

Lower intra-abdominal pressure has no cardiopulmonary benefits during laparoscopic colorectal surgery: a double-blind, randomized controlled trial

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Abstract

Background Higher intra-abdominal pressure may impair cardiopulmonary functions during laparoscopic surgery. While 12–15 mmHg is generally recommended as a standard pressure, the benefits of lower intra-abdominal pressure are unclear. We thus studied whether the low intra-abdominal pressure compared with the standard pressure improves cardiopulmonary dynamics during laparoscopic surgery.

Methods Patients were randomized according to the intra-abdominal pressure and neuromuscular blocking levels during laparoscopic colorectal surgery: low pressure (8 mmHg) with deep-block (post-tetanic count 1–2), standard pressure (12 mmHg) with deep-block, and standard pressure with moderate-block (train-of-four count 1–2) groups. During the laparoscopic procedure, we recorded cardiopulmonary variables including cardiac index, pulmonary compliance, and surgical conditions. We also assessed postoperative pain intensity and recovery time of bowel movement. The primary outcome was the cardiac index 30 min after onset of laparoscopy.

Results Patients were included in the low pressure with deep-block (*n*=44), standard pressure with deep-block (*n*=44), and standard pressure with moderate-block $(n=43)$ groups. The mean (SD) of cardiac index 30 min after laparoscopy was 2.7 (0.7), 2.7 (0.9), and 2.6 (1.0) L min⁻¹ m⁻² in each group ($P=0.715$). The pulmonary compliance was higher but the surgical condition was poorer in the low intra-abdominal pressure than the standard pressure (both $P < 0.001$). Other variables were comparable between groups.

Conclusion We observed few cardiopulmonary benefits but poor surgical conditions in the low intra-abdominal pressure during laparoscopy. Considering cardiopulmonary dynamics and surgical conditions, the standard intra-abdominal pressure may be preferable to the low pressure for laparoscopic surgery.

Keywords Cardiac output · Laparoscopy · Lung compliance · Neuromuscular blockade · Sugammadex

The laparoscopic surgical space is created by insufflating a gas and increasing the pressure in the abdominal cavity

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[[1,](#page-8-0) [2](#page-8-1)]. However, excessively high intra-abdominal pressures may impair cardiovascular or pulmonary functions, decreasing the cardiac output or pulmonary compliance [[2–](#page-8-1)[7\]](#page-8-2). Therefore, 12–15 mmHg is generally recommended as a standard intra-abdominal pressure for laparoscopic surgery $[1-3, 6]$ $[1-3, 6]$ $[1-3, 6]$ $[1-3, 6]$ $[1-3, 6]$.

In addition to the intra-abdominal pressure, the neuromuscular block may affect the laparoscopic view [[1,](#page-8-0) [2,](#page-8-1) [7](#page-8-2)–[11](#page-8-5)]. Several previous studies suggested that the deep neuromuscular block compared with the moderate block provided acceptable surgical conditions even in the intraabdominal pressure lower than the standard level [[7](#page-8-2), [10,](#page-8-6) [11](#page-8-5)]. However, cardiopulmonary benefits of this lower intraabdominal pressure are unclear, although a few animal

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studies suggested the possibility [[12](#page-8-7), [13\]](#page-8-8). We thus studied whether the low intra-abdominal pressure compared with the standard pressure improves cardiopulmonary dynamics during laparoscopic surgery.

Materials and methods

Patients

This prospective, double-blind, single-center, parallel-group, randomized controlled trial was approved by the Institutional Review Board of Seoul National University Hospital (1405- 010-576; Seoul, Korea), and registered at ClinicalTrials.gov (NCT02249585). This trial followed the CONSORT guideline (Supplementary Material). After obtaining written informed consents, we enrolled patients aged 20–80 years with American Society of Anesthesiologists physical status I–II, and undergoing elective laparoscopic colorectal surgery. We excluded patients with allergies to anesthetic drugs, neuromuscular dysfunctions, severe cardiovascular or respiratory diseases, irregular cardiac rhythms, or body mass index of > 35 kg m⁻². Patients were randomized to one of the three groups depending on the intra-abdominal pressures and neuromuscular blocking levels during laparoscopy: the low pressure with deep-block, standard pressure with deep-block, and standard pressure with moderate-block groups. An assistant not involved in the trial created the randomization in a 1:1:1 ratio and concealed it in sealed opaque envelopes. The group assignment was blinded to patients and investigators.

Anesthesia and surgery

Attending anesthesiologists were instructed about the study protocol but not related to data analyses. Without premedication, patients were monitored with non-invasive blood pressure, pulse oximeter, three-channel electrocardiograph, bispectral index (A-2000 XP; Aspect Medical Systems, Newton, MA, USA), and two-channel cerebral oximeter (Somanetics INVOS oximeter; Covidien, Mansfield, MA, USA). For neuromuscular monitoring, an acceleromyograph (TOF-watch SX; Organon, Dublin, Ireland) was applied to the patient's left hand to obtain responses of the adductor pollicis muscle. Two stimulating electrodes were attached on the wrist over the ulnar nerve, a temperature sensor on the palm, and an acceleration transducer on the thumb.

For anesthetic induction, propofol and remifentanil were administered intravenously via effect-site target-controlled infusion (Base Primea; Fresenius Vial, Brezins, France) with Schnider [[14](#page-8-9)] and Minto [[15\]](#page-8-10) pharmacokinetic models, respectively. The initial effectsite concentrations were 4 μ g mL⁻¹ for propofol and 4 ng mL−1 for remifentanil and lactated Ringer's solution was infused at 10 mL kg⁻¹ h⁻¹. Before giving rocuronium (Esmeron; MSD, Kenilworth, NJ, USA), the acceleromyograph was calibrated and stabilized: a 50-Hz tetanic stimulation for 5 s followed by serial train-of-four (TOF) measurements within a 5% variation [[1,](#page-8-0) [7,](#page-8-2) [8,](#page-8-11) [11,](#page-8-5) [16](#page-8-12)]. During TOF stimulation every 10 s, rocuronium 0.8 or 0.4 mg kg^{-1} was given intravenously to induce deep or moderate neuromuscular blocks, respectively (Fig. [1](#page-2-0)). At the TOF count of 0 and bispectral index of < 60 , the patient's trachea was intubated with a polyvinylchloride tracheal tube with an inner diameter of 7.0 and 7.5 mm for women and men, respectively. The intra-cuff pressure was adjusted to 20–25 cm H₂O (VBM Medizintechnik GmbH, Sulz am Neckar, Germany).

A 20-gauge catheter was inserted into the right radial artery and connected to an arterial waveform analysis system (FloTrac/EV1000, version 4.0; Edwards Life Sciences, Irvine, CA, USA) for hemodynamic monitoring and blood sampling. The FloTrac sensor was placed at the level of the right atrium in the supine position, and adjusted according to the patient's positional changes. A nasogastric tube and a temperature probe were placed in the stomach and the nasopharynx, respectively.

During anesthetic maintenance, the effect-site concentrations of propofol and remifentanil were titrated within the bispectral index of 40–60, and lactated Ringer's solution was infused at 5 mL kg⁻¹ h⁻¹. The neuromuscular blocking level was checked every 10 min. Rocuronium 0.3 or 0.15 mg kg^{-1} was intermittently administered to maintain the deep neuromuscular block with a post-tetanic count 1–2 or the moderate block with a TOF count 1–2, respectively (Fig. [1\)](#page-2-0) [[7](#page-8-2), [11](#page-8-5), [17\]](#page-8-13). The blocking level was maintained until the end of surgery. During laparoscopic procedures, the patient's lungs were ventilated (Primus; Dräger, Lübeck, Germany) with a tidal volume of 6–8 mL kg−1 of predicted body weight, PEEP of 5 cm H2O, inspiratory-to-expiratory ratio of 1:2, plateau time of 10%, respiratory rate of 12–16 min−1, and inspired oxygen fraction of 0.5 with a gas flow of 2 L min⁻¹ of oxygen and air. Ephedrine 5 mg, phenylephrine 30 µg, or lactated Ringer's solution 200 mL were given at a mean blood pressure of <60 mmHg, urine output of <0.5 mL kg⁻¹ h⁻¹, or stroke volume variation of $>13\%$.

Two surgeons (S-YJ and JWP) conducted all laparoscopic procedures under the lithotomy with a 30° head-down position. Carbon dioxide $(CO₂)$ was insufflated (Pneumo Sure High Flow Insufflator; Stryker Endoscopy, San Jose, CA) into the abdominal cavity and the intra-abdominal pressure was set at 8 or 12 mmHg for the low or standard pressure

Fig. 1 Study protocol and flowchart

levels, respectively (Fig. [1](#page-2-0)) [\[2,](#page-8-1) [6\]](#page-8-4). If the laparoscopic view was too poor to continue the procedures, the intra-abdominal pressure was increased by 4 mmHg at the surgeon's request. The intra-abdominal pressure and neuromuscular blocking levels were blinded to the surgeons by concealing the monitor of $CO₂$ insufflator and acceleromyograph.

At the skin closure, an intravenous patient-controlled analgesia (Anaplus; Ewha Biomedics, Goyang-si, Korea) was initiated with a 100-mL mixture of morphine 30–60 mg, fentanyl 1000–1500 µg, and normal saline, and infused at 1 mL h−1, bolus 0.5 mL, and lockout time 15 min until the third postoperative day. Ramosetron 0.3 mg was given to prevent postoperative nausea or vomiting.

At the end of surgery, all anesthetic drugs were discontinued, and sugammadex (Bridion; MSD, Kenilworth, NJ, USA) 4 mg kg^{-1} was administered to reverse the neuromuscular block. When the patient was able to breathe spontaneously and respond to verbal commands at the TOF ratio of > 0.9 , the trachea was extubated and the patient was transferred to the postanesthesia care unit. In the postoperative period, fentanyl 50 µg was given as a rescue analgesic at the patient's request. The patient was discharged from the postanesthesia care unit with a modified Aldrete score of 9–10 [\[18\]](#page-8-14) and discharged from the hospital when the patient can tolerate food and ambulate safely without severe pain, fever, and complications [[19\]](#page-8-15).

Outcomes

We collected baseline data of patients, surgery, and anesthesia. Intraoperative cardiopulmonary variables were recorded at six-time points: 1 min after skin incision and $CO₂$ insufflation in the supine position, and 30, 60, 90, and 120 min after $CO₂$ insufflation in the head-down position. Stroke volume index, cardiac index, mean blood pressure, and heart rate were obtained from the EV1000 platform; plateau and peak inspiratory airway pressures from the Primus anesthesia machine; arterial partial pressures of oxygen and $CO₂$ from the blood gas analyzer (GEM Premier 3000, Model 5700; Instrumentation Laboratory, Lexington, MA, USA); and left or right cerebral oxygen saturations from the INVOS cerebral oximeter. The static and dynamic pulmonary compliances were calculated from the plateau and peak inspiratory pressures, PEEP, and tidal volume [\[20\]](#page-8-16). We checked amounts of fluids, transfusion, urine output, estimated blood loss, and inotropic requirements.

After the laparoscopic procedure, the surgeon subjectively assessed the quality of surgical conditions using a five-point scale as follows: optimal, a wide visible laparoscopic working field without any movements or contractions; good, a wide laparoscopic field with sporadic muscle contractions or movements; acceptable, a wide visible laparoscopic field with regular muscle contractions or movements causing some interference with the surgeon's work; poor, a visible laparoscopic field with continuous muscle contractions or movements causing severe interference with the surgeon's work; extremely poor, the inability to obtain a visible laparoscopic field because of inadequate muscle relaxation or coughing [\[8,](#page-8-11) [16\]](#page-8-12). We also recorded the insufflated $CO₂$ volume and number of patients receiving elevation of the intra-abdominal pressure during laparoscopy. After surgery, we checked the durations of eye opening or tracheal extubation after the administration of sugammadex, and the length of stay in the postanesthesia care unit or hospital. An investigator (HP) blinded to the group assignment confirmed the TOF ratio of ≥ 1.0 to exclude residual paralysis 30 min after surgery [[21\]](#page-8-17). The investigator also evaluated the pain intensity using an 11-point visual analogue scale (0, no pain; 10, worst pain imaginable), and the sedation level using a seven-point Leiden observer's assessment of alertness/sedation scale (0, normal alertness; 6, not aroused by a painful stimulus) [[16](#page-8-12)]. We recorded rescue analgesic requirements, recovery time of bowel movement, and any perioperative adverse events.

The primary outcome was the cardiac index 30 min after $CO₂$ insufflation. The secondary outcomes were other cardiopulmonary variables, surgical conditions, and $CO₂$ consumption during laparoscopy; and recovery times and pain intensity after surgery.

Statistical analysis

In our pilot study $(n=10)$, the mean (SD) of cardiac index was 2.6 (0.6) L min⁻¹ m⁻² at 30 min after CO₂ insufflation under the intra-abdominal pressure of 12 mmHg and the post-tetanic count of 1–2 during laparoscopic colorectal surgery. To detect a 15% difference in the cardiac index by lowering the pressure to 8 mmHg, 41 patients were needed in each group with a type-I error risk of 0.05 and a power of 0.8 for two-tailed analysis.

Continuous variables were presented as mean (SD) or median (interquartile range) after checking the normality with Shapiro–Wilk test. Repeatedly measured continuous variables were analyzed with linear mixed models, ANOVA or Kruskal–Wallis test, and unpaired *t* or Mann–Whitney *U* tests as appropriate. In the mixed model, fixed effects were the group, time, and interaction between group and time, and a random effect was the subject.

Categorical variables were the number of patients (proportion) and were compared with Chi-Squared test or Fisher's exact test. Effect sizes with 95% CI were calculated. A P -value of < 0.05 was considered significant and adjusted with Bonferroni correction. All analyses were conducted in an intention-to-treat manner. STATA (Special Edition 14.2; Stata Corporation, College Station, TX, USA) was used for sample size calculation, randomization, and statistical analyses.

Results

After screening 150 patients, 131 patients were included in the low pressure with deep-block $(n=44)$, standard pressure with deep-block $(n=44)$, and standard pressure with moderate-block $(n=43)$ groups between December 2014 and October 2016 (Fig. [1](#page-2-0)). However, at 90 and 120 min after $CO₂$ insufflation, we obtained cardiopulmonary data only from 103 and 70 patients because of the shorter laparoscopic procedure time (Fig. [1](#page-2-0)). The characteristics of patients, surgery, and anesthesia were comparable between groups except for the dose of rocuronium (Table [1\)](#page-4-0). No patients received conversion to open laparotomy or transfusion.

The mean (SD) of the cardiac index at 30 min after CO₂ insufflation was 2.7 (0.7), 2.7 (0.9), and 2.6 (1.0) L min⁻¹ m⁻² in the low pressure with deep-block, standard pressure with deep-block, and standard pressure with moderate-block groups $(P=0.715, ANOVA)$ and similar throughout the entire laparoscopic procedure (Fig. [2B](#page-5-0), $P=0.192$, linear mixed model). The stroke volume index $(P=0.213)$, mean blood pressure $(P=0.814)$, and heart rate $(P = 0.543)$ were also comparable between groups (Fig. [2](#page-5-0)). The static and dynamic pulmonary compliances were significantly higher in the low pressure group than in the standard pressure groups at 1, 30, and 60 min after $CO₂$ insufflation (Fig. [3](#page-6-0)A, B, $P < 0.001$, ANOVA). The arterial partial pressures of oxygen (Fig. $3C$, $P = 0.651$) and CO₂ (Fig. [3](#page-6-0)D, $P = 0.338$), or the left ($P = 0.745$) and right $(P=0.712)$ cerebral oxygen saturations were similar between groups.

The laparoscopic surgical condition was better in the deep neuromuscular block than in the moderate block under the standard intra-abdominal pressure, but worse in the low pressure than the standard pressure under the deep-block (Fig. [4\)](#page-7-0). Moreover, in 12/44 (27%) patients in the low pressure with deep-block group, the surgeon asked to increase the intra-abdominal pressure because of the unacceptable laparoscopic view (Table [2\)](#page-7-1). The insufflated $CO₂$ volume was comparable between groups (Table [2](#page-7-1)).

After surgery, recovery times and pain intensity were similar between groups (Table [2\)](#page-7-1). No patients showed residual paralysis or severe complications.

Table 1 Characteristics of patients, surgery, and anesthesia

Values are mean (SD) or number of patients (proportion)

a By ANOVA

Discussion

In this randomized controlled trial, the low intra-abdominal pressure (8 mmHg) compared with the standard pressure (12 mmHg) showed similar hemodynamic responses and higher pulmonary compliances, but poor surgical conditions during laparoscopic colorectal surgery.

The intra-abdominal pressures higher than 15 mmHg may compress the inferior vena cava or mediastinum and decrease the cardiac preload, and thus the stroke volume and cardiac output $[2, 3]$ $[2, 3]$ $[2, 3]$. These effects can be aggravated in cardiovascular-compromised patients [[2](#page-8-1), [3](#page-8-3), [22,](#page-8-18) [23\]](#page-8-19). However, because our participants were relatively healthy without severe cardiovascular diseases, they might be hemodynamically tolerable even in the increased intra-abdominal pressures. Furthermore, the leg-up (i.e., lithotomy) and head-down position may facilitate venous return to the heart $[3, 6, 24]$ $[3, 6, 24]$ $[3, 6, 24]$ $[3, 6, 24]$ $[3, 6, 24]$ $[3, 6, 24]$, compensating for negative inotropic effects of the elevated intra-abdominal pressure. These could explain our findings of similar hemodynamic status between the low and standard intra-abdominal pressures during laparoscopic colorectal surgery.

The high pressure in the abdomen can be transmitted to the thorax by pushing up the diaphragm, thereby reducing the efficiency of mechanical ventilation $[2, 4-6, 25, 26]$ $[2, 4-6, 25, 26]$ $[2, 4-6, 25, 26]$ $[2, 4-6, 25, 26]$ $[2, 4-6, 25, 26]$ $[2, 4-6, 25, 26]$ $[2, 4-6, 25, 26]$. We observed that the lower intra-abdominal pressure provided

Fig. 2 Mean (circle) and SD (bar) of hemodynamic variables before and 1, 30, 60, 90, and 120 min after onset of laparoscopy

higher pulmonary compliances but not better oxygenation nor $CO₂$ $CO₂$ $CO₂$ elimination [2, [11](#page-8-5), [27\]](#page-9-0). Thus, the lower intraabdominal pressure seems to have only limited benefits for pulmonary functions.

Deeper neuromuscular blocks can reduce abdominal muscle tones, thereby expanding the laparoscopic working spaces under the same intra-abdominal pressure [\[1,](#page-8-0) [2](#page-8-1), [8,](#page-8-11) [9](#page-8-24)]. However, it remains controversial whether the deep-block enables laparoscopic procedures to be performed even in the low intra-abdominal pressure [\[10,](#page-8-6) [28,](#page-9-1) [29](#page-9-2)]. In our study, the deeper block provided better surgical conditions in the standard intra-abdominal pressure, but unacceptable conditions in the low pressure. Moreover, in 12 patients with a pressure of 8 mmHg, the surgeon requested higher pressure because of unacceptable laparoscopic views. Therefore, the intra-abdominal pressure is more likely to affect the laparoscopic conditions compared with the neuromuscular blocking level, especially under lower pressures.

Although $CO₂$ is commonly used for laparoscopic surgery, its systemic absorption may cause adverse effects such as embolism, acidosis, or hemodynamic instability [[2,](#page-8-1) [6,](#page-8-4) [11](#page-8-5), [26,](#page-8-23) [30\]](#page-9-3). Theoretically, lower intra-abdominal pressures require a lower volume of $CO₂$ [[26,](#page-8-23) [31](#page-9-4)], but we found no difference between groups. This is probably because the intraabdominal pressure was increased from 8 to 12 mmHg in the 12 patients, and their data were included for the intentionto-treat analysis.

Fig. 3 Mean (circle) and SD (bar) of pulmonary variables before and 1, 30, 60, 90, and 120 min after onset of laparoscopy. *Mean difference (95% CI) 5.8 (1.9–9.7) mL cm⁻¹ H₂O, $P = 0.004$ and 5.6 (1.5–9.7) mL cm⁻¹ H₂O, *P* = 0.007 compared with the standard pressure with deep- and moderate-block groups, respectively, by unpaired *t* test. [†]4.1 (1.7–6.5) mL cm⁻¹ H₂O, *P*=0.001 and 4.6 (2.2–7.1)

Intraoperative deep neuromuscular blocks may lead to postoperative residual paralysis and delayed recovery [\[32–](#page-9-5)[34\]](#page-9-6). However, because sugammadex is known to completely antagonize any level of rocuronium-induced neuromuscular block within 3 min [\[32](#page-9-5), [34](#page-9-6), [35](#page-9-7)], we observed similar durations to tracheal extubation or discharge from the postanesthesia care unit without recurarization in all groups. Higher intra-abdominal pressures may compress the nerves or vessels in the abdominal cavity, thus can intensify postoperative pain or prolong the recovery of bowel movement, but previous findings were inconsistent

[[2,](#page-8-1) [3](#page-8-3), [6](#page-8-4), [10](#page-8-6), [17,](#page-8-13) [36\]](#page-9-8). We also observed no differences in mL cm⁻¹ H₂O, $P = 0.004$

mL cm−1 H2O, *P*<0.001. ‡ 4.2 (1.2–7.2) mL cm−1 H2O, *P*=0.006 and 4.0 (1.0–7.1) mL cm⁻¹ H₂O, *P* = 0.009. [§]5.1 (1.6–8.6) mL cm⁻¹ H₂O, $P=0.005$ and 5.8 (1.8–9.7) mL cm⁻¹ H₂O, $P=0.004$. [¶]4.9 (2.3–7.4) mL cm⁻¹ H₂O, *P* < 0.001 and 5.9 (3.4–8.4) mL cm⁻¹ H₂O, *P*<0.001. [∥]3.6 (1.2–6.0) mL cm⁻¹ H₂O, *P* = 0.003 and 4.0 (1.3–6.6)

the postoperative outcomes although the analyses were

underpowered. Our study has limitations. The pulmonary artery catheter is the gold standard for cardiac output monitoring, but we did not use it because of its invasiveness [[37](#page-9-9), [38\]](#page-9-10). The arterial waveform analysis is known to have low accuracy and precision to predict the absolute value of cardiac output and can be biased by hemodynamic instability [[39\]](#page-9-11). However, it can estimate the cardiac output reliably in a stable hemodynamic status with a regular cardiac rhythm as in our

Fig. 4 Laparoscopic surgical conditions. $*P < 0.001$, $^{\dagger}P = 0.013$, and ‡ *P*=0.012 by Chi-Squared test

study [[37,](#page-9-9) [40](#page-9-12), [41](#page-9-13)]. In addition, although cardiopulmonary responses can be affected by the patient's condition, position, or anesthetic type during laparoscopy $[3, 6, 25, 26]$ $[3, 6, 25, 26]$ $[3, 6, 25, 26]$ $[3, 6, 25, 26]$ $[3, 6, 25, 26]$ $[3, 6, 25, 26]$ $[3, 6, 25, 26]$. we only investigated relatively healthy patients in the lithotomy and head-down positions under the intravenous anesthesia. Our findings thus may not be extrapolated to other clinical situations.

Nevertheless, we found few advantages in cardiopulmonary dynamics, but poor surgical conditions in the low intra-abdominal pressure compared with the standard pressure during laparoscopic colorectal surgery even under the deep neuromuscular block. Therefore, when considering cardiopulmonary effects and surgical conditions, the standard intra-abdominal pressure may be preferable to the low pressure for successful laparoscopic colorectal surgery and patient safety.

Table 2 Variables during and after laparoscopic surgery

Values are number of patients (proportion) or mean (SD)

a By Chi-Squared test

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Compliance with ethical standards

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