Surg Endosc (2009) 23:2543–2549
DOI 10.1007/s00464-009-0388-4

Effect of different intra-abdominal pressure levels on QT dispersion in patients undergoing laparoscopic cholecystectomy

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Received: 30 August 2008 / Accepted: 22 January 2009 / Published online: 5 March 2009

Abstract

Background Hemodynamic changes caused by carbon dioxide (CO_2) insufflation occur frequently in patients who undergo laparoscopic surgery. One indicator of these changes is corrected QT dispersion (QTcd), an index of myocardial function. Prolongation of QTcd has been associated with cardiovascular morbidity and mortality. We compared the effects of high-pressure (15 mmHg) and low-pressure (7 mmHg) CO_2 pneumoperitoneums on the QT interval, the rate-corrected QT interval (QTc), the QT dispersion (QTd), and the corrected QT dispersion (QTcd) during laparoscopic cholecystectomy.

Methods Twenty consecutive patients were in a low-pressure pneumoperitoneum group and 32 were in a high-pressure pneumoperitoneum group. A 12-lead electrocardiogram was used to monitor cardiac variables. In all patients, serial electrocardiograms were recorded before anesthesia induction (baseline), immediately after the pneumoperitoneum had been created, every 15 minutes during CO_2 insufflation, and 5 minutes after deflation. Two observers measured the QT intervals independently, and the QTcd was calculated using Bazett's formula.

Results The QT interval and the QTc interval did not change significantly during the study in either group. The QTd and QTcd in the high-pressure pneumoperitoneum group increased significantly during CO_2 insufflation and were significantly higher in the high-pressure pneumoperitoneum group compared with the low-pressure pneumoperitoneum group. Changes caused by CO_2 insufflation were reversible.

Conclusions Statistically significant increases of QTd and QTcd, which are associated with an increased risk of arrhythmias and cardiac events, occur during CO_2 insufflation in both high-pressure and low-pressure pneumoperitoneums. QTd and QTcd were significantly higher in the high-pressure pneumoperitoneum group than they were in the low-pressure pneumoperitoneum group. QT interval changes were not related to anesthetic agents, surgical stress, hypercapnia, or duration of CO_2 insufflation. Increased intra-abdominal pressure may have caused these changes.

Keywords Laparoscopic cholecystectomy · High-pressure and low-pressure pneumoperitoneum · Electrocardiography · QT dispersion

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Laparoscopic cholecystectomy (LC) has become a routine surgical procedure for the treatment of gallbladder disease. Despite its advantages and wide acceptance, cardiac adverse effects of a CO_2 pneumoperitoneum are well established [1, 2]. Creating a pneumoperitoneum may increase the cardiovascular complication rate in patients who undergo LC; however, lower intra-abdominal pressure levels have been shown to be feasible, safe, and to reduce the cardiovascular consequences of a high-pressure CO_2 pneumoperitoneum [3, 4]. Eisenberg and associates found intraoperative myocardial ischemia in 39% of their patients who underwent conventional noncardiac surgery when monitored; however, routine anesthetic monitoring identified myocardial ischemia in only 2% of these same patients [5]. A further concern centers on cardiovascular changes induced by a positive-pressure CO_2 pneumoperitoneum.

Cowan and associates popularized the concept of QT dispersion (QTd) and found that measures of interlead QT intervals were greater in patients with myocardial infarction than they were in patients without myocardial infarction [6]. The QT interval corresponds to ventricular depolarization and repolarization, and QTd or corrected QT dispersion (QTcd) reflects electrical instability in the ventricles. In the general patient population, prolongation of the QT interval and QTd, as shown on a 12-lead electrocardiogram (ECG), has been correlated with cardiovascular mortality [7]. In elderly persons, intraperitoneal CO_2 insufflation during LC is associated with increases in the QT interval and the QTd [8].

Investigators have studied the effects of intra-abdominal CO_2 insufflation on QTd as an indicator of myocardial function in elderly patients, but to our knowledge, there have been no studies regarding the QTd and QTcd in high-pressure and low-pressure CO_2 pneumoperitoneums. The goal of this study, therefore, was to evaluate changes in the QT, the corrected QT (QTc) interval, the QTd, and the QTcd of patients who undergo LC with a high-pressure (15 mmHg) or low-pressure (7 mmHg) CO_2 pneumoperitoneum.

Patients and methods

The project was approved by the Baskent University research council and the local ethics committee. All patients provided written, informed consent. This prospective, randomized, controlled, single-blind clinical study enrolled consecutive patients of American Society of Anesthesiologists grade 1 and 2 undergoing LC. The indication for LC was ultrasonographically proven uncomplicated symptomatic cholelithiasis. Patients with cardiac diseases, conduction disorders, metabolic problems, previous history of atrial fibrillation, or those taking antiarrhythmic medications were excluded from the study, as were those who were converted to open surgery, refused LC, or refused to give informed consent. Patients who required perioperative position change or the use of suction and irrigation and laparoscopic retractor were excluded from this study.

Between October 2006 and November 2007, 52 patients were allocated to two groups: the low-pressure CO_2 pneumoperitoneum (7 mmHg; $n = 20$) and the high-pressure CO_2 pneumoperitoneum (15 mmHg; $n = 32$). Randomization to the high-pressure or the low-pressure group was done before the operation, and the surgeon was informed of the randomization at the time of the first skin incision. In addition to demographic data, previous abdominal operations, accompanying systemic diseases, and body mass index were recorded. An electrocardiogram was performed, and noninvasive blood pressure, heart rate, peripheral oxygen saturation, and end-tidal carbon dioxide values were monitored with a SIEMENS SC7000 Monitor (Siemens Medical Solutions USA, Inc., Malvern, PA). Anesthesia was induced with intravenous propofol (2 mg/kg) and fentanyl (1 μg/kg). Endotracheal intubation was facilitated with intravenous vecuronium bromide (1 mg/kg); anesthesia was maintained with 1 minimum alveolar concentration sevoflurane in a 50% O_2/air mixture. Laparoscopic procedures were performed in a standard manner in all patients. End tidal carbon dioxide was maintained between 35 and 40 mmHg by changing the respiratory rate during pneumoperitoneum. All patients received a continuous infusion of crystalloid solution of 5 ml/kg per hour during the study.

Four experienced surgeons performed the laparoscopic cholecystectomies. In both groups, after intubation, the patient was prepared in a standard manner. The abdomen was insufflated with CO_2 via a Veress needle through an infraumbilical incision. Two 10-mm and two 5-mm trocars were inserted through the appropriate infraumbilical, subxiphoid, subcostal midclavicular, and subcostal anterior axillary incisions. The cystic duct and the cystic artery were clipped twice and incised. Blood pressure and pulse rate counts were recorded continuously during surgery.

In the low-pressure group, a laparoscopic retractor was used to elevate the edge of the liver whenever needed. The position of the patients was mainly supine; however, the head-up tilt position was used in six patients (three patients in each group).

The 12-lead electrocardiogram was recorded at a paper speed of 50 mm per second and at a voltage of 20 mm/mV. Electrocardiograph recordings were made and recorded before anesthetic induction (baseline), immediately after the pneumoperitoneum had been created, every 15 minutes during CO_2 insufflation, and 5 minutes after deflation. A cardiologist blinded to the study protocol did the measurement of the QT duration. Using calipers on printed electrocardiograms, each QT interval was measured from the beginning of the QRS complex to the visual return of the T wave to the isoelectric line. When the T wave was interrupted by the U wave, the end of the T wave was defined as the nadir between the T and U waves. The heart rate QTc interval was calculated using Bazett's formula. QT dispersion was defined as the difference between the maximum and minimum QT intervals; QTc dispersion was defined as the difference between the maximum and minimum Bazett rate corrected QT intervals. The repeatability of the QT and QTc measurements was tested by a second observer, who measured the same intervals of lead 2 in ten randomly selected electrocardiograms.

All data are presented as mean ± standard deviation. An analysis of variance test was used for repeated measurements. The Scheffe test was used to make comparisons between the groups. $p < 0.05$ was accepted as statistically significant.

Results

Between October 2006 and November 2007, 14 patients were excluded as a result of protocol violation and 70 patients were allocated to 2 groups: 35 patients in each group. In the high-pressure group, 3 patients were put into head-up tilt position, leaving 32 patients. In the low-pressure group, three patients had marked gallbladder adhesions. Four patients had gallbladder perforations, which required suction and irrigation. One patient bled from the cystic artery; the patient had been converted to a high-pressure pneumoperitoneum, which allowed us an improved view to apply clips to the artery to stop the bleeding. A laparoscopic retractor was used in four patients, and three patients were put into a head-up tilt position. This left 20 patients.

Fourteen patients were excluded as a result of protocol violations; therefore, 52 patients were included in the analysis (6 men, 46 women; mean age, 50 ± 11.18 years). There were no differences between groups regarding previous abdominal operations, accompanying systemic diseases, body mass index, age, sex, duration of anesthesia, duration of surgery, and amount of gas used during LC (Table 1). There were no conversions to open cholecystectomy in the groups.

The mean arterial blood pressure increased significantly in both groups after CO_2 insufflation (low-pressure, $p = 0.05$; high-pressure, $p = 0.01$) and remained higher than the baseline value after desufflation (low-pressure, $p = 0.05$; high-pressure, $p = 0.01$). There was no statistically significant difference between the groups (Fig. 1).

There was a moderate increase in heart rate that reached statistical significance for the high-pressure group ($p = 0.05$). The increased heart rate returned to normal after desufflation. There was no statistically significant difference between the two groups (Fig. 2). No statistically significant differences in QT interval and QTc interval were observed for either group during the study (Figs. 3 and 4).

In both groups, QTd increased significantly from immediately after insufflation until desufflation. In the high-pressure group, mean baseline QTd was 39.7 ± 8.6 msec, and the peak value was 62.9 ± 13 msec immediately after the start of insufflation ($p < 0.01$). In the low-pressure group, mean QTd at baseline was 37.4 ± 7.2 msec, which increased to a peak value of 47.8 ± 4.8 msec immediately after insufflation ($p < 0.05$). During the insufflation period, the mean QTd was significantly higher in the high-pressure group than it was in the low-pressure group. Three patients in the low-pressure group with a mean baseline QTd of 36.1 ± 2.2 msec and a peak value of 46.4 ± 1.1 msec immediately after CO_2 insufflation were placed in a head-up tilt position, and three patients in the high-pressure group with a mean QTd value of 35.2 ± 1.7 msec at baseline and a peak value of 60.4 ± 2.3 msec immediately after CO_2 insufflation were placed in the head-up tilt position. (Figs. 5 and 6)

In both groups, the QTcd increased significantly from immediately after insufflation through desufflation. In the high-pressure group, mean baseline QTcd was 43.5 ± 6.4 msec, and the peak value was 69.1 ± 8.3 ms ($p < 0.01$) immediately after the start of insufflation. In the low-pressure group, the mean baseline QTcd was 41.6 ± 6.1 msec and increased to a peak value of 47.7 ± 6.8 ms ($p < 0.05$) immediately after insufflation.

The QTcd was significantly higher during insufflation period in the high-pressure group than it was in the low-pressure group. Three patients in the low-pressure group who were put into a head-up tilt position had a baseline mean QTcd of 40.1 ± 1.2 msec; their peak value immediately after CO_2 insufflation was 45.4 ± 2.0 msec. Three patients in the high-pressure group had a baseline mean QTcd value of 41.0 ± 1.3 msec; the peak value immediately after CO_2 insufflation was 65.1 ± 2.2 msec.

Table 1 General characteristics of the patients

	Low-pressure group ($n = 20$)	High-pressure group ($n = 32$)
Male/female ratio	2/18	6/26
Age (yr)	52.2 ± 10.05	49.3 ± 12.64
Body mass index	28.5 ± 4.76	28.4 ± 5.13
Comorbid disease	6/20	7/32
Previous UAO	1/20	2/32
Previous LAO	1/20	3/32
Duration of operation (min)	55.05 ± 20.19	51.02 ± 17.23
Duration of anesthesia (min)	73.4 ± 21.8	69.1 ± 18.7
Amount of gas used (L)	42.7 ± 24.3	38.9 ± 25.1

UAO upper abdominal operation, *LAO* lower abdominal operation

Discussion

In patients without cardiovascular disease who undergo LC, QTd and QTcd are prolonged with intraperitoneal CO_2 insufflation; this effect is more pronounced at higher pressures. There was no cardiac morbidity or mortality in the perioperative period in this study. The reported cardiovascular effects of pneumoperitoneum and prolonged

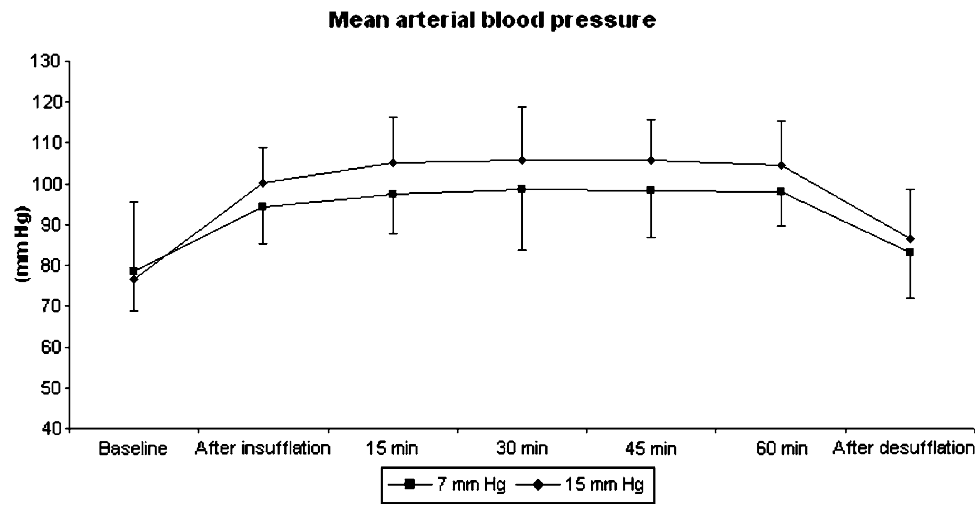

Fig. 1 Changes in mean arterial blood pressure. All values are means ± standard deviations

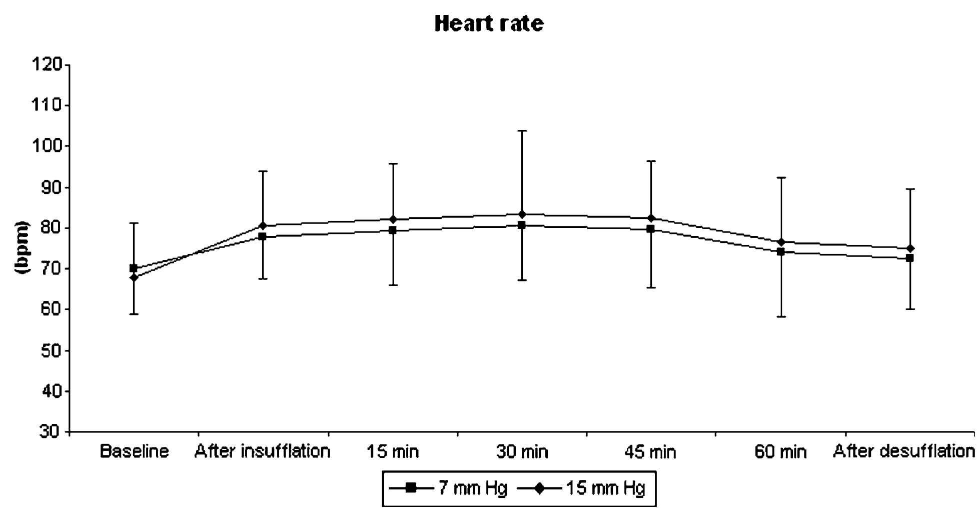

Fig. 2 Changes in heart rate. All values are means ± standard deviations

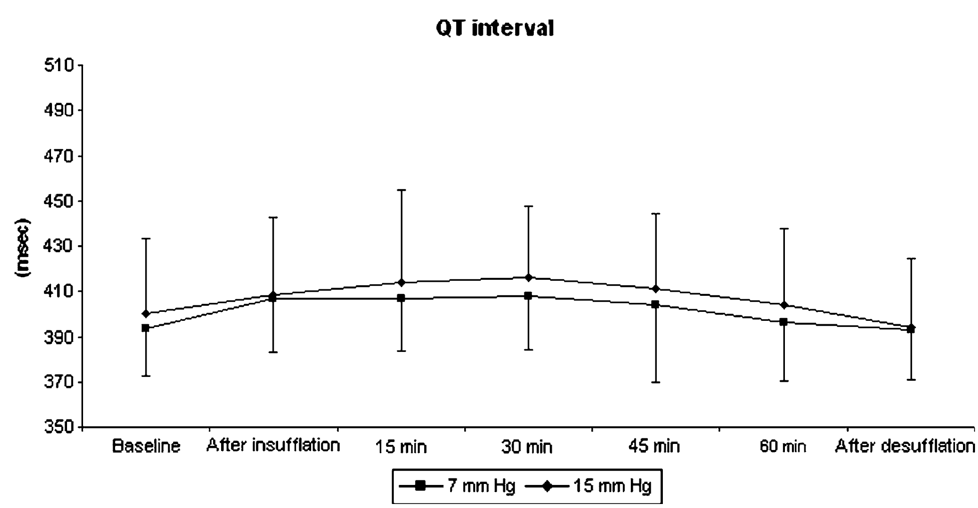

Fig. 3 Changes in QT interval. All values are means ± standard deviations

QTc and QTcd are not expected to have clinical significance in healthy patients during elective laparoscopic operations, except elderly persons with cardiac problems during prolonged operations [9–11].

Carbon dioxide insufflation and the patient's volemic status, age, position, presence of hypercapnia, anesthetic agents, surgical stress, and level of intra-abdominal pressure also may affect QT interval and QTd.

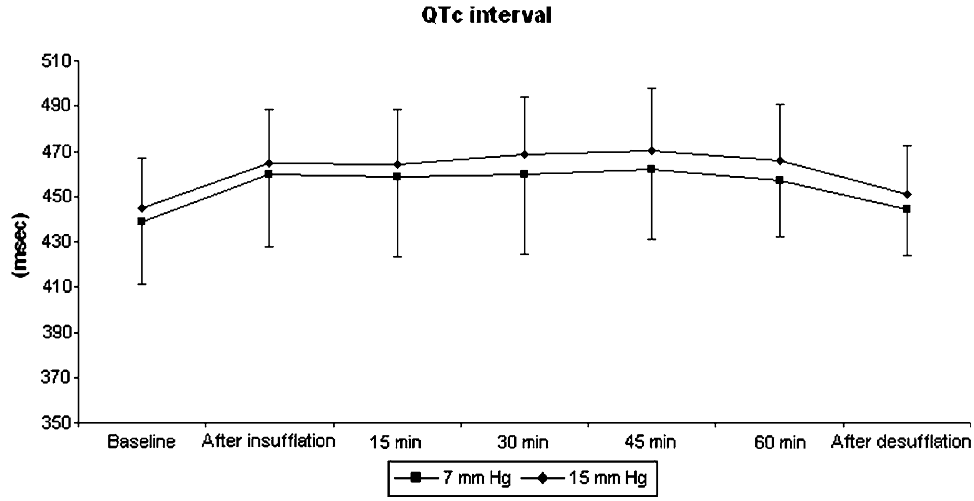

Fig. 4 Changes in corrected QT interval. All values are means ± standard deviations

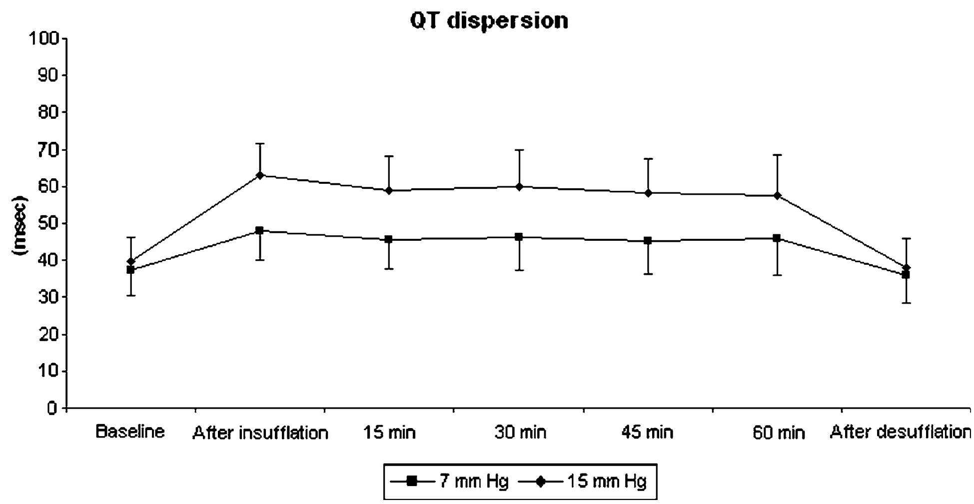

Fig. 5 Changes in QT dispersion. All values are means ± standard deviations

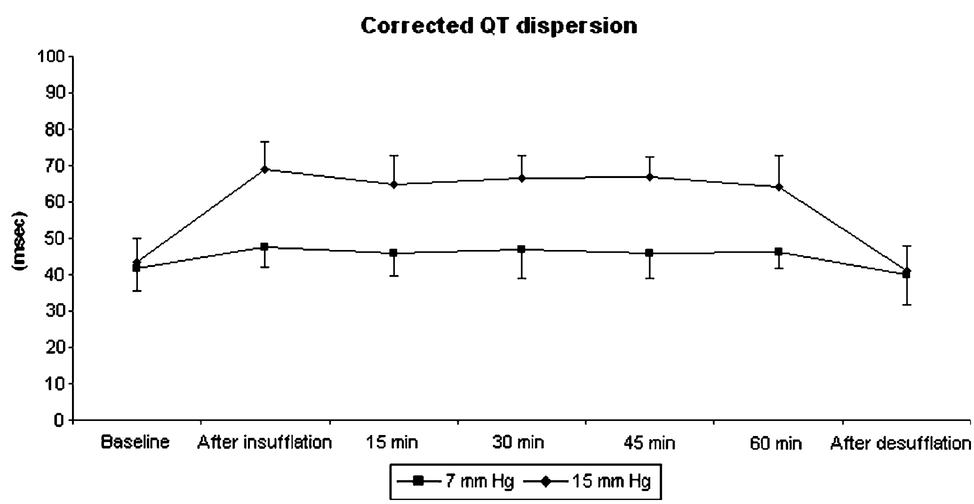

Fig. 6 Changes in corrected QT dispersion. All values are means ± standard deviations

In the current study, the amounts of insufflating gas used in each group were similar, and we found no differences in volemic status between the groups. The preoperative characteristics of the patients were similar in both groups. The position of the patients was supine; however, three patients from each group were placed in a head-up tilt position, and we used a laparoscopic liver retractor in one patient. During the study, the overall effect of these positions on patients and the use of a liver retractor was negligible.

Hypercapnia has been thought to produce an increase in the QTd interval and QTcd [12]. Actually, hypercapnia activates the sympathetic nervous system leading to an increase in blood pressure, heart rate, myocardial contractility, and arrhythmias [13]. Nevertheless, in our study, end-tidal CO_2 values were monitored, and no hypercapnia was observed during the procedure.

In our study, propofol was used for induction of and sevoflurane was used to maintain anesthesia. QTc changes during the procedures were caused by the insufflation of CO_2 and were reversed by desufflation. Thus, QTc changes during laparoscopic surgery seem to be unrelated to the use of propofol or sevoflurane.

Additionally, it is thought that surgical stress also affects QTd and QTcd [8]. Surgical exertion may prolong QT duration, but this effect was the same in both groups in our study. There seem to be different factors that affect QT duration during LC. Compared with a low-pressure pneumoperitoneum, a high-pressure pneumoperitoneum (15 mmHg) increased minute ventilation and shifted the diaphragm cephalad, resulting in an increase in intrathoracic pressure. In the high-pressure group, intrathoracic pressure was relatively higher compared with the low-pressure group. Because of the higher intrathoracic pressures, QTd and QTcd levels may be increased more in the high-pressure group than in the low-pressure group. Although Egawa and colleagues demonstrated that QTd changes were related to the duration of CO_2 insufflation during LC, we were not able to find such a relationship [8]. Increases in the mean QTc and QTcd in our series seemed to be independent of the duration of CO_2 insufflation.

Day and associates proposed the use of QT dispersion measurement as an index of the inhomogeneity of myocardial repolarization, which could be applied as a potential prognostic tool in detecting future ventricular tachyarrhythmic events and death [14, 15]. The Strong Heart Study showed that QTcd was a strong predictor of all-cause mortality and a weaker predictor of cardiovascular mortality, and that QTd is a significant predictor of cardiovascular mortality [15]. QTd analysis has been associated with an adverse prognosis in a variety of patient populations [16–19]. Several factors may account for the increased left ventricular arrhythmic activity in the patients who underwent LC during pneumoperitoneum. Intraperitoneal CO_2 insufflation induces alteration of electrophysiologic changes, including QT prolongation [8]. Left ventricular hypertrophy, myocardial infarction, dilated cardiomyopathy, altered membrane permeability for sodium ions, increased sympathetic activity all have been shown to significantly increase QTd from baseline [20–29]. It should be mentioned that we did not measure variables, such as cardiac output or autonomic activity in correlation with our findings, because the changes that follow pneumoperitoneum have already been well documented in many studies.

Although there were 14 protocol violations in the study, there were enough patients in each group. Our results suggest that during LC, a low-pressure pneumoperitoneum (compared with a high-pressure pneumoperitoneum) has a minimal effect on electrophysiologic changes, as shown on an electrocardiogram. Electrocardiographic changes returned to baseline after desufflation. In our study, the finding that prolonged QT duration time can expose some functional and structural cardiac changes (physiological and molecular) that reflect certain cardiac derangements during induction of pneumoperitoneum.

Eventually, such changes were well-tolerated in the vast majority of the operated population and did not result in cardiac morbidity (because of their good health and the short duration time of pneumoperitoneum during elective LC). However, our findings should raise concerns regarding choosing a low-pressure pneumoperitoneum for LC (which may prevent patients from cardiac risks whenever we perform prolonged and complicated laparoscopic procedures), especially in elderly and cardiac-diseased patients.

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