# Investigation of the Onset of Ventricular Tachyarrhythmias in Patients Treated with Implantable Cardioverter Defibrillator

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**Summary**

*The role of different arrhythmia mechanisms in the onset and maintenance of spontaneous life threatening ventricular arrhythmia has not been elucidated in detail. The aim of this study was to investigate different pathomechanisms of spontaneous malignant arrhythmia based on it's onset and the analysis of the efficient therapy from the implantable cardioverter defibrillator (ICD). 65 patients (44 male, 21 female) were included into the study with a mean follow up period of 16.5 ± 14.7 months. Arrhythmia events were grouped according to four classes based on the RR intervals preceding the onset: tachycardia (HR > 100/min), bradycardia (HR < 60/min), ventricular extrasystoles (VES) and short-long cycle-length sequences. In the case of monomorphic ventricular tachycardia (MVT) the efficiency of antitachycardia stimulation (ATS) was determined. Altogether 295 episodes of ventricular tachyarrhythmia were collected from 32 patients (23 males, 9 females), of which 147 (68 VF's and 79 VT's) could be evaluated regarding the onset. 50 episodes of ventricular arrhythmia (10 VF's, 24 polymorphic ventricular tachycardias (PVT), 16 MVT's) evolved from tachycardia, 12 episodes (8 VF's, 3 PVT's, 1 MVT) from bradycardia. 62 episodes (28 VF's, 2 PVT's, 32 MVT's) were induced by a VES, whereas short-long cycle-length sequences induced 23 episodes (21 VF's, 2 MVT's). Bradycardia and short-long cycle-length sequences as trigger mechanisms were found to induce only 23% of the analyzed events. The majority (83%) of these triggered arrhythmias resulted in VF. To 67% MVT's were caused by the a reentry mechanism (VES onset and efficient ATS).*

**Key Words**

ICD, heart rate variablity, ventricular tachycardia

## Introduction

Life threatening arrhythmias (i.e. ventricular fibrillation (VF) and ventricular tachycardia (VT)) are the most frequent cases of sudden cardiac death. Structural abnormalities of the heart and transient myocardial malfunctions both play an important role in the pathomechanism of these arrhythmias. Such electrophysiologic abnormalities are caused either by disorders of impulse conduction (reentry excitation), or by disorders of impulse formation (pacemaker activity), or by the combination of both.

Each of these two mechanisms are subclassified. Reentrant excitation occurs when the propagating impulse is not extinguished after complete activation of the heart, as is normally the case, but persists to reexcite the atria or ventricles after the end of the refractory period. Reentrant excitation can be subdivided into reflected reentry and circus movement excitation. In circus movement reentry, the activation wavefront encounters a site of unidirectional conduction block and propagates in a circuitous pathway before reexciting the tissue proximal to the site block after the refractory period has ended. By contrast, in the reflection model of reentrant excitation, impulses in both directions transmit over the same pathway.

Circus movement reentry can be classified into anatomical and functional types. Models with anatomically defined pathways block the impulse in one pathway and whereas it slowly propagates in the adjacent pathway, because of the two (or more) different electrophysiological properties (e.g. a difference refractory

| Mechanism | Induction | Termination |
|---|---|---|
| Reentry | extrastimulus (ES) | ES, overdrive |
| EAD | pause, bradycardia | spontaneous, defibrillation |
| DAD | fast stimulation, ES | overdrive (rarely), defibrillation |
| Abnormal automaticity | not inducible, warm up | cannot be terminated |

*Table 1. Characteristics of pathomechanisms of ventricular arrhythmia.*

period). If conduction in this alternative route is sufficiently depressed, the slow propagating impulse excites tissue beyond the blocked pathway and returns in a reversed direction along the pathway initially blocked to reexcite tissue proximal to the site of block. Functional reentry lacks confining anatomical boundaries and can occur in contiguous fibers that exhibit functionally different electrophysiological properties. This depends on heterogenous electrophysiological properties of cardiac muscle caused by local differences in the transmembrane action potentials. Dispersion of excitability and/or refractoriness, as well as anisotropic distributions of intercellular resistances, permits initiation and maintenance of reentry. The arrhythmias induced by reentry mechanisms can be initiated and terminated by extrastimuli.

On the other hand, pacemaker activity occurs when a cell or a group of closely knit cells begin to generate impulses. The mechanism can be normal automatic activity, abnormal automatic activity, or triggered activity. Abnormal automaticity differs from normal automaticity in that it occurs at a level of transmembrane potential considerably less negative than the normal maximum diastolic potential or normal resting potential of the fibers involved. Abnormal automaticity can neither be initiated nor terminated electrophysiologically, but its very important feature is the gradual acceleration into tachycardia (warm up phenomenon).

Triggered activity is initiated by afterdepolarisations in membrane voltage induced by one or more preceding action potentials. These depolarisations can occur before or after full repolarisation of the fiber and are best termed early afterdepolarisations (EADs) when they arise from a reduced level of membrane potential during phase 2 or 3 of the cardiac action potential and late or delayed afterdepolarisations (DADs) when they occur after completion of repolarisation (phase 4) generally at a more negative membrane potential than EADs. Not all afterdepolarisations reach threshold potential, but if they do, they can trigger another afterdepolarisation and thus self-perpetuate.

The ionic base of EADs is unclear but may be via the L-type $Ca^{2+}$-channel. EADs that arise at voltages close to the plateau (phase 2) appear to result from time- and voltage-dependent reactivation of L-type calcium channels. Lengthening action potential by a variety of ways allows development of this type of EADs. Thus, bradycardia and pause can initiate them, while they can cease spontaneously or sometimes only by defibrillation.

DADs appear to be caused by a transient inward current that is small or absent under normal physiological conditions. When intracellular calcium overload occurs, as during extensive sympathetic stimulation or after large doses of digitalis, oscillatory release of $Ca^{2+}$ from the sarcoplasmatic reticulum activates a nonselective cation channel (or an electrogenic $Na^{+}$-$Ca^{2+}$ exchange). This results in a transient inward current carried primarily by $Na^{+}$, that generates the DAD. DADs can be initiated by fast stimulation and extrastimuli and may be terminated by overdrive pacing. It is more likely, however, that overdrive accelerates these types of the arrhythmias.

Pacemaker cardioverter defibrillators (ICD's) are used in the non-pharmacological management of malignant ventricular arrhythmia since 1980. These devices may reduce the incidence of sudden cardiac death from 10-30% to 1% in patients suffering from major ventricular arrhythmia. RR intervals before, during and after the observed and treated arrhythmia can be retrieved from the memory of the ICD. Furthermore, ICD's are capable of recording intracardiac electrograms. Fourth generation ICD's have individual detection and therapy zones for bradycardia, VT and VF. The device detects and selects the observed arrhythmia according to it's rate and the respective programmed RR-interval zone. Therapy can either be antitachycardia stimulation and/or cardioversion or defibrillation.

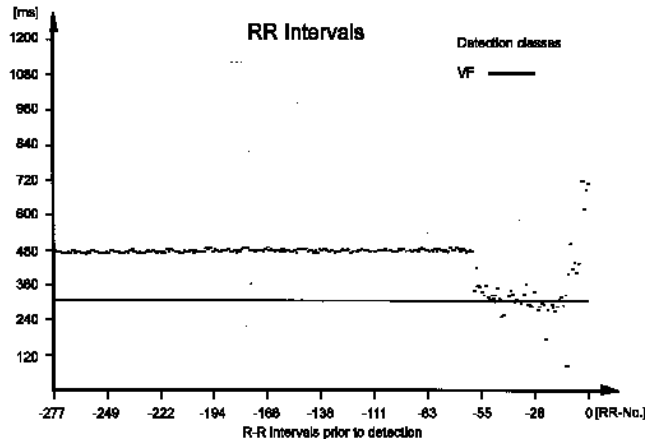


*Figure 1. Onset of a ventricular tachycardia initiated by sinus tachycardia. The x-axis represents the number of RR-intervals, the y-axis the cycle length in ms.*

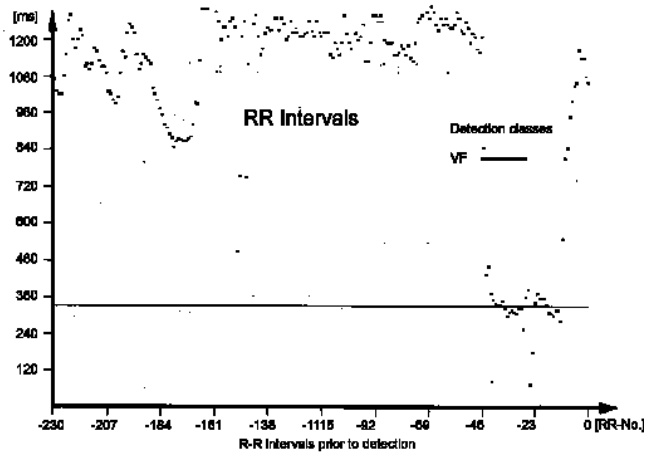


*Figure 2. Bradycardia (HR<60/min, RR>1000ms) triggered ventricular tachyarrhythmia.*

The aim of this study was to investigate the pathomechanisms of the spontaneous malignant arrhythmia based on the onset and the analysis of the efficient therapy in patients with implantable cardioverter defibrillator.

## Methods and Patients

65 patients (44 male, 21 female) were followed up over a mean period of 16.5 ± 14.7 months for spontaneous arrhythmia episodes, using RR-interval Holter and stored intracardiac electrograms from the ICD. Ventricular arrhythmia was grouped according into four classes based on the RR intervals preceding the onset of arrhythmia: tachycardia (heart rate >100/min), bradycardia (heart rate < 60/min), ventricular extrasystoles (VES) and short-long cycle-length sequences. The criterion of short-long cycle length is that the short cycle should be at least 100 ms shorter, the long cycle at least 100 ms longer than the mean RR-interval of the preceding rhythm.

VT's were also grouped according to regularity. The arrhythmia was considered as monomorphic (MVT) if the difference in RR-intervals of the first 5 beats was less than 40 ms. In case of a delta larger than 40 ms the VT was considered as polymorphic (PVT). In the case of MVT the efficiency of antitachycardia stimulation (ATS) was evaluated.

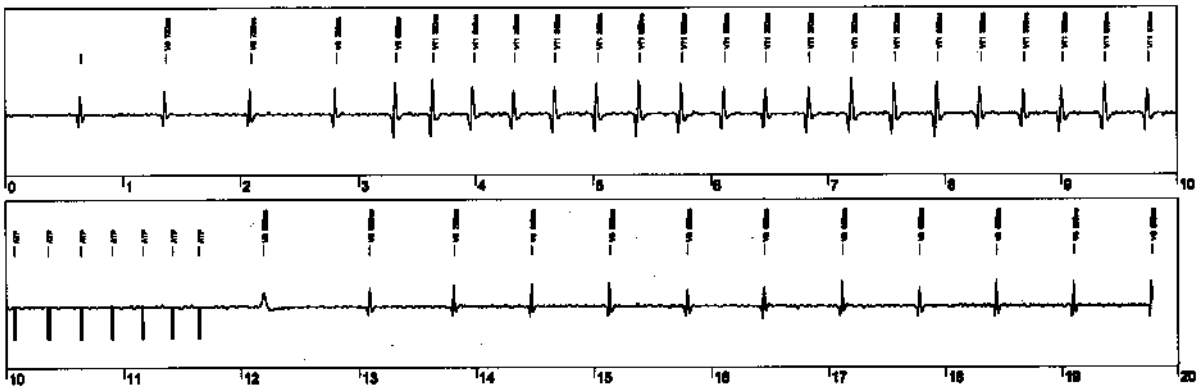


*Figure 3. Intracardiac electrogram from ICD Holter shows the onset of a monomorphic VT, which was initiated by VES and terminated by antitachycardia pacing.*

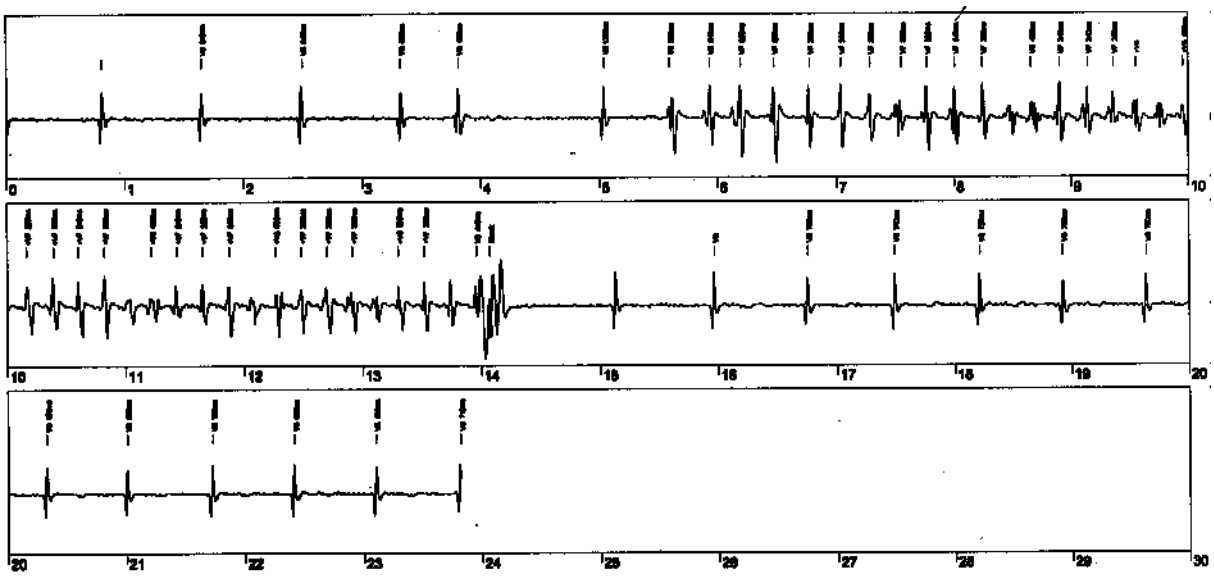

*Figure 4. Intracardiac electrogram shows ventricular fibrillation preceded by a short-long cycle sequence. Arrhythmia with RR-intervals shorter than 250 ms (300 ms in amiodarone treated patients) are defined as VF.*

32/65 patients (23 male, 9 female) presented at follow up with arrhythmia episode recordings in the ICD Holter. Patient characteristics are presented in Table 1. Mean age was 53.6 ± 13.8 years. Mean ejection fraction was 37.5 ± 10.2%. Two patients were classified as NYHA I, 18 as NYHA II, 10 as NYHA III and 2 as NYHA IV. The underlying diseases were coronary heart disease (23 patients), congestive cardiomyopathy (5 patients) and hypertrophic cardiomyopathy (1 patient). No structural abnormalities could be determined in 3 cases. Indications for ICD implant were hemodynamically relevant, sustained VT (15 patients), VT with history of sudden cardiac death (8 patients) and VF (8 patients).

## Results

147/295 episodes of ventricular tachyarrhythmia (68 VF's and 79 VT's) could be included into analysis as of documentation of the onset within the ICD Holter. 50 episodes of ventricular arrhythmia (10 VF's, 24 PVT's, 16 MVT's) evolved from tachycardia. 12 episodes (8 VF's, 3 PVT's, 1 MVT) developed from bradycardia. 62 episodes (28 VF's, 2 PVT's, 32 MVT's) were induced by single or coupled VES, whereas short-long cycle-length sequences induced 23 episodes in total (21 VF's, 2 MVT's).

## Conclusions

Bradycardia and short-long cycle-length sequences, which mostly are referred to as an arrhythmia triggering mechanism were found to induce only 23% of the recorded episodes. The majority (83%) of the resulting triggered arrhythmia was VF.
67% of the MVT's were induced by VES and thus maintained by reentry mechanism (VES onset and efficient ATS).

## Discussion

In our clinical study we elucidated the onset and maintenance of spontaneous life threatening ventricular arrhythmia in a large group of patients for the first time in Hungary. As a complement of the limited data it can be supposed, that more then half of the VT's and VF's, which frequently cause sudden death, are induced by triggering activity and the presumption that MVT's are caused mostly by reentry mechanism can be confirmed.

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