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# Investigating Short Term Heart Rate Variability in Patients with Implantable Cardioverter Defibrillator

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## **Summary**

The aim of the present study was to analyze the value of short-term heart rate variability (HRV) recording in the investigation of the relationship between ventricular arrhythmias and the changes of autonomic nervous system in patients with implantable cardioverter defibrillator (ICD). 32 arrhythmias (10 VTs and 22 VFs) were analyzed in 13 patients. We compared the HRV statistical values of the 10 minute period before the onset of arrhythmias to the 10 minute period minimum 30 minutes before the arrhythmia stored in the memory of the device. The statistical values: MeanNN - the average of normal to normal intervals; SDANN - standard deviation of the average NN intervals calculated over 5 minute period; pNN50-percent of difference between adjacent normal RR intervals that are greater than 50 msec; rMSSD - root mean square of successive differences. Decreases of short-term heart rate variability parameters before the onset of arrhythmias safely prove the influence of autonomic nervous imbalance on the cardiovascular system, by this means facilitates the judgment of onset mechanisms of ventricular tachyarrhythmias and the application of adequate therapy.

## **Keywords**

Heart rate variability, ventricular arrhythmias autonomic nervous system

#### Introduction

Ventricular arrhythmias such as ventricular tachycardia and fibrillation are the main cause of sudden cardiac death (SCD). Arrhythmogenic substrates, trigger mechanisms and modulating factors have to be present simultaneously in pathogenesis of these arrhythmias. Arrhythmogenic substrates are ischemic or infarcerated, dilated-fibrotic and hypertrophic myocardium. The trigger is often a supraventricular or ventricular premature beat, bradycardia or tachycardia. Modulating factor can be the electrolyte disturbance (e.g. hypokalaemia), haemodynamic factors (e.g. left ventricular failure, increased end-diastolic pressure), drugeffects, and the imbalance of the autonomic nervous system. The investigations of the last two decades revealed that there was significant association among the increased sympathetic tone, the decreased reflexactivity of the parasympathetic nervous system, and the onset of malignant ventricular tachyarrhythmias (Figure 1). The dominance of the sympathetic tone basically changes the electrophysiological circumstances in the heart by increasing the electrical instability of the myocardium, thus increases the risk of life threatening ventricular arrhythmias [1,6]. The aim of the present study was to analyze the value of short-term time domain heart rate variability (HRV) recording in case of spontaneous onset of ventricular tachycardia (VT) and fibrillation (VF).

#### **Materials and Methods**

We analyzed data of patients treated with implantable cardioverter defibrillator (ICD) for life threatening malignant ventricular tachyarrhythmias to investigate the relationship between ventricular arrhythmias and the changes of autonomic nervous system [4,5]. The implanted device is Phylax Extended Memory (XM) (BIOTRONIK), which has a telemetrically interrogatable long time memory that is able to store among others the therapy history of the recent 31 episodes, up to 18000 RR-intervals preceding arrhythmia per device, up to 16 x 1 minutes of pre-episode IEGM.

By means of statistical analysis of the successive RR

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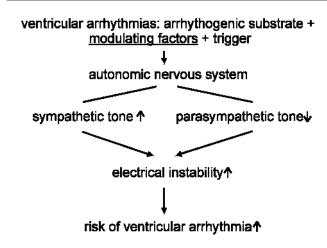


Figure 1. Arrhythmogenic effect of autonomic imbalance.

intervals we obtained heart rate variability parameters (HRV) that characterize the state of autonomic influence - serum catecholamine level, direct sympathomimetic effect, reduction of the vagal tone - on the cardiovascular system [3,7].

Patients were eligible for the study if they had at least 3000 RR intervals preceding the spontaneous arrhythmia stored in the Holter memory of the device, if they were not pacemaker dependent, did not have other pacemaker devices, did not have atrial fibrillation and did not suffer from incessant ventricular arrhythmias. Further exclusion criteria were high dose (over 100 mg metoprolol) beta-blocker therapy or high dose (320 mg) d,l-Sotalol therapy (Table 1) [2].

HRV statistical values of the 10 minute period before the onset of the arrhythmias to the 10 minute period minimum 30 minutes before the arrhythmia of the RRintervals were stored in the memory of the device and

Inclusion criteria ICD Holter	Exclusion criteria pacemaker-dependence atrial fibriliation
min. 3000 RR intervals arrhythmia	Incessant arrythmia
	ICD + pacemaker
	high dose beta-blocker

Table 1. Methods.

Etiology	n	
Coronary artery disease + myocardial infarction	7	
hypertrophic cardiomyopathy	1	
congestive cardiomyopathy	2	
valvular disease	1	
primary	2	

Table 2. Etiology.

compared by paired t-test. The statistical values: MeanNN - the average of normal to normal intervals; SDANN - standard deviation of the average NN intervals calculated over 5 minute period; pNN50 - percent of difference between adjacent normal RR intervals that are greater than 50 msec - this parameter is considered to be the most significant representative value for the vagal tone; rMSSD - root mean square of successive differences. To exclude premature beats, a 150 ms interval filter was used [3,7-10]. During the average of  $10.3 \pm 5.7$  month follow up period 32 arrhythmias (10 VTs and 22 VFs) were analyzed in 13 patients - 6 women, 7 men. Average age of the patients was  $59.2 \pm 10.6$  years. Etiology was mostly ischemic heart disease and congestive or hypertrophic cardiomyopathy. Two patients did not have any structural cardiac abnormality (Table 2). Left Ventricular Ejection Fraction was: 41.4 ± 12.1%. Indications for ICD implantation were: sustained VT (n = 6), VF (n = 6), VF+VT (n = 1). NYHA classification were as follows: Class I: n = 2, Class II: n = 5, Class III: n = 5, Class IV: n = 1.

#### Results

In case of the spontaneous arrhythmias the MeanNN, RMSSD and pNN50% parameters of the 10 minute period preceding the arrhythmia proved to be significantly (p < 0.05) lower than in the control period. The SDANN parameter was not significantly lower than in the control period (Table 3). Decreases of short-term heart rate variability parameters before the onset of arrhythmias may indicate that the imbalance of the autonomic nervous regulation plays important role in the pathogenesis of certain arrhythmias. This suggests that in the therapy of those patients who had an arrhythmia generated mainly by the increased sympa-

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	Period before the arrhythmia (mean ± sd)	p-value	Control period (mean ± sd)
MeanNN (ms)	733.05±220.48	0.0069	821.58±182.84
SDANN (ms)	99.90±56.38	0.2136	91.74±49.66
RMSSD (ms)	42.95±39.91	0.0072	56.51±65.44
pNN50 (%)	13.71±14.00	0.0071	19.24±20.24

Table 3. Time domain parameters.

thetic tone additional high dose antiadrenergic drugs are necessary beside the ICD and other antiarrhythmic drug therapy. Figure 2 shows a Holter of over 16000 RR-intervals. In this case the indication of implantation was SCD caused by ventricular fibrillation. The patient has coronary artery disease, had two MI. NYHA Class III, LVEF 30%. Pre- and postoperative antiarrhythmic drug therapy was Amiodarone 200 mg. It is well shown that there is a continuous reduction in the beat-to-beat intervals. A 480 ms RR-interval sinus tachycardia precedes the ventricular premature contraction - induced ventricular fibrillation - proving the influence of increased sympathetic dominance.

Figure 3 facilitates the visual judgment of HRV. This is a map of dots in Cartesian coordinates. Each pair of successive beat-to-beat intervals is plotted as a dot with coordinates. Preserved physiological HRV leads to a wide spreading plot, while records of reduced HRV produces a compact plot (\_Figure 3) that is classified as "comet" or "torpedo" [11].

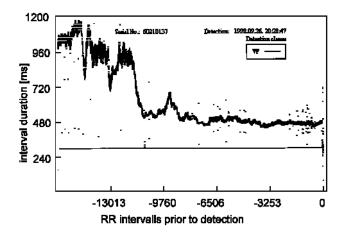


Figure 2. RR-Holter.

#### **Discussion**

The imbalance of the autonomic nervous system plays an important role in the pathogenesis of most malignant ventricular tachyarrhythmias. The individual investigation of HRV parameters of each arrhythmia is an additional useful method to understand the pathomechanism thus to apply adequate individual therapy. In case of patients with decreased short-term time domain HRV parameters directly preceding the arrhythmia it is important to treat the imbalance of the autonomic tone. Therefore it is necessary to apply relatively high doses of antiadrenergic drugs beside the ICD and other antiarrhythmics.

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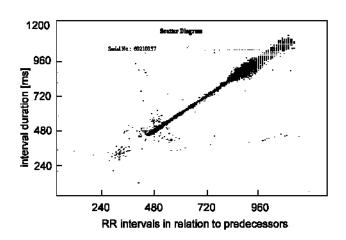


Figure 3. Scatter diagram of the arrhythmia shown in Figure 2.

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