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Original Article

Association of sleep-disordered breathing and disturbed cardiac repolarization in patients with ST-segment elevation myocardial infarction

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ABSTRACT

Objective: In patients with ST-segment elevation myocardial infarction (STEMI), disturbed cardiac repolarization before percutaneous coronary intervention (PCI) is a risk factor for malignant ventricular arrhythmia. We tested the hypothesis that sleep-disordered breathing (SDB) in patients with STEMI is associated with disturbed cardiac repolarization.

Methods: Thirty-three patients with STEMI who underwent PCI were prospectively enrolled. To assess cardiac repolarization, the heart-rate corrected interval from the peak of the T wave to the end of the T wave (TpTec) and QTc intervals were assessed with 12-lead electrocardiography before PCI, within 24 h after PCI, and 12 weeks after PCI. SDB defined as an apnea–hypopnea index (AHI) ≥15 per hour was diagnosed by polysomnography.

Results: Before PCI, patients with SDB had a significantly prolonged TpTec interval compared to patients without SDB (133 vs 104 ms, $p = 0.035$). Within 24 h after PCI, the TpTec interval was 107 vs 92 ms ($p = 0.178$). QTc intervals showed a similar pattern (pre-PCI: 443 vs 423 ms, $p = 0.199$; post-PCI: 458 vs 432 ms, $p = 0.115$). In multiple linear regression analyses, AHI was significantly associated with prolonged TpTec intervals (pre-PCI: B-coefficient = 1.11, 95% confidence interval (CI) 0.48–1.74, $p = 0.001$; post-PCI: B = 0.97, 95% CI 0.29–1.65, $p = 0.007$), prolonged QTc intervals (pre-PCI: B = 1.05, 95% CI 0.20–1.91, $p = 0.018$; post-PCI: B = 1.37, 95% CI 0.51–2.24, $p = 0.003$), and higher TpTe/QT-ratios (pre-PCI: B = 0.16, 95% CI 0.05–0.27, $p = 0.007$; post-PCI: B = 0.13, 95% CI < 0.01–0.25, $p = 0.036$), independent of known risk factors for cardiac arrhythmia.

Conclusion: In patients with STEMI, SDB was significantly associated with disturbed cardiac repolarization before and after PCI, independent of known risk factors. These findings suggest that SDB may contribute to the risk of developing malignant ventricular arrhythmia.

1. Introduction

Sleep-disordered breathing (SDB) is characterized by nocturnal intermittent apneas and hypopneas associated with hypoxia, negative intrathoracic pressure swings, and arousals from sleep resulting in increased sympathetic activation, cardiac afterload, and heart rate [1–3]. SDB in patients without any known cardiac disease has been linked to disturbed cardiac repolarization and thus to an increased risk of cardiac arrhythmia, such as atrial fibrillation and

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ventricular arrhythmia [4,5]. Parameters in the electrocardiogram (ECG) describing cardiac repolarizations, such as prolonged QT and prolonged intervals from the peak of the T wave to the end of the T wave (TpTe), predict malignant ventricular arrhythmia and cardiac death in various clinical conditions [6–9]. A recent study has shown significantly prolonged QTc, TpTe, and TpTe/QT ratios in patients with SDB but without any heart disease who were withdrawn from continuous positive airway pressure (CPAP) for two weeks and compared to a standard CPAP group [10].

Notably, some evidence suggests that a prolonged TpTe interval is associated with sudden cardiac death in the general population [7]. A recent study has shown that, in the first hours after ST-elevation myocardial infarction (STEMI), the uncorrected TpTe interval was significantly longer in patients with sustained ventricular fibrillation than in patients without ventricular fibrillation [9]. Furthermore, prolonged TpTe intervals and increased TpTe/QT ratios in patients with STEMI before percutaneous coronary intervention (PCI) seems to be associated with increased short-term and long-term incidence of major adverse cardiac events.

The association of SDB and disturbed cardiac repolarization in STEMI patients, namely QTc, TpTec, and TpTe/QT-ratio, has not yet been investigated. Therefore, we tested the hypothesis that SDB in patients with STEMI is associated with disturbed cardiac repolarization, independent of known risk factors for cardiac arrhythmia.

2. Methods

A sub-analysis of the prospective observational study on patients with acute myocardial infarction was conducted at the University Medical Center Regensburg (Regensburg, Germany) [11–13]. Details of the study design have been published previously [11–13].

2.1. Patients

The inclusion criteria of this sub-analysis were as follows: patients with STEMI and PCI aged 18–80 years, who were treated at the University Medical Center Regensburg (Regensburg, Germany) within 24 h of symptom onset. Key exclusion criteria were previous myocardial infarction or previous myocardial revascularization (PCI or surgical), indication for surgical myocardial revascularization, cardiogenic shock, implantation of a cardiac device, or other contraindications for cardiac magnetic resonance, known treated SDB, and unfeasible follow-up (eg, length of distance to place of residence, language, and so on).

Between March 2009 and March 2012, we evaluated 252 consecutive patients who received PCI because of acute MI. Seventy-four patients fulfilled the inclusion and exclusion criteria of the prospective observational study [12]. Forty-one patients were excluded because of missing ECG, the impossibility to conduct an ECG analysis, or because they had myocardial infarction other than STEMI. The final analysis included 33 patients, who were stratified by the presence or absence of SDB.

2.2. Study design

The study protocol was reviewed and approved by the local institutional Ethics Committee. The study was conducted according to the Declaration of Helsinki on Good Clinical Practice. Written informed consent was obtained from all patients prior to enrollment.

Eligible patients underwent an overnight in-laboratory sleep study (polysomnography, PSG) 3–5 days after PCI [11–13]. Twelve-lead ECGs conducted before, ≤24 h after, and 12 weeks after PCI were analyzed.

Clinical management and medication was at the discretion of the responsible physician according to current practice and guidelines. SDB of an at least moderate degree was defined as an apnea–hypopnea index (AHI) of ≥15 events per hour of sleep. According to these specifications, patients were stratified into two groups: without SDB (AHI <15 events per hour) and with SDB (AHI ≥15 events per hour). None of the patients received treatment with positive airway pressure within the first 12 weeks after STEMI.

2.3. Polysomnography

All patients underwent PSG with standard polysomnographic techniques (Alice System; Respironics, Pittsburgh, PA, USA) [11–13]. The sleep laboratory is located in the cardiology ward of the University Medical Center to which participants with STEMI are admitted. The median time to baseline PSG after STEMI was three days. Respiratory efforts were measured by means of respiratory inductance plethysmography, and airflow was measured with a nasal pressure cannula. Sleep stages, arousals, apneas, and hypopneas were determined according to the criteria of the American Academy of Sleep Medicine [14] by an experienced sleep technician blinded to the clinical data. Apnea was defined as cessation of inspiratory airflow for ≥10 s. Hypopnea definition A was used (≥30% airflow reduction and ≥4% desaturation) [15]. AHI was defined as the number of apneas and hypopneas that occurred per hour of sleep.

2.4. ECG measurements – arrhythmia and cardiac repolarization

The ECG lead recorded during PSG was extracted and visually analyzed supported by the holter ECG software QRS-Card™ Cardiology Suite (Pulse Biomedical Inc., King of Prussia, USA). The software recorded the number of normal, ventricular, and supraventricular premature beats as well as the occurrence of premature couplets and triplets. Supraventricular and ventricular tachycardia, atrioventricular blocks, and pauses were registered. Automated analysis was visually verified by a scorer blinded to the clinical data.

Cardiac repolarization was analyzed with routine 12-lead ECG before PCI, 24 h after PCI, and 12 weeks after PCI. ECG intervals were measured manually with analysis software (DatInf Measure 2.1d, DatInf GmbH Tübingen, Germany) including QT, TpTe, and RR intervals that were measured in three consecutive heart beats in one lead. The preferential lead for measurement was V5, followed by V4, V6, II, and I. This selection was based on the experience in previous studies that faced difficulties in measuring leads V1 and V2 because of augmented quantity of T wave morphology that possibly resulted in longer or shorter TpTe times [16]. TpTe was measured by the 'tail method': the length of the T wave from the nadir to the end of the wave crossing the isoelectric line. QT interval was defined as the time of the earliest onset of the Q peak to the end of the T wave. The arithmetic mean was calculated using three consecutive measurements of one lead. QT and TpTe intervals were corrected for heart rate using the formula developed by Bazett (QTc, TpTec). The TpTe/QT ratio was calculated as the ratio of TpTe and the corresponding QT in that lead. The following values were considered as high risk: TpTe >100 ms [16,17], TpTe/QT ratio >0.29 [18].

2.5. Statistical analysis

All quantitative data are expressed as mean ± standard deviation unless otherwise indicated. Continuous and normal distributed variables were compared using Student's *t*-test for equal variances and Welch's test for unequal variances. Not normally distributed variables were compared using Mann–Whitney U-