QT dispersion and heart rate variability in sudden death risk stratification in patients with ischemic heart disease

Ina Blužaitė1,2, Julija Braždžionytė2, Remigijus Žaliūnas3, Hans Rickli1, Peter Ammann1
1Kantonsspital St. Gallen, Switzerland. 2Institute of Cardiology, Department of Cardiology, Kaunas University of Medicine, Lithuania

Key words: QT dispersion, heart rate variability, sudden death risk stratification.

Summary. The aim of the article is to review the literature data about the significance and problems of the QT dispersion and heart rate variability in sudden death risk stratification in patients with coronary heart disease. QT dispersion is defined as the difference between the longest and the shortest QT intervals as measured in the 12-lead electrocardiogram. A direct relationship between the prolongation of QT dispersion and myocardial ischemia has been reported by several authors. Our previous study showed that QT dispersion assessed immediately after bicycle exercise test was significantly higher in patients with coronary stenoses of >50% as compared to the patients without coronary artery disease. Despite some controversial data, several studies showed that QT dispersion is a significant predictor of cardiovascular mortality. Heart rate variability representing a relationship between the autonomic nervous system and cardiovascular mortality, including sudden cardiac death, is one of the most promising markers. The predictive value of heart rate variability is independent of other factors established for postinfarction risk stratification, such as depressed left ventricular ejection fraction, increased ventricular ectopic activity, and presence of late potentials. For prediction of all-cause mortality, the value of heart rate variability is similar to that of left ventricular ejection fraction, but heart rate variability is superior to left ventricular ejection fraction in predicting arrhythmic events (sudden cardiac death and ventricular tachycardia).

The clinical usefulness of measuring changes in the duration of the QT interval in the standard 12-lead electrocardiogram (ECG) is a topic of growing interest. C. P. Day et al. (1) proposed the use of QT dispersion (QTd) measurement as an index of the inhomogeneity of myocardial repolarization, which could be applied as a potential prognostic tool in the detection of future ventricular tachyarrhythmic events and death (2). QTd is defined as the difference between the longest and the shortest QT intervals as measured in the 12-lead ECG and can be assessed computerized and manually as well. QT dispersion at rest varies from 30–60 ms in healthy subjects and 60–80 ms in patients with coronary artery disease (CAD) (3). From a practical point of view when a precise determination of QT interval is needed, the heart rate correction should be optimized for the given person (4), and heart rate-corrected QTd should be used (QTcd), but until now there are contradictory data as well, whether QTd should be corrected for heart rate values (5).

A relation between QTd and the extent of myocardial ischemia has been reported indicating a direct correlation between myocardial lactate extraction ratio (a metabolic marker of myocardial ischemia) and QTd in patients undergoing rapid atrial pacing (6). A direct relationship between the prolongation of the QT interval and myocardial ischemia has been reported by G. Roukema et al. (7), who observed increased QTd in patients with exercise-induced myocardial ischemia. In both experimental animal and patient studies, it has been shown that the QT interval shortens in acutely hypoperfused areas, whereas in infarcted myocardium there is a prolonged repolarization time associated with QT prolongation on the ECG (8). Our previous study showed (9) that QTd assessed immediately after bicycle exercise test was significantly higher in patients with coronary stenoses of >50% as compared to the patients without CAD. There are some controversial data that QT dispersion significantly decreases during positive dobutamine stress testing in patients with CAD (10) or fails to correlate with changes in regional wall motion during dobutamine stress echocardiography (11), and that QTd...
correlates only with the parameters of vectorcardiographic T loop morphology (12). M. Bountiokos et al. (13) found that QT dispersion negatively correlated to myocardial viability (number of viable segments) assessed by dobutamine stress echocardiography in patients with severely depressed left ventricular function due to CAD (13). P. Lancellotti et al. (14) claim that dobutamine-induced increase in QT dispersion is associated with viable and jeopardized myocardium, and unchanged QT dispersion during dobutamine stress is a simple marker of extensive necrosis.

J. Perkimki et al. (15) claim that increased QTd is related to susceptibility to reentry ventricular tachyarhythmias, independent of degree of left ventricular dysfunction or clinical characteristics of the patient, suggesting that the simple, noninvasive measurement of this interval from a standard 12-lead ECG makes significant contribution to identifying patients at risk for life-threatening arrhythmias after a previous myocardial infarction. The Strong Heart Study of assessment of QT interval and QTd for prediction of all-cause cardiovascular mortality in American Indians (1,839 participants) showed that QTcd was a strong predictor of all-cause mortality and a weaker predictor of cardiovascular mortality, and that QTd is a significant predictor of cardiovascular mortality (2). A subgroup analysis of 313 patients with heart failure in ValHeFT (Valsartan Heart Failure Trial) study showed that QTcd of >70 ms was associated with significant higher mortality (16). Rotterdam study (more than 5,000 ECG’s of 78% of inhabitants aged >55 years living in the Rotterdam district Ommoord) revealed that QTcd was an independent predictor for cardiovascular mortality in senior persons (17).

There are some controversial data that the determination of QTd from the surface ECG even when performed with the best available methodology failed to predict subsequent risk in infarct survivors (18), and that QT parameters are not influenced by infarct size (19) and do not predict inducibility of life-threatening arrhythmias during electrophysiological study (2). Reasons for these contradictory results are, for example, the difficulties in determining the end of the T-wave and the missing standard in QT-interval measurement methods (20). QTd is time-variable as well and is biphasic with two peaks (at night or in the morning and in the afternoon) (21), so this time-variability could make additional difficulties in QTd assessment.

The last three decades have witnessed the recognition of a significant relationship between the autonomic nervous system and cardiovascular mortality, including sudden cardiac death (22, 23). Heart rate variability (HRV) represents one of the most promising markers (24). Analysis of HRV consists of a series of measurements of successive RR interval variations of sinus origin which provide information about autonomic tone (25). Different physiological factors may influence HRV such as gender, age, circadian rhythm, respiration, and body position (26). Measurements of HRV may generally be performed on the basis of 24-hour Holter recordings or on shorter periods ranging from 0.5 to 5 minutes (24, 27). Most Holter apparatus manufacturers nowadays propose HRV analysis programs which are incorporated into their instrument systems (28). Although computer analysis of tape recordings has improved, human interventions are required in most measurements of HRV parameters in order to detect erroneous beats, artefacts, and alterations in tape speed that may alter timing intervals (27).

In 1996, a Task Force of the European Society of Cardiology (ESC) and the North American Society of Pacing and Electrophysiology (NASPE) defined and established standards of measurement, physiological interpretation, and clinical use of HRV (24). Time domain indices, geometric measures, and frequency domain indices constitute nowadays the standard clinically used parameters (27). The time domain measures, perhaps, are the simplest to perform. With this method either the heart rate at any point of time or the intervals between successive normal complexes are determined (24). Among the various time domain and geometric methods available, the Task Force of the ESC and the NASPE have recommended the use of four measures for HRV assessment: SDNN (ms) – standard deviation of all NN (normal to normal complex) intervals, SDANN (ms) – standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording, RMSSD (ms) – the square root of the mean of the sum of the squares of differences between adjacent NN intervals, and the HRV triangular index (24). Frequency domain (power spectral density) analysis describes the periodic oscillations of the heart rate signal decomposed at different frequencies and amplitudes and provides information on the amount of their relative intensity in the heart’s sinus rhythm (24). Frequency domain parameters include total power – variance of all NN intervals (≤0.4 Hz), ULF – power in the ultra-low-frequency range (≤0.003 Hz), VLF – power in the very-low-frequency range (0.003–0.04 Hz), LF – power in the low-frequency range (0.04–0.15 Hz), HF – power in the high-frequency range (0.15–0.4 Hz) (24, 27). In general, time-domain methods are useful in short- and long-term recordings; the frequency methods are usually
able to provide more easily interpretable results in short recordings (24).

Since the first report by M. M. Wolf et al. (29) in 1978 on the association between decreased HRV and increased mortality after myocardial infarction, numerous studies have been performed using HRV alone or in combination with other variables (30–32). The predictive value of HRV is independent of other factors established for postinfarction risk stratification, such as depressed left ventricular ejection fraction, increased ventricular ectopic activity, and presence of late potentials (24). For prediction of all-cause mortality, the value of HRV is similar to that of left ventricular ejection fraction, but HRV is superior to left ventricular ejection fraction in predicting arrhythmic events (sudden cardiac death and ventricular tachycardia) (33). Taken alone the positive predictive accuracy of HRV hardly reaches 40% (27). It has, however, a higher negative predictive value, which means that post-MI patients with normal HRV can be considered at low risk for cardiac or arrhythmic events. Combined to other variables, such as diminished left ventricular ejection fraction, premature ventricular couplets >10/ hour, runs of nonsustained ventricular tachycardia, late potentials, its positive predictive accuracy can be improved (27). In the large international ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) trial (32) the concomitant use of HRV and baroreflex sensitivity for post-MI risk stratification showed that the values of SDNN of <70 ms or baroreflex sensitivity of <3.0 ms/mmHg were both independent predictors of cardiac mortality. Furthermore, the association of low SDNN and baroreflex sensitivity with a left ventricular ejection fraction of <35% carried a relative risk of cardiac mortality (6.7 and 8.7, respectively).

In 2005, S. Guzzetti et al. analyzing different spectral components of 24 h HRV in chronic heart failure detected that depressed power of night-time HRV below 0.04 Hz (very low frequency) was independently related to death for progressive pump failure, while the reduction of power between 0.04 and 0.15 Hz at night was linked to sudden mortality (34).

In an era of sophisticated tests of the autonomic system, A. Katz et al. (1999) found out that a simple 1-minute deep breathing test (five seconds for each inhalation and five seconds for each exhalation) of HRV in patients after myocardial infarction appears to be a good predictor for all-cause mortality and sudden death and may be used as a clinical test for risk stratification after myocardial infarction (35). The authors claim that the sensitivity and specificity of this test for cardiovascular mortality is 90 and 68%, respectively, and that HRV <10 beats/min remains a significant predictor of death after adjusting for clinical, demographic, and left ventricular function with an odds ratio of 1.38 (95% confidence interval 1.13–1.63) (35).

The time after acute myocardial infarction at which the depressed HRV reaches the highest predictive value has not been investigated comprehensively. Nevertheless, the general consensus is that HRV should be assessed shortly prior to hospital discharge, i.e. approximately one week after index infarction. Such a recommendation also fits well into the common practice of hospital management of survivors of acute myocardial infarction (24). HRV is decreased early after acute myocardial infarction and begins to recover within a few weeks; it is maximally but not fully recovered by 6–12 months after myocardial infarction (31). HRV measured one year after acute myocardial infarction also predicts further mortality (36).

Despite the large number of experimental and clinical studies published the measurement of HRV is still a research technique and not a routine clinical tool (27). There are several potential reasons that can explain this situation. First, the clinical application of HRV assessment is limited by lack of standardized methodology due to variability of the parameters according to gender, age, drug interferences, and concomitant diseases. Second, despite the relative evidence of the robust character of parameters such as SDNN and the HRV index, there is still no consensus about the most accurate HRV parameter for clinical use (27). Third, the sensitivity, specificity, and positive predictive accuracy of HRV are limited. Particularly, its positive predictive accuracy is modest, ranging from 14 to 40% (27). It has, however, a higher negative predictive value ranging from 77 to 98% (27). The combination of HRV with other risk stratifiers, including left ventricular ejection fraction, nonsustained ventricular tachycardia, premature ventricular beats >10/h, late potentials, baroreflex sensitivity, T-loop morphology, spatial QRS-T angle, etc., may increase the overall predictive accuracy (27, 32, 33, 37–39).

Given the human and economic costs of sudden cardiac death and the potential benefits to be gained by early identification of patients at increased risk and by the use of implantable cardioverter defibrillator (ICD) devices, today the most important problem is to identify patients best suited for this treatment and those who do not need an ICD (27). An important challenge for the near future will be to obtain a universally accepted standardization of HRV methodology and improvement of its positive predictive accuracy mostly by combining it to other risk stratifiers.
QT dispersija ir širdies ritmo dažnio variabilumas įvertinant staigios mirties riziką sergantiesiems išimine širdies ligą

Ina Blužaitė1, 2, Julija Braždžionytė1, Remigijus Žaliūnas1, Hans Rickli1, Peter Ammann1
1St. Galeno kantono ligoninė, Šveicarija, Kauno medicinos universiteto 2Kardiologijos institutas, Kardiologijos klinika, Lietuva

Raktas: QT dispersija, širdies ritmo dažnio variabilumas, staigios mirties rizikos įvertinimas.


Adresas susirūsinėti: J. Braždžionytė, KMU Kardiologijos klinika, Eivenių 2, 50009 Kaunas
El. paštas: julbra@kmu.lt

References


Received 30 January 2006, accepted 26 May 2006

Straipsnis gautas 2006 01 30, priimtas 2006 05 26