

CLINICAL PRACTICE

## Acid–base alterations during laparoscopic abdominal surgery: a comparison with laparotomy

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### Key points

- Carbon dioxide insufflation during laparoscopic surgery results in an acid–base imbalance.
- The decrease in the pH during the pneumoperitoneum is caused by the increase in  $P_{a_{CO_2}}$ , which promptly returns to a normal value after the desufflation.
- In contrast, during laparotomy, a decrease in the pH is mostly caused by the metabolic factors, which persists an hour after the surgery.

**Background.** Carbon dioxide insufflation during laparoscopic surgery results in an acid–base imbalance. The purpose of this study was to investigate the effect of pneumoperitoneum on the acid–base status using Stewart’s approach.

**Methods.** Thirty patients undergoing abdominal surgery were allocated to the laparotomy group ( $n=15$ ) or the laparoscopy group ( $n=15$ ). The acid–base parameters were measured 10 min after the induction (T1), 40 min after opening the peritoneum or pneumoperitoneum according to the group (T2), at the end of the surgery (T3), and 1 h after the surgery (T4).

**Results.** There were no significant differences in the standard base excess (SBE), strong ion gap, or anion gap between the two groups. In both groups, the SBE decreased at T2, T3, and T4 compared with baseline value. At T3 and T4 in the laparotomy group, the apparent strong ion difference (SIDa) and pH were decreased whereas the lactate and chloride were increased compared with their baseline values. At T2 in the laparoscopy group, the pH was decreased whereas  $P_{a_{CO_2}}$  was increased compared with their baseline values.

**Conclusions.** The decrease in the pH during the pneumoperitoneum was affected by the increase in  $P_{a_{CO_2}}$ , which promptly returned to a normal value after the desufflation. On the other hand, the decrease in the pH after laparotomy was affected by the metabolic factors, which persisted an hour after the surgery.

**Keywords:** chemistry, analytical; complications, acid–base disorders; surgery, laparoscopy

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The abdominal laparoscopic surgery is replacing a variety of laparotomy procedures because it is a relatively non-invasive procedure with fast recovery and less pain. However, the laparoscopic technique requires carbon dioxide (CO<sub>2</sub>) insufflation with positive pressure to allow optimal visualization. The resulting acid–base imbalance may be different from that during traditional laparotomy. The CO<sub>2</sub> pneumoperitoneum causes an increase in the abdominal pressure and CO<sub>2</sub> absorption through the peritoneal serosa,<sup>1 2</sup> which may result in hypercarbia and respiratory acidosis. However, controversy exists, among different authors, over which factor in the acid–base imbalance is basically disrupted—the respiratory or the metabolic factor. The experimental and clinical studies have demonstrated some risks of acid–base balance alterations with CO<sub>2</sub>

pneumoperitoneum towards metabolic acidosis.<sup>3 4</sup> Moreover, Taura and colleagues<sup>5</sup> have reported that prolonged pneumoperitoneum at 15 mm Hg causes lactic acidosis due to impaired regional oxygenation/perfusion.

The traditional approach by the Henderson–Hasselbalch equation is often inadequate to explain the complexity of acid–base derangements during the surgery.<sup>6</sup> Stewart’s approach offers clinicians a theoretical framework to better understand the development of an acid–base disorder and the physiology of treatments such as the buffers and haemofiltration.<sup>6</sup> Since no report has been issued regarding the effects of a surgical technique on the acid–base balance in patients undergoing major abdominal surgery, this study investigated the effect of the pneumoperitoneum on the acid–base status during laparoscopic surgery and the result

was compared with that during the laparotomy using the Stewart's physicochemical approach.

## Methods

After procedure approval of the institutional review board, 30 adult patients undergoing major abdominal surgery gave informed consent and were studied prospectively. Patients with coagulopathy, anaemia, chronic renal failure, respiratory insufficiency, or pre-existing metabolic acidosis were excluded. The patients were distributed to receive either a laparotomy (laparotomy group,  $n=15$ ) or the laparoscopy (laparoscopy group,  $n=15$ ) according to the decision of the medical team, and therefore, they were not randomized.

The laparoscopic surgeries requiring pneumoperitoneum more than 90 min such as a gastrectomy, colectomy, and low anterior resection were included in this study. The pneumoperitoneum pressure was restricted to 15 mm Hg.

The patients were premedicated with i.m. injection of midazolam 2 mg and glycopyrrolate 0.2 mg. On arrival at the operating theatre, the standard vital signs monitors were attached and a 20 G catheter was inserted into the radial artery under local anaesthesia for continuous arterial pressure monitoring and blood sampling. Anaesthesia was induced with remifentanyl, propofol, and rocuronium. The lungs were ventilated with a tidal volume of 7–10 ml  $\text{kg}^{-1}$  and a ventilatory frequency of 8–12 bpm to maintain an end-tidal carbon dioxide concentration ( $\epsilon'_{\text{CO}_2}$ ) of 4.00–4.66 kPa at a 60% inspired oxygen with air. In the laparoscopy group, the tidal volume and ventilatory frequency were reset to maintain an  $\epsilon'_{\text{CO}_2}$  between 4.66 and 5.33 kPa after pneumoperitoneum. Anaesthesia was maintained with sevoflurane 0.8–1.2 vol% and remifentanyl 0.1–0.2  $\mu\text{g kg}^{-1} \text{min}^{-1}$ . After the induction, a central venous catheter was inserted through the right jugular vein and a urinary catheter was inserted to measure hourly urine output.

The oesophageal temperature was kept between 36°C and 37°C. For the i.v. fluids, Hartmann's solution and 6% hydroxyethyl starch in normal saline (NS) solution (Voluven™, Fresenius Kabi, Bad Homburg, Germany) were administered according to the following protocol. Hartmann's solution was infused at a constant rate of 6 ml  $\text{kg}^{-1} \text{h}^{-1}$ . The triggers

for infusion of 6% hydroxyethyl starch in NS solution were a systolic arterial pressure of <90 mm Hg and/or decrease of >20% from baseline, a heart rate of >100 beats  $\text{min}^{-1}$  and/or an increase of >30% from baseline, and/or urine output of <0.4 ml  $\text{kg}^{-1} \text{h}^{-1}$ . The maximum dose of 6% hydroxyethyl starch in NS solution was 50 ml  $\text{kg}^{-1}$ . Packed red blood cells were transfused when the haemoglobin decreased below 8 g  $\text{dl}^{-1}$ .

The arterial samples were obtained 10 min after the induction of anaesthesia (T1), 40 min after opening the peritoneum in the laparotomy group or pneumoperitoneum in the laparoscopy group (T2), at the end of the surgery (T3), and 1 h after the surgery (T4). The samples were analysed for pH,  $P_{\text{aCO}_2}$  (standard electrodes), and serum lactate (enzymatic method, quantification of  $\text{H}_2\text{O}_2$ ), all integrated in the blood gas analyser (GEM Premier 3000, Instrumentation Laboratory, MA, USA). Additionally, the concentrations of sodium ( $\text{Na}^+$ ), potassium ( $\text{K}^+$ ), and chloride ( $\text{Cl}^-$ ) (ion-selective electrode), serum phosphate ( $\text{Pi}^-$ ; ultraviolet photometry of a phosphomolybdate complex), serum total protein concentration (Biuret method), and albumin concentration (colorimetry of bromocresol complex) were measured using the same blood samples. The standard base excess (SBE) and bicarbonate were taken from the blood gas analyser, which uses the Henderson–Hasselbalch equation and the Van Slyke equation. For each sample, the apparent and effective strong ion difference (SIDa and SIDe), strong ion gap (SIG), and anion gap (AG) were calculated (for abbreviations and calculations, see Table 1).

Statistical analyses were performed using the statistical package (SAS Institute Inc., Cary, NC, USA). Sample size was calculated based on the previous study.<sup>7</sup> In each group, 12 patients were needed to detect the intergroup difference of 1.5 mmol  $\text{litre}^{-1}$  in SIDa with a power of 0.8 and at a 0.05 level of significance. To compensate a dropout rate 20%, 30 patients were included in this study. Data are presented as median (inter-quartile range), mean (SD), or number of patients. The distribution of all measure and calculated data is tested by one-sample Kolmogorov–Smirnov tests. Patients' characteristics were compared with the Mann–Whitney *U*-test or Fisher's exact test where appropriate. For other variables, data within the group were analysed with repeated-measures ANOVA with Bonferroni's

**Table 1** Abbreviations and calculations

Abbreviation	Definition	Calculation
$A_{\text{TOT}}$ (mmol $\text{litre}^{-1}$ )	Sum of all anion charges of weak plasma acid	$A_{\text{TOT}} = \text{Alb}^- + \text{Pi}^-$
$\text{Alb}^-$ (mmol $\text{litre}^{-1}$ )	Negative charges displayed by serum albumin	$\text{Alb}^- = \text{serum albumin concentration} \times (0.123 \times \text{pH} - 0.631)$
$\text{Pi}^-$ (mmol $\text{litre}^{-1}$ )	Negative charges displayed by inorganic phosphate	$\text{Pi}^- = \text{serum phosphate concentration} \times (0.309 \times \text{pH} - 0.469)$
SIDa (mmol $\text{litre}^{-1}$ )	Apparent strong ion difference	$\text{SIDa} = \text{Na}^+ + \text{K}^+ - \text{Cl}^- - \text{Lac}^-$
SIDe (mmol $\text{litre}^{-1}$ )	Effective strong ion difference	$\text{SIDe} = \text{HCO}_3^- + \text{Alb}^- + \text{Pi}^-$
SIG (mmol $\text{litre}^{-1}$ )	Strong ion gap	$\text{SIG} = \text{SIDa} - \text{SIDe}$
AG (mmol $\text{litre}^{-1}$ )	Anion gap	$\text{AG} = \text{Na}^+ + \text{K}^+ - \text{Cl}^- - \text{HCO}_3^-$

correction. Student's *t*-test was performed to compare inter-group differences. A value of  $P < 0.05$  was considered statistically significant.

**Table 2** Patient characteristics and data from the perioperative period. Values are median (inter-quartile range) or number of patients. DM, diabetes mellitus; laparotomy group, patients with laparotomy; laparoscopy group, patients with laparoscopic abdominal surgery. There were no significant differences between the groups

	Laparotomy (n=13)	Laparoscopy (n=14)
Age (yr)	51 (43–63)	56 (48–64)
Weight (kg)	62 (52–71)	57 (51–67)
Sex (M/F)	10/3	6/8
Medical history (n)		
Hypertension/DM	3/2	2/2
Operation time (min)	265 (195–307)	210 (173–240)
Pneumoperitoneum time (min)	—	130 (100–185)
Operation (n)		
Low anterior resection/ colectomy/ gastrectomy	3/4/6	7/3/4
Fluid balance, intraoperative		
Crystalloid (ml)	1350 (1050–1675)	900 (750–1600)
Colloid (ml)	650 (500–900)	500 (300–687)
Fluid balance, postoperative 1 h		
Crystalloid (ml)	200 (100–400)	150 (100–400)
Colloid (ml)	50 (40–100)	100 (43–163)
Urine output, intraoperative (ml h <sup>-1</sup> )	51 (44–60)	52 (34–77)
Estimated blood loss (ml)	300 (213–500)	300 (200–400)

## Results

Two patients in the laparotomy group were excluded for analysis due to loss of data and a patient in the laparoscopy group due to change in the surgical method to laparotomy.

The patient characteristics and data from the perioperative period are presented in Table 2. There were no significant differences in the age, weight, sex, preoperative medical history, and the type of operation between the groups. There were no statistical significance between the groups with respect to the anaesthesia time, fluid balance, urine output, estimated blood loss, and blood transfusion.

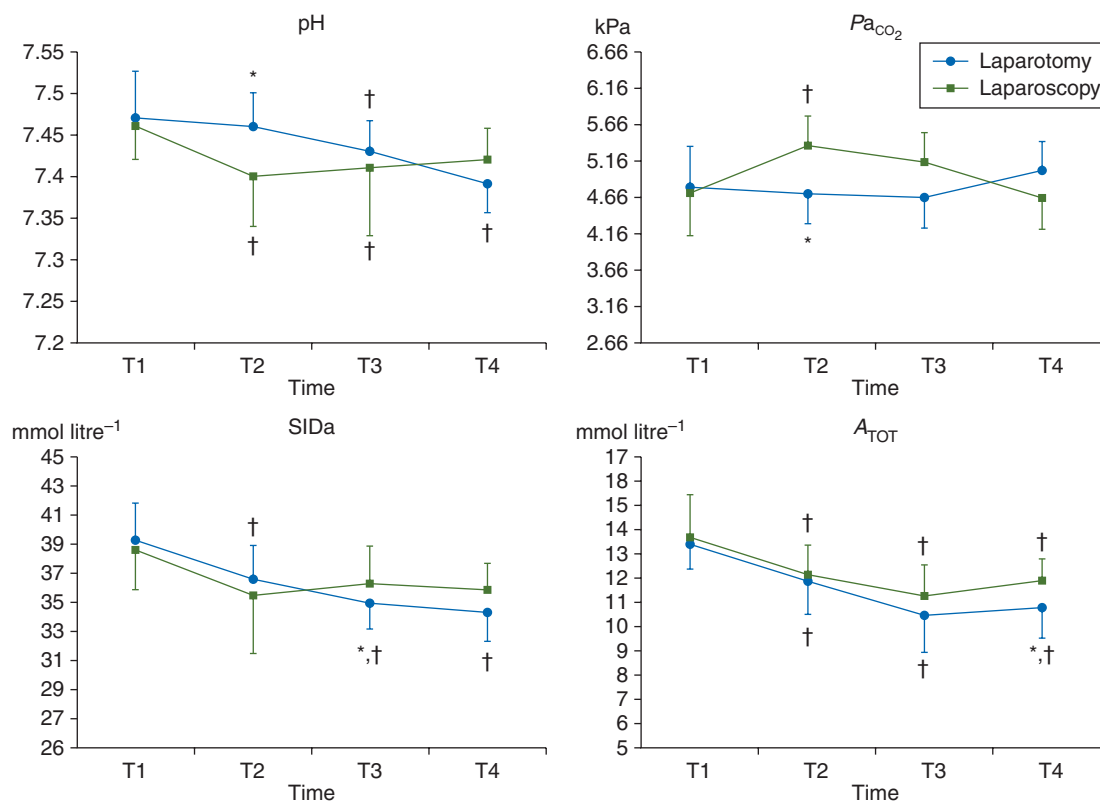
The haemodynamic variables and body temperatures (BTs) are listed in Table 3. There were no differences in MAP and BT between the two groups. The HR was significantly lower and central venous pressure (CVP) was higher in the laparoscopy group than that in the laparotomy group at T2. The CVP was significantly increased at T2 compared with the baseline value in the laparoscopy group.

The changes of acid–base status were illustrated in Figures 1 and 2. At T3 and T4 in the laparotomy group, the SIDa and pH were decreased whereas the lactate and Cl<sup>-</sup> were increased compared with their baseline values. At T3, the lactate was higher and the SIDa was lower in the laparotomy group compared with those in the laparoscopy group. The baseline SIDa value at T1 was about 38 mmol litre<sup>-1</sup> in both groups, which is within the normal range. At T2 in the laparoscopy group, the pH was decreased whereas Pa<sub>CO2</sub> was increased compared with their baseline values. At T2, the pH was lower and Pa<sub>CO2</sub> was higher in the laparoscopy group compared with those in the laparotomy group.

The calculation of the unmeasured anions is listed in Table 4. There were no significant differences in the SBE, SIG, and AG between the two groups throughout the whole investigation period. After the surgery (T4), the SBE significantly decreased in both groups and mean (SD) decrease in the SBE from the baseline value (T1) was

**Table 3** Haemodynamic variables and BT. Values are means (SD). Laparotomy group, patients with laparotomy; laparoscopy group, patients with laparoscopic abdominal surgery; MAP, mean arterial pressure; HR, heart rate; CVP, central venous pressure; BT, body temperature; T1, 10 min after the induction of anaesthesia; T2, 40 min after opening the peritoneum in the laparotomy group or pneumoperitoneum in the laparoscopy group; T3, at the end of surgery; T4, 1 h after the surgery. \* $P < 0.05$ , vs the laparotomy group; † $P < 0.05$ , vs baseline values (T1) within the group

	T1	T2	T3	T4
MAP (mm Hg)				
Laparotomy	81 (9)	87 (10) <sup>†</sup>	88 (12)	94 (10) <sup>†</sup>
Laparoscopy	85 (11)	91 (16)	84 (12)	96 (20)
HR (beats min <sup>-1</sup> )				
Laparotomy	68 (15)	72 (13)	65 (12)	80 (16)
Laparoscopy	65 (13)	60 (10)*	55 (5)*	80 (9) <sup>†</sup>
CVP (mm Hg)				
Laparotomy	7 (3)	8 (4)	7 (3)	7 (3)
Laparoscopy	8 (3)	13 (4)* <sup>†</sup>	9 (2)	8 (2)
BT (°C)				
Laparotomy	35.9 (0.6)	35.8 (0.5)	35.7 (0.6)	36.0 (0.5)
Laparoscopy	36.1 (0.4)	35.7 (0.4) <sup>†</sup>	35.6 (0.6) <sup>†</sup>	36.1 (0.3)



**Fig 1** Changes of acid–base state in patients undergoing major abdominal surgery at four measure points. T1, 10 min after the induction of anaesthesia; T2, 40 min after opening the peritoneum in the laparotomy group or pneumoperitoneum in the laparoscopy group; T3, at the end of surgery; T4, 1 h after the surgery. Bar displays the standard deviation. \* $P < 0.05$ , vs the laparotomy group; † $P < 0.05$ , vs baseline values (T1) within the group.

4.0 (1.6) mmol litre<sup>-1</sup> in the laparotomy group ( $P < 0.001$ ) and 2.9 (1.3) mmol litre<sup>-1</sup> in the laparoscopy group ( $P < 0.001$ ).

## Discussion

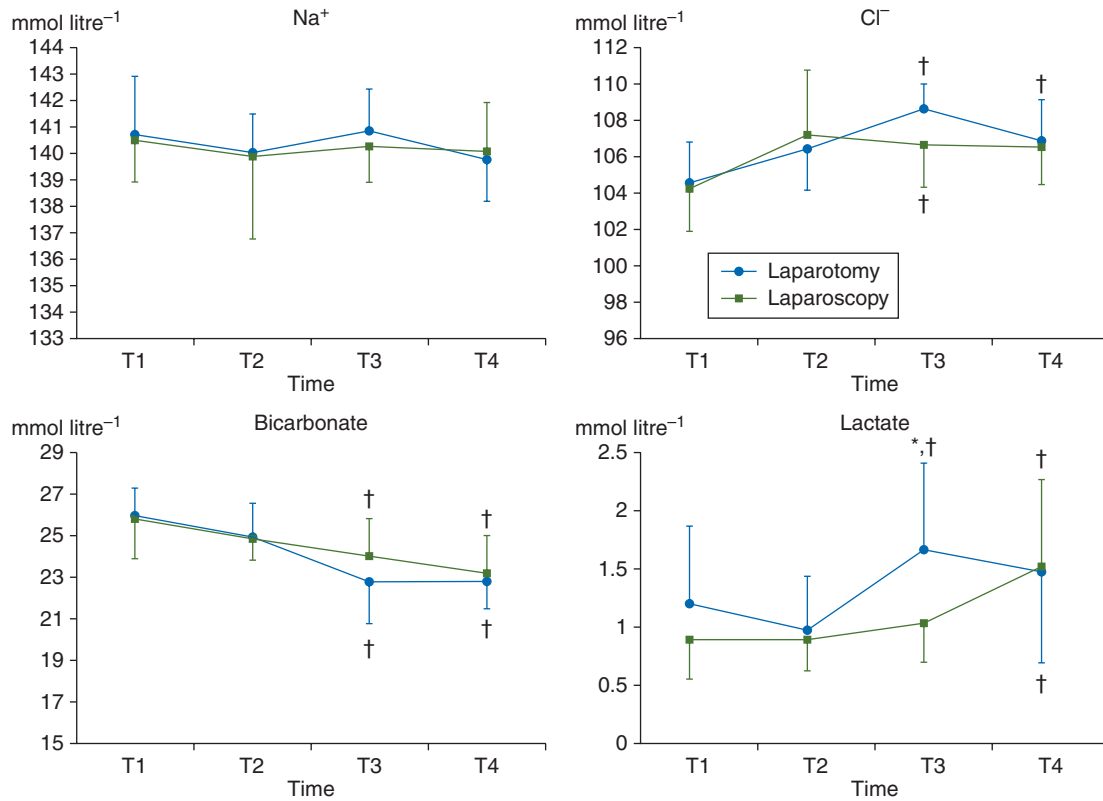
In this study, we found that in the laparoscopy group, the pH was decreased and  $Pa_{CO_2}$  was increased only during  $CO_2$  pneumoperitoneum. The decrease in the pH and SIDa with elevated lactate was observed after laparotomy but not after laparoscopic surgery.

Previous investigations on the acid–base imbalance during laparoscopic surgery with  $CO_2$  pneumoperitoneum reported controversial results. Some reported respiratory acidosis due to the transperitoneal absorption of  $CO_2$  and others reported metabolic acidosis.<sup>1–3</sup> Sefr and colleagues<sup>8</sup> reported that carbon dioxide pneumoperitoneum causes alterations of the acid–base balance, mostly of respiratory or mixed type. In this study, the decrease in the blood pH was noted in conjunction to increased  $Pa_{CO_2}$  without a significant change in the SID and lactate during  $CO_2$  pneumoperitoneum in the laparoscopy group. The pH increased after the desufflation with the decrease in  $Pa_{CO_2}$ , which suggest a respiratory factor as the cause of the decreased pH during laparoscopic surgery. On the other hand, the pH in the

laparotomy group decreased after the surgery with decreased SIDa and increased lactate level, which suggest a metabolic factor. The lactate was significantly increased at T3 and T4 in the laparotomy group, which suggests the lactic acid accumulation with hypoperfusion after laparotomy.

The SIG calculated by the Stewart's approach could provide an estimate of the unmeasured anion. The SIG is similar in concept to the AG and the 'normal' value is zero. In this study, significant within-group change was not observed in unmeasured, unidentified cations or anions as assessed by calculating the SIG in both groups.<sup>9–11</sup> Therefore, the metabolic factor of the decreased pH after laparotomy may have been influenced by the water excess or hyperchloraemia.

The hypoalbuminaemia is ubiquitous during large amounts of fluid administration after the surgery and the Stewart's approach offers a better understanding of the acid–base status of a patient.<sup>6</sup> Despite the significant decreases in  $A_{TOT}$ , the pH decreased after the surgery in both groups. This suggests that the decrease in SID overwhelms the countercurrent  $A_{TOT}$  dilutional metabolic alkalosis. This mechanism was supported by the result of this study, in which the mean decrease of SIDa was larger than that of  $A_{TOT}$  (3 vs 1.5 mmol litre<sup>-1</sup>).



**Fig 2** Changes of electrolyte and lactate in patients undergoing major abdominal surgery at four measure points. T1, 10 min after the induction of anaesthesia; T2, 40 min after opening the peritoneum in the laparotomy group or pneumoperitoneum in the laparoscopy group; T3, at the end of surgery; T4, 1 h after the surgery. Bar displays the standard deviation. \* $P < 0.05$ , vs the laparotomy group; † $P < 0.05$ , vs baseline values (T1) within the group.

**Table 4** Calculation of unmeasured anions. Values are means (sd). Laparotomy group, patients with laparotomy; laparoscopy group, patients with laparoscopic abdominal surgery; SBE, standard base excess; SIG, strong ion gap; AG, anion gap; T1, 10 min after the induction of anaesthesia; T2, 40 min after opening the peritoneum in the laparotomy group or pneumoperitoneum in the laparoscopy group; T3, at the end of surgery; T4, 1 h after the surgery. † $P < 0.05$ , vs baseline values (T1) within the group

	T1	T2	T3	T4
SBE (mmol litre <sup>-1</sup> )				
Laparotomy	2.4 (1.7)	0.8 (2.3) <sup>†</sup>	-1.2 (1.6) <sup>†</sup>	-1.6 (1.6) <sup>†</sup>
Laparoscopy	2.0 (1.8)	-0.3 (1.4) <sup>†</sup>	-0.5 (1.8) <sup>†</sup>	-0.9 (1.8) <sup>†</sup>
SIG (mmol litre <sup>-1</sup> )				
Laparotomy	-0.2 (2.6)	-0.5 (1.3)	1.2 (2.6)	0.8 (2.7)
Laparoscopy	-0.9 (2.7)	-1.6 (4.1)	1.0 (2.1)	0.5 (2.3)
AG (mmol litre <sup>-1</sup> )				
Laparotomy	14.2 (2.8)	12.4 (1.6)	13.7 (2.2)	12.9 (2.4)
Laparoscopy	13.6 (3.2)	11.5 (4.3)	13.2 (2.5)	14.0 (2.7)

There are several limitations to this study. One of them is the lack of the ionized calcium ( $\text{Ca}^{2+}$ ) and magnesium ( $\text{Mg}^{2+}$ ) in the formula for the apparent strong ion difference. The  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  were omitted because the measurement of an ionized divalent cation concentration was not available in the ABGA machine at the time of the study. Theoretically,

when a strong cation is added, the SID increases. The hydrogen ions are withdrawn from the solution to maintain an electrochemical neutrality, which promotes alkalinity. Therefore, the pH increases when the SID increases. However, the strong cations other than  $\text{Na}^+$ , such as  $\text{Mg}^{2+}$ ,  $\text{K}^+$ , and  $\text{Ca}^{2+}$ , do not change significantly to affect the acid-base status.

In fact,  $\text{Ca}^{2+}$  and  $\text{Mg}^{2+}$  were often omitted in the formula depending on its availability,<sup>12–14</sup> and Story and colleagues<sup>15</sup> reported that a simplified Fencl–Stewart approach using only  $\text{Na}^+$  and  $\text{Cl}^-$  agree well with the previous, more complex equations. In addition, the calcium containing solution was infused in this study. Lanzinger and colleagues<sup>16</sup> reported that when the average calcium intake was 6.24 mmol, the change in ionized calcium level was only 0.04 mmol litre<sup>-1</sup> in patients undergoing abdominal surgery. In this study, the mean (SD) of calcium intake was 2.2 (0.79) mmol in the laparotomy group and 1.8 (0.7) mmol in the laparoscopy group. Since there was no difference in the calcium intake between the two groups in this study, the effect of the calcium containing solution would not have affected the result of this study. Another limitation in this study is the fluctuation of  $\text{Pa}_{\text{CO}_2}$  during laparoscopy. The ventilation was adjusted to maintain  $\text{Et}'_{\text{CO}_2}$  between 4.00 and 4.66 kPa except during  $\text{CO}_2$  pneumoperitoneum, which was 4.66–5.33 kPa. Constant maintenance of  $\text{CO}_2$  level may have provided better understanding of the acid–base status during pneumoperitoneum. Lastly, this study is not a randomized study because patients were treated with laparoscopy or laparotomy according to the decision of the medical team.

In conclusion, the decrease in the pH during the pneumoperitoneum was affected by the increase in  $\text{Pa}_{\text{CO}_2}$ , which promptly returned to a normal value after the desufflation. On the other hand, the decrease in the pH after laparotomy was affected by the metabolic factors, which persisted an hour after the surgery.

## Conflict of interest

None declared.

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