

## Does increasing end-tidal carbon dioxide during laparoscopic cholecystectomy matter?

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**Abstract:** To examine the adverse effects of peritoneal carbon dioxide (CO<sub>2</sub>) insufflation during laparoscopic cholecystectomy, both hemodynamic and respiratory alterations were continuously monitored in 17 adult patients using noninvasive Doppler ultrasonography and a continuous spirometric monitoring device. During the surgery, which was performed under inhalational general anesthesia, intraabdominal pressure was maintained automatically at 10mmHg by a CO<sub>2</sub> insufflator, and a constant minute ventilation, initially set to 30–33mmHg of end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>), was maintained. Despite considerable depth of anesthesia, peritoneal CO<sub>2</sub> insufflation induced a significant and immediate increase of mean blood pressure (+42%) and systemic vascular resistance (+62%), accompanied by a slight depression of cardiac index (–12%, nonsignificant), while the ETCO<sub>2</sub> gradually increased and maximized around 30min following the initial CO<sub>2</sub> insufflation. The stress of 10mmHg pneumoperitoneum was a major cause of hemodynamic changes during laparoscopic cholecystectomy. Some clinical strategies such as deliberate intraabdominal insufflation at the initial phase might be required to minimize these hemodynamic changes.

**Key words:** Cardiac output, Cholecystectomy, Doppler ultrasonography, End-tidal CO<sub>2</sub>, Laparoscopy

### Introduction

Laparoscopic cholecystectomy has become a rapidly standardized procedure for gallbladder removal with the benefits of lower mortality, fewer complications, and shorter hospital stay compared to the traditional open operation [1–3]. The adverse effects of increasing PaCO<sub>2</sub> induced by intraabdominal carbon dioxide (CO<sub>2</sub>)

insufflation to produce pneumoperitoneum have already been highlighted [4,5], and this surgical procedure apparently results in dramatic changes of the circulatory state [6]. By using noninvasive monitoring systems, we monitored both hemodynamic and respiratory alterations continuously during laparoscopic cholecystectomy.

### Methods

After having obtained the approval of our institutional ethics committee and informed consent from all participants, we studied 17 adult patients scheduled for elective laparoscopic cholecystectomy. All patients received 150mg ranitidine orally at 21:00 the day before surgery, and 50mg hydroxyzine and 0.5mg atropine intramuscularly 30min before transfer to the operating room.

In the operating room, routine monitors (ECG, pulse oximetry, noninvasive blood pressure) were placed. General anesthesia was induced with intravenous injection of thiopental (4mg·kg<sup>-1</sup>), and succinylcholine (1mg·kg<sup>-1</sup>) was injected to facilitate endotracheal intubation. Following tracheal intubation, general anesthesia was maintained with nitrous oxide (4l·min<sup>-1</sup>) in oxygen (2l·min<sup>-1</sup>) and sevoflurane in a semiclosed circular system with CO<sub>2</sub> absorber. The inhaled concentration of sevoflurane was set at 2.5% unless hemodynamic stability was lost. Adequate muscle relaxation was achieved by intermittent injection of vecuronium bromide. All patients were mechanically ventilated at a constant minute ventilation (10ml·kg<sup>-1</sup> × 8–10 breaths per min; Aika Anesthetic System 210, Aika, Tokyo, Japan) to keep end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>) between 30 and 33mmHg. These ventilatory settings were retained for the remainder of the operation. An esophageal Doppler the ultrasound probe (Accucom, Datascope, Paramus, NJ, USA) was inserted and positioned to maximize audible signals as previously described [7]. The patients

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were placed in a 15° head-up position, which was maintained until removal of the laparoscope. Following placement in the head-up position, laparoscopy was performed using a standardized technique; the CO<sub>2</sub> gas was employed to inflate the abdominal cavity, and the intraabdominal pressure (IAP) was maintained automatically at 10 mmHg by a CO<sub>2</sub> insufflator (System 3000 electronic insufflator, Cabot Medical, Langhorne, PA, USA). During the initial phase of insufflation, the CO<sub>2</sub> gas flow rate was set at 1 l·min<sup>-1</sup> and then raised 1 l·min<sup>-1</sup> every 8–10 s up to 10 l·min<sup>-1</sup>.

After baseline measurements of blood pressure, heart rate, pulse oximetry, and capnography, intraabdominal insufflation of CO<sub>2</sub> was started and recorded at 5, 10, 20, 30, 45, 60, and 90 min later. During surgery, the sevoflurane concentration, ETCO<sub>2</sub>, peak airway pressure (P<sub>aw</sub>), and volume expired during the 1st s of expiration (V<sub>1.0%</sub>), indicating changes in airway resistance on a breath-by-breath basis during general anesthesia, were continuously monitored by a Capnomac Ultima anesthetic gas analyzer with a sidestream spirometer (Datex, Helsinki, Finland). Cardiac output was measured by Doppler ultrasonography (Accucom, Datascope) and subsequently indexed (cardiac index; CI) for body surface area as previously described [8]. Briefly, on the presumption that the cross-sectioned area of the aorta would remain constant, the built-in nomogram that estimates the inner diameter of the ascending aorta just above the sinus of Valsalva in relation to the patients' sex, age, height, and body weight was used during Doppler calibration. Then, a continuous-wave Doppler transducer was placed in the suprasternal notch to measure ascending aortic blood flow velocity. At the highest possible signal level, a high-pitched Doppler sound without low-frequency noise was searched for by proper positioning of the transducer. Cardiac output was then calculated as the mean of five single cardiac output values from the Doppler probe placed in the esophagus.

Systemic vascular resistance (SVR) was calculated from cardiac index and mean blood pressure, when central venous pressure (CVP) was assumed to be constant at 3 mmHg.

Data are expressed as mean ± standard error of mean (SEM) unless otherwise specified. Data were analyzed by Student paired *t*-test and corrected for multiple comparison. A *P* value less than 0.05 was considered statistically significant.

## Results

The demographic data of the patients are shown in Table 1. No patient had coexisting cardiac disease or excessive obesity. The skin incision, placement of the laparoscope, and head-up positioning caused few hemodynamic changes (data not shown). Immediately following intraabdominal insufflation, both mean blood pressure (MBP) and SVR significantly increased (+42% and +62%, respectively) and remained at a similarly high level until 30 min after insufflation compared to the baseline period (Table 2). Thereafter, both parameters were gradually depressed. The cardiac index showed a depressed tendency during CO<sub>2</sub> insufflation (-12%; not significant). Heart rate and pulse oximetry did not change significantly throughout the study period (Table 2). In contrast, ETCO<sub>2</sub> increased gradually and maximized around 30 min following insufflation of CO<sub>2</sub> (Table 2). Both V<sub>1.0%</sub> and P<sub>aw</sub> increased immediately (+10% and +34%, respectively;

**Table 1.** Patients' demographic data

Sex (female/male)	11/6
Age (years)	50.5 ± 3.3
Height (cm)	159 ± 3
Body weight (kg)	61.3 ± 2.5

Data are expressed as mean ± SEM.

**Table 2.** Changes in hemodynamic and respiratory parameters during laparoscopic cholecystectomy

	ETCO <sub>2</sub> (mmHg)	V <sub>1.0%</sub> (%)	P <sub>aw</sub> (cmH <sub>2</sub> O)	SVR (k·dyne per s <sup>5</sup> )	CI (l·min <sup>-1</sup> ·m <sup>-2</sup> )	MBP (mmHg)	HR (bpm)
Baseline	30 ± 1	84 ± 1	16 ± 1	1.67 ± 0.13	3.8 ± 0.3	77 ± 2	80 ± 2
5 min	33 ± 1*	92 ± 1*	22 ± 1*	2.63 ± 0.23*	3.3 ± 0.3	108 ± 4*	88 ± 3
10 min	35 ± 1*	92 ± 1*	21 ± 1*	2.66 ± 0.27*	3.6 ± 0.4	109 ± 4*	86 ± 3
20 min	38 ± 1*	92 ± 1*	22 ± 1*	2.77 ± 0.27*	3.4 ± 0.2	111 ± 5*	89 ± 3
30 min	39 ± 1*	93 ± 1*	22 ± 1*	2.71 ± 0.25*	3.4 ± 0.2	110 ± 5*	90 ± 3
45 min	39 ± 1*	92 ± 1*	22 ± 1*	2.38 ± 0.19*	3.5 ± 0.2	101 ± 4*	90 ± 3
60 min	39 ± 1*	93 ± 1*	22 ± 1*	2.39 ± 0.19*	3.4 ± 0.3	95 ± 4*	86 ± 3
90 min	40 ± 2*	93 ± 1*	23 ± 1*	2.39 ± 0.28	3.5 ± 0.3	94 ± 3*	86 ± 3

ETCO<sub>2</sub>, end-tidal carbon dioxide; V<sub>1.0%</sub>, volume expired during the 1st second of expiration; P<sub>aw</sub>, peak airway pressure; SVR, systemic vascular resistance; CI, cardiac index; MBP, mean blood pressure; HR, heart rate. Data are expressed as mean ± SEM. \**P* < 0.05 versus baseline value.

$P < 0.05$ ) and remained at the elevated levels during intraperitoneal insufflation (Table 2).

## Discussion

This study demonstrates that the major physiological alterations occurring during laparoscopic cholecystectomy include a prompt and notable increase of systemic vascular resistance, resulting in elevated blood pressure immediately following the pneumoperitoneum. However, the  $\text{ETCO}_2$  increased gradually and maximized around 30 min after the insufflation of  $\text{CO}_2$ , accompanied by a prompt increase of peak airway pressure and an augmentation of expiration speed probably due to raised intraabdominal pressure. Since we did not change the initial ventilatory settings to regulate  $\text{ETCO}_2$  within the normal range, this study allows us to suggest that the increasing  $\text{ETCO}_2$  is unlikely to play an important role in creating the dramatic increase of SVR during laparoscopic cholecystectomy. Although some previous reports have overstressed the fact that ventilatory settings should be carefully employed to avoid hypercapnia during  $\text{CO}_2$  insufflation [5,9], a recent review also indicated that one must clearly distinguish between the sequential hemodynamic effects of anesthesia and positioning, the mechanical and neuroendocrine effects of pneumoperitoneum, and those resulting from absorbed carbon dioxide [6].

A couple of substantial factors contributing to increased SVR during laparoscopic cholecystectomy have been proposed [6]. First, the prompt increase of intraabdominal pressure or distention of the peritoneum causes sympathoadrenal discharge, associated with the release of vasoconstricting hormones [10]. Second, an increase of IAP to over 10 mmHg probably compresses the inferior vena cava and then diminishes venous return to the right atrium [11]. Tilting the patient to the head-up position also reduces venous return. Consequently, cardiac output may be depressed, resulting in further discharge of the sympathetic nervous system, although depressed cardiac output in our study was not statistically significant. Third, increasing IAP likely augments transmural pressure on either the capillary bed or on venules of the splanchnic circulation. The changes in venous resistance have a far greater effect on cardiac output than similar changes in arterial resistance [12], and the stability of the heart rate throughout the study period may suggest that the direct effects of pneumoperitoneum on the capillary bed in the splanchnic circulation played a major role in the elevation of SVR rather than occurring through the sympathetic nervous system. Interestingly, both SVR and MBP tended to return to baseline levels 45 min after the

pneumoperitoneum, although a similar IAP was maintained. Thus, the hosts might be able to compensate the high level of intraabdominal pressure during this period. In other words, when  $\text{CO}_2$  insufflation is carried out more slowly than as currently employed, these hemodynamic changes might be minimized.

The differences in head-up positioning, IAP, ventilatory settings, and/or assessment techniques between various previous reports have resulted in the variety of hemodynamic responses seen during laparoscopic cholecystectomy [6]. However, the overall effects of this surgical procedure reported in previous studies are similar to our results; i.e., elevation of blood pressure and vascular resistance and depression of cardiac output [1,6,13]. There are several limitations to interpretation of the data in the current study. We assumed CVP to be constant at 3 mmHg during the study period. Although there is no reason to believe that this determination was correct during surgery, the change in CVP, which was considered to be within the low-pressure range, would have been unable to modify the calculation of cardiac output and SVR to any large extent. Thus, the changes in blood pressure, considered significantly greater than those in CVP, were probably able to overcome such changes in low-pressure parameters. The validity of Doppler ultrasonography for the measurement of cardiac output might also be questioned [7,14,15]. Although the issue still remains controversial, a newer study has suggested that this device may be regarded acceptable for cardiac output trend monitoring in sedated, paralyzed patients [14]. Since the relative changes in cardiac output rather than absolute values were more consequential in this study, we believe the data shown were a valid basis for discussion.

Laparoscopic cholecystectomy is currently being performed and advocated for elderly patients with coexisting cardiac disease [2,16], since it appears to be minor surgery with a small incision. Cunningham and co-workers reported that left ventricular function determined by transesophageal echocardiographic estimation of ejection fraction was well preserved during  $\text{CO}_2$  insufflation despite an augmentation in left ventricular end-systolic wall stress [1]. The indication for this surgery is becoming increasingly widespread compared to conventional open cholecystectomy [2]. However, we wish to emphasize that the abrupt increase of afterload during intraabdominal insufflation might have a detrimental influence on patients with poor myocardial reserve. Some clinical strategies such as deliberate intraabdominal insufflation at the initial phase might be required to minimize the adverse changes occurring during the initial phase of pneumoperitoneum. Further studies are warranted to examine the efficacy of such strategies.

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