

Effects of long periods of pneumoperitoneum combined with the head-up position on heart rate-corrected QT interval during robotic gastrectomy: an observational study

Na Young Kim¹ , Sun-Joon Bai¹,
Hyoung-Il Kim² , Jung Hwa Hong³,
Hoon Jae Nam¹, Jae Chul Koh^{4,#}  and
Hyun Joo Kim^{1,#} 

Abstract

Objective: Pneumoperitoneum and the head-up position reportedly stimulate the sympathetic nervous system, potentially increasing the risk of cardiac arrhythmia. We evaluated the effects of a long duration of pneumoperitoneum in the head-up position on the heart rate-corrected QT (QTc) interval during robotic gastrectomy.

Methods: This prospective observational study involved 28 patients undergoing robotic gastrectomy. The QTc interval was recorded at the following time points: before anaesthetic induction (baseline); 10 minutes after tracheal intubation; 1, 5, 30, 60, and 90 minutes after pneumoperitoneum induction in the head-up position; after pneumoperitoneum desufflation in the supine position; and at the end of surgery. The primary outcome was the QTc interval, which was measured 90 minutes after pneumoperitoneum combined with the head-up position.

¹Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea

²Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea

³Department of Policy Research Affairs National Health Insurance Service Ilsan Hospital, Goyang, Gyeonggi-do, Republic of Korea

⁴Department of Anesthesiology and Pain Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Republic of Korea

#These authors contributed equally to this work.

Corresponding author:

Hyun Joo Kim, Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea.
Email: jjlong@yuhs.ac



Results: Compared with baseline, the QTc interval was significantly prolonged at 1 and 60 minutes after pneumoperitoneum, peaked at 90 minutes, and was sustained and notably prolonged until the end of surgery. However, no considerable haemodynamic changes developed.

Conclusion: A long period of carbon dioxide pneumoperitoneum application in a head-up position significantly prolonged the QTc interval during robotic gastrectomy. Therefore, diligent care and close monitoring are required for patients who are susceptible to developing ventricular arrhythmia.

Trial Registration: Registered at ClinicalTrials.gov; <https://clinicaltrials.gov/ct2/show/NCT02604979>; Registration number NCT02604979

Keywords

Carbon dioxide pneumoperitoneum, head-up position, QTc interval, robotic gastrectomy, anaesthesia, cardiac arrhythmia

Date received: 3 April 2018; accepted: 29 May 2018

Introduction

Gastric cancer is a leading cause of cancer-related death worldwide, and surgical treatment of this disease has been performed via both conventional and minimally invasive techniques.¹ Robotic gastrectomy is being increasingly regarded as an alternative minimally invasive technique that may help surgeons to overcome the principal drawbacks of laparoscopic gastrectomy.^{2–4} Robotic-assisted systems are particularly helpful when precise dissection is required because such systems can attenuate the surgeon's tremor, improve the surgeon's wrist articulation, and produce three-dimensional high-resolution surgical fields.^{1,3}

However, because of the additional time necessary for docking and other technical factors, a longer operation time is typically required for robotic surgery, although this additional time is gradually decreasing.⁵ During robotic gastrectomy, the patient must be under pneumoperitoneum and in the head-up position for a long period to achieve a better view of the surgical site. Pneumoperitoneum and the head-up

position are reportedly predisposing conditions for autonomic nervous system imbalance.^{6,7} Such an imbalance exacerbates prolongation of the heart rate-corrected QT (QTc) interval, which may be closely related to the development of potentially dangerous malignant cardiac arrhythmias.^{7,8} Cardiac arrhythmias occur fairly frequently during pneumoperitoneum and can progress to serious consequences such as ventricular fibrillation or cardiac arrest.^{9–11} However, in previous studies investigating the effects of pneumoperitoneum, QTc interval prolongation either did not occur^{7,11} or only occurred in patients of advanced age.¹² In contrast, the QTc interval has been demonstrated to increase during head-up tilt.¹³ To the best of our knowledge, no study has been performed to investigate changes in the QTc interval during robotic gastrectomy, which is usually conducted with a long duration of pneumoperitoneum while the patient is in the head-up position.

Therefore, our hypothesis was that a long period of pneumoperitoneum combined with the head-up position prolongs the QTc interval during robotic gastrectomy. To test this

hypothesis, we evaluated the QTc interval changes from the induction of anaesthesia to the end of surgery in patients undergoing robotic gastrectomy.

Materials and methods

Study population

This was a single-centre, prospective observational study. After obtaining approval from the Institutional Review Board and Hospital Research Ethics Committee of Severance Hospital, Yonsei University Health System in Seoul, Korea (IRB approval no. 4-2015-0607) on 21 August 2015, this study was registered at ClinicalTrials.gov (registration no. NCT02604979). Patients with an American Society of Anesthesiologists physical status of I or II who were concurrently scheduled to undergo robotic gastrectomy from September 2015 to February 2016 were evaluated for study eligibility. Written informed consent was obtained from all patients. The exclusion criteria were preoperative electrocardiography (ECG) abnormalities including a QTc interval of >440 ms and arrhythmias; a history of cardiac disease such as unstable angina, congestive heart failure, coronary artery disease, or valvular heart disease; prior pacemaker implantation; electrolyte imbalance; use of antiarrhythmic agents or any drugs that could affect the QTc interval other than antihypertensive agents; hepatic or renal failure; and neurological or psychiatric impairment.

Anaesthesia

All patients were premedicated with 0.1 mg of intravenous glycopyrrolate. ECG, oxygen saturation, noninvasive blood pressure, and the bispectral index (A-2000; Aspect Medical Systems Inc., Newton, MA, USA) were monitored. Anaesthesia was induced with 1.5 to 2.0 mg/kg of propofol, 0.5 μ g/kg of remifentanyl, and 1.2 mg/kg of rocuronium.

Mechanical ventilation was maintained at a tidal volume of 8 mL/kg and a positive end-expiratory pressure of 5 cmH₂O. The respiratory rate was adjusted to maintain the end-tidal carbon dioxide (CO₂) at 35 to 45 mmHg. After induction, a radial artery catheter was placed for continuous arterial pressure monitoring. Anaesthesia was maintained with desflurane (age-adjusted minimum alveolar concentration of 0.7–1.2) and remifentanyl (0.02–0.1 μ g/kg/min) to adjust the bispectral index from 40 to 60.

Data collection

The QT interval (from the onset of the QRS complex to the end of the T wave) was continuously monitored in lead V5 and recorded using LabChart software (Pro Version 7; ADInstruments, Inc., Sydney, Australia) and a data acquisition system (PowerLab; ADInstruments, Inc.). The QT interval was measured at the following nine time points: before anaesthetic induction (baseline); 10 minutes after tracheal intubation; 1, 5, 30, 60, and 90 minutes after the application of pneumoperitoneum in the head-up position; after desufflation of the pneumoperitoneum in the supine position; and at the end of surgery. In the event of automatic measurement failure, the QT interval was manually measured.¹⁴ At each time point, the interval was measured for four successive beats and then averaged. The QTc interval was calculated using the Bazett's formula:

$$QTc = QT/\sqrt{RR}$$

All measurements and analyses were performed by one of the authors. Haemodynamic data including the mean arterial pressure and heart rate were collected at each time point. Hypotension (mean arterial pressure of <60 mmHg) and bradycardia (heart rate of <40 beats/min) were treated with 4 mg of intravenous ephedrine

and 0.5 mg of atropine, respectively. The CO₂ insufflator was used to maintain an intra-abdominal pressure of 12 mmHg in the 15-degree head-up position. The peak inspiratory pressure, end-tidal CO₂, and concentration of desflurane were also recorded 10 minutes after tracheal intubation; 5, 30, 60, and 90 minutes after the start of pneumoperitoneum induction in the head-up position; and after desufflation of the pneumoperitoneum in the supine position.

Statistical analysis

The primary outcome was the QTc interval, which was measured 90 minutes after pneumoperitoneum combined with the head-up position. A QTc interval of 440 ms was considered the cut-off value that indicated abnormal prolongation according to a previous study.¹⁵ Therefore, the occurrence of a prolonged QTc interval of >440 ms as well as prolongation of more than 30, 60, or 100 ms from the baseline value were assessed.¹⁵ Statistical analyses were performed using SAS software version 9.2 (SAS Inc., Cary, NC, USA). The independent *t*-test and Mann–Whitney U test were used to compare mean values of parametric and non-parametric data, respectively. A linear mixed model analysis was used to compare changes in the QTc interval, peak inspiratory pressure, end-tidal CO₂, concentration of desflurane, and haemodynamics. Bonferroni correction was performed to adjust for multiple comparisons in the post-hoc analysis. A *p* value of <0.05 was regarded as statistically significant.

Results

Of 32 patients who were evaluated for eligibility, two patients with a preoperative QTc interval of >440 ms on ECG were excluded. Moreover, two patients were excluded due to a change in the type of surgery from robotic gastrectomy to open

Table 1. Patient demographics and intraoperative variables.

Characteristic	N = 28
Age (years)	54.3±10.9
Sex	
Male	17 (60.7)
Female	11 (39.3)
Height (cm)	165.4±8.9
Weight (kg)	61.5±10.8
ASA physical status classification	
I	19 (67.9)
II	9 (32.1)
Duration of surgery (min)	174.6±42.2
Duration of pneumoperitoneum (min)	164.1±63.1
Duration of anaesthesia (min)	211.4±41.6
Total CO ₂ amount (L)	838.0±366.1
Fluid intake (mL)	1358.9±448.5
Blood loss (mL)	33.4±33.2
Urine output (mL)	108.6±64.4
Administered dose of remifentanyl (µg)	806±254
Administered dose of ephedrine (mg)	2.9±5.1

Data are presented as mean ± standard deviation or number (percentage). ASA = American Society of Anesthesiologists, CO₂ = carbon dioxide.

gastrectomy and the development of pneumothorax during surgery, respectively. Thus, the remaining 28 patients were evaluated in this study.

The patient characteristics and intraoperative variables are presented in Table 1. The mean duration of surgery and anaesthesia was 174.6 and 211.4 minutes, respectively. The total amount of CO₂ used for pneumoperitoneum maintenance was 838 L during a mean duration of 164.1 minutes.

The QTc interval was significantly prolonged at 1 and 60 minutes after pneumoperitoneum, peaked at 90 minutes, and was sustained and notably prolonged until the end of surgery (*p* < 0.05) (Figure 1). Linear mixed model analysis revealed significant differences in the QTc interval over time (*p* < 0.001). Following post-hoc analysis

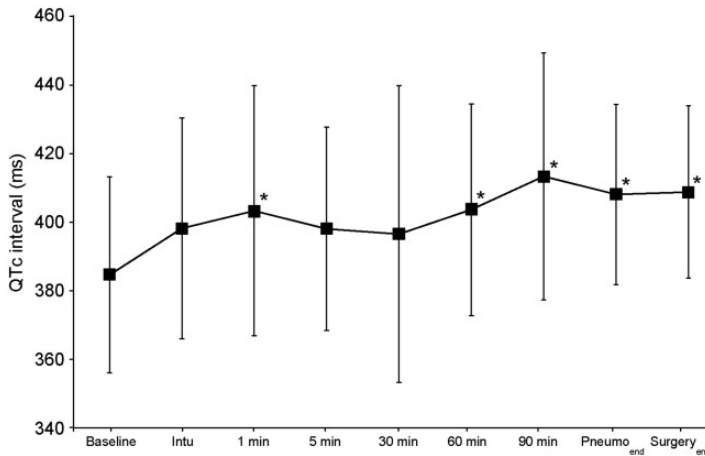


Figure 1. QTc interval from baseline until the end of surgery during robotic gastrectomy. QTc = heart rate-corrected QT interval; Baseline = before anaesthesia induction; Intu = 10 minutes after tracheal intubation; 1, 5, 30, 60, and 90 minutes = 1, 5, 30, 60, and 90 minutes after the start of pneumoperitoneum induction in the head-up position; Pneumo_{end} = desufflation of pneumoperitoneum in the supine position; Surgery_{end} = end of surgery. Data are expressed as mean \pm standard deviation. * $p < 0.05$ versus baseline value (Bonferroni-corrected).

with Bonferroni correction, the QTc interval was significantly prolonged at 1, 60, and 90 minutes after the application of pneumoperitoneum in the head-up position; after desufflation of the pneumoperitoneum in the supine position; and at the end of surgery compared with the baseline value ($p = 0.004$, $p = 0.034$, $p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). Meanwhile, no considerable haemodynamic changes in the mean arterial pressure or heart rate developed, while the QTc interval was significantly prolonged ($p < 0.05$) (Figure 2).

Nine patients exhibited a QTc interval of >440 ms, and extension of the interval was most remarkable at 90 minutes after pneumoperitoneum induction (five patients), although none of the patients had a QTc interval of >440 ms before surgery. Twenty (71.4%) patients had a prolonged QTc interval of >30 ms from baseline during surgery. Moreover, the QTc interval was prolonged by a maximum of 108.1 ms from baseline in one patient; this occurred 90 minutes after

pneumoperitoneum in the head-up position (Table 2).

The peak inspiratory pressure 5 minutes after the start of pneumoperitoneum application in the head-up position until desufflation of the pneumoperitoneum in the supine position was significantly higher than that at baseline ($p < 0.001$ for all). The end-tidal CO₂ ($p = 0.006$, 0.004, 0.001, 0.006, and 0.003) and desflurane concentrations ($p < 0.001$ for all) were significantly higher than the baseline values at the same time points as the peak inspiratory pressure, but they were not significantly different throughout the application of pneumoperitoneum (Table 3). None of the patients developed arrhythmias during surgery.

Discussion

To our knowledge, this prospective observational study is the first to investigate the influence of long periods of pneumoperitoneum application and head-up position

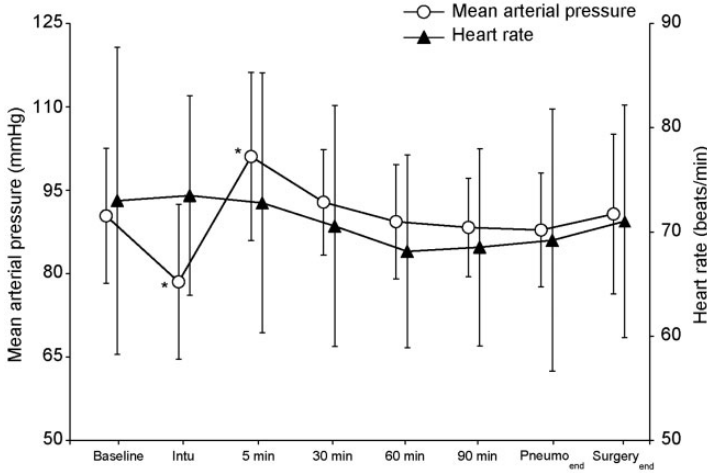


Figure 2. Intraoperative haemodynamics Baseline = before anaesthesia induction; Intu = 10 minutes after tracheal intubation; 1, 5, 30, 60, and 90 minutes = 1, 5, 30, 60, and 90 minutes after the start of pneumoperitoneum induction in the head-up position; Pneumo_{end} = desufflation of pneumoperitoneum in the supine position; Surgery_{end} = end of surgery. Data are expressed as mean ± standard deviation. *p < 0.05 versus baseline value (Bonferroni-corrected).

Table 2. QTc interval changes during robotic gastrectomy.

	N = 28
QTc interval > 440 ms	9 (32.1)
Prolonged QTc interval > 30 ms from baseline	20 (71.4)
Prolonged QTc interval > 60 ms from baseline	13 (46.4)
Prolonged QTc interval > 100 ms from baseline	1 (3.6)

Values are presented as number (percentage). QTc interval = heart rate-corrected QT interval.

maintenance on the QTc interval in patients undergoing robotic gastrectomy. The proportion of robotic surgeries performed for gastric cancer continues to increase; therefore, it is important to both prevent possible complications and maximize the benefits of robotic surgery. We observed prolongation of the QTc interval immediately and 60 minutes after the application of pneumoperitoneum in the head-up position; the QTc interval peaked at 90 minutes and

was sustained and significantly prolonged until the end of the robotic gastrectomy. Meanwhile, no considerable haemodynamic changes developed, while prolongation of the QTc interval was significantly sustained.

In the present study, we monitored the QTc interval for up to 90 minutes after the start of pneumoperitoneum induction. After desufflation of pneumoperitoneum, we continued to monitor the QTc interval until the end of the surgery, which lasted for a mean of 164 minutes because of the relatively longer duration of robotic surgery. As a result, the QTc interval increased most significantly at 90 minutes after the start of insufflation in the present study, suggesting that a long CO₂ insufflation time is closely related to increases in the QTc interval.¹² The creation of pneumoperitoneum using CO₂ insufflation is reportedly a predisposing factor for autonomic imbalance, resulting in a possible risk of cardiac arrhythmia. Increased intra-abdominal pressure might cause reflex sympathetic stimulation due to the decrease in

Table 3. Intraoperative parameters for ventilation.

	Intu	5 min	30 min	60 min	90 min	Pneumo _{end}
PIP, cmH ₂ O	13.0 ± 0.3	17.2 ± 0.4*	17.9 ± 0.5*	18.3 ± 0.4*	18.5 ± 0.5*	15.5 ± 0.4*
EtCO ₂ , mmHg	37.1 ± 0.6	38.9 ± 0.6*	39.1 ± 0.5*	39.4 ± 0.7*	39.4 ± 0.7*	40.8 ± 1.0*
Et _{DES} , vol %	3.8 ± 0.1	4.6 ± 0.1*	5.2 ± 0.1*	5.2 ± 0.1*	5.3 ± 0.1*	5.3 ± 0.1*

Values are presented as mean ± standard deviation. PIP = peak inspiratory pressure; EtCO₂ = end-tidal carbon dioxide; Et_{DES} = end-tidal desflurane; Intu = 10 minutes after tracheal intubation; 5, 30, 60, and 90 minutes = 5, 30, 60, and 90 minutes after start of pneumoperitoneum under head-up position; Pneumo_{end} = after desufflation of pneumoperitoneum *p < 0.05 versus baseline value (Bonferroni-corrected).

cardiac output. Moreover, hypercarbia might also directly or indirectly stimulate the sympathetic system via an increase in catecholamine release and induce nociceptive stimulation by distension of the abdominal muscles and diaphragm.^{6,7,12,16} For these reasons, prolonged maintenance of pneumoperitoneum might be a predisposing condition for further increases in the QTc interval.

In other studies, however, pneumoperitoneum with the head-up position did not increase the QTc interval,^{7,11,16} and Egawa et al.¹² only observed pneumoperitoneum-induced QTc interval prolongation in patients older than 65 years. Nevertheless, in the present study, we observed a significant increase in the QTc interval after the application of pneumoperitoneum in young adults (mean age of 54 years). In addition, we identified the number of patients who exhibited a QTc interval of >440 ms and relative prolongation of the QTc interval from the baseline value of >30 ms and >60 ms, which is considered abnormal and indicative of an increased risk of torsades de pointes.^{15,17} Although none of the patients exhibited a QTc interval of >440 ms before surgery, pneumoperitoneum with the head-up position led to QTc interval prolongation of >440 ms in 9 patients and prolongation of the QTc interval from the baseline value of >60 ms in 13 patients; this prolongation was even >100 ms in one patient.

The above-described findings may be attributed to the type of surgery, different inhalational anaesthetics, or degree of intra-abdominal pressure, which strengthen the effects of sympathetic stimulation and ultimately increase the QTc interval. With regard to the type of surgery, thoracic and upper abdominal surgeries appear to be associated with a higher risk of arrhythmia than surgeries at other sites.^{18,19} For a better surgical view and approach, robotic gastrectomy is usually performed under the head-up position. The head-up position might have been a contributing factor to the results of the present study. This position is closely related to changes in the autonomic nervous system, which might cause an imbalance in autonomic cardiac control.^{7,12,13} Differences in inhalational anaesthetics may have also affected the results. We used desflurane for anaesthetic maintenance in this study. Desflurane is our institution's standard of care because of its rapid emergence. Previous studies have indicated that desflurane prolongs the QTc interval more than sevoflurane, and direct effects on cardiac myocytes or sympathetic stimulation have been suggested as possible mechanisms.^{17,20} Therefore, desflurane may contribute to QTc interval prolongation during pneumoperitoneum, even in young adults. However, the significant differences in QTc interval prolongation observed with several types of inhalational agents remain controversial.^{21,22} Low doses of desflurane, such as those used in our study, may not

significantly prolong the QTc interval.²³ Moreover, our study results showed that most of the QTc interval prolongation occurred at 90 minutes of pneumoperitoneum application with an intra-abdominal pressure of 12 mmHg, which is similar to the 8 to 12 mmHg used in other studies performed to investigate the effects of pneumoperitoneum on the QTc interval.^{7,11,12} Imbalance of the autonomic nervous system with CO₂ insufflation and an increase in abdominal pressure might cause QTc interval prolongation. In addition, a longer duration of pneumoperitoneum in the head-up position may lead to a longer period of QTc interval prolongation with a higher possibility of arrhythmia risk even if no haemodynamic changes have occurred.

The present study has several limitations. First, the QTc interval was used to evaluate the risk of cardiac arrhythmia. In previous studies, other variables such as QT interval dispersion and the Tp-e interval combined with the QTc interval were also evaluated.^{7,21,24} However, there remains no definitive proof of a combined effect of these parameters under surgical and anaesthetic conditions.²⁵ Moreover, the QTc interval is still mainly used to analyse the risk of arrhythmia associated with specific drugs or procedures.^{26,27} Second, the small sample size of this study could be a limitation. However, the post-hoc power analysis showed a power of 0.987 when using the mean value of the QTc interval before anaesthetic induction and 90 minutes after pneumoperitoneum. Therefore, our sample size seems sufficient to support the primary endpoint of the current study. Third, for clarity, the increase in the QTc interval from baseline to the end of surgery should have been measured every 30 minutes. However, we only measured the QTc interval up to 90 minutes after pneumoperitoneum because pneumoperitoneum during robotic gastrectomy is terminated as early as 100 minutes in some cases; hence,

some data may not be available. Finally, in the current study, measurement of the QTc interval was not performed postoperatively in the ward despite the fact that the QTc interval was sustained and significantly prolonged at the end of surgery. However, in a previous study,¹⁵ QTc interval prolongation was not present after postoperative day 1 despite prolongation of the QTc interval at the end of surgery. Therefore, we expected that the prolonged QTc interval would return to the normal value postoperatively. However, ECG monitoring until 24 hours after surgery can be suggested because arrhythmias may possibly develop within 24 hours after surgery even if no arrhythmias developed during surgery. Thus, further studies evaluating the QTc interval for several postoperative days are required.

In conclusion, a long period of CO₂ pneumoperitoneum application in the head-up position significantly prolonged the QTc interval during robotic gastrectomy. Moreover, a longer duration of pneumoperitoneum in the head-up position may lead to a longer period of QTc interval prolongation with a higher risk of arrhythmia. Therefore, diligent care and close monitoring are required for patients who are susceptible to developing ventricular arrhythmias during robotic gastrectomy even if no haemodynamic changes have occurred.

Acknowledgements

The authors thank the biostatisticians of the Department of Research Affairs for their statistical comments and analysis as well as Dong-Su Jang, MFA (medical illustrator, Medical Research Support Section, Yonsei University College of Medicine) for his help with the figures.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ORCID iD

Na Young Kim  <http://orcid.org/0000-0003-3685-2005>

Hyoung-II Kim  <http://orcid.org/0000-0002-6134-4523>

Jae Chul Koh  <http://orcid.org/0000-0002-1625-8650>

Hyun Joo Kim  <http://orcid.org/0000-0003-1963-8955>

References

- Alimoglu O, Atak I and Eren T. Robot-assisted laparoscopic (RAL) surgery for gastric cancer. *Int J Med Robot* 2014; 10: 257–262.
- Lim SH, Lee HM, Son T, et al. Robotic surgery for gastric tumor: current status and new approaches. *Transl Gastroenterol Hepatol* 2016; 1: 28.
- Caruso S, Franceschini F, Patriiti A, et al. Robot-assisted laparoscopic gastrectomy for gastric cancer. *World J Gastrointest Endosc* 2017; 9: 1–11.
- Acquafresca PA, Palermo M, Rogula T, et al. Most common robotic bariatric procedures: review and technical aspects. *Ann Surg Innov Res* 2015; 9: 9.
- Vilallonga R, Fort JM, Caubet E, et al. Robotic sleeve gastrectomy versus laparoscopic sleeve gastrectomy: a comparative study with 200 patients. *Obes Surg* 2013; 23: 1501–1507.
- Sato N, Kawamoto M, Yuge O, et al. Effects of pneumoperitoneum on cardiac autonomic nervous activity evaluated by heart rate variability analysis during sevoflurane, isoflurane, or propofol anesthesia. *Surg Endosc* 2000; 14: 362–366.
- Di Iorio C, Cafiero T and Di Minno RM. The effects of pneumoperitoneum and head-up position on heart rate variability and QT interval dispersion during laparoscopic cholecystectomy. *Minerva Anesthesiol* 2010; 76: 882–889.
- Straus SM, Kors JA, De Bruin ML, et al. Prolonged QTc interval and risk of sudden cardiac death in a population of older adults. *J Am Coll Cardiol* 2006; 47: 362–367.
- Scott DB and Julian DG. Observations on cardiac arrhythmias during laparoscopy. *Br Med J* 1972; 1: 411–413.
- Uemura N, Nomura M, Inoue S, et al. Changes in hemodynamics and autonomic nervous activity in patients undergoing laparoscopic cholecystectomy: differences between the pneumoperitoneum and abdominal wall-lifting method. *Endoscopy* 2002; 34: 643–650.
- Egawa H, Morita M, Yamaguchi S, et al. Comparison between intraperitoneal CO₂ insufflation and abdominal wall lift on QT dispersion and rate-corrected QT dispersion during laparoscopic cholecystectomy. *Surg Laparosc Endosc Percutan Tech* 2006; 16: 78–81.
- Egawa H, Minami J, Fujii K, et al. QT interval and QT dispersion increase in the elderly during laparoscopic cholecystectomy: a preliminary study. *Can J Anaesth* 2002; 49: 805–809.
- Findler M, Birger A, Diamant S, et al. Effects of head-up tilt-table test on the QT interval. *Ann Noninvasive Electrocardiol* 2010; 15: 245–249.
- Kim Y, Kim SY, Lee JS, et al. Effect of dexmedetomidine on the corrected QT and Tp-e intervals during spinal anesthesia. *Yonsei Med J* 2014; 55: 517–522.
- Nagele P, Pal S, Brown F, et al. Postoperative QT interval prolongation in patients undergoing noncardiac surgery under general anesthesia. *Anesthesiology* 2012; 117: 321–328.
- Ekici Y, Bozbas H, Karakayali F, et al. Effect of different intra-abdominal pressure levels on QT dispersion in patients undergoing laparoscopic cholecystectomy. *Surg Endosc* 2009; 23: 2543–2549.
- Staikou C, Stamelos M and Stavroulakis E. Impact of anaesthetic drugs and adjuvants on ECG markers of torsadogenicity. *Br J Anaesth* 2014; 112: 217–230.
- Mohamad MF, Mohammad MA, Hetta DF, et al. Thoracic epidural analgesia reduces myocardial injury in ischemic patients

- undergoing major abdominal cancer surgery. *J Pain Res* 2017; 10: 887–895.
19. Vretzakis G, Simeoforidou M, Stamoulis K, et al. Supraventricular arrhythmias after thoracotomy: is there a role for autonomic imbalance? *Anesthesiol Res Pract* 2013; 2013: 413985.
 20. Silay E, Kati I, Tekin M, et al. Comparison of the effects of desflurane and sevoflurane on the QTc interval and QT dispersion. *Acta Cardiol* 2005; 60: 459–464.
 21. Min JJ, Lee J, Lee HC, et al. A comparison of the effects of sevoflurane and desflurane on corrected QT interval prolongation in patients undergoing living donor liver transplantation: a prospective observational study. *Transplant Proc* 2016; 48: 96–101.
 22. Yildirim H, Adanir T, Atay A, et al. The effects of sevoflurane, isoflurane and desflurane on QT interval of the ECG. *Eur J Anaesthesiol* 2004; 21: 566–570.
 23. Kim SH, Park SY, Chae WS, et al. Effect of desflurane at less than 1 MAC on QT interval prolongation induced by tracheal intubation. *Br J Anaesth* 2010; 104: 150–157.
 24. Xia Y, Liang Y, Kongstad O, et al. Tpeak-Tend interval as an index of global dispersion of ventricular repolarization: evaluations using monophasic action potential mapping of the epi- and endocardium in swine. *J Interv Card Electrophysiol* 2005; 14: 79–87.
 25. Tse G and Yan BP. Traditional and novel electrocardiographic conduction and repolarization markers of sudden cardiac death. *Europace* 2017; 19: 712–721.
 26. Elliott A, Johan Mork T, Hojlund M, et al. QTc interval in patients with schizophrenia receiving antipsychotic treatment as monotherapy or polypharmacy. *CNS Spectr* 2017; 1–6. doi:10.1017/S1092852917000402.
 27. Gibbons JA, Mojica AJ and Peele ME. Human electrical muscular incapacitation and effects on QTc interval. *J Forensic Sci* 2017; 62: 1516–1521.