THE WEDENSKY MODULATION IN INVESTIGATING THE RISK FOR MALIGNANT VENTRICULAR ARRHYTHMIA

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REZUMAT

Obiective: investigarea tehnicii modulării Wedensky. Acest studiu se bazează pe o metodă introdusă recent de Hoium și colab. care încearcă să diferențieze pacienții cu risc de tahicardii sau fibrilații ventriculare de cei fără riscul unor aritmii ventriculare maligne. **Material și metode:** În studiul nostru am inclus 40 de pacienți cu infarct miocardic (IM) pe care i-am impărțit în funcție de rezultatul studiului electrofiziologic invaziv (EPS) în inductibili si ne-inductibili pentru aritmii maligne. Am făcut comparații în cele două grupuri referitoare la durata QRS filtrată din electrocardiograma cu semnal medianizat, fracția de ejecție, suprafața reziduală în ferestre de 1ms și 10ms și indexul modulării Wedensky. **Rezultate:** Într-un grup mic am obținut diferențe semnificative ale mediilor parametrilor modulării Wedensky între pacienții post-IM cu tahicardii ventriculare (TV) sau fibrilații ventriculare (FV) si cei fără aritmii ventriculare maligne documentate prin studiul electrofiziologic invaziv. **Concluzii:** Studiul pare să indice faptul că pacienții cu IM si TV sau FV sunt mai puțin sensibili la modularea Wedensky comparativ cu pacienții fără TV sau FV în studiul electrofiziologic invaziv.

Cuvinte cheie: infarct miocardic (IM), tahicardie ventriculară (TV), fibrilație ventriculară (FV), modularea Wedensky

ABSTRACT

Objectives: To investigate the Wedensky modulation technique. This study, based on a method recently introduced by Hoium et.al, intends to confirm its capacity to distinguish between patients at risk for ventricular tachycardia (VT) or ventricular fibrillation (VF) and patients without a risk for VT/VF. **Material and methods:** In our study of 40 patients with myocardial infarction (MI) we compared 2 subgroups of patients with VT/ VF and without VT/ VF in the electrophysiological study (EPS). We compared in the two groups several accepted risk factors: filtered QRS duration from the signal-averaged ECG (SAECG), the ejection fraction (EF), as well as the Wedensky modulation parameters: the wavelet surface residuum (WSR) in 1 ms and 10 ms windows and the Wedensky modulation index. **Results:** In our small group we obtained a significant difference of the averages of the Wedensky parameters between the patients with and those without VT/VF in the EPS. **Conclusions:** Our results suggest that MI patients with propensity to develop VT/VF in the EPS are less sensitive to the Wedensky modulation than MI patients without VT/VF.

Key Words: myocardial infarction (MI), ventricular tachycardia (VT), ventricular fibrillation (VF), Wedensky modulation

INTRODUCTION

Sudden cardiac death often caused by a ventricular arrhythmia is a major cause of death in coronary artery disease patients. Implantable cardioverter defibrillator (ICD) systems have first been implanted 24 years ago by Michael Mirowski.[1] After the development of subpectorally implanted devices with transvenous leads the number of implantations has increased rapidly. Over the last decade attempts have been made to improve the indication for ICD implantation by identifying reliable risk stratifiers for sudden cardiac death. Recently, The Second Multicenter Automated Defibrillator Implantation Trial (MADIT II) showed a 31% reduction in global mortality in the patients with a history of MI and low left ventricular ejection fraction ≤30%.[2-4] Except for the QRS duration of >120 ms, there was no relevant risk factor to identify subgroups of patients who would benefit mostly from the ICD implantation. These results suggest that the ICD therapy may be indicated for the primary prevention in all post-MI patients with an EF ≤30%. Consequently, a further increase in implantation numbers threatens to have a serious impact on public health-care spending in developed countries and make this therapy

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unaffordable in countries with less financial resources. As shown by the MADIT II study several risk stratifiers have failed to prove their utility in the identification of high-risk groups. As a result new techniques are being implemented in order to achieve a non-invasive detection of patients at risk.[2-6]

More than a hundred years ago, Wedensky, a Russian neuro-physiologist, demonstrated on a frog neuro-muscular preparation that a sub-threshold stimulus evokes a muscular response if preceded by a strong stimulus.[7] This phenomenon is called the Wedensky effect. Another phenomenon described by Wedensky is the Wedensky facilitation, which represents a lowering of the threshold below a block region caused by a normal stimulus that reaches the block region. Both, the Wedensky effect and the Wedensky facilitation were confirmed in cardiac tissue as well.[8,9]

Based on these two properties of the cardiac tissue, Hoium et al developed a technique called the Wedensky modulation.[10] It consists in the modulation of the QRS complex by means of a subthreshold stimulus of 20 mA and 2 ms duration, delivered synchronously (R+0 ms protocol), and respectively 20 ms after the R detect point (R+20 ms protocol), between two external electrodes at each second heart beat. 200 modulated and 200 non-modulated QRS complexes are computed for each study protocol by applying the Morlet wavelet decomposition. Several Wedensky modulation parameters can be obtained: the wavelet surface residuum (WSR) in 1ms and 10ms windows and the Wedensky modulation index, which is a number designed to be directly proportional to the risk of sudden cardiac death (SCD).[11-13]

MATERIAL AND METHODS

A total group of 70 patients with various cardiac diseases including myocardial infarction, coronary artery disease, dilative cardiomyopathy, Brugada syndrome, right ventricular dysplasia, etc. participated in the Wedensky modulation study in the Cantonal Hospital of Lucerne between November 2003 and June 2004 after signing an informed consent. For the purposes of our study all patients with a complete data set were selected from the entire group resulting in a total number of 40 post-MI patients. In all patients the Wedensky test was performed with an MI-1000 device from Harbinger Medical Inc. For the needs of our study we computed for the two modulation protocols the WSR in 1 ms and 10 ms windows and the Wedensky modulation index (Fig. 1). Subsequently, an SAECG and an echocardiography were done followed by an EPS. A positive SAECG was considered when two of three criteria were positive: high filtered QRS duration >115 ms, RMS <21 microV, LAS >35 ms. Noise levels had to be less than 0.4 microV.

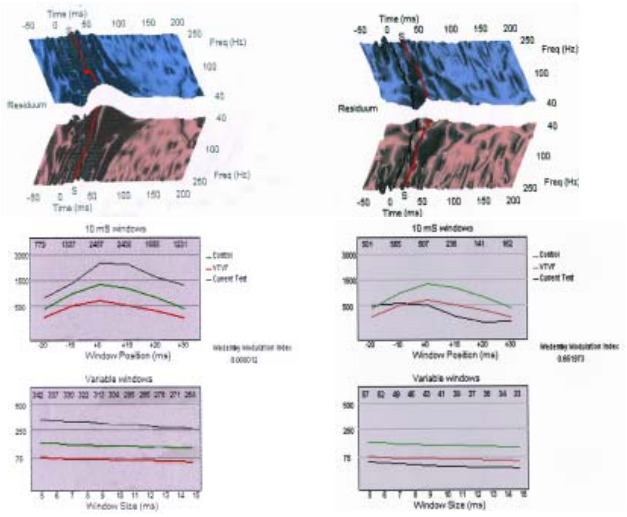

Figure 1.

A complete transthoracic echocardiography was performed in each patient with the EF measurement in the 4-chamber view using the Simpson formula. The EPS testing was inducible when sustained monomorphic or polymorphic ventricular tachycardia with ≤3 extrastimuli or ventricular fibrillation with ≤2 extrastimuli could be provoked.

Two subgroups with inducible and non-inducible EPS were obtained. For the two groups we compared the EF, the filtered QRS duration and the Wedensky modulation parameters by using the Mann-Whitney non-parametric test.

RESULTS

We included a total number of 40 patients (37 men and 3 women). In all these patients several investigations were performed including ECG, SAECG, echocardiography, Wedensky modulation and the invasive electro-physiologic testing. 12 patients were inducible in the EPS study and 28 non-inducible. The median age of the inducible patient group was 61.46 ± 8.62 years and the median age of the non-inducible patients was 55.5 ± 9.76 years.

We compared both groups for the EF, the filtered QRS duration as the most powerful predictive SAECG parameter, the WSR in 1 ms and 10 ms windows following the stimulus delivery for both protocols (R+0 ms and R+20 ms) and the Wedensky modulation index.

We were not able to find any statistical significant difference for the EF value in the two groups. The median EF in the non-inducible group was 42 ± 12.16 and in the inducible group 37.77 ± 10.03. Using the Mann-Whitney test there was no significant difference between the two patient groups (p=0.2534).

The filtered QRS duration in the non-inducible group was 132.12 ± 34.2 ms and in the inducible group 127.54 ± 23.29 ms without a significant difference in the Mann-Whitney test (p=0.72).

The averaged WSR in 10 ms modulation windows didn't reach significance (p=0.26) but they became highly significant in 1 ms modulation windows (p=0.000071), when the R+0 ms protocol was performed. (Figures 2,3)

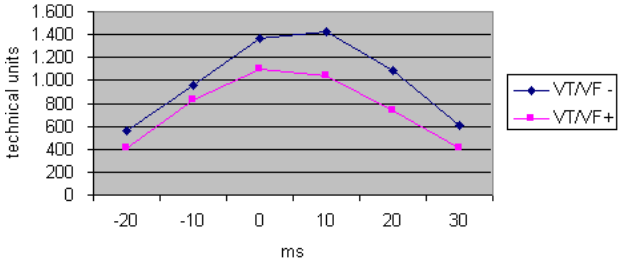

Figure 2. WSR averages in 10 ms windows in the R + 0 ms protocol.

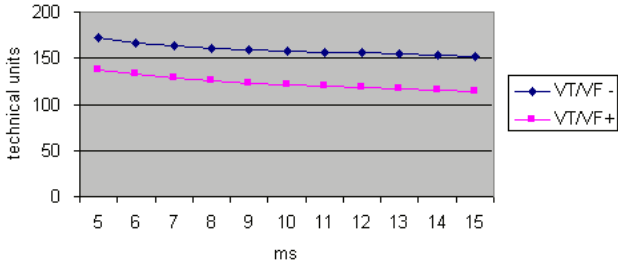

Figure 3. WSR averages in 1 ms windows in the R + 0 ms protocol.

Another statistical significant difference was found for the averages of WSR in 10 ms modulation windows (p=0.025) and in 1 ms modulation windows (p=0.000071) when the R+20 ms protocol was performed. (Figures 4,5). There was no significant difference for the Wedensky index between the two groups.

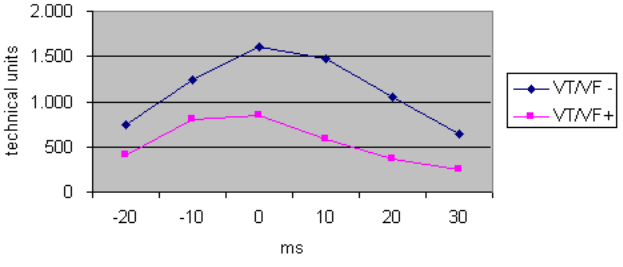

Figure 4. WSR averages in 10 ms windows in the R + 20 ms protocol.

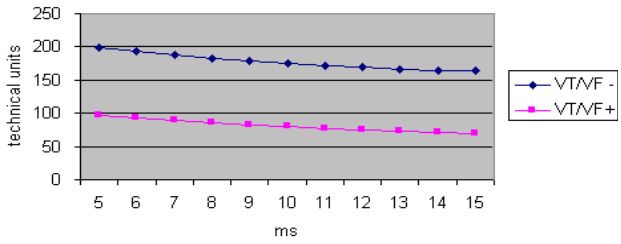

Figure 5. WSR averages in 1 ms windows in the R + 20 ms protocol.

DISCUSSIONS

The Wedensky modulation is a new non-invasive approach for the risk assessment for lethal ventricular rhythm disturbances, recently introduced by Hoium et al.[10] In a pilot study published in 2002 it was demonstrated that the Wedensky modulation was able to detect the modulation within the QRS complex.[13] Patients with inducible EPS seem to be less sensitive to the Wedensky modulation than patients without VT/VF in the EPS.[10-13] Using the MI-1000 device of the Harbinger Medical Inc. and two modulation protocols R+0 ms and R+20 ms we confirmed in a small group of 40 post-MI patients a significant difference of several Wedensky modulation parameters between those with documented VT/VF in the EPS and patients without VT/VF. There was no evident difference between the two groups, concerning the other established risk stratifiers, such as: EF or filtered QRS duration. Although, according to MADIT II the EPS hasn't proven to be a reliable risk stratifier in the post MI population with an EF less than 30% it is still the golden standard in patients with EF 30-40% in MADIT I and the Multicenter Unsustained Tachycardia Trial (MUSTT).[5]

In our study the number of patients with severely impaired ventricular function (EF ≤30%) was 5 (18%) in the non-inducible group and 5 (38%) in the inducible group. Globally, there was no significant difference of the EF in the two groups, but the proportion of patients with severely deteriorated left ventricular function was higher in the inducible group.

Obviously, due to the small number of investigated patients the difference didn't reach significant values. The filtered QRS values have shown no significant difference in our study. This is quite puzzling, since several studies have documented the importance of the global QRS duration and the filtered QRS duration of the SAECG in the risk stratification for sudden cardiac death.[15,16] This might be explained by the different protocol used in the SAECG of the Wedensky study.

On the other hand, there was a significant association between inducible EPS and lower Wedensky

modulation parameters. Whether such values are also associated with an increased risk for sudden cardiac death has to be established by the prospective study, still ongoing. It must also be emphasized that, because of the small number of patients, a control group couldn't be selected. This is why a comparison was possible only between two groups of MI patients with and without VT/VF in the EPS. We hope that the continuation of the study will offer more support to the preliminary findings from Hoium et al, that suggest the method distinguishes patients with an increased risk for ventricular lethal arrhythmia from controls and patients with other cardiac diseases without a risk for VT/VF.

CONCLUSIONS

In our study we demonstrated that the QRS modulation produced by a subliminal stimulus synchronously with the R wave (named Wedensky modulation) is stronger in MI patients without VT/VF in the EPS and weaker in MI patients with VT/VF in the EPS and hence potentially offers a non-invasive alternative to the risk stratification for ventricular malignant rhythm disturbances. Further studies, including the multicentric HIP study (Harbinger implantable defibrillator study), are expected to give a clear answer to the question.

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