Validation of Heart Rate Variability Analysis Based on the RR Intervals Recorded by Implantable Cardioverter-Defibrillators

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Summary

Heart rate variability (HRV) assesses the autonomic balance of the heart. Certain measures of heart rate variability can predict the risk of ventricular tachycardia and fibrillation (VT/VF) in specific patient groups. Recently attention is focusing on the mechanisms initiating episodes of VT/VF by analysing the time period immediately preceding such episodes. HRV preceding episodes of VT/VF can now be systematically analysed in patients with an implantable cardioverter defibrillator (ICD) by utilising the long term RR interval Holter, which is available in the ICD Phylax XM and it's successors mycroPhylax and mycroPhylax plus (BIOTRONIK). Simultaneous recordings of a standard surface electrocardiogram (ECG) using the Medilog Excel-2 (OXFORD Instruments) and the intracardiac electrogram (IEGM) generated by the Phylax XM were obtained and subsequently analysed in 16 patients under standardised conditions in supine and upright positions. Time and frequency domain HRV parameters of 5 minute sections of each recording were determined and evaluated for significant equivalence using the population bioequivalence test. The HRV parameters derived from the two systems showed a high degree of correlation and the major parameters were significantly equivalent independent of the patients' position. The Phylax XM is a suitable tool to systematically and accurately evaluate the major time and frequency domain parameters of HRV during a time period of up to five hours preceding the detection of a VT/VF in patients.

Key Words

Heart rate variability, implantable cardioverter-defibrillator, ventricular tachycardia, ventricular fibrillation

Introduction

Experimental and clinical observations have shown that an imbalance of the autonomic nervous system, especially reduced parasympathetic (vagal) activity, is a risk factor for precipitating ventricular tachycardia and ventricular fibrillation (VT/VF) [1,2]. The suggested underlying pathophysiologic mechanism is that high sympathetic activity, and concurrent lack of the protective effect of parasympathetic tone, predisposes to VT/VF [3, 4]. Variations in autonomic balance are reflected in the heart rate. Determination of cyclic changes in heart rate - the heart rate variability (HRV) - is thus a suitable instrument for indirect measurement of autonomic activity. It has been well established in recent years by several studies that changes in HRV correlate with the occurrence of VT/VF of different etiology [5-8]. It has also been shown that certain measures of HRV constitute independent statistical predictors of sudden death in specific patient groups, for example in post myocardial infarction patients [9-12], and in patients with idiopathic dilated cardiomyopathy [13,14].

Recently more attention is being focused on the time period immediately preceding episodes of VT/VF for analysis of the mechanisms initiating these arrhythmias. It is of special interest to identify specific changes in HRV and possibly specific critical

sequences of RR intervals in order to predict future episodes of VT/VF before their occurrence. Up to now systematic investigation concerning this aspect of HRV has been limited by the small number of episodes available for analysis, these usually being coincidentally recorded by Holter electrocardiography [15,16].
It is now possible to systematically and prospectively assess the HRV preceding episodes of spontaneous VT/VF on a routine basis, by utilising the long term RR interval Holter which is available in the ICD Phylax XM (BIOTRONIK).

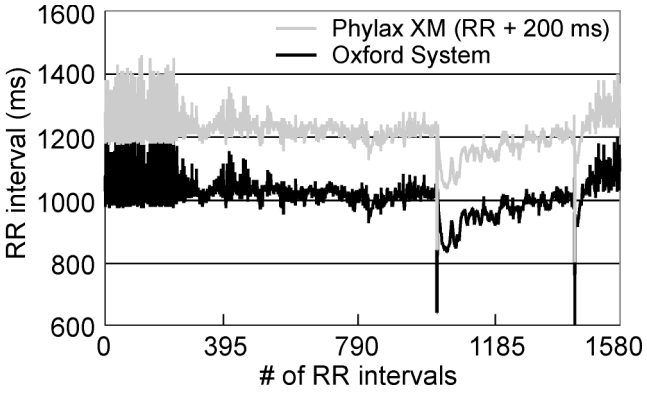

Figure 1. Interval tachogram recorded with Phylax XM and OXFORD system.

Materials and Methods

The RR interval Holter memory of the ICD Phylax XM features a storage capacity of 18,000 RR intervals, derived from a near field bipolar ventricular intracardiac electrogram (IEGM), with a sampling rate for detection of the QRS complex of 8 kHz. The re-sampling for RR interval storage is done with a time resolution of 3.9 ms. The extended RR interval Holter of the Phylax XM is expected to enable a comprehensive and accurate analysis of HRV parameters in a time period of up to five hours preceding the detection of a VT/VF.
The purpose of this study was to investigate the suitability of the Phylax XM for accurate determination of HRV parameters. The main objective was to show a significant equivalence of the most relevant time and frequency domain parameters of HRV derived from the near field IEGM compared to a standard high time resolution digitally processed surface electrogram (ECG).
16 patients referred for ICD implantation according to accepted guidelines who gave their informed consent were included in the study. Patients with intermittent bundle branch block, polyneuropathy, endocrine disorders and patients not in sinus rhythm or with a high proportion of anti-bradycardia pacing were excluded from the study. All patients were assessed during the morning to exclude circadian influences on HRV. All pertinent patient data including concomitant disease, cardiac status and antiarrhythmic medication were documented.
Simultaneous recordings of a standard ECG using the Medilog Excel-2 (OXFORD Instruments) and the IEGM generated by the Phylax XM were obtained from each patient under standardised conditions and subsequently analysed.
According to the test protocol, RR intervals during sinus rhythm were recorded for 10 min while the patient was breathing normally in the supine position, for 5 min while the patient was breathing deeply while supine and for 5 min while the patient was in an upright position. An allowance of approximately one minute was made after the orthostatic manoeuvre for circulatory adjustment (Figure 1). The RR interval data stored in the Holter memory of the Phylax XM were retrieved and saved using the patient data management system PDM2000 (BIOTRONIK) for further processing.
Ectopic beats were filtered from the recordings of the surface ECG and the IEGM respectively, using an interval filter of 150 ms. The HRV of 5 minute sections of each recording was assessed using standard time and frequency domain parameters 17, 18 as follows:

- MeanRR (mean of all normal RR intervals);
- SDNN (standard deviation of the mean of all RR intervals);
- rMSSD (root-mean square of differences between consecutive RR intervals);
- pNN50 (percentage of adjacent RR intervals varying by more than 50 ms);
- COVR (SDNN in relation to MeanRR);
- LF (power of low frequency band: 0.040-0.150 Hz);
- HF (power of high frequency band: 0.150-0.500 Hz);
- TP (total power: 0.040-0.500 Hz)

The frequency domain parameters LF, HF and TP were calculated by a fast Fourier transformation (FFT) non-parametric algorithm using a Hanning window.
The correlation between the individual HRV parameters obtained from the OXFORD Medilog system and the Phylax XM respectively was calculated.

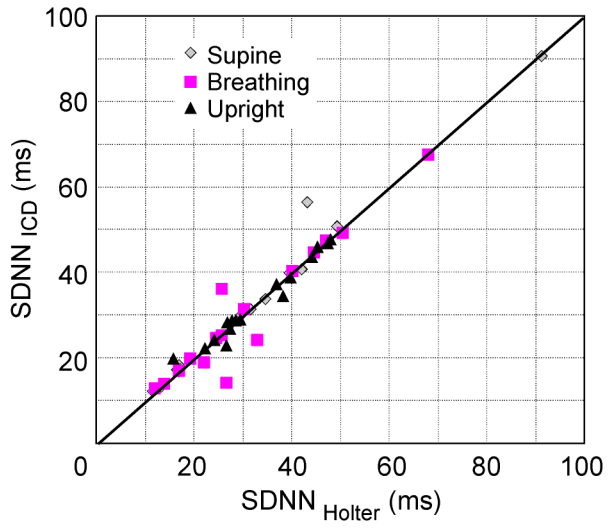

Figure 2. Correlation plot of SDNN obtained from Phylax Xm and OXFORD system.

	Supine	Breathing deeply	Upright
Mean RR	1.0*	1.0*	1.0*
SDNN	0.99*	0.95*	0.98*
rMSSD	0.99*	0.78	0.92
pNN50	0.99	0.66	0.98
COVR	0.99*	0.97*	0.99*
LF	0.97*	0.96*	0.99*
HF	0.98*	0.98	0.99*
TP	0.97*	0.98	0.99*

* significant ($p < 0.05$) population bioequivalence [80 %, 125 %]

Table 1. Correlation coefficients and equivalence of HRV parameters obtained from the OXFORD system and the Phylax XM.

The HRV parameters derived from the two different systems were subsequently evaluated for significant equivalence using the population bioequivalence test with the OXFORD system as reference (equivalence range 80%, 125%) with a Type I error of 5% ($p < 0.05$).

Results

The time domain parameters MeanRR, SDNN and COVR showed a high degree of correlation while the patients were supine and upright and while the patients breathed deeply (e.g. Figure 2). Table 1 shows the calculated values for the correlation coefficient to be between 0.95 and 1.0. The parameters rMSSD and pNN50 correlated well in both the supine and upright position with the correlation coefficient being between 0.92 and 0.99, but not while the patients breathed deeply. All frequency domain parameters (LF, HF, TP) showed a high correlation in the supine and upright position, as well as during deep breathing with the correlation coefficient found to be between 0.96 and 0.99. As determined by the population bioequivalence test, there was a significant equivalence ($p < 0.05$) for the time domain parameters MeanRR, SDNN and COVR and the frequency domain parameter LF in the supine and upright position as well as during deep breathing. The parameters HF and TP also reached significant equivalence during the supine and upright position, but not while the patients were breathing deeply.

Discussion

The time domain parameters MeanRR, SDNN and COVR and the frequency domain parameters LF, HF and TP showed a high degree of correlation independent of the patients' position and during deep breathing.

There was a significant equivalence ($p < 0.05$) for the time domain parameters MeanRR, SDNN and COVR and the frequency domain parameters LF, HF and TP in the supine and upright position. These parameters, except HF and TP, also reached significant equivalence while the patients breathed deeply. Although HF and TP, which is dependent on HF, showed a high correlation, these parameters could not reach significance with the available sample size due to the higher values of their respective standard deviations.

The Phylax XM is a suitable tool to systematically and accurately evaluate the major time and frequency domain parameters of HRV. The Phylax XM and it's direct successor models mycroPhylax and mycroPhylax plus, which feature the same long term RR interval Holter, enable the investigation of the HRV parameters during a time period of up to five hours preceding the detection of a VT/VF. This feature offers the unique possibility to prospectively evaluate HRV in ICD patient collectives. It is expected that future studies will be conducted which may lead to new approaches to the diagnosis and therapy of ventricular arrhythmias.

References

[1] Cerati D, Schwartz PJ. Single cardiac vagal fiber activity, acute myocardial ischemia, and risk for sudden death. Circ Res. 1991; 69 (5): 1389-1401.

[2] Fei L, Statters DJ, Hnatkova K, et al. Change of autonomic influence on the heart immediately before the onset of spontaneous idiopathic ventricular tachycardia. J Am Coll Cardiol. 1994; 24 (6): 1515-1522.

[3] Lown B, Verrier RL. Neural activity and ventricular fibrillation. N Engl J Med. 1976; 294 (21): 1165-1170.

[4] Vanoli E, De Ferrari GM, Stramba-Badiale M, et al. Vagal stimulation and prevention of sudden death in conscious dogs with a healed myocardial infarction. Circ Res. 1991; 68 (5): 1471-1481.

[5] Hohnloser SH, Klingenheben T, van de Loo A, et al. Reflex versus tonic vagal activity as a prognostic parameter in patients with sustained ventricular tachycardia or ventricular fibrillation. Circulation. 1994; 89 (3): 1068-1073.

[6] Hull SS Jr, Vanoli E, Adamson PB, et al. Do increases in markers of vagal activity imply protection from sudden death? The case of scopolamine. Circulation. 1995; 91 (10): 2516-2519.

[7] Filipecki A, Trusz-Gluza M, Szydlo K, et al. Value of heart rate variability parameters for prediction of serious arrhythmic events in patients with malignant ventricular arrhythmias. Pacing Clin Electrophysiol. 1996; 19 (11 Pt 2): 1852-1856.

[8] Perkiomaki JS, Huikuri HV, Koistinen, JM et al. Heart rate variability and dispersion of QT interval in patients with vulnerability to ventricular tachycardia and ventricular fibrillation after previous myocardial infarction. J Am Coll Cardiol. 1997; 30 (5): 1331-1338.

[9] Bigger JT, Fleiss JL, Rolnitzky LM, et al. The ability of several short-term measures of RR variability to predict mortality after myocardial infarction. Circulation. 1993; 88 (3): 927-934.

[10] Schwartz PJ, La Rovere MT, Vanoli E. Autonomic nervous system and sudden cardiac death, experimental basis and clinical observations for post-myocardial infarction risk stratification. Circulation. 1992; 85 (1 Suppl): I77-I91.

[11] Singer DH, Martin GJ, Magid N et al. Low heart rate variability and sudden cardiac death. J Electrocardiol. 1988; 21 Suppl: 46-55.

[12] Dougherty CM, Burr RL. Comparison of heart rate variability in survivors and nonsurvivors of sudden cardiac arrest. Am J Cardiol. 1992; 70 (4): 441-448.

[13] Fauchier L, Babuty D, Cosnay P et al. Heart rate variability in idiopathic dilated cardiomyopathy: characteristics and prognostic value. J Am Coll Cardiol. 1997; 30 (4):1009-1014.

[14] Ponikowski P, Anker SD, Chua TP et al. Depressed heart rate variability as an independent predictor of death in chronic congestive heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. Am J Cardiol. 1997; 79 (12): 1645-1650.

[15] Pozzati A, Pancaldi LG, Di Pasquale G et al. Transient sympathovagal imbalance triggers "ischemic" sudden death in patients undergoing electrocardiographic Holter monitoring. J Am Coll Cardiol. 1996; 27 (4): 847-852.

[16] Martin GJ, Magid NM, Myers G et al. Heart rate variability and sudden death secondary to coronary artery disease during ambulatory electrocardiographic monitoring. Am J Cardiol. 1987; 60 (1): 86-89.

[17] Burr R, Dougherty C, Buchanan L. Using heart rate variability measures in clinical research designs. J Electrocardiol. 1990; 23 Suppl: 203.

[18] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation. 1996; 93 (5): 1043-1065.