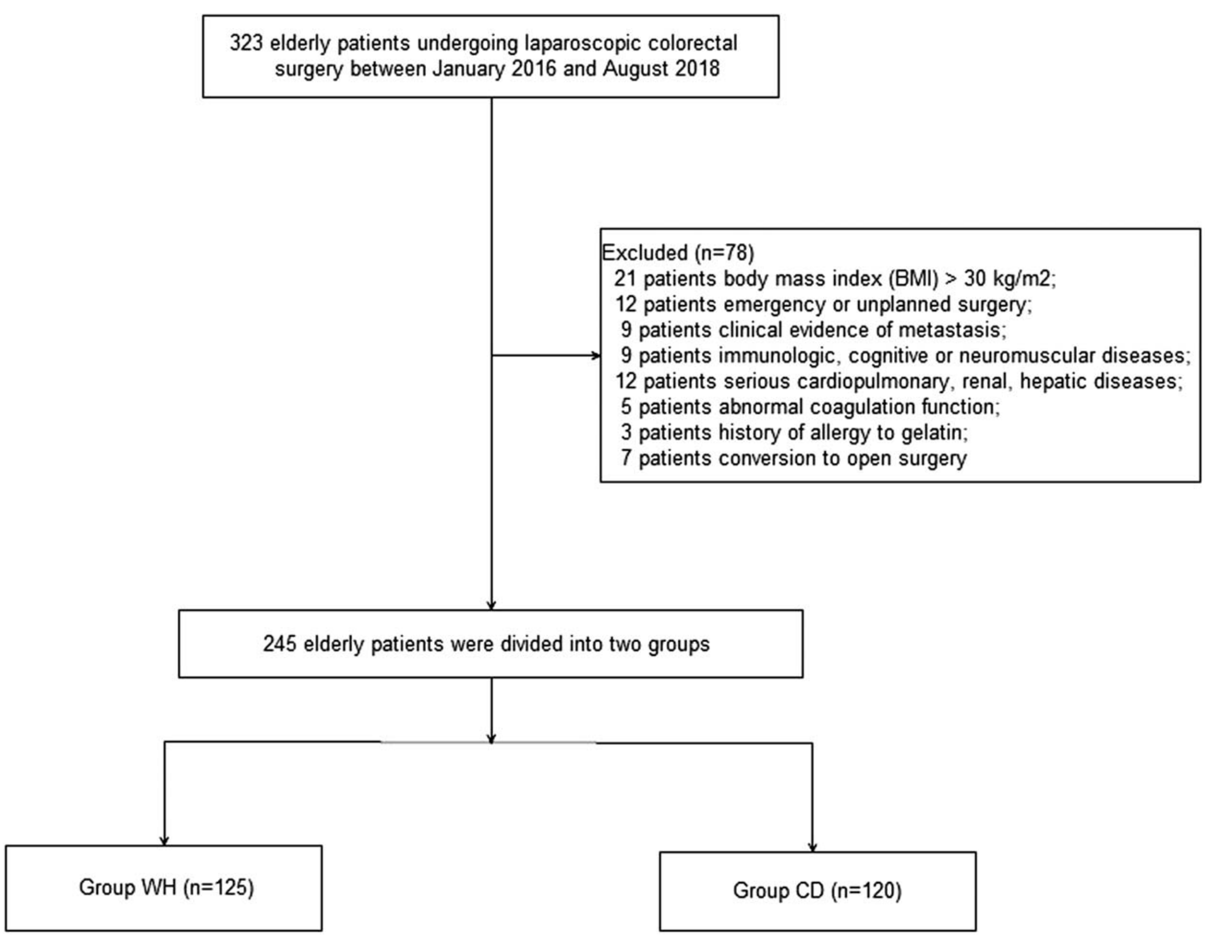

Figure 1. Patient enrollment diagram illustrating the flow of all patients screened and excluded.

Table 1

Patients' characteristics and intraoperative data.

	Group WH (n=125)	Group CD (n=120)	*P*-values
Age, yr	68.81±5.23	67.53±5.16	.054
BMI, kg/m^2	24.32±4.01	23.88±3.92	.385
Gender (M/F)	65/60	55/65	.334
ASA I/II/ III (n)	22/76/27	27/73/20	.470
OR temperature, °C	23.53±1.94	23.89±1.12	.165
Comorbidity, n (%)			.957
Hypertension	73 (58.40%)	77 (64.17%)	
Diabetes mellitus	24 (19.20%)	27 (22.50%)	
Coronary heart disease	16 (12.80%)	19 (15.83%)	
Atrial fbrillation	7 (5.60%)	5 (4.17%)	
Cerebral infarction	5 (4.00%)	6 (5.00%)	
Total infused fluid, mL	1150 (825–2215)	1230 (725–2550)	.271
Intraoperative blood loss, mL	200 (105–315)	175 (85–275)	.065
Duration of surgery, min	152.78±25.38	148.82±38.37	.317
Duration of anesthesia, min	182.64±37.72	179.71±29.95	.512
Conversion to laparotomy, n (%)	12 (9.60%)	14 (11.67%)	.600
Intra-abdominal	12.83±2.31	13.44±3.55	.112
Pressure, mm Hg			
Volume CO_2 used, L	103.29±20.38	100.23±25.16	.056
Recovery time of PACU, min	25.17±5.45	36.74±9.02*	.012

The variables are presented as mean±SD, median (interquartile range) or number of patients, n (%).
ASA=American Society of Anesthesiologists, BMI=body mass index, CD = cold, dry CO_2/control group, OR=operating room, WH = warming and humidification group.
* $P<.05$ versus Group WH.

were noted in the time to tolerance of semiliquid food and time of discharge between the 2 groups ($P>.05$, Table 3). The incidence of vomiting and diarrhea in the WH group was significantly lower than that in the CD group ($P<.05$, Table 3). However, no significant differences were noted in the occurrence of SSIs between the 2 groups ($P>.05$, Table 3).

Compared to patients in the WH group, those in the CD group had a significantly higher incidence of shivering ($P<.05$, Table 4). The number of patients with a shivering grade of 0 was significantly higher in the WH group, whereas the number of patients with a shivering grade of 3 was significantly higher in the CD group ($P<.05$, Table 5). In contrast, no significant differences were noted between the 2 groups with respect to the incidence of arrhythmia, hypertension, hypotension, and delirium ($P>.05$, Table 4).

4. Discussion

Our study found that warming and humidification of insufflation CO_2 in elderly patients undergoing laparoscopic colorectal surgery could maintain the stability of hemodynamics, and reduce lactic acid levels, recovery time in the PACU, and the incidence of acute gastrointestinal injury (AGI)-related symptoms, such as time to first flatus/defecation and bowel movement. In addition, the satisfaction scores of both patients and surgeons were significantly higher.

A previous study found that a gelatin solution could maintain favorable splanchnic perfusion in elderly patients undergoing laparoscopic surgery, in comparison to both a balanced solution, and hypertonic sodium chloride hydroxyethyl starch solution.[20] Thus, all patients in the present trial received an intravenous infusion of 10 mL/kg of gelatin within 30 minutes of entering the operating room. Previous studies have also reported that acute hypervolemic fluid infusion (AHFI) before the induction of anesthesia is 1 method of intraoperative volume management, which could improve tissue oxygen supply, stabilize hemodynamics during anesthesia, and reduce the loss of blood, especially in elderly patients who depend mainly on an increase in the end-diastolic volume to improve cardiac output.[21,22] The GI mucosa is very sensitive to both ischemia and hypoxia, and its recovery is slower than that of other organs.[23] The method of AHFI applied may partly account for the lower levels of lactic acid, hemodynamic fluctuations, and incidence of AGI-related symptoms observed in the present study, in comparison to those reported in a previous study.[24]

Laparoscopic colorectal surgery routinely uses a 15 mm Hg CO_2 pneumoperitoneum and an anti-Trendelenberg position to maintain sufficient intra-abdominal space for the surgical procedure. However, this may be deleterious to the respiratory and circulatory systems, and maintenance of the acid–base balance, especially in elderly patients.[6] A previous study found that a multifaceted individualized pneumoperitoneum strategy is feasible, and can create adequate working space in most patients, without major changes in cardiac output due to compensatory mechanisms.[7] We adopted a multifaceted pneumoperitoneum strategy based on a previous study: ventilation with low tidal volume (6–8 mL/kg); a modified lithotomy position; deep neuromuscular blockade (maintained TOF of 0, and PTC between 1 and 5); prestretching of the abdominal wall; and individualized IAP titration (PEEP set at 5 mm Hg, oxygen inspiratory fraction of 0.8, and respiratory rate of 12 to 15 per minute to maintain $ETCO_2$ of 35–45 mm Hg, Ppeak $\leq$25 cm H_2O) and most of all warmed to 37°C and humidified to 98% CO_2 pneumoperitoneum. As a result, the number of patients with shivering was less than previous studies, at the same time, the recovery time was shorter.[4,14] We also found no significant differences in IAP during surgery between the groups. Increasing evidence shows that elevated IAP could disturb the mesenteric circulation. Splanchnic hemodynamics are generally considered to change drastically if IAP exceeds 15 mm Hg.[25] Several

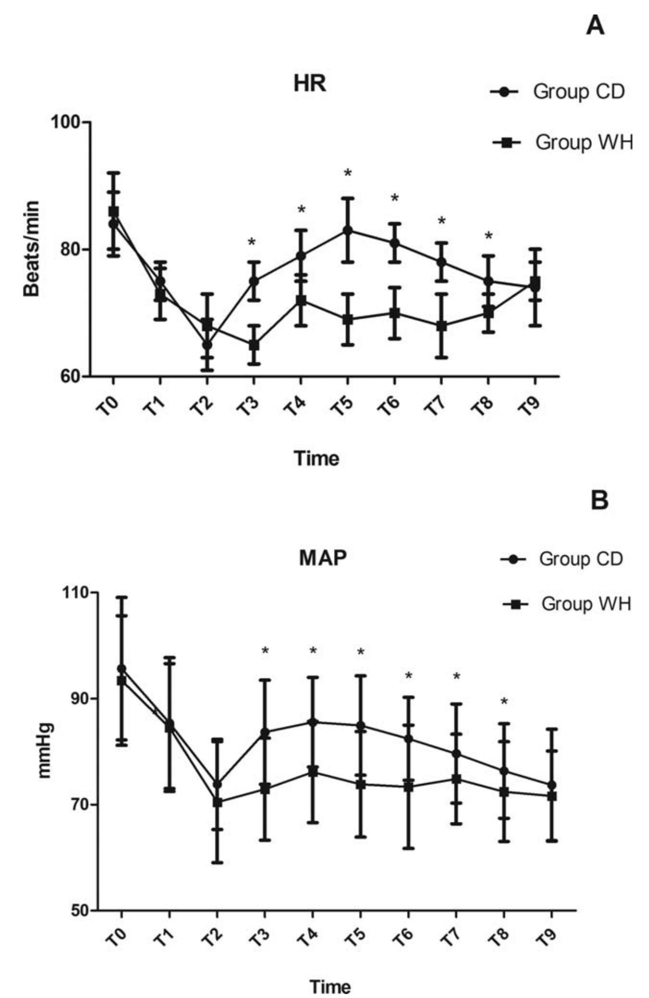

Figure 2. Intraoperative hemodynamic data monitored between the 2 groups at the following time points: at baseline (T0); before induction (T1); before pneumoperitoneum (T2); 10 (T3), 30 (T4), 60 (T5), and 90 min (T6) into pneumoperitoneum; and 5 (T7), 10 (T8), and 15 min (T9) after pneumoperitoneum. *$P < .05$ versus the WH group. WH = warming and humidification group.

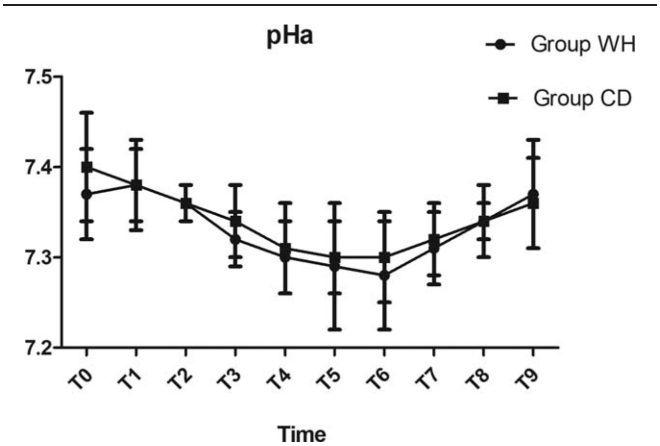

Figure 3. Intraoperative pHa monitored between the experimental (WH) and control (CD) groups at the following time points: at baseline (T0); before induction (T1); before pneumoperitoneum (T2); 10 (T3), 30 (T4), 60 (T5), and 90 min (T6) into pneumoperitoneum; and 5 (T7), 10 (T8), and 15 min (T9) after pneumoperitoneum. CD = cold, dry CO_2/control group, pHa = arterial blood pH, WH = warming and humidification group.

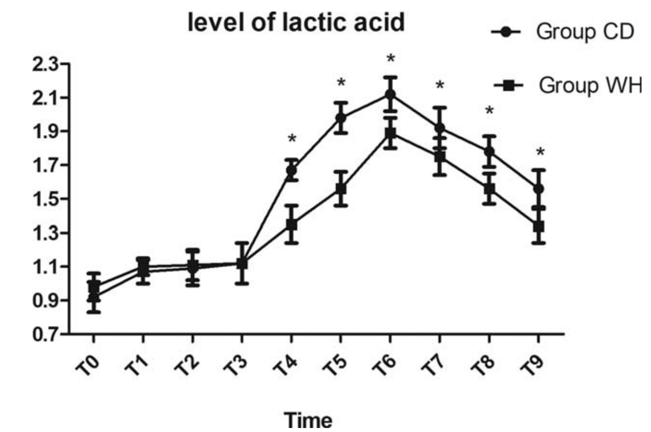

Figure 4. Intraoperative levels of lactic acid monitored between the 2 groups at the following time points: at baseline (T0); before induction (T1); before pneumoperitoneum (T2); 10 (T3), 30 (T4), 60 (T5), and 90 min (T6) into pneumoperitoneum; and 5 (T7), 10 (T8), and 15 min (T9) after pneumoperitoneum. *$P < .05$ versus the WH group. WH = warming and humidification group.

mechanisms have been considered. First, increased IAP has a direct effect. The intrathoracic pressure will be increased as the diaphragm is pushed upward. As a result, visceral vessels of the abdominal organs can be indirectly affected, as the trunks of these major vessels are located within the thoracic cavity. Second, hypercapnia-induced sympathicotonus may be the result of peripheral and mesenteric vasoconstriction. Third, decreased renal perfusion due to kidney compression could lead to angiotensin release. Finally, hemodynamic disturbances during laparoscopic surgery are mainly due to a reduction in venous return.[26–28] Furthermore, reperfusion injury eventually leads to free radical-induced damage, which may contribute to bacterial translocation and septic complications in elderly patients.[29]

The ideal gas for pneumoperitoneum should be nontoxic, colorless, readily soluble in blood, easily ventilated through the lungs, and inexpensive. Throughout the history of laparoscopic procedures, many gases have been used to establish pneumoperitoneum, including room air, nitrous oxide, oxygen, and CO_2.[30,31] Patients undergoing laparoscopic colorectal surgery often suffer from hypercapnia and serum acidosis due to the long-term absorption of CO_2. Hypercapnia increases the incidence of cardiac arrhythmias and decreases cardiac output.[32] Consistent with a previous study, we also observed electrolyte disturbances and metabolic acidosis. However, these parameters gradually returned to baseline levels after surgery. Moreover, the overall variations were within our management, and patients had no complaints of severe discomfort.[4]

Table 2

Satisfaction scores of patients and surgeons.

	Group WH (n=125)	Group CD (n=120)	*P*-values
Patients satisfaction score	8.25 (7.25–9.75)	7.50 (6.75–9.25)*	.012
Surgeon satisfaction score	9.25 (8.25–9.75)	8.75 (7.25–9.75)*	.045

Variables presented as median (interquartile range).

CD = cold, dry CO_2/control group, WH = warming and humidification group.

*$P < .05$ versus Group WH.

Table 3

AGI correlated parameters between the 2 groups.

	Group WH (n=125)	Group CD (n=120)	*P*-values
Time to first flatus/defecation, h	20.23 (14.35–24.65)	28.25 (17.45–38.65)*	.023
Time to first bowel movement, h	18.84 (15.65–22.31)	25.37 (18.69–32.17)*	.045
Time to tolerance of semiliquid food, h	125.27 (110.54–142.37)	137.69 (116.43–156.32)	.268
The occurrence of vomiting, n (%)	93 (74.40%)	105 (87.50%)*	.009
The occurrence of diarrhea, n (%)	102 (81.60%)	113 (94.17%)*	.003
The occurrence of SSI, n (%)	7 (5.60%)	11 (9.17%)	.285
The discharge time, d	8.5 (6.5–10.5)	9.0 (7.0–11.5)	.132

Variables presented as median (interquartile range).
AGI = acute gastrointestinal injury, CD = cold, dry CO_2/control group, SSI=surgical site infections, WH = warming and humidification group.
* $P<.05$ versus Group WH.

As proposed by the Working Group on Abdominal Problems of the European Society of Intensive Care Medicine in 2012, AGI can be commonly observed in postoperative patients after abdominal surgery.[33] The incidence of AGI has been significantly reduced within recent years owing to improvements in laparoscopic colorectal surgery and perioperative care. Postoperative AGI-related symptoms are induced by the insufflation and desufflation of CO_2 pneumoperitoneum, while IAP is increased up to 12 mm Hg. The times to first bowel movement, first flatus/defecation, and tolerance of semiliquid food in the WH group were consistent with the results of a previous study.[24]

Other previous studies have reported that warming and humidifying CO_2 significantly decreases the risk of SSIs, and reduces readmission rates and length of hospital stay.[13,34] This differences may be due to the different types of surgery and insulation measures. Hypothermia results in subcutaneous vasoconstriction, and decreased oxygen tension in this layer at a wound site increases the risk of SSIs.[35] Hypothermia also has a detrimental effect on the host's ability to mount an immune response in vitro, and decreases the ability of leucocytes to migrate, produce antibodies, and phagocytose.[36] However, we did not observe any such differences between the 2 groups in the present study, partly because of the warming strategy adopted.

The limitations of our study are as follows: First, we only compared the occurrence and recovery of GI symptoms, and thus lacked the use of objective serum biomarkers for GI function/dysfunction. Second, esophageal catheters were not used to estimate intrapleural pressures. The transpulmonary pressure ΔP, calculated from intrapleural pressures, could be more informative than the ΔP_{RS}.[37] Third, we did not adopt gastric tonometry to monitor GI perfusion, which is the only method approved by the United States Food and Drug Administration.[38] Finally, this was a single-center, retrospective trial. A multicenter prospective controlled trial would be necessary to verify the conclusion of this study.

In summary, warming and humidification of insufflation CO_2 in elderly patients undergoing laparoscopic colorectal surgery could maintain the stability of hemodynamics, and reduce lactic acid levels, recovery time in the PACU, and incidence of AGI-related symptoms.

Table 4

Comparison of the adverse events between the 2 groups.

	Group WH (n=125)	Group CD (n=120)	*P*-values
Arrhythmia	8 (6.40%)	12 (10.00%)	.304
Hypertension	12 (9.60%)	21 (17.50%)	.070
Hypotension	8 (6.40%)	10 (8.33%)	.562
Shivering	19 (15.20%)	47 (39.17%)*	.000
Delirium	7 (5.60%)	12 (10.00%)	.198

The variables are presented as number of patients, n (%).
CD = cold, dry CO_2/control group, WH = warming and humidification group.
* $P<.05$ versus Group WH.

Table 5

Comparison of the shivering grade between the 2 groups.

	Group WH (n=125)	Group CD (n=120)	*P*-values
Grade 0	75 (27.34%)	36 (13.55%)*	.000
Grade 1	28 (14.06%)	38 (4.52%)*	.102
Grade 2	12 (6.25%)	27 (4.52%)	.006
Grade 3	7 (4.69%)	13 (1.94%)	.135
Grade 4	3 (0.78%)	6 (1.94%)	.326

The variables are presented as number of patients, n (%).
CD = cold, dry CO_2/control group, WH = warming and humidification group.
* $P<0.05$ versus Group WH.

Author contributions

Liping Liu, Na Lv, Chunmiao Hou conceived and designed the trial. Liping Liu and Na Lv collected the data. Chunmiao Hou analyzed the data. Liping Liu, Na Lv, Chunmiao Hou wrote this paper.
Conceptualization: Liping Liu, Na Lv, Chunmiao Hou.
Data curation: Na Lv, Chunmiao Hou.
Writing – original draft: Liping Liu, Na Lv, Chunmiao Hou.
Writing – review and editing: Chunmiao Hou.

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