Role of Shortened QTc Dispersion in In-hospital Cardiac Events in Patients Undergoing Percutaneous Coronary Intervention for Acute Coronary Syndrome

Chi-Cheng Lai¹, Hsiang-Chiang Hsiao¹,², Shin-Hung Hsiao¹, Wei-Chun Huang¹, Chuen-Wang Chiou¹,², Tung-Cheng Yeh¹, Hwong-Ru Hwang¹, Doyal Lee¹, Guang-Yuan Mar¹, Shih-Kai Lin¹, Kuan-Rau Chiou¹,², Shoa-Lin Lin¹,², Chun-Peng Liu¹,²*

¹Division of Cardiology, Department of Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, and ²National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.

Background: QT dispersion (QTD) refers to the difference between maximal and minimal QT values on the electrocardiogram (ECG). QTD values are calculated and corrected with Bazett’s formula (corrected QTD = QTcD = QTD/√RR). QTcD increases in patients with acute coronary syndrome (ACS). Recovery of increased QTcD (shortened QTcD) develops after successful revascularization, but prolonged QTcD occurs in certain patients. The aim of this study is to ascertain the clinical significance between shortened and prolonged QTcD groups after percutaneous coronary intervention (PCI).

Methods: We retrospectively enrolled 128 patients with ACS who had received PCI. The values of QTcD were measured manually on 12-lead standard ECGs obtained within 3 days before and after PCI (pre-PCI QTcD and post-PCI QTcD). All the patients were divided into 2 groups. The shortened QTcD group was defined as those patients with a decrease in QTcD after PCI and the prolonged QTcD group as those with an increase in QTcD after PCI. The underlying diseases, various clinical classifications and some prognostic factors were taken into comparison and statistical analysis between these 2 groups.

Results: The shortened QTcD group showed a significantly higher rate of in-hospital cardiac death (13% vs. 0%, p = 0.006) and a greater pre-PCI QTcD (100.8 ± 39.5 vs. 61.3 ± 24.1 ms, p < 0.001) than the prolonged QTcD group. There was a significantly greater pre-PCI QTcD in patients with cardiac death than those without cardiac death (111.6 ± 38.3 vs. 83.3 ± 38.3 ms, p = 0.027). Furthermore, the patients with in-hospital cardiac death presented with a significantly more frequent occurrence of in-hospital ventricular arrhythmia, compared with those without cardiac death (30.0% vs. 4.0%, p = 0.014).

Conclusion: Among the patients with ACS undergoing PCI, directly divided into shortened and prolonged QTcD groups regardless of initial pre-PCI QTcD, the shortened QTcD group showed a higher occurrence of in-hospital cardiac death and a greater pre-PCI QTcD. Shortened QTcD might be 1 risk factor for in-hospital cardiac death. [J Chin Med Assoc 2006;69(7):297–303]

Key Words: acute coronary syndrome, acute myocardial infarction, cardiac death, percutaneous coronary intervention, QT dispersion

Introduction

QT dispersion (QTD) is defined as the difference between maximum and minimum QT on the 12-lead electrocardiogram (ECG). QTD values are calculated and corrected with Bazett’s formula (corrected QTD = QTcD = QTD/√RR). Greater QTD and/or QTcD (QTcD/QTD) usually represents more electrical heterogeneity and instability of ventricular myocardium. It has been reported that increased QTD/QTcD is useful to predict the potential risk of ventricular arrhythmogenesis and/or mortality.¹⁻⁶
Increased QTD/QTcD is found in most patients with acute coronary syndrome (ACS). It has also been published that increased QTD/QTcD recovers after successful reperfusion, such as therapy with thrombolytic agents or percutaneous coronary intervention (PCI). These dynamics of QTD/QTcD after PCI serve as a valuable marker of successful revascularization and clinical prognosis. The “shortened QTcD” group is defined as patients with a decrease in QTcD after PCI and the “prolonged QTcD” group as those with an increase in QTcD after PCI. Among patients with ACS after coronary intervention, there is a paucity of published information comparing the clinical differences between shortened QTcD and prolonged QTcD. The aim of this study is to determine the clinical significance in patients with ACS after PCI between these 2 groups.

Methods

Study population
We retrospectively investigated 176 consecutive patients with ACS who had undergone emergent interventional therapy at Kaohsiung Veterans General Hospital between December 2002 and 2004. Exclusion criteria included atrial fibrillation or flutter, pacing rhythm, bundle branch block, complete atrioventricular block, marked change of rhythm, more than 6 missing leads or sequentially received coronary artery bypass surgery. Therefore, 128 patients were included in this study. All the patients were divided into 2 groups: the shortened QTcD group and the prolonged QTcD group. The incidence of baseline characteristics, various clinical classifications, and some prognostic factors were taken into consideration for statistical analysis and a comparison between these 2 groups was made (Table 1).

12-lead ECGs
The QT intervals and QTcD were measured manually from the standard ECGs available within 3 days before and after PCI by 2 cardiac electrophysiologists. The 12-lead surface ECGs were recorded at a paper speed of 25 mm/second and were amplified to 1.4 times in length. The QT interval was defined as the interval between the beginning of the Q wave and termination of the T wave. The terminated point of the T wave

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics of the 2 study groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shortened QTcD (n = 77)</td>
</tr>
<tr>
<td>Age (yr)</td>
</tr>
<tr>
<td>Male (%)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
</tr>
<tr>
<td>Prior MI (%)</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
</tr>
<tr>
<td>Peak of CK (mean)</td>
</tr>
<tr>
<td>Peak of CK–MB (mean)</td>
</tr>
<tr>
<td>Unstable angina (%)</td>
</tr>
<tr>
<td>NSTEMI (%)</td>
</tr>
<tr>
<td>STEMI (%)</td>
</tr>
<tr>
<td>LAD artery disease</td>
</tr>
<tr>
<td>Pre-PCI TIMI grade 0 or 1 (%)</td>
</tr>
<tr>
<td>Single-vessel disease (%)</td>
</tr>
<tr>
<td>Double-vessel disease (%)</td>
</tr>
<tr>
<td>Triple-vessel disease and/or left main disease (%)</td>
</tr>
<tr>
<td>Re-intervention* (%)</td>
</tr>
<tr>
<td>Usage of aspirin (%)</td>
</tr>
<tr>
<td>Usage of beta-blocker (%)</td>
</tr>
<tr>
<td>Usage of ACEI (%)</td>
</tr>
<tr>
<td>Usage of statin (%)</td>
</tr>
</tbody>
</table>

*Re-intervention is the presence of intervention again before April 2005, and not limited to the same target lesions for coronary intervention. MI = myocardial infarction; CK = creatine kinase; CK–MB = isoform of creatine kinase; NSTEMI = non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction; LAD artery = left anterior descending artery; Pre-PCI QTcD = QT dispersion before percutaneous coronary intervention; TIMI = thrombolysis in myocardial infarction; ACEI = angiotensin-converting enzyme inhibitor.
was defined as the cross-point of the baseline and slope tangent line if the endpoint was undetermined classically (Figure 1). Each measurement was taken as the mean value of 2–3 consecutive RR and QT intervals. The leads with isoelectrical lines (absent or too small amplitude of T waves), uncertainties or variations of QT intervals and wandering waveforms were omitted. The goal of all these considerations is to decrease the variation, increase the reproducibility, and improve the accuracy of measurement. The typical examples for QTcD measurement in these 2 groups are depicted in Figures 2 and 3.

Cardiac catheterization
All the enrolled patients received coronary angiography and interventional therapy. The severities of diseased coronary arteries and grade flows of thrombolysis in myocardial infarction (TIMI) were determined by 2 independent cardiologists. Significant lesions of diseased coronary arteries were defined as the narrowing of coronary arteries by at least 50% in lumen diameter or by 75% in lumen area compared with adjacent segments of coronary artery. Coronary intervention was operated in the infarct-related arteries or culprit lesions, and the other significantly stenotic lesions were not managed simultaneously. Successful revascularization was defined as the restoration of TIMI grade 3 flow with less than 50% residual stenosis in lumen diameter; whether or not to deploy the stents and types of stents was left to the judgment of the operators.

Statistical analysis
Categorical data are presented as absolute values and percentages, whereas continuous variables are summarized as mean values ± standard deviation. The $\chi^2$ test was used to compare the categorical data. Independent sample $t$ test was performed to compare the continuous data. A $p < 0.05$ was considered statistically significant. Univariate and multivariate logistic regression analyses were performed, with the risk variables for ventricular tachycardia or fibrillation and in-hospital cardiac death assessed including age, prior MI, ST elevation MI (STEMI), pre-PCI TIMI grade 0 and 1, usage of aspirin, beta-blocker, ACE inhibitor and statin, pre-PCI QTcD, post-PCI QTcD, and difference between QTcD before and after PCI (Table 2).

Results

Demographic data
The 128 patients included in this study were divided into 2 groups: the shortened QTcD group and the prolonged QTcD group. Demographic baseline and clinical characteristics of these 2 groups are shown in Table 1.

QTc dispersion before PCI
The shortened QTcD group manifested a significantly greater pre-PCI QTD/QTcD than the prolonged QTcD group (101.9 ± 40.3/100.8 ± 39.5 vs. 54.9 ± 21.3/61.3 ± 24.1 ms, $p < 0.001$).

In-hospital cardiac death and ventricular tachycardia or fibrillation
This study demonstrated that there was a significantly higher rate of in-hospital cardiac death in the shortened QTcD group than in the prolonged QTcD group ($n = 10$, 13.0% vs. $n = 0$, 0%, $p = 0.006$). Moreover, the patients with cardiac death had a greater pre-PCI QTcD compared with those without cardiac death (111.5 ± 38.3 vs. 83.3 ± 38.3 ms, $p = 0.027$), and significantly more frequent occurrence of in-hospital ventricular arrhythmia ($n = 3$, 30% vs. $n = 5$, 4%, $p = 0.014$) compared with survivors. All risk variables for ventricular tachycardia or fibrillation (VT/VF) and in-hospital cardiac death were collected for univariate and multivariate analyses (Table 2). Some variables of multivariate analysis presented as significant risk factors for in-hospital cardiac death (Table 2), including STEMI, usage of beta-blocker, and shortened QTcD group, but none of the variables presented as a significant risk factor for VT/VF.
Figure 2. A typical example of QTcD measurement was demonstrated in the shortened QTd group. (A) QTcD measurement before PCI (pre-PCI QTcD). (B) QTcD measurement after PCI (post-PCI QTcD) (ms = millisecond).
Figure 3. A typical example of QTcD measurement was demonstrated in the prolonged QTcD group. (A) Before PCI (pre-PCI QTcD). (B) After PCI (post-PCI QTcD).
Discussion

In the present study, the shortened QTcD group had a significantly higher rate of in-hospital cardiac death among the patients with ACS after receiving PCI, compared with the prolonged QTcD group. Although shortened QTcD after PCI represented a marker of successful reperfusion and better outcome in previous studies, surprisingly, our study displayed results against the prediction. How to explain the presence of higher rates of cardiac death in the shortened QTcD group? First, the shortened QTcD group had a significantly greater pre-PCI QTcD, which might serve as a predictor of worse outcome. Also, an increased QTcD is usually associated with old age, ventricular arrhythmia, unsuccessful reperfusion, or mortality. In this study, the prognostic factors did not reach statistical significance between these 2 groups. Increased electrical stability and homogeneity regained after PCI in patients with greater pre-PCI QTcD, which certainly displayed as much more reduction of QTcD. The adverse effects of greater pre-PCI QTcD might overcome the beneficial effects of PCI in the shortened QTcD group. In other words, pre-PCI QTcD should be taken into account if shortened QTcD after PCI was shown as a predictor of good outcome. Otherwise, the shortened QTcD group after PCI showed significantly opposite result if they were divided regardless of initial pre-PCI QTcD. The prolongation of QTcD after PCI has previously been regarded as a marker for unsuccessful revascularization.

In our opinion, the prolongation of post-PCI QTcD seemed to be attributed to multiple factors, including the presence of revolution of ST segments and T waves, timing of ECG examination, and the existence of the late deflection of T wave (discordant negative or positive component of T waves). The effect became more dramatic in the prolonged QTcD group due to shorter baseline QTcD.

As shown in Table 2, STEMI, usage of beta-blocker, and shortened QTcD were risk factors for in-hospital cardiac death after multivariate analysis. It was reasonable that patients with STEMI had higher in-hospital mortality rate than those with unstable angina or non-STEMI. However, the significance of usage of beta-blockers might have contributed to selection bias; beta-blockers were held or withdrawn in patients with more severe clinical presentations, such as hemodynamic compromise, heart conduction block, pulmonary edema, asthma, and coexisting lung disease.

The current study has several limitations. First, the number of patients enrolled, in-hospital cardiac deaths, and ventricular arrhythmias was small, which restricted the statistical analysis and clinical applications. More prospective studies with greater case numbers are warranted to confirm the significance of shortened QTcD and in-hospital cardiac deaths in patients with ACS after PCI. Second, the QTcD was measured manually, which resulted in more variation and inaccuracy. However, this method of QTcD measurement serves

<table>
<thead>
<tr>
<th>Risk variables</th>
<th>VT/VF (p)</th>
<th>Cardiac death (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate</td>
<td>Multivariate</td>
</tr>
<tr>
<td>Age</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Prior MI</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>STEMI</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>CK</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>CK–MB</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Usage of aspirin</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Usage of beta-blocker</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Usage of ACEI</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Usage of statin</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-PCI TIMI 0 or 1</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-PCI QTcD</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Post-PCI QTcD</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Difference between QTcD before and after PCI</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Shortened QTcD group</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = non-significant; VT/VF = ventricular tachycardia or fibrillation; MI = myocardial infarction; STEMI = ST elevation myocardial infarction; CK = creatine kinase; CK–MB = isoform of creatine kinase; ACEI = angiotensin-converting enzyme inhibitor; Pre-PCI TIMI = TIMI flow grade before PCI; Pre-PCI QTcD = QTc dispersion before percutaneous coronary intervention; Post-PCI QTcD = QTc dispersion after percutaneous coronary intervention.
as an available, simple, and inexpensive technique not just as a research tool but also as an easy clinical application. Without doubt, QTcD measurement remains a technologic and methodologic problem. Although this assessment is easy to utilize in routine clinical situations, this issue still remains to be solved.

In conclusion, this study established that patients with ACS after PCI presenting with shortened QTcD have significantly higher occurrence of in-hospital cardiac deaths, which seem to be the result of greater pre-PCI QTcD. Furthermore, patients with in-hospital cardiac death have a significantly greater pre-PCI QTcD and higher occurrence of in-hospital ventricular arrhythmia than those without in-hospital death. Shortened QTcD might be 1 risk factor for in-hospital cardiac death regardless of initial pre-QTcD.

Acknowledgments

The authors wish to thank assistant Ya-Ting Wu for her secretarial work.

References