

Elective lung resection increases spatial QRS-T angle and QTc interval

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Abstract

Background: Lung resection changes intra-thoracic anatomy, which may affect electrocardiographic results. While postoperative cardiac arrhythmias have been recognized after lung resection, no study has documented changes in vectorcardiographic variables in patients undergoing this surgery. The purpose of this study was to analyse changes in spatial QRS-T angle (spQRS-T) and corrected QT interval (QTc) after lung resection.

Methods: Adult patients undergoing elective lung resection under general anaesthesia were studied. The patients were allocated into four groups: those undergoing (1) left lobectomy (LL); (2) left pneumonectomy (LP); (3) right lobectomy (RL); and (4) right pneumonectomy (RP). The spQRS-T angle and QTc interval were measured one day before surgery (baseline) and 24, 48 and 72 h after surgery.

Results: Seventy-one adult patients (47 men and 24 women) aged 47–80 (65 ± 7) years were studied. In the study group as a whole, lung resection was associated with significant increases in spQRS-T ($p < 0.001$) and QTc ($p < 0.05$ at 24 and 48 h and $p < 0.01$ at 72 h). The greatest changes were noted in patients undergoing LP. Postoperative atrial fibrillation (AF) was noted in 6.4% of patients studied, in whom the widest spQRS-T angle and the most prolonged QTc intervals were also noted.

Conclusions: Lung resection widens the spQRS-T angle and prolongs the QTc interval, especially in patients undergoing LP. While postoperative AF was a relatively rare complication after lung resection in this study, it was associated with the widest spQRS-T angles and most prolonged QTc intervals. (Cardiol J XXXX; XX, X: xx–xx)

Key words: vectorcardiography, spatial QRS-T angle, corrected QT interval, atrial fibrillation, general anaesthesia

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Introduction

Cardiac arrhythmias, including atrial fibrillation (AF), have been recognized as frequent complications after thoracic surgery [1–4]. Different kinds of cardiac arrhythmias have been noted in one-fifth of patients after lung resection, AF being the most common [4, 5]. Many studies have documented an increased risk of morbidity and mortality in thoracic surgical patients with postoperative cardiac arrhythmias [5–11]; however, only some have proposed risk factors for predicting postoperative cardiac disorders [9–11]. A history of ischemic heart disease, cardiovascular disorders and electrocardiographic Q waves are known predisposing factors for postoperative cardiac arrhythmias [10, 11].

Postoperative cardiopulmonary complications occur within 30 days after pulmonary resection and include pulmonary edema, ventricular fibrillation, complete heart block, various cardiac arrhythmias and sudden cardiac death [10, 11]. Changes in intra-thoracic anatomy following lung resection may affect heart function, leading to hemodynamic and electrocardiographic disorders. Experimental studies have documented supraventricular tachycardia (sinus tachycardia and AF) occurring within 2 weeks after lobectomy or pneumonectomy [12]. Other electrocardiographic changes following pneumonectomy or lobectomy have included increases in P duration, ST-depression, delayed precordial R-wave transition and displacement of the QRS vector. The most striking changes were noted in patients who underwent left pneumonectomy or left upper segmentectomy and left lower lobectomy [7]. However, according to available research, no study has documented changes in spatial QRS-T angle (spQRS-T) or corrected QT interval (QTc) after lung resection.

Vectorcardiography (VCG) is a spatial method of electrocardiography (ECG) that enables visualizing, through the cardiac cycle, the continuous moments of the cardiac vector as loops. Vectorcardiograms and associated parameters such as the spQRS-T, i.e., the spatial angle between cardiac depolarization and repolarization, can also now be easily derived from standard 12-lead ECGs [13, 14]. While normal ranges for spQRS-T vary by method and by study, most studies have suggested that normal values lie below 100–110° for men and below 90° for women [14–17]. Of note, a widened spQRS-T is an independent predictor of cardiac arrhythmias and sudden cardiac death [14–17]. In healthy patients without apparent ECG pathol-

ogy, cardiovascular mortality has been found to be 0.8% for spQRS-T between 0 and 50°, increasing to 2.3% for borderline spQRS-T (50–100°) and to 5.1% for spQRS-T angle between 100° and 180° [15, 17]. Additionally, spQRS-T wider than 100° can identify cardiomyopathic patients at a high risk of life-threatening ventricular arrhythmias for whom cardioverter-defibrillator devices might be most appropriate [18].

The corrected QT interval is an electrocardiographic parameter providing information on both cardiac depolarization and repolarization, especially the latter. Its prolongation has been observed in patients with electrolyte disorders and coronary diseases who are treated with antiarrhythmics or subjected to general anaesthesia with a volatile anesthetic [19–21]. A prolonged QTc interval has been well recognized as a parameter indicating an increased risk of malignant ventricular arrhythmias [22, 23]. Although a prolonged QTc has been noted in patients undergoing surgery with pneumoperitoneum [24, 25] and cardiac surgery [26], changes in QTc have not been recognised in patients undergoing lobectomy or pneumonectomy. It should be noted that severe right and/or left ventricular dysfunction has been documented echographically following lobectomy or pneumonectomy [27]. The purpose of this study was to analyze changes in spQRS-T and QTc in patients undergoing lung resection.

Methods

Ethical considerations

This prospective observational study was conducted in adult patients undergoing elective thoracic surgery under general anesthesia. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board and the Bioethical Committee for Human Studies of the Medical University at Lublin, Poland (KE-0254/220/2016). Written informed consent was obtained from all participants. One day before surgery all patients were examined and a 12-lead ECG without overt clinical abnormality was the main criterion for patient inclusion. The exclusion criteria were: congenital heart defects, myocardial infarct and myocarditis history, cerebral stroke history, endocrine and metabolic diseases. Patients who required re-thoracotomy due to postoperative bleeding were also excluded.

Patient description

Anaesthesia. One day before surgery, routine blood examination was performed to assess

complete blood count, blood glucose and urea, creatinine, serum electrolytes and blood type. All patients received the same premedication composed of a single oral dose (2 mg) of estazolam (Polfa, Warsaw, Poland). Just before anaesthesia induction, all patients were routinely monitored with continuous ECG for heart rate, intermittent and non-invasive arterial blood pressure measurements and continuous pulse oximetry (SpO₂). The urinary bladder was catheterized in all patients before anaesthesia induction.

General anaesthesia was induced intravenously with a single dose of fentanyl (Polfa, Warsaw, Poland) and propofol (AstraZeneca, United Kingdom). A single bolus of rocuronium (0.6 mg/kg body weight) (Rocuronium B. Braun, Germany) was administered to each patient before tracheal intubation with a double-lumen tracheal tube, the placement of which was controlled with bronchoscopy. All participants were ventilated using intermittent positive pressure ventilation, and anaesthesia was maintained throughout the procedure using 100% oxygen and inhaled sevoflurane (AbbVie, UK) at a dose of 0.8–1.2 minimal alveolar concentration and fractionated doses of fentanyl. Intra-operative ventilation was performed with an expiratory/inspiratory ratio of 1:2, a tidal volume of 5–6 mL/kg body weight, a respiration rate of 9–12/min and positive end-respiratory pressure (PEEP) + 5 cm H₂O. Ventilation was controlled by EtCO₂ and SpO₂, which were maintained between 35–40 mmHg and 92–100% saturation during surgery with both double and single lung ventilation monitored via SpaceLabs monitor (SpaceLabs Healthcare, OSI systems, USA). During surgery, all patients received a continuous infusion of balanced crystalloids (Sterofundin ISO, B. Braun Melsungen, Germany). In patients not responding adequately to the crystalloid infusion, a single dose of ephedrine (Ephedrine hydrochlorici, Polfa Warsaw, Poland) was administered. Anaesthesia was used to maintain mean arterial pressure above 70 mmHg. After completion of the surgery, sevoflurane was discontinued. The neuromuscular blockade was reversed using a single dose of atropine (0.5 mg) and neostigmine (2.5 mg). Patients were extubated upon satisfactory emergence from general anaesthesia and admitted to the Postoperative Intensive Care Unit. Postoperative pain was treated with fractionated doses of paracetamol (Bristol Myers Squibb, Warsaw, Poland). During the first and second postoperative days, all patients received intravenous mixture of potassium and magnesium at doses that depended on blood concentrations.

Surgery. After induction of anaesthesia, pneumonectomy or lobectomy was performed with thoracotomy through the 4th or 5th intercostal space. Then, pleuraecotomy was performed through the 6th intercostal space. The chest was closed in layers, including muscle, subcutaneous tissue, and the subcuticular layer, using resorbable sutures. Skin staples were used for the final cutaneous suture (Johnson and Johnson, New Jersey, USA).

Measurements

ECG, derived VCG. The method used for VCG measurement was presented previously [23]. Surface 12-lead resting ECG was recorded using a Cardiax device (IMED Co., Ltd., Budapest, Hungary). The recordings in each time period were automatically averaged to a single beat and transformed into three orthogonal leads, X, Y and Z, according to the inverse Dower method [14, 28]. The projections of maximum vectors of QRS and T-waves in frontal, transverse, and left sagittal planes and on x, y, and z axes were then obtained. Next, the value for the spatial QRS-T angle automatically calculated from the maximum spatial QRS and T vectors, as well as the values for the QTc interval, were obtained directly from Cardiax software. For detection of the QT interval and calculation of QTc, Cardiax software utilizes a median-beats related “global QT interval” algorithm similar to that described by Xue [29].

Study protocol and patient division. Electrocardiography was performed at four time points: 1 day before surgery (baseline value) and 24, 48 and 72 h after surgery. All measurements were performed in the horizontal position. Patients were allocated into four groups: patients undergoing left pneumonectomy (LP), left lobectomy (LL), right pneumonectomy (RP) or right lobectomy (RL), respectively.

Statistical analysis

A statistical analysis was performed using Statistica 12 software (StatSoft). Demographic data were summarized as frequencies and percentages. Categorical variables were compared using the χ^2 and Fisher exact test or χ^2 with the Yates correction where applicable. For variables with a normal distribution, means and standard deviations (SD) were calculated, and the Student unpaired *t*-test was used for variables with a normal distribution as confirmed by the Shapiro-Wilk test. For variables with a non-normal distribution, the Wilcoxon signed-rank, Mann-Whitney-U, Kruskal-Wallis ANOVA and post hoc Dunnett’s multiple compari-

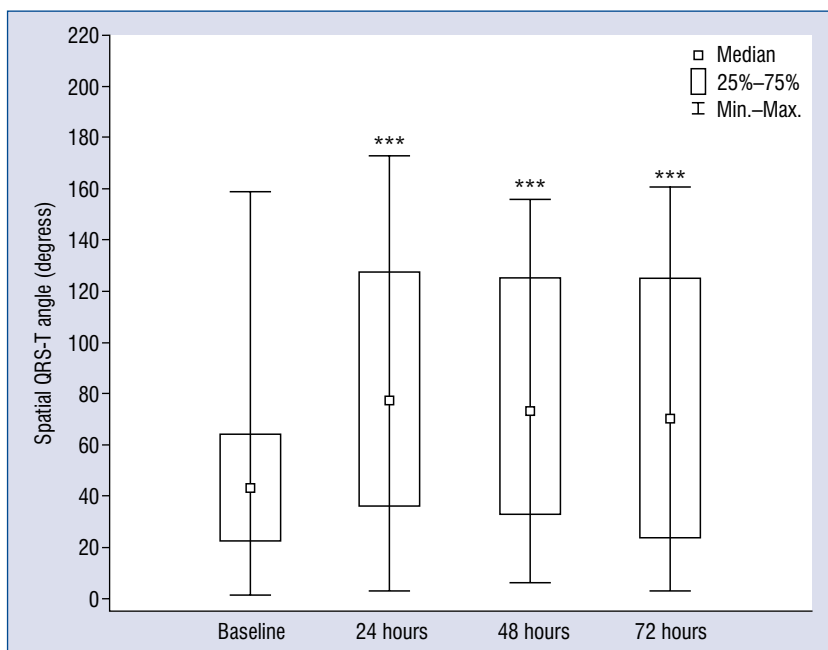


Figure 1. Changes in spatial QRS-T angle in the studied population. Time points: baseline — 1 day before surgery, and 24, 48 and 72 hours after surgery; ***p < 0.001 in comparison with baseline.

son tests were used. A $p < 0.05$ was considered significant. The power of the statistical tests was assessed by the G*Power test.

Results

Seventy-one adult patients (47 men and 24 women) aged 65 ± 7 years (range 47–80), undergoing general anaesthesia and elective lung surgery for pulmonary neoplasm were included. In the studied group: 32 patients underwent left lobectomy (group LL: 14 patients — upper lobectomy and 18 patients — lower lobectomy), 9 — left pneumonectomy (group LP), 23 — right lobectomy (group RL: 10 patients — upper lobectomy and 13 patients — lower lobectomy) and 7 — right pneumonectomy (group RP). Forty-nine patients were treated for concomitant arterial hypertension (I° or II° according to the World Health Organization classification) with beta-blockers (38 patients), Ca^{+2} blockers (9 patients), angiotensin converting enzyme inhibitors (44 patients) and diuretic drugs. Twenty-six patients were prescribed magnesium and 10 both magnesium and potassium for more than 1 month prior to surgery. Among all participants, the mean time of anaesthesia was 161 ± 45 min, and the surgical time was 115 ± 30.7 min. The mean body mass index was 26.6 ± 5.2 kg/m². The mean arterial pressure and SpO₂ were 68–100 mmHg and 92–100%, respectively, during anaes-

thesia and surgery. None of the patients required intensive fluid therapy during surgery or the early postoperative period, and a possible insufficiency of intravascular fluids was supplemented with crystalloid infusion (Sterofundin ISO, B. Braun Melsungen, Germany). Immediately after anaesthesia completion, all patients were transferred to the Postoperative Intensive Care Unit. A sinus rhythm was noted in all participants with mean heart rates of 76.4 ± 15.7 /min, 78.5 ± 14.8 /min and 81.5 ± 14.1 /min at postoperative days 1, 2 and 3, respectively.

Atrial fibrillation was noted in 9 (6.4%) patients at 5–10 postoperative days — 7 after left lung surgery and 2 after right lung surgery ($\chi^2 = 1.69$, $p = 0.19$, χ^2 with Yates correction = 0.89 for $p = 0.35$). Additionally, postoperative AF was noted in 6 patients after pneumonectomy (LP) and 3 after lobectomy (1 after LL and 2 after RL) ($\chi^2 = 11.5$, $p = 0.001$, χ^2 with Yates correction = 8.79 for $p = 0.01$). None of the other patients required treatment for postoperative cardiac arrhythmias, and the 12-lead ECG showed a sinus rhythm throughout the study period.

In the patient group as a whole, spQRS-T increased at 24, 48 and 72 h after surgery (Fig. 1). Changes in spQRS-T were similar in patients undergoing left and right lung surgery; however, a significantly wider spQRS-T was noted in patients after pneumonectomy than lobectomy (Table 1).

Table 1. Comparison of changes in spatial QRS-T angle and QTc intervals in patients undergoing left lobectomy (group LL) pneumonectomy (group LP), right lobectomy (group RL) and right pneumonectomy (group RP).

	Baseline	24 hours	48 hours	72 hours
Spatial QRS-T angle				
LL	38.5 [31; 56]	80** [63.25; 93.5]	70.5* [48; 87]	67.5 [21.25; 115.5]
LP	56‡ [50.25; 84.25]	129*†‡ [128; 133.5]	147*††‡ [130.5; 149.25]	145*††‡‡ [134.5; 154]
RL	47.5†† [24.75; 97.75]	47 [31.25; 135]	72* [38.25; 137]	65* [30.5; 120.75]
RP	20 [6; 27]	33 [10.5; 47]	42* [9.5; 99.5]	43* [15; 109.5]
Corrected QT interval				
LL	425.5 [420; 442.2]	439.5 [429.5; 452.75]	435 [420.5; 558]	446** [430.5; 455.75]
LP	443.5‡ [59.25; 85]	462.5‡‡ [98; 147]	464.5 [111.5; 156.3]	462* [93.6; 174.5]
RL	428 [418.5; 478]	434 [421; 465.25]	431.5 [407.5; 480]	444.5 [427.75; 480.75]
RP	411 [406; 414]	421 [412; 423]	414 [409; 443]	406 [403; 423]

Values shown are medians [quartile 1 and 3]. LL (n = 32), LP (n = 9), RL (n = 23), RP (n = 7). The small number of patients with pneumonectomy limits statistical power ($1 - \beta \geq 0.8$).

*p < 0.05 versus Baseline; †p < 0.05 and ††p < 0.01 — pneumonectomy versus lobectomy (LP vs. LL and RP vs. RL, respectively); ‡p < 0.05 and ‡‡p < 0.01 — left versus right pneumonectomy or left versus right lobectomy (LP vs. RP and LL vs. RL, respectively).

Table 2. Comparison of changes in spatial QRS-T angle and QTc intervals in patients with atrial fibrillation (AF) in the late postoperative period and patients with an uncomplicated postoperative period (n-AF).

	Baseline	24 hours	48 hours	72 hours
Spatial QRS-T angle				
AF	50 [47; 56]	129*† [88; 135.5]	143* [75; 147]	102 [59; 145]
n-AF	33.5 [20.25; 68.75]	69** [32.25; 116.75]	71.5** [26.25; 120.75]	66** [24.; 123.5]
Corrected QT interval				
AF	439 [427.5; 445.5]	453 [439; 462.75]	469† [455; 470.5]	462* [451.5; 467]
n-AF	425 [414; 445.5]	434 [421.25; 455.5]	434.5 [412.5; 458.75]	435 [423; 455.75]

Values shown are medians [quartile 1 and 3]. AF (n = 9), n-AF (n = 62). The small number of patients with postoperative AF limits statistical power ($1 - \beta \geq 0.8$).

*p < 0.05 and **p < 0.001 versus Baseline; †p < 0.05 — complicated postoperative period by AF versus uncomplicated postoperative period

Additionally, a wider spQRS-T was noted after LP than RP at all time points whereas this angle was comparable in patients undergoing LL and RL (Table 1). In patients with, compared to those without postoperative AF, the spatial QRS-T angle was significantly wider only at 24 h postoperatively (Table 2). Representative serial 12-lead ECGs from a patient who underwent LP are presented in Figure 2.

In the patient group as a whole, QTc intervals were also prolonged after lung resection (Fig. 3). Although prolongation of the QTc was similar in patients undergoing left and right lung surgery independent of the type of surgery, LP prolonged the QTc significantly more than RP (Table 1). The corrected QT interval was also significantly longer at 48 and 72 h in patients with versus those without postoperative AF (Table 2).



Figure 2. Representative changes in the spatial QRS-T angle and 12-lead electrocardiogram of a patient who underwent left pneumonectomy.

Discu/ssion

According to available research, this is the first study documenting effects of lung resection on spQRS-T and QTc. Pneumonectomy and lobectomy affected spQRS-T and QTc; however, the most striking changes were noted in patients undergoing left rather than right lung surgery, especially LP. Additionally, patients with postoperative AF had wider spQRS-T and longer QTc in the early postoperative period.

The spQRS-T angle presents the directional differences between the ventricular repolarization and depolarization [30]. It has been suggested to be a strong predictor for all-cause and cardiac mortality in middle-aged and elderly patients [15, 17, 30]. Additionally, a wide spQRS-T has been shown to predict life-threatening ventricular arrhythmias [15–18] and silent myocardial ischemia/infarction [31, 32]. Several factors affect spQRS-T. The spQRS-T angle evolves with age and depends

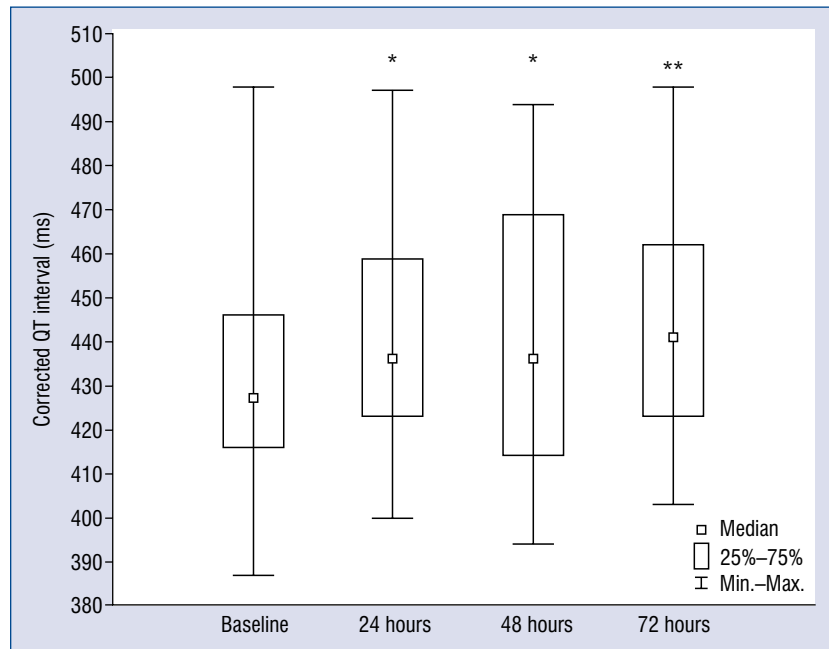


Figure 3. Changes in the corrected QT interval of the studied population. Time points: baseline — 1 day before surgery, and 24, 48 and 72 hours after surgery; * $p < 0.05$ and ** $p < 0.01$ in comparison with baseline.

on sex and physical condition [13–17, 33, 34]. Changes in body position as well as in intra-thoracic volume following diaphragm elevation due to increases in intra-abdominal pressure, which may also disturb ventricular repolarization, thus widening the spQRS-T [25, 35, 36]. Gul and colleagues documented a completely altered QRS complex in patients with changes in intra-thoracic anatomy following eventration of the diaphragm and displacement of the bowels into the thoracic cavity [37].

In the present study, an increase in spQRS-T in patients after lung resection was observed, the most substantive changes occurring in patients after LP. A lack of or significant reduction in heart compression during respiration probably disturbs the QRS loop configuration and affects the heart's hemodynamic function. In people with normal pulmonary function, the amplitude of the maximum leftward force affects the QRS vector, decreasing significantly during inspiration, whereas the amplitude of the maximum posterior force increases. The QRS vector displaces posteriorly and inferiorly with a decrease in spatial magnitude of approximately 10%, leading to an increase in the spQRS-T angle [37]. Previous studies have shown that right-lung resection causes a right-sided QRS vector shift in 100% of patients after RP and in 75%, 58.3% and 50% after right upper segmentectomy, lower left lobectomy and right upper segmentectomy,

respectively [7]. On the other hand, left-lung resection results in a left-sided QRS vector shift in 100% of patients after LP and in 87%, 66.7%, 57.9% and 55.6% of patients after left upper lobectomy, left upper segmentectomy, right lower lobectomy and right middle lobectomy, respectively [7]. The present study was not focused on, and thus did not fully confirm these disturbances. However, LP spectacularly increased spQRS-T in the patient group as a whole, with disturbances in spQRS-T being significantly lower in patients after RP. It should be noted that the small number of patients with pneumonectomy limited the power of the analysis, and may have impacted results.

A 6.4% incidence of postoperative AF was lower than that in other reports [1–6]. A significantly wider spQRS-T angle was noted in all of these patients. Several studies have confirmed a strong relationship between a wider spQRS-T and the occurrence of potentially lethal arrhythmias in patients with left ventricular systolic dysfunction [15–17, 30, 38]. The risk of cardiac arrhythmia significantly increases with spQRS-T wider than 100° [15, 16, 30]. It should be noted that spQRS-T increased above 100° in relatively more patients with postoperative AF and that the higher angle was observed 48 h after surgery.

Postoperative AF might result from postoperative electrolyte disorders; however, all affected

patients received potassium and magnesium supplementation, and their blood potassium concentration was higher than 4.0 mmol/L (data not shown). The incidence of AF was significantly higher in patients after pneumonectomy, in agreement with other studies [4–6]. Although none of the patients presented with myocardial ischemia, it can also be speculated that postoperative AF might be a result of silent myocardial ischemia. Many patients had a history of smoking and chronic obstructive pulmonary disease, which are often associated with atherosclerosis and coronary diseases. Indeed, silent myocardial ischemia/infarct has been shown to be associated with a widened spQRS-T angle [32]; however, this speculation would require further dedicated confirmation.

In the present study, QTc was prolonged after left-side resection and was significantly longer than after right-side resection. Additionally, QTc was longer in patients with postoperative AF. The QTc interval represents myocardial depolarization and repolarization. Its normal value is below 460 ms for women and below 440 ms for men, with borderline values ranging 461–479 ms and 441–459 ms for women and men, respectively; a prolonged value is defined as a value higher than 480 ms and 460 ms for women and men, respectively [23].

A prolonged QTc interval is also associated with an increased risk of life-threatening arrhythmias, including polymorphic ventricular tachycardia (torsade de points), and a significant increase in the risk for such pathology increases markedly in patients with QTc intervals longer than 500 ms. However, the risk of cardiac arrhythmia also increases when QTc lengthens more than 60 ms compared with the baseline value [39].

Female sex and older age predisposes QTc interval prolongation. Pathologically prolonged QTc has been noted in patients with electrolyte disturbances such as hypokalemia, hypomagnesemia and/or hypocalcemia, myocardial ischemia, heart failure and severe bradycardia [19, 20, 31]. Many medications can also result in asymptomatic or symptomatic QTc interval prolongation, their administration sometimes being associated with an increased risk for cardiac arrhythmias [22].

It should be noted that volatile anaesthetics and some opioids, including fentanyl, significantly prolong QTc. However, there is controversy as to whether propofol has an effect [22, 40–42]. Chang et al. [41] documented a prolongation of QTc following propofol anesthesia. Oji et al. [40] noted the shortening of QTc after target-controlled infusion of propofol. In contrast, Kleinsasser et al. [42] did

not observe an effect of propofol on QTc interval. Additionally, some local anaesthetics used for epidural anaesthesia during lung surgery can also affect QTc [9]. In the present study, a prolonged QTc only in patients undergoing left-lung resection was observed, but all participants received the same kind of anesthesia. Unfortunately for reasons of logistics, it was not possible to study changes in QTc more immediately after surgery.

Limitations of the study

An important limitation of the present study was the small number of patients undergoing elective pneumonectomy, which notably limits study-related statistical power. Generally, the available screening examinations enable cancer diagnosis in its early stages and have a fundamental role in the possible kinds of treatment. The lack of an analysis of spQRS-T and QTc as a function of blood electrolyte concentration or preoperative or postoperative spirometric features or pharmacological treatment was also considered a limitation.

Conclusions

In the present study, an effect of lung resection on spQRS-T and the QTc interval was documented. Generally, lung resection induced spQRS-T widening and QTc prolongation; however, the most striking widening and prolongation were noted in patients undergoing LP. Additionally, AF episodes were primarily noted in patients after left-lung resection who had prolonged QTc interval.

Conflict of interest: None declared

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