The Ventricular Evoked Response as Clinical Marker in Patients with Dilatative Cardiomyopathy

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Summary

Echocardiographic determination of a patient's cardiac state, as well as of the success of pacemaker therapy, is a very time-consuming procedure in patients with cardiomyopathies. It would be advantageous if this evaluation could be performed with a cardiac pacemaker during a standard follow-up examination instead. Earlier studies have shown that the ventricular evoked response, a unipolarly measured intracardiac signal, reflects the activity of the myocardium and the geometric expansion of the heart. Therefore, it can be assumed that the ventricular evoked response is suited for evaluating the cardiac state in patients with cardiac diseases, such as cardiomyopathies. This study was performed on 23 patients (age 69.1 ± 11.8 years) who were implanted with Physios CTM 01 dual-chamber pacemakers. All patients underwent an examination, in the course of which the ventricular evoked response was determined using the pacemaker (pacing rate PR = 90 bpm, AV delay AVI = 100 ms), as well as hemodynamic parameters, using echocardiography. For the analysis, the patients were divided into two groups, according to either their basic cardiac disease (dilatative cardiomyopathy) or their NYHA classification. Both the hemodynamic parameters and the ventricular evoked response showed significant differences in a direct comparison between the groups. The results indicate that poor cardiac function seems to be associated with low values of the ventricular evoked response amplitude. Generally, it becomes obvious that it is promising to evaluate the cardiac state primarily based on the recording and analysis of the ventricular evoked response under well-defined conditions. The results of further studies concerning the specificity will show whether the ventricular evoked response will have a future as an alternative in diagnosis and in the evaluation of the therapeutic success, at least in patients with congestive cardiac diseases.

Key Words

Ventricular evoked response, echocardiography, cardiomyopathy, NYHA

Introduction

It often takes considerable time and effort to evaluate the cardiac state of a patient or the therapeutic success of a pacemaker implantation in patients with congestive cardiac diseases, such as cardiomyopathies. Echocardiography is used for the diagnosis and to classify the severity of the disease. It would be advantageous if the cardiac state of a patient could be evaluated via cardiac monitoring by a pacemaker as part of a standard follow-up examination.

The ventricular evoked response (VER), a unipolarly measured intracardiac signal, is defined as the myocardial response to an electrical stimulus. It is a sum signal of the action potentials of all myocardial cells. Fractal coated electrodes allow recording this signal without stimulation artifacts [1]. Previous studies have shown that the VER reflects the activity of the myocardium and the geometric expansion of the heart, as well as the influences of inotropic and chronotropic regulation, and, thus, the cardiac state [2-4]. It can be assumed that the VER is suited for evaluating the cardiac state and the success of a pacemaker therapy in patients with cardiac diseases, such as cardiomyopathies.

The presented study had the goal of investigating the behavior of the VER in patients with and without cardiomyopathies, and to test whether this signal is suitable for monitoring the cardiac state. Furthermore, it aimed to show whether and to what degree the VER indicates the detected severity of the disease in the sense of a NYHA classification of the patients. The results of the echocardiographic examination were used as reference.

Materials and Methods

In the context of this controlled singlecenter study, 23 patients with a mean age of 69.1 ± 11.8 years (min. 47, max. 88; 14 m, 9 f) were enrolled. All patients had indications for a DDD pacemaker. Depending on their diagnosis, the patients were divided into three groups:

- dilatative cardiomyopathy (DCM),
- hypertrophic non-obstructive cardiomyopathy, and
- other cardiac diseases.

Patients whose hyperthrophy was only a secondary disease were also assigned to the group with hypertrophic non-obstructive cardiomyopathy. Each patient was implanted with a Physios CTM 01 (Biotronik, Germany) dual-chamber pacemaker, an atrial lead, and a bipolar, fractal coated ventricular lead (Polyrox, Biotronik). The latter allowed measurement of the VER without stimulation artifacts. All patients underwent an examination in addition to the regular follow-up at 2 or 4 weeks after implantation. During this examination, the VER was measured with the pacemaker, and an echocardiographic examination was performed. For these measurements, the pacemaker was programmed to a pacing rate PR = 90 bpm and an AV delay AVI = 100 ms. With these pacemaker settings, the IEGM (VER) was recorded for 60 s with the help of the laptop programming system SWM/SWD 1000 (Biotronik). The recording took place 2 min after programming, ensuring that a hemodynamically stationary state had been reached and that the transient response of the pacemaker input amplifier's filter did not distort the measurement. Additionally, hemodynamic and geometric parameters were determined by echocardiography. This measurement was carried out with the patient lying down, and it was repeated after 10 min.

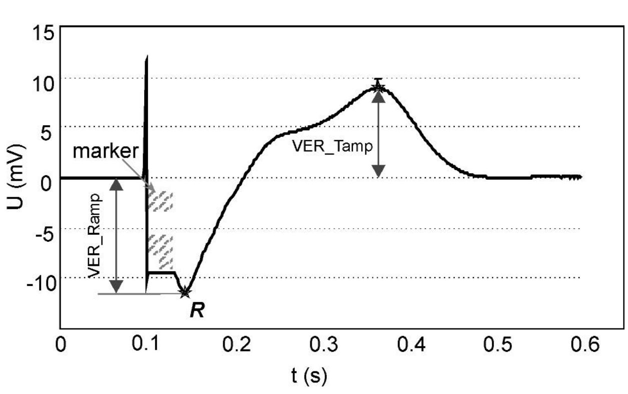

Figure 1. Parameters extracted from the VER.

The IEGM analysis and evaluation and their statistical processing in connection with the recorded echocardiographic parameters were performed by Cortronik (Graz, Austria), using fully automated methods [5]. In a first step, the signals in each recording were classified as VER, in order to detect fusion beats and intrinsic events. Next, all signals classified as VER were averaged. From the resulting signal, the minimum during the depolarization phase of the VER (VER_Ramp) and the maximum of the T wave (VER_Tamp) were determined (Figure 1).

From the echocardiographic images, the left-ventricular end-diastolic and end-systolic diameters (ECHO_LVDD, ECHO_LVSD), the left-ventricular end-diastolic and end-systolic wall thickness (ECHO_LVDWT, ECHO_LVSWT), and the stroke volume index ECHO_SVI were determined. In each case, three measuring results were averaged. The left-ventricular myocardial mass (ECHO_LVMM) was automatically determined from the echocardiographic examination.

For statistical statements, methods of descriptive statistics and the two-tailed t-test were used. The results were considered to be statistically significant if the probability of error was < 5 %. To quantify the correlation of two parameters, the respective correlation coefficient was calculated.

Results

Reproducibility

All patient examinations were performed without complications. In order to study their reproducibility, all measured parameters were compared, and the correlation coefficients as well as the statistical significance were determined (Table 1). As an example, Figures 2 a and 2b graphically show the results of the regression

Parameter	Correlation coefficient	N	p-value
VER_Ramp	0.994	20	0.0001
VER_Tamp	0.909	20	0.0001
ECHO_SVI	0.870	20	0.0001
ECHO_LVDD	0.961	18	0.0001
ECHO_LVSD	0.970	18	0.0001
ECHO_LVDWT	0.742	20	0.0002
ECHO_LVSWT	0.536	20	0.02

Table 1. Correlation coefficients as well as the statistical significance for all parameters at PR = 90 bpm and AVI = 100 ms.

analyses of VER_Ramp with a correlation coefficient of r = 0.994, and of ECHO_LVDD with r = 0.961.

NYHA Class

Table 2 compares the results for the respective parameters after the patients had been assigned to one of two groups according to their NYHA class (group 1: NYHA = IV; group 2: NYHA < IV). The p-values were determined using the two-tailed t-test. VER_Ramp, VER_RTamp, ECHO_SVI, and ECHO_LVMM show a significant difference between the two groups. All other parameters show differences, however, they are not statistically significant. Figures 3 a and b graphically depict the distribution of the values of VER_Ramp and of ECHO_SVI for both groups

Parameter	Unit	NYHA < IV M ± SD	NYHA = IV M ± SD	N	p-value
VER_Ramp	mV	12.2 ± 3.07	7.91 ± 3.97	14/7	< 0.02
VER_Tamp	mV	6.27 ± 1.83	4.56 ± 1.85	14/7	0.06
ECHO_SVI	ml	99.3 ± 29.1	66.7 ± 38.9	14/7	< 0.05
ECHO_LVDD	mm	52.7 ± 12.2	60.6 ± 16.7	12/7	0.25
ECHO_LVSD	mm	34.9 ± 14.4	45.8 ± 20.1	12/7	0.18
ECHO_LVDWT	mm	13.8 ± 2.08	14.8 ± 2.71	14/7	0.37
ECHO_LVSWT	mm	18.7 ± 2.70	19.6 ± 4.65	14/7	0.58
ECHO_LVMM	g	325 ± 104	494 ± 189	12/7	< 0.05

Table 2. Differences of the VER- and ECHO-parameters with respect to the two patient-groups with different NYHA-class.

as examples. It can be seen that both the VER_Ramp and the ECHO_SVI decrease significantly at NYHA IV.

Cardiomyopathies

According to whether a DCM was diagnosed or not, the patients were divided into two groups (group 1: without DCM; group 2: with DCM). Table 3 displays the differences in the distribution of the VER- and ECHO-parameters in the two groups. With the exception of ECHO-SV, ECHO_LVDWT, and ECHO_LVMM, all parameters show significant differences. In cases of DCM, all VER amplitudes

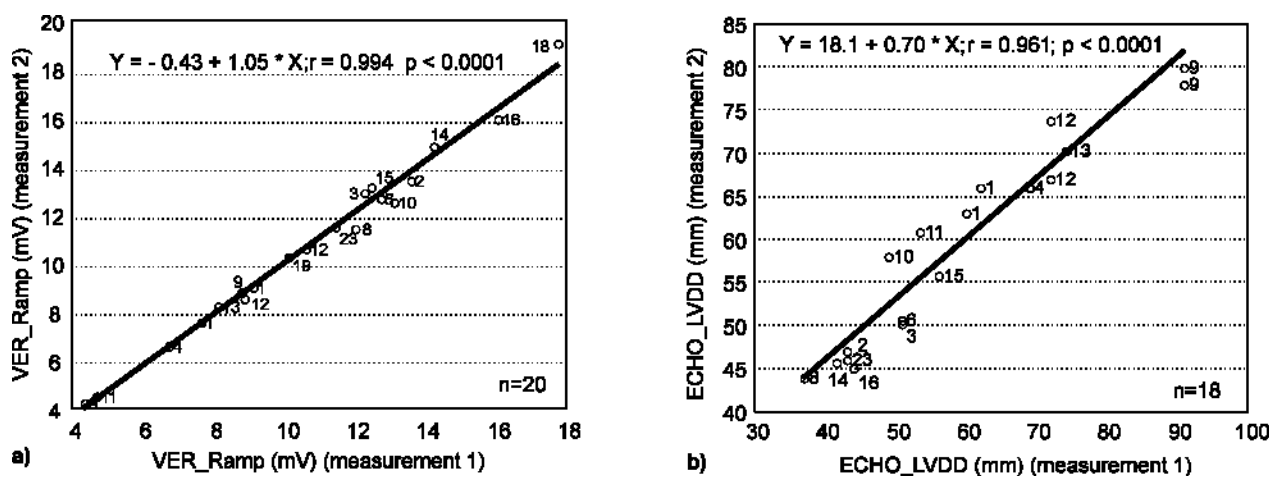

Figure 2. Illustration of the regression analyses concerning the VER_Ramp with a correlation coefficient of r = 0.994, and of ECHO_LVDD with r = 0.961.

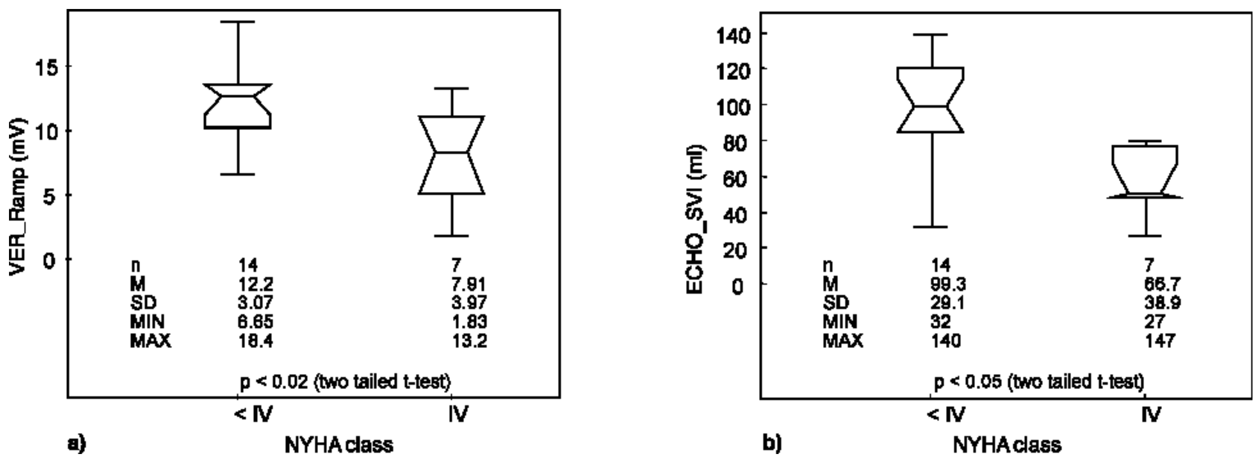

Figure 3. Statistic distribution of the VER_Ramp and ECHO_SVI with respect to the two patient groups with different NYHA-class.

(VER_Ramp (Figure 4a), VER_Tamp) are clearly lower than in patients without DCM. Corresponding to the diagnosis, the wall thickness is smaller in patients with DCM, and the ventricular diameter (Figure 4b) is larger.

Discussion

Reproducibility

The analyses show a clearly higher reproducibility for the VER parameters, i.e., higher correlation coefficients, than for the majority of the parameters from the echocardiographic examination. A possible reason might be that the VER measurements can be repeated without any changes in the measuring set-up. Thus, the VER_Ramp shows by far the highest correlation coefficient with r = 0.994. In comparison, the transducer must be repositioned for each measurement during the echocardiographic examination, necessarily leading to a scattering of the results.

Unfavorable physical sound conditions at the thorax of elderly patients make clear delineations more difficult, resulting in a certain imprecision of the measurement. Accordingly, the lowest correlation coefficients were found here. To make up for this, a larger number of measurements should be performed. Clearly better results were achieved when measuring the diameter of the ventricle.

NYHA Class and Cardiomyopathy

The VER_Ramp is smaller in patients with a diagnosed DCM, as well as with NYHA class IV, as in patients without DCM or with NYHA < IV. This indicates that poor cardiac function is apparently associated with low VER_Ramp values. However, whether the reverse is true can only be proven with specificity measurements that include a larger number of patients. A discriminatory threshold value of 10 mV appears appropriate in both cases in the studied patient group. The main reason for the modifications in the VER can probably be found in the geometric changes of the heart in patients with DCM. Dilatative cardiomyopathy is characterized by a lesser wall thickness and a larger ventricular diameter. Possible structural remodeling processes, such as increase of the interstitial tissue, reduction in the amount of extracellular fluid, and a morphological change and/or redistribution of the myofibrils, must be regarded as background, influencing the VER morphology in their totality. Previous studies have proven that the VER_Ramp is clearly correlated to geometric changes of the heart [3-6]. This is confirmed in the studied patient group by the results from the echocardiographic examination. Additionally, the changed course of myocardial contraction is reflected in the signal morphology, as it can also be described by echocardiography, especially by determining the digital velocity profile with tissue velocity imaging of the left ventricle. From the results of this study, it cannot be deduced to what degree possible conduction disturbances influence the VER. However, this should be clarified by another study. The same is true for patients with a pronounced hypertrophic non-obstructive cardiomyopathy. In the respective patient

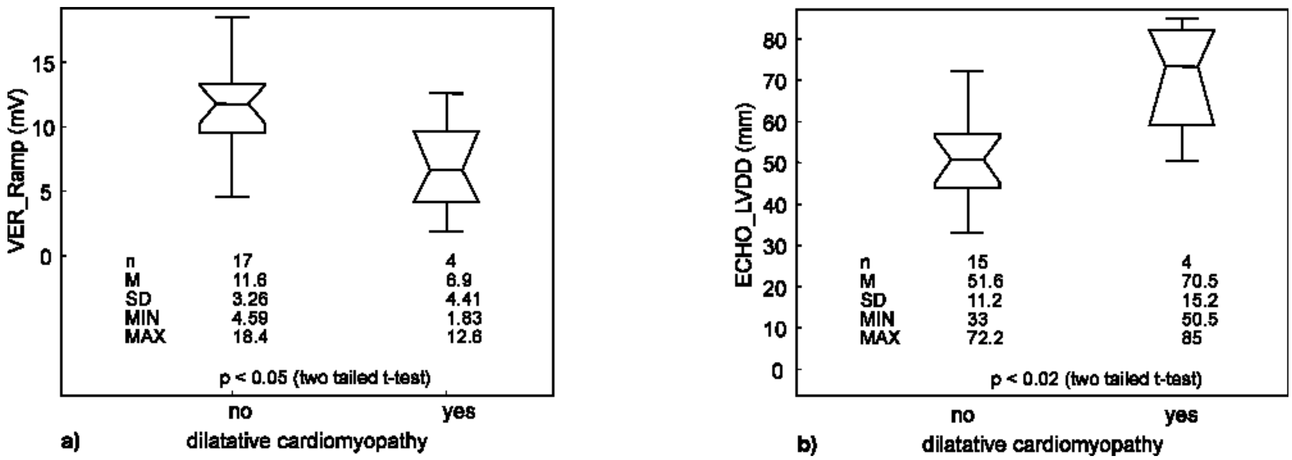

Figure 4. Statistic distribution of the VER_Ramp and ECHO_LVDD with respect to the two patient groups with or without DCM.

group of the presented study, most patients exhibited only a hypertrophy, without any indication of a cardiomyopathy, but usually with a coronary heart disease. This might be the reason why no significant changes of the VER and echocardiographic parameters could be found in this patient collective when compared with patients without cardiomyopathies.

When dividing the groups according to the NYHA class, the stroke volume index shows a significant decrease, while the increase in the ECHO_LVDD is of statistical significance if the groups are formed according to a diagnosed DCM. In general, the results of the echocardiographic examination have shown that the end-diastolic diameter of the left ventricle and the stroke volume index are the parameters with the highest reproducibility and are, thus, best suited as comparative parameters.

Conclusion

Measuring the VER is reliable and highly reproducible under defined conditions. Moreover, it is associated with a short time expenditure and can be performed as often as desired. In general, the results show that it is promising to evaluate the cardiac state primarily based on the recording and analysis of the VER under well-defined conditions. Results of future studies concerning the specificity will show whether the VER will have a future as a diagnostic alternative in the diagnosis and evaluation of the therapeutic success, at least in patients with congestive cardiac diseases. Regularly scheduled control or follow-up examinations via the cardiac pacemaker would not put any strain on the patient and constitute a progress, especially in clinical-therapeutic and also deleterious final stages.

References

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Parameter	Unit	No dil. CMP M ± SD	Dil. CMP M ± SD	N	P-Value
VER_Ramp	mV	11.6 ± 3.26	6.90 ± 4.41	17/4	< 0.05
VER_Tamp	mV	6.20 ± 1.75	3.59 ± 1.50	17/4	< 0.02
ECHO_SVI	ml	92.7 ± 33.8	70.1 ± 41.1	17/4	0.26
ECHO_LVDD	mm	51.6 ± 11.2	70.5 ± 15.2	15/4	< 0.02
ECHO_LVSD	mm	33.6 ± 11.7	58.9 ± 20.7	15/4	< 0.005
ECHO_LVDWT	mm	14.2 ± 2.13	13.5 ± 3.19	17/4	0.58
ECHO_LVSWT	mm	19.8 ± 3.14	15.9 ± 2.72	17/4	< 0.05
ECHO_LVMM	g	364 ± 126	511 ± 289	16/3	0.15

Table 3. Differences of the VER- and ECHO-parameters with respect to the two patient-groups with or without DCM.

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