QT Dispersion and Sleep related Breathing Disorders in Recipients of Implantable Cardioverter Defibrillator

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Introduction

QT dispersion (QTD) has been proposed as a descriptor of ventricular repolarisation inhomogeneity, a precursor of life-threatening arrhythmias, and as a predictor of cardiovascular mortality [1, 2]. However, data concerning these topics remain contradictory. As proposed by some authors for example, an increased QTD might be the consequence of an unusual vectorcardiographic projection of the T wave loop [3, 4].

The presence of sleep related breathing disorders (SRBD) has been shown to be associated with cardiovascular diseases, such as coronary artery disease, or with the presence of pulmonary hypertension [5]. Furthermore severe SRBD have been discussed to have a major impact on cardiac arrhythmias [6]. It has been demonstrated recently, that repolarisation inhomogeneity as assessed with the heart rate corrected QTd (QTcD) correlates with the severity of SRBD [7]. Simantirakis et al [8] using a subcutaneously implanted loop recorder, investigated the impact of SRBD treatment by means of continuous positive airway pressure therapy and found a significant reduction in ventricular ectopy beats in 21 patients with moderate and severe SRBD after 8 weeks of this therapy, and no ectopy was recorded during the last 6 months of follow-up.

The two sleep-apnea syndromes that are listed as subtypes of SRBD are the obstructive and the central sleep apnea [9]. In general diagnosis of SRBD requires a history of symptoms related to disturbed sleep (choking or gasping during sleep, recurrent awakenings, unrefreshing sleep, excessive daytime sleepiness, impaired concentration and documented respiratory events [10, 11]. Polysomnography allows differentiation of the above-mentioned subtypes of SRBD, by recording the breathing effort. However, although overnight polysomnography is the gold standard diagnosing test for SRBD, ApneaLinkR (commercially available device) is highly sensitive to diagnose SRBD (sensitivity 97.3% compared to polysomnography) [12]. However, ApneaLinkR does not allow further differentiation of SRBD, and we therefore employed the term SRBD to account for both entities.

To assess the impact of SRBD on QTD, we prospectively investigated patients with an ICD, while it allows automatically monitoring and evaluation of life-threatening arrhythmias over a long time interval.

Patients and methods

We prospectively studied 44 unselected ICD recipients with ischemic (n=36) and non-ischemic (n=8) cardiomyopathy at the Kantonsspital St.Gallen: 39 males and 5 females with a mean age of 62 ± 9 years and a reduced left ventricular ejection fraction (LVEF) of 29 ± 6 %. QT intervals were analysed at rest electrocardiogram performed in supine position. QTd was defined as the difference between the maximum and minimum QT values assessed in the standard 12 lead surface electrocardiogram. QTd and QTcD were automatically assessed by means of Schiller CS electrocardiography software and were revised and corrected manually, if necessary.

Assessment of cardiac arrhythmias. We prospectively interrogated the ICD devices over a 12-month period for the presence of life threatening arrhythmias.
Screening for the presence of SRBD. An overnight screening analysis was performed at study inclusion using a commercially available highly sensitive device (ApneaLinkR, ResMed, GmbH, Martinsried, Germany). This device allows respiratory pressure measurements through a nasal canula and therefore determination of the respiratory flow. The oxygen saturation is measured by pulse oxymetry. An apnea was defined as cessation of airflow > 10 seconds and hypopnea as a > 50% reduction of airflow lasting > 10 seconds. The Apnoe Hypopnoe Index (AHI) is calculated by dividing the number of apneas and hypopneas by the number of hours of sleep and is an index of disease severity. Data from sleep studies were stored digitally and reviewed by an experienced pneumonologist.

All patients completed the Epworth sleepiness scale questionnaire (ESS), which is used to determine the level of daytime sleepiness. A score of 10 or more is considered sleepy. We defined the presence of significant SRBD as an AHI ≥ 15/h corresponding to at least moderate SRBD according to international guidelines [11]. Those patients with significant SRBD were invited to perform an overnight polysomnography to confirm diagnosis and differentiation of SRBD.

Statistical analysis. Continuous data are expressed as mean ± standard deviation. Group comparisons were calculated using 2-tailed T-test. A two-tailed p value <0.05 was considered as statistically significant. Spearman correlation analysis was applied between the QTD, QTcD and Apnea-Hypopnea Index.

Results

Patients were divided in two groups, which consisted of patients without or mild SRBD (group I, n= 29) and those with at least moderate SRBD (group II, n=15). The groups did not differ according to their age, sex, LVEF and the use of antiarrhythmic medication (beta-blocking agents (BB) or amiodarone) (Table 1).

Table 1. Baseline characteristics of ICD recipients with and without significant sleep related breathing disorders

<table>
<thead>
<tr>
<th>Variable, n (%)</th>
<th>no SRBD n=29</th>
<th>SRBD n=15</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>63 ± 10</td>
<td>62 ± 10</td>
<td>0.90</td>
</tr>
<tr>
<td>Male</td>
<td>26(79)</td>
<td>13(87)</td>
<td>1.0</td>
</tr>
<tr>
<td>LVEF</td>
<td>29 ± 5</td>
<td>28 ± 6</td>
<td>0.73</td>
</tr>
<tr>
<td>Betablocker</td>
<td>26(79)</td>
<td>15(100)</td>
<td>0.54</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>7(24)</td>
<td>3(20)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Data in Table 1 is presented as numbers or mean values with standard deviation.

QTD did not differ between the groups: 63.4 ± 17.9 ms in group I and 60.3 ± 25.7 ms in group II, p=0.64 (Fig 1). QTcD did not differ between the groups as well (66.7 ± 19.5 ms in group I and 67.6 ± 30.4 ms in group II, p=0.91).

![Fig. 1. QT dispersion in ICD recipients with and without significant sleep related breathing disorders](image1.png)

Spearman correlation analysis between the QTD, QTcD and Apnea-Hypopnea Index did not show any significant correlations (Fig. 2).

![Fig. 2. Spearman correlation between QT dispersion and Apnea-Hypopnea Index in ICD recipients](image2.png)

As shown in Table 2 QTD and QTcD analysis with respect to life-threatening arrhythmias revealed no correlation between those patients with and those without ventricular tachycardia and/or ventricular fibrillation (VT/VF) during a prospective observation period of 12 months. However, patients without VT/VF had a higher
prescription rate of amiodarone compared to those in whom life-threatening arrhythmias occurred (p=0.03).

**Table 2.** Characteristics of ICD recipients with and without life threatening arrhythmias

<table>
<thead>
<tr>
<th>Variable, n (%)</th>
<th>no VT / VF n=25</th>
<th>VT / VF n=19</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>64 ± 9</td>
<td>60 ± 10</td>
<td>0.20</td>
</tr>
<tr>
<td>Male</td>
<td>21(84)</td>
<td>18(95)</td>
<td>0.37</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>29 ± 6</td>
<td>29 ± 6</td>
<td>0.99</td>
</tr>
<tr>
<td>QTD (ms)</td>
<td>59.7 ± 20.1</td>
<td>66.4 ± 21.3</td>
<td>0.30</td>
</tr>
<tr>
<td>QTcD (ms)</td>
<td>64.7 ± 22.6</td>
<td>70.4 ± 24.6</td>
<td>0.45</td>
</tr>
<tr>
<td>Betablocker</td>
<td>23(92)</td>
<td>18(95)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cordarone</td>
<td>9(36)</td>
<td>1(5)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Data in Table 2 is presented as numbers or mean values with standard deviation. Abbreviations: VT – ventricular tachycardia; VF – ventricular fibrillation; LVEF – left ventricular ejection fraction; QTD – QT dispersion; QTcD – heart rate corrected QT dispersion.

**Discussion**

Several studies showed that increased QTD is a significant predictor of cardiovascular mortality [1, 2] and is related to susceptibility to life-threatening ventricular arrhythmias, independent of left ventricular dysfunction [13]. There are controversial data, that QTD correlates only with the parameters of vectorcardiographic T-loop morphology [3] and does not predict the occurrence of life-threatening ventricular arrhythmias. Investigations regarding the relation between SRBD and QTD demonstrated, that QTcD was increased in patients with moderate-severe obstructive sleep apnea syndrome [7]. Increased QTcD was observed in hypertensive patients with sleep apnea during episodes of apneas and hypopneas compared to those without sleep apnea syndrome [14]. Our results, however, demonstrate that neither QTD (60.3 ± 25.7 ms vs. 63.4 ± 17.9 ms, p= 0.64) nor QTcD (67.6 ± 30.4 ms vs. 66.7 ± 19.5 ms, p=0.91) assessed at rest electrocardiography, did differ significantly between the groups with and without significant SRBD in patients at high risk for life threatening arrhythmias - ICD recipients. Moreover QTD and QTcD were not predictive for the occurrence of life threatening arrhythmias during the observation period of 12 months as well. These results confirm our previous data of QTD investigations in another contingent of ICD recipients [15].

**Study limitations**

As previously discussed, QTD and QTcD might change during episodes of apnea or hypopnea in subjects with SRBD. However, QTD measurements were performed at daytime, which might be seen as a limitation to this study.

**Conclusion**

QT dispersion and heart rate corrected QT dispersion did not differ in recipients of implantable cardioverter defibrillator with and without significant sleep related breathing disorders.

**References**


The aim was to investigate a high risk group of patients with an implantable cardioverter defibrillator (ICD) and to evaluate the relation of QT dispersion and sleep related breathing disorders (SRBD). The study population consisted of 44 unselected ICD recipients. The patients were divided in two groups: group I consisted of 29 pts without or only with mild SRBD, group II – 15 pts with at least moderate SRBD. The groups did not differ according to the age, sex, ejection fraction and use of beta-blocking agents or amiodarone. QT dispersion (QTD) did not differ between the groups: 63.4±17.9 ms in group I and 60.3±25.7 ms in group II, p=0.64. Heart rate corrected QT dispersion (QTcD) did not differ between the groups as well (67.6±19.5 ms in group I and 67.6±20.6 ms in group II, p=0.91). Spearman correlation analysis between the QTD, QTcD and Apnea-Hypopnea Index did not show any significant correlations in this contingency. Ill. 2, bibl. 15 (in English; summaries in English, Russian and Lithuanian).


Цель – анализ больных с повышенным риском, которым имплантированы кардиовертеры – дефibrillatorы (ICD) – и выяснение связи дисперсий QT интервала (QTD) с нарушениями дыхания во время сна (SRBD). В обследование были включены 44 больные с имплантированными ICD. Они были распределены на 2 группы. В первую группу включены 29 больных без или с лёгкими SRBD, во вторую группу – 15 больных с умеренными и тяжёлыми SRBD. Между группами не было различий по полу, возрасту, фракции изгнания левого желудочка, приёму β-блокаторов, амиодарона. Не выяшено различий по QTD между группами: QTD в 1-ой группе (63.4±17.9 мс) и во 2-ой группе (60.3±25.7 мс), p=0.64. По частоте сердцебиений корректированная QT дисперсия (QTcD) не отличалась (соответственно 67.6±19.5 мс и 67.6±20.6 мс, p=0.91). Коррелятивный Спирман анализ QTD, QTcD и Apnea/Hypopnea indeksа не показал значительных взаимосвязей. Ил. 2, библ. 15 (на английском языке; рефераты на английском, русском и литовском языках.).


Darbo tikslas – ištirti didelės rizikos ligonių su implantuotu kardioverterių defibrilatoriumi (ICD) kontingentai ir nustatyti, ar QT dispersija yra susijusi su kvėpavimo sutrikimais miego metu (SRBD). Tiriamaujų kontingentai sudarė 44 ligonai, kuriems implantuotas ICD. Ligoniai buvo suskirstyti į dvi grupes: pirmąją grupę sudarė 29 ligoniai tik su lengvais SRBD arba be jų, antrąją grupę – 15 ligonų su vidutiniu ir sunkaus laipsnio SRBD. Grupės nesiskyrė pagal amžių, lytį, išsitūrimą frakciją, beta blokiatorius ir amiodarono vartojimą. Panėsi buvo ir grupių QT dispersija (QTD): 63.4±17.9 ms (pirmą grupę) ir 60.3±25.7 ms (andra grupę), p=0.64. Pagal širdies dažnį koreguota grupių QT dispersija (QTcD) taip pat beveik nesiskyrė (atitinkamai 66.7±19.5 ms ir 67.6±3.4 ms, p=0.91). QTD, QTcD ir Apnoe/Hypopnoe indeksø Spearman koreliacinë analizë neparodë patikimą tarpusavyje ryši. Il. 2, bibl. 15 (anglų kalba; santraukos anglų, rusų ir lietuvių k.).