Influence of AV-Delay on the Intracardiac Signal of Pacemaker Patients with Different Cardiac Diseases

E. EBNER
Sophien- und Hufelandklinikum gGmbH, Weimar, Germany

Summary

The ventricular evoked response (VER) represents the summed signal of the transmembrane action potentials of all myocardial cells. As changes in the electrophysiological state of the myocardial cells are reflected in the morphology of the VER, the variation of the heart rate, the AV-delay and the contractility leads to changes in the VER [4]. In addition the size and the geometrical modifications of the heart cause different spread of excitation which modify the morphology as well. Due to this fact, it shall be illustrated in this study, that the monitoring of the VER can be used either for the improvement of the therapy with dual chamber pacemakers or as an diagnostic tool according to diseases like dilative cardiomyopathy. The present study involved examination of 10 patients (4 female, 6 male) with a mean age of 68.5 ± 10.2 years of which three suffered under dilative cardiomyopathy. During the investigation the stroke volume and the VER was measured at three pacing rates (60 bpm, 90 bpm, 120 bpm) and five AV-delays each (50 ms, 100 ms, ... 250 ms). This examination was repeated after four and eight months. The results illustrate general changes in the signal duration and an increased amplitude of the VER with higher rates. The variation of AV-delays at 60 bpm leads to small but systematic changes in the morphology of the VER which show correlation to the stroke volume. In addition, the therapeutic success of a dilative cardiomyopathy leads to modified VER signals. Therefore it could be used on the one hand side as a diagnostic tool for the detection of the state of dilative cardiomyopathies. On the other hand, the observed modifications of the VER according to the AV-delay demonstrates, that the intracardiac signal is a suitable tool for the improvement of the therapy of cardiac disease.

Key Words

Ventricular evoked response, AV-delay, stroke volume, cardiomyopathy

Introduction

The ventricular evoked response (VER), measured between the tip of the ventricular electrode and the pacemaker case, represents a summed signal of the action potentials of all myocardial cells. Therefore changes in the electrophysiological state of the myocardial cells are reflected in the morphology of the VER. A number of analyses showed that hemodynamic and neurohumoral influences can be extracted from the morphology of the VER signal [5].

In healthy subjects as well as in patients with cardiac diseases the autonomic nervous system endeavours to supply all organs in an optimal way. For that reason among others the heart rate, the AV-delay and the contractility of the myocardium are adapted, which necessarily leads to changes in the electrophysiological state of the myocardial cells [4]. Due to this fact, conclusions can be drawn from characteristic changes in the morphology of the VER to the present value of the stroke volume. In addition, geometric modifications have an influence on the morphology of the VER signal, which is due to the superposition of all action potentials of the myocardium. The therapeutic success of a pacemaker in the case of dilative cardiomyopathy could be registered by measuring the VER.

This investigation shall demonstrate whether the monitoring of the VER can be used either for the improvement of the therapy with dual chamber pacemakers or as an diagnostic tool according to diseases like dilative cardiomyopathy.

Methods

The present study involved examination of 10 patients (4 female, 6 male) with a mean age of 68.5 ± 10.2 years. In addition to the usual DDD indications the patients have the following secondary symptoms: 3 with dilative cardiomyopathy; 1 with restrictive cardiomyopathy; 5 with coronary heart disease and 1 with chronic disease of the lung. In these patients dual chamber pacemakers (Physios CTM 01, BIOTRONIK) were implanted which allow to transmit intracardiac signals to the programmer without any falsification of the original signal. Therefore, the VER can be measured with a high resolution so that even small changes in the morphology are registered. For further evaluations the VER was stored on a PC.

The measuring of the stroke volume was carried out with a NICaS 2001 NON-INVASIVE Cardio-respiratory system (NI Medical), which allows to evaluate hemodynamic parameters on the basis of measurement of body electrical bioimpedance. The attachment of 2 disposable NICaS electrodes is necessary for the measurement.

During the investigation VER and stroke volume of each patient (supine position, no load) have been measured with 15 different pacing parameters. The pacemaker had been programmed to 60, 90 and 120 bpm. For each pacing rate signals have been recorded with an AV-delay of 50 ms, 100 ms, 150 ms, 200 ms and 250 ms. The recording of the stroke volume and VER was performed two minutes after parameter programming, so that a stable state had been reached. The stroke volume used is the mean value of three measurements which is evaluated each out of 20 events. The investigation was repeated after four and eight months, in order to investigate the correlation of secondary disease and general changes in the morphology of VER. The stored signals were analysed with evaluation software (Bioview, BIOTRONIK). The time after stimulation and the corresponding amplitude of the VER were determined at the position of the T wave maximum, the R^- wave and the R^+ wave.

Results

As a first result, the morphology of VER shows general changes in the signal duration and the maximum amplitude. The increasing pacing rate leads to a decrease in the signal duration and an increase in the amplitude of the T wave.

In Figure 1a-c the observed changes of the VER at different pacing rates and AV-delays are illustrated exemplary. At a pacing rate of 60 bpm the maximum T wave amplitude decreases with increasing AV-delay up to 200 ms and increases again for 250 ms. Furthermore, the moment of the R^+ wave moves towards the stimulus and back in the same manner. The mean values of these variations and the corresponding mean stroke volumes are visualised in Figure 2a and 2b. In spite of the big standard deviations, a correlation between the stroke volume and the changes of the VER can be observed. The rise of the stroke volume from 70.8 ml to 85.1 ml with an AV-delay up to 200 ms is reflected in the percentile decrease of the T wave amplitude. At an AV-delay of 250 ms the stroke volume decreases and the amplitude of the T wave rises again. The same behaviour can be observed with movement of the R^+ wave. At a pacing rate of 90 bpm and 120 bpm no significant and regular changes in the morphology of the T and R^+ wave can be observed. Figure 3 shows mean values of the stroke volume at 120 bpm and the decrease of the amplitude of the negative R wave. Although the stroke volume does not rise significantly with AV-delays bigger than 100 ms the amplitude of the R^- wave decreases up to 25% at an AV-delay of 250 ms. This behaviour was obtained at 90 bpm and 60 bpm as well but the variations of the amplitude were little.

In Table 1 the T-wave amplitudes and the corresponding stroke volumes of two patients with and without dilative cardiomyopathy (DCM) are listed over a time of four follow-up checks. In the case of the DCM-patient, the data show an increase of the T-wave amplitu-

	Patient with DCM		Patient without DCM	
60 bpm AV 50 ms	T wave mV	SV ml	T wave mV	SV ml
1. follow-up	2.94	38	5,4	99
2. follow-up	4.03	93	5,6	95
3. follow-up	3.98	93	5,1	55
4. follow-up	3.29	73	-	-

Table 1. Stroke volume and T-wave amplitude during several follow-up checks of two patients, one with and one without DCM.

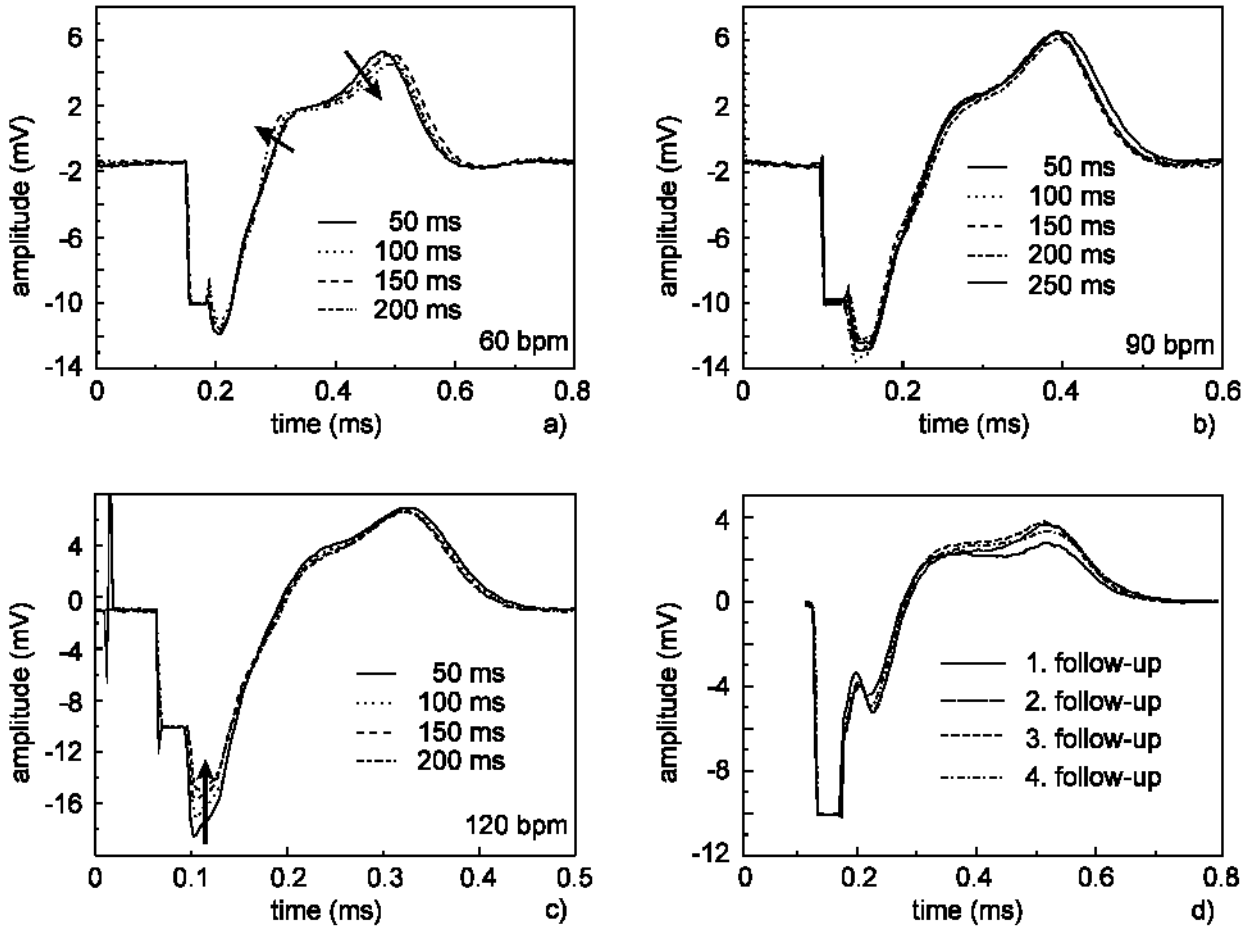

Figure 1. VER at different pacing rates with varying AV-delays (a-c). In d) the VER of a patient with dilative cardiomyopathy during several follow up checks are illustrated.

de (Figure 1d) according to the stroke volume. In contrast to these results the data of the patient without DCM show no significant changes.

Discussion

The results illustrate, that the modifications of the VER are based on two effects, the increased heart rate and the variations of the AV-delay. After a short discussion of the pacing rate induced variations, a description of AV-delay based changes follows. In the edge the discussion goes into with the results concerning the dynamics of the VER of patients with DCM.

The increased pacing rate results in a general rise of the T-wave amplitude and shortened VER signals. The reason for that behaviour lies in the frequency based shortening of the action potentials of the myocardial cells [5]. Furthermore the spread of excitation decreases with higher rates [2], which is reflected in a lower gradient of the action potential and therefore leads to changes in the R^- wave of the VER.

The variation of the AV-delay at a fixed pacing rate causes different filling states of the ventricle, which lead to geometric changes of the heart and a stronger stretching of the myocardial fibres. The geometric arrangement of the single myocardial cells (dependent from the ventricle geometry) induces different spread of excitation which is responsible for the shape of the VER signal. Furthermore the stretching of the fibres correlating with the filling of the ventricle leads to an increase of cytosolic Ca^{2+}-concentration and therefore to a slightly stronger contraction. This contraction

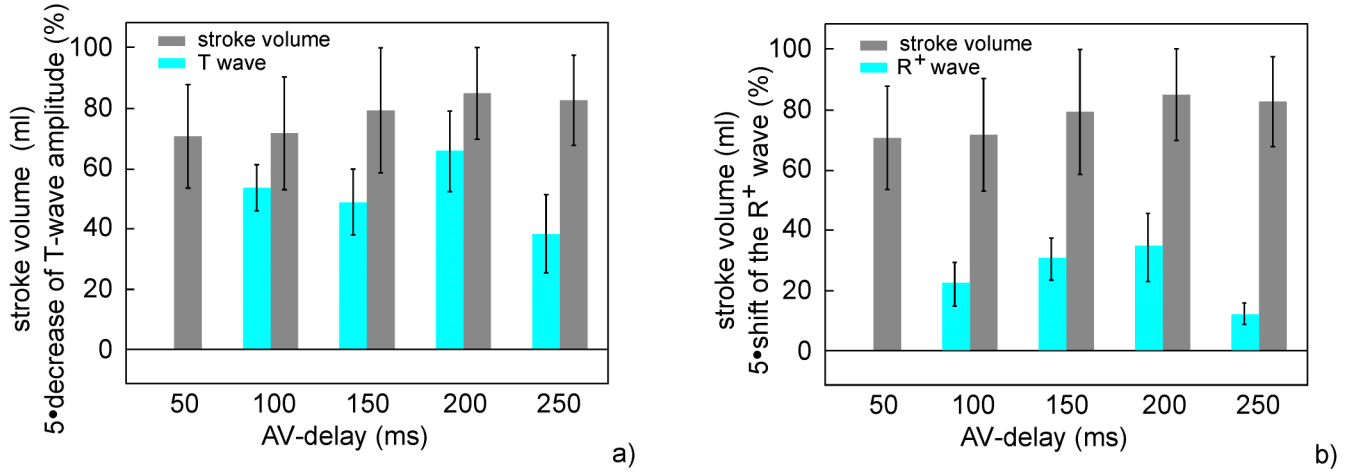

Figure 2. Average stroke volume at 60 bpm with varying AV-delays in correlation to the T wave amplitude (a) and the time shift of the R^+ wave (b), respectively. The percentile decrease of the T wave amplitude is normalized to the amplitude of the T wave at an AV-delay of 50 ms. The time shift of the R^+ wave is normalized to the time of the R^+ wave after stimulus at an AV-delay of 50 ms.

increase changes the action potential which is reflected in the VER [1].

An additional reason for the observed changes can be seen in the improved supply of the body which is reached with a higher stroke volume. In comparison to the lower cardiac output at lower AV-delays the sympathetic tone is reduced. This causes a reduction of the contraction which is based on a lower Ca^{2+}-concentration in the intercellular area. As a consequence, the gap junctions of the myocardial cells change their permeability [2]. This leads to an increased spread of excitation velocity which also has an influence on the VER morphology, especially in the areas of the R^+ and T wave. On the basis of the available data no exact conclusions can be drawn which of the mentioned effects dominate and which causes the observed changes. All these effects contribute to the variations in the VER signals, which only can be observed at a pacing rate of 60 bpm.

In the case of higher rates like 90 bpm and 120 bpm no significant changes can be measured, for which two reasons might be responsible. First of all, the optimal AV-delay at higher rates is shorter than at lower ones. Due to this fact, no changes do occur in the filling volume, which is shown by the results concerning the stroke volume. On the other hand the patient is at rest during the measurement. This is the reason why a heart rate of 90 or 120 bpm lowers the sympathetic tone, so that the contraction of the ventricle is reduced. In this case the varying AV-delay does not change anything at the sympathetic tone and thus no modifications in the VER can be seen.

In addition, increased AV-delays lead to geometric changes of the heart which result in different spread of excitation and therefore in a variation of the R^- wave.

The therapeutic success of a pacemaker in the case of DCM patients can be seen in the morphologic change of the VER signal which is correlated to the stroke volume (Table 1). The increased T-wave amplitude results from the decreased size of the ventricle and there-

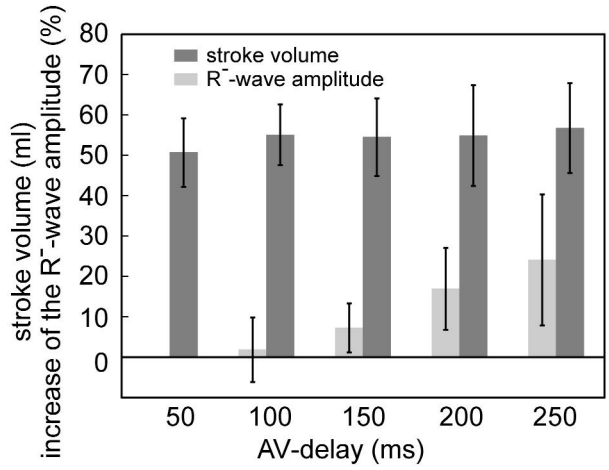

Figure 3. Average stroke volume at 120 bpm in correlation to the percentile increase of the R-wave amplitude, which is normalized to the amplitude at an AV-delay of 50 ms.

fore leads to modified spread of excitation. Furthermore, the contraction of the ventricle changes with its size and therefore the Ca^{2+}-concentration in the myocardial cells.

Conclusion

The presented results show that the variation of AV-delay and heart rate leads to small but systematic changes in the VER signal. At a rate which corresponds to the load of the patient, changes of the VER correlate with the resulting stroke volume. In order to get exact explanations about the observed behaviour of the VER morphology additional investigations are necessary. Furthermore the sensitivity and specificity has to be improved so that the optimal AV-delay can be determined exactly.

As the state of dilative cardiomyopathies shows a significant influence on the VER, it could be used as a diagnostic tool for the detection of dilative cardiomyopathies and the monitoring of the therapeutic effects. The results of this investigation demonstrate that the measurement of intracardiac signals is a promising tool in diagnosis and therapy of cardiac diseases.

References

[1] Lab MJ. Mechanoelectrical feedback (transduction) in heart: Concepts and implications. Cardiovascular Research 32 (1): 15-24, July 1996.

[2] Shaw RM, Rudy Y. Ionic Mechanisms of Propagation in Cardiac Tissue. Circulation Research 81: 727-741, 1997.

[3] Ten Eick RE, Whalley DW, Rasmussen HH. Connections heart disease, cellular electrophysiology, and ion channels. FASEB J. 6: 2568-2580, 1992.

[4] Wetzig T, Fischer G, Worth H, et. al. Analyse evozierter Myokardpotentiale in Abhängigkeit von Ergometrischer Belastung und Schlagfrequenz für die Anwendung in frequenzadaptiven Herzschrittmachern. Biomedizinische Technik 40: 9-13, 1995.

[5] Whalley DW, Wendt DJ, Grant AO. Basic Concepts in Cellular Cardiac Electrophysiology. PACE 18, 1556-1574, August 1995.