Beat-to-beat QT interval variability before and after cardiac surgery

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Abstract

Non-uniform recovery of excitability may be essential in triggering malignant ventricular tachycardia after cardiac surgery. Thirty-five channels ECG was recorded for 6 min in 27 patients before and after heart surgery and in 20 control subjects. Off-line analysis was performed. RR interval duration, RR SD, QT SD and power spectra of RR variability were computed from 256 s stable RR and QT interval series. When compared to controls, patients had decreased RR SD and increased QT SD before surgery (p<0.002 and p<0.0005, respectively); RR SD further decreased and QT SD increased after the surgery (p<0.0001 and p<0.0002, respectively). Increase of QT variability and decrease of RR variability after cardiac surgery may reflect disrupted electrophysiological stability of the myocardium and thus electrophysiological substrate for triggering malignant arrhythmia.

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1. Introduction

Development of ventricular tachycardia (VT) after cardiac surgery is associated with high in-hospital mortality rate of 25% [1]. Although uncommon [2], cardiac arrest due to malignant ventricular arrhythmia occurring after cardiac surgery is a catastrophic event. Studies indicate that the postoperative sustained VT or fibrillation may evolve due to the transient features such as reperfusion of ischemic myocardium [1,3], occult perioperative damage of myocardium [4], graft occlusion [5] and the influence of endogenous and exogenous catheholamines [6]. Another study suggests that

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myocardial structural damage from the surgery results in persistent susceptibility to arrhythmia [2]. An etiology of VT is not readily apparent [5] and apart from the history of myocardial infarction, significant left ventricular dysfunction and clinically evident chronic heart failure [1] there are no consistent clinical features predicting the development of malignant arrhythmia in patients after cardiac surgery.

There is a strong evidence that non-uniform recovery of myocardial excitability may be essential in triggering malignant VT in different heart diseases [7]. Non-uniform recovery of myocardial excitability seems to be reflected in increased temporal fluctuations of QT interval [8]. Beat-to-beat oscillations of the QT interval have not been studied in patients undergoing cardiac surgery. The aim of this study was to evaluate and quantify beat-to-beat RR and QT variability in patients prior and after different cardiac surgery.

2. Materials and methods

2.1. Patient population and data acquisition

A study population included 27 patients (mean age 61.7 ± 9.4; 15 males) scheduled for elective cardiac surgery. All patients were operated on at the University Clinical Center in Ljubljana. Sex, age distribution and clinical data for these patients are shown in Table 1. Inclusion criteria were: stable sinus rhythm prior to the cardiac surgery without atrioventricular or intraventricular conduction disturbances. The presence of atrial or ventricular ectopy was allowed unless such beats represented more than 5% of total beats over 6 min interval. Patients with ECG rhythm other than normal sinus, patients who were administered class I antiarrhythmic drugs and those with low amplitude T-wave were excluded from the study.

Control group included 20 healthy volunteers (mean age 50.6 ± 9.6; 13 males) without a history or evidence of heart disease and with normal 12 lead surface ECG. Informed consent was obtained from all the subjects before the study.

Two measurements were obtained from each patient: first one, a single day before the surgery and second one, in the period from the 5th to the 7th day after the surgery. Multi-channel ECG (MECG) [9] was recorded for 360 s after 10 min rest in the supine position. Body surface potentials

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Clinical characteristics of patient population before heart surgery</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>CABG (N = 15)</td>
</tr>
<tr>
<td>Male/female</td>
<td>9/6</td>
</tr>
<tr>
<td>Age</td>
<td>60.3 ± 9.7</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>2.6 ± 0.8</td>
</tr>
<tr>
<td>LVEF &lt; 50%, N</td>
<td>3</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting, LV = left ventricle, LVEF = left ventricle ejection fraction, N = number of patients, NYHA = New York Heart Association, VALVE = valve repair or replacement.
were measured with 35 unipolar lead (each with 14 bits/sample, 1000 samples/s), 32 placed on the thorax and three electrodes placed on both arms and left leg. The electrodes and their positions were numbered from 1 to 35. For detailed placing of electrodes see [10,11].

After electrode positioning the data acquisition started, collecting data for 360 s. All data were immediately checked for the quality of signal in general as well as the quality of signal from each individual electrode. In case of defect measurement, the cause of disturbance was identified and the problem immediately solved, then the data acquisition was restarted following the same protocol. Good-quality data was saved on computer disc for further analysis.

2.2. QT variability algorithm

The method introduced by Berger et al. [12] was used in the analysis of RR and QT variability with the following modifications. Matching of beats to the template is achieved by shifting the template in discrete steps rather than stretching. Baseline wander is removed by linear correction of ECG. The modified algorithm implemented on a personal computer (IBM PC compatible) is described in the following steps:

(1) The time $t_R$ of each R-wave is identified with an automated peak detection algorithm using a channel with high R-wave amplitude.

(2) A channel with high T-wave amplitude is selected by the operator and a typical T-wave (template) is determined by the following three points: the first point before P-wave is used for baseline wandering removal, the second and the third point determine the beginning and the end of T-wave template denoted by $\phi(n)$

$$\phi(n) = x(n), \quad n = [n_0, \ldots, n_1],$$

where $n$ is the sample number, $x(n)$ is the ECG signal and $n_0$ and $n_1$ are the beginning and the end of T-wave template. Template T-waves $\phi(n)$ for all the other channels $k$ are automatically identified from the same interval.

(3) Error function $e_k(n)$ is computed:

$$e_k(n) = \sum_{j=0}^{n_1-n_0} [\phi(n_0 + j) - x(n + j)]^2, \quad n = [1, \ldots, N - (n_1 - n_0)],$$

where $N$ is the number of samples in each channel and $k$ is the channel number. The low value of error function means that the difference between template and ECG signal is also low.

(4) The best match of ECG signal to T-wave template is found for each beat. The best match is defined as time $t_T$ where the error function has lowest value in an interval restricted to the T-wave vicinity.

(5) Finally, the algorithm computes QT interval deviation from the first QT interval found in ECG. This deviation is defined as time series denoted by $QTV_k$

$$QTV_k(t_T(i)) = [t_T(i) - t_R(i)] - [t_T(1) - t_R(1)],$$

where $i$ is the beat number, $t_T$ is the time where best match of T-wave was found, $t_R$ is the time of R-wave peak and $k$ is the channel number.
For further analysis we used only QTV of the channel with the highest T-wave amplitude computed from the samples of T-wave template. Root mean squares for channel templates are used as a measure of the channel accuracy.

Time series of R-wave peaks $t_R(i)$ are used in the analysis of the RR interval variability. RR interval is defined as

$$RR(i) = t_R(i) - t_R(i - 1).$$

Rectangular windowing and fast Fourier transformation is used to compute power spectra density from the RR interval series. The power spectrum is analyzed in two frequency bands: low-frequency (LF = 0.04–0.15 Hz) and high-frequency (HF = 0.15–0.4 Hz). The power in each frequency band is obtained by summing the spectral components inside the band.

2.3. Statistical analysis

Comparison between the control group and group of patients before and after cardiac surgery was performed using a non-parametric independent sample $t$-test (Mann–Whitney $U$-test). Data in the group of patients were compared statistically by Wilcoxon matched pairs test. Statistical significance was accepted at probability value $p < 0.05$.

3. Results

3.1. Patient characteristics

Surgery data and clinical characteristics after the surgery are described in Table 2. The percentage of deletion of ectopic beats due to atrial or ventricular arrhythmia was $> 5\%$ in four patients, thus among 27 patients enrolled, a total of 23 fulfilled clinical and technical inclusion criteria. Four patients developed a single episode of atrial fibrillation in postoperative period that was in three cases coupled with amiodarone. None of the patients died before the discharge. Patients were hospitalized a median of 8 days.

| Clinical characteristics of the patient population after cardiac surgery |
|-----------------------------|---------------------|---------------------|---------------------|---------------------|
|                           | CABG                | VALVE               | CABG+VALVE          | LV aneurysmectomy   |
| ICU (day)                  | 4.6 ± 2.3           | 3.7 ± 1             | 5.5 ± 1             | 2                   |
| Arrhythmic events, $N$     | 2(16.7%)            | 0                   | 2(50%)              | 0                   |
| Medications, $N$ (B/A)     | 10/11               | 3/1                 | 4/3                 | 1/1                 |
| $\beta$-blocker            | 7/6                 | 3/3                 | 4/3                 | 0/0                 |
| ACE inhibitor              | 3/2                 | 1/1                 | 2/2                 | 1/0                 |
| Calcium antagonist         | 0/0                 | 0/0                 | 0/0                 | 0/0                 |
| Digitalis                 | 2/2                 | 0/0                 | 0/1                 | 0/0                 |
| Amiodarone                | 0/2                 | 0/0                 | 0/0                 | 0/0                 |

B/A = before the surgery/after the surgery, CABG = coronary artery bypass grafting, ICU = intensive care unit, LV = left ventricle, $N$ = number of patients, VALVE = valve repair or replacement. Values are expressed as mean ±SD.
Table 3
Statistical data for study variables in control group and groups of patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (C)</th>
<th>Before surgery (B)</th>
<th>After surgery (A)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR mean (ms)</td>
<td>969.5 ± 141.9</td>
<td>959.8 ± 189.4</td>
<td>760.5 ± 154.3</td>
<td>0.696</td>
</tr>
<tr>
<td>RR SD (ms)</td>
<td>40.7 ± 14.5</td>
<td>25.2 ± 12.8</td>
<td>9.8 ± 6.3</td>
<td>0.002</td>
</tr>
<tr>
<td>QT SD (ms)</td>
<td>1.51 ± 0.69</td>
<td>2.24 ± 1.3</td>
<td>3.4 ± 2.61</td>
<td>&lt; 0.0005</td>
</tr>
<tr>
<td>RR LF (ms²)</td>
<td>624.0 ± 541.8</td>
<td>167.0 ± 185.5</td>
<td>25.7 ± 37.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>RR HF (ms²)</td>
<td>466.4 ± 593.5</td>
<td>145.3 ± 148.6</td>
<td>20.7 ± 28.5</td>
<td>0.007</td>
</tr>
</tbody>
</table>

A = after surgery, B = before surgery, C = control group, RR mean = mean RR interval duration, RR SD = RR interval standard deviation, QT SD = QT standard deviation, LF = power in low-frequency band (0.04 – 0.15 Hz), HF = power in high-frequency band (0.15 – 0.4 Hz). Values are expressed as mean ± SD.

3.2. Temporal RR and QT variability

RR interval duration (RR mean), RR variability (RR SD) and QT variability (QT SD) and results of spectral analysis of RR interval variability comparing control group, patients before and after the surgery are presented in Table 3. No difference was found in RR mean between healthy subjects and patients before the surgery, but there was significantly lower RR SD and higher QT SD in patients before the surgery. After the surgery, patients exhibited lower RR mean, RR SD and higher QT SD in comparison to the control group as well as to the results obtained before the surgery. Results of power spectral analysis of RR interval variability are shown in the bottom two lines of Table 3. Patients before the surgery had smaller power in low- and high-frequency bands when compared to controls. After the surgery, patients exhibited further decrease of power in both frequency bands.

Examples of RR and QT interval series during 256 s epoch in a control subject and in a patient before and after the surgery are presented in Fig. 1. In the control subject (Fig. 1C) RR interval exhibited substantial beat-to-beat variability; QT interval variability was small. Before the surgery (Fig. 1B), patient had lower, but still substantial heart rate variability and increased QT variability. After the surgery (Fig. 1A), RR variability was reduced and QT interval variability increased compared with the result obtained before the surgery.

4. Discussion

The principal finding of this study is that the cardiac surgery increases beat-to-beat QT interval variability. Significantly, higher QT interval variability after the surgery reflects disrupted electrophysiological stability of myocardium and may therefore present an increased risk for developing ventricular arrhythmia. Increased QT interval variability was also found in our patients before the surgery. This finding is in accordance with other studies. Increased QT interval variability was found in patients with ischemic and non-ischemic dilated cardiomyopathy [12], hypertrophic cardiomyopathy [13] and angina pectoris [14]. A large proportion of our patients had ischemic heart disease, which may be the principal source of altered myocardial repolarization, reflected in in-
Fig. 1. A single epoch of RR interval and QT deviation from the first QT interval in the series. C = control subject, B = a patient before the surgery, A = a patient after the surgery.
creased QT interval variability before the surgery. Our group of patients was too small to analyze possible patient characteristics, which might importantly contribute to increased postoperative electrical myocardial instability. The clinical implication and importance of increased QT variability for a purpose of risk stratification of developing malignant arrhythmia after heart surgery is yet to be determined.

We observed increase of heart rate and a marked decrease of RR interval variability in both spectral components of power spectra after cardiac surgery. Therefore, both vagal and sympathetic regulation of heart rate seems to be disrupted in the postoperative period. These findings are consistent with prior studies [15–17]. Disrupted autonomic control of sinus node does not seem to predict short-term cardiovascular instability [18]. However, direct autonomic regulation of myocardial repolarization was proposed [19]. Disturbance of direct myocardial autonomic innervation after cardiac surgery might contribute to the loss of coupling between the heart rate and the ventricular repolarization [12,20,21].

Several important factors should to be considered in interpreting the results of this study. First, data presented in this study can only be applied to the patients defined by our inclusion and exclusion criteria. Four of the 27 patients were ineligible for the study, which limits the value of the results. Second, patients were taking a variety of medications: β-blockers, amiodarone, benzodiazepines and opiates that could have influenced ventricular repolarization [22]. Since clinical trials do not indicate an increase of QT variability after β-blocker admission [23,24] and similar number of patients was receiving β-blockers before and after the surgery (a total of 17/16 patients), we did not attempt to exclude these patients from the study. A third limitation is the use of different methods in measurement of QT interval variability in different studies without universally accepted standards of analysis. The observed QT variability was much smaller (QT SD in control group was 1.5±0.69 ms, before the surgery 2.24±1.3 ms and after the surgery 3.4±2.61 ms) than in the previous studies [12,22]. We contribute this discrepancy to different methodology and possibly higher accuracy of the method introduced in this article. Because of 35 available ECG channels we always selected one with the most emphasized T-wave.

The problem of reproducibility of the QT measurements is also in question. Data presented are based on 256 s ECG measurements. It is possible that repolarization varies over the course of day or from one day to another [12]. This could effect QT variability measurements obtained in individual subject, but the finding that patients after the heart surgery exhibit higher QT variability than before the surgery as well as compared with the control subjects, cannot be explained on this basis. To avoid the influence of diurnal variation [25], posture [26] on heart rate variability indexes, all ECG recordings were performed under standardized conditions. All postoperative measurements were obtained on the 5th to 7th day after the surgery when patients were already transferred to the general ward and intensive treatment including inotropic support had been withdrawn.

5. Conclusion

This study provides evidence of the impact of the heart surgery on myocardial repolarization and confirms the findings of severe cardiac autonomous dysfunction in early postoperative period. The fact that the cardiac surgery causes an increase of QT interval variability in the face of decreased RR interval variability suggests a loss of coupling between the heart rate and the ventricular repolarization
and represents previously unrecognized phenomenon in the setting of cardiac surgery. On this basis, the study to test QT variability as prognostic factor in developing malignant arrhythmia after cardiac surgery could be designed.

6. Summary

It has already been established that the increase in beat-to-beat QT interval variability is an electrocardiographic marker of myocardial repolarization abnormalities. The uncoupled QT-RR variability has been associated with high incidence of malignant ventricular arrhythmias and sudden cardiac death. This study was designed to provide us with the information on RR and QT interval variability after heart surgery. The study population included 27 patients scheduled for elective cardiac surgery and 20 control subjects. Thirty-five channel ECG (each with 14 bits/sample, 1000 samples/s) was recorded for 6 min 1 day before and on the 5th to 7th day after the surgery. Computer analysis was performed, selecting the best channels for further analysis. The duration of RR interval (RR mean), RR interval variability (RR SD), QT interval variability (QT SD) and power spectra of RR interval variability were computed from 256 s recording.

This study revealed that the heart surgery causes an increase of QT interval variability in face of decreased RR interval variability. This finding implicates increased myocardial electrical instability after cardiac surgery. A loss of coupling between heart rate and ventricular repolarization was proposed. This represents previously unrecognized phenomenon and provides us with basic ground for further investigation of changes in ventricular repolarization and its connection with development of malignant ventricular arrhythmias in the setting of cardiac surgery.

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References


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