THERAPEUTIC APPROACH IN PATIENTS WITH ASYMPTOMATIC NONSUSTAINED VENTRICULAR TACHYCARDIA AFTER MYOCARDIAL INFARCTION

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SUMMARY – Although nonsustained ventricular tachycardia after myocardial infarction may be associated with an increased risk of sudden cardiac death, there are no clear guidelines as to which is the most effective management of this arrhythmia. In this paper, we present our experience in the treatment of patients with asymptomatic nonsustained ventricular tachycardia, prior myocardial infarction, and left ventricular ejection fraction <40%, based on electropharmacological testing performed in 130 patients. Eighty-two of them had noninducible, and 48 inducible sustained monomorphic ventricular tachycardia. Patients with noninducible ventricular tachycardia were randomized to treatment with no antiarrhythmogenic drugs (n=46) or beta-blockers (n=36). Among patients with inducible ventricular tachycardia, 23 were treated with electropharmacologically guided drug therapy, and 25 with drugs slowing inducible ventricular tachycardia. During a mean follow-up period of 24 months, seven patients died suddenly, five survived cardiac arrest, and 12 suffered nonsudden death. The overall incidence of sudden cardiac death and total mortality were significantly higher in patients with inducible than in those with noninducible ventricular tachycardia. The incidence of sudden cardiac death at 2 years was 33% in patients with inducible and nonsuppressible ventricular tachycardia, 7% in patients with inducible and electropharmacologically guided therapy, 9% in patients with noninducible ventricular tachycardia treated without drugs, and 8% in patients with noninducible ventricular tachycardia treated with beta-blockers. In conclusion, patients with asymptomatic nonsustained ventricular tachycardia, prior myocardial infarction, ejection fraction <40%, and excluded active ischemia should be submitted to electropharmacological testing. Patients with noninducible ventricular tachycardia may be followed with no drugs. Patients with inducible and suppressible ventricular tachycardia may be treated by effective drug if their ejection fraction is higher than that recorded in the Multicenter UnSustained Tachycardia Trial population. Patients with inducible and nonsuppressible ventricular tachycardia are candidates for cardioverter-defibrillator implantation, because they are at a high risk of sudden cardiac death.

Key words: Myocardial infarction, complications; Myocardial infarction, therapy; Tachycardia, ventricular, therapy

Introduction

Although nonsustained ventricular tachycardia (VT) after myocardial infarction (MI) may be associated with an increased risk of sudden cardiac death, there are no clear guidelines as to which is the most effective management of this arrhythmia. Over the last ten years, programmed ventricular stimulation was used by some authors to guide therapy in such patients, and noninducibility of sustained monomorphic VT after electropharmacological testing was considered as a predictor of successful antiarrhythmic therapy1-4. Recently, two studies have shown that patients with asymptomatic nonsustained VT, MI, low left ventricular ejection fraction, and inducible sustained monomorphic VT have a significantly better clini-
cal outcome if treated by implantable cardioverter-defibrillator than by antiarrhythmic drugs, contesting the empirical and electrophysiologically guided antiarrhythmic therapy in these patients\textsuperscript{5,6}.

The purpose of this paper is to present our experience in the treatment of asymptomatic nonsustained VT in patients after MI, based on the electropharmacological evaluation. Study results have previously been reported in the abstract form\textsuperscript{7}.

**Patients and Methods**

**Study patients**

Study population consisted of 130 consecutive patients referred to our Department of Arrhythmias for evaluation of nonsustained VT between March 1989 and March 1995. Criteria for inclusion in the study were as follows: 1) asymptomatic nonsustained VT (duration of >6 beats to 30 seconds, rate >120 beats/min) documented by ambulatory monitoring or telemetry recordings; 2) a Q-wave positive myocardial infarction more than 2 months before entry; 3) left ventricular ejection fraction <40%; and 4) life expectancy of more than one year. Patients with a history of sustained VT or ventricular fibrillation (VF), active myocardial ischemia, functional class IV, or significant comorbidity were excluded from the study.

Left ventricular function was assessed by radionuclide ventriculography. Active myocardial ischemia was excluded by clinical evaluation, coronaryography (30 patients), or exercise stress testing (100 patients).

**Electrophysiologic and electropharmacologic evaluation**

The electrophysiologic study was performed in the absence of antiarrhythmic therapy for at least ten days. All patients gave written informed consent. Three to four quadripolar electrode catheters were introduced percutaneously through femoral veins and positioned in the high right atrium, His bundle area and right ventricular apex. Five surface electrocardiograms and three intracardiac recordings were made simultaneously at paper seeds of 25 and 100 mm/s by a Siemens Mingograf 7 recorder. Intracardiac pacing was performed at twice diastolic threshold with a pulse duration of 2 ms. Ventricular stimulation was performed at the apex and outflow tract of the right ventricle using three drive ventricular cycles (500, 400 and 350 ms) and up to three extrastimuli. The end point of stimulation was the induction of sustained monomorphic VT, or completion of the entire stimulation protocol without induction of this arrhythmia.

In patients with baseline inducible sustained monomorphic VT, the protocol of ventricular stimulation was repeated after intravenous loading of sotalol (1.5 mg/kg/15 min) or amiodarone (10 mg/kg/10 min). If the induction of sustained monomorphic VT was suppressed by one of these antiarrhythmic agents, the patient was long-term treated with the respective drug per os. If the induction of sustained monomorphic VT was not suppressed by these antiarrhythmic agents, the patient was treated with the drug that made the induced tachycardia best tolerated. Patients with noninducible sustained monomorphic VT were randomized to be off drugs or to take beta-blockers.

The following definitions were used with regard to the electrophysiologic study: sustained monomorphic VT was defined as having a uniform beat-to-beat QRS morphology lasting for more than 30 seconds, rate >120 beats/min, or requiring earlier termination by external electroshock because of hemodynamic compromise. Polymorphic VT was defined as having a variable QRS morphology.

**Follow-up**

All patients were prospectively followed at our Arrhythmia Center every 6 months. Each control included history, physical examination, 12-lead electrocardiogram, and Holter monitoring. The end points of the follow-up were the occurrence of VF successfully resolved by external electroshock and resuscitation, sudden death, and nonsudden cardiac death.

Sudden cardiac death was defined as a death due to documented ventricular tachyarrhythmia, or death which occurred within minutes of the onset of symptoms, or during sleep in a previously stable patient. On statistical analysis, patients with resuscitated VF were also classified as having sudden cardiac death. Nonsudden cardiac deaths were those due to acute MI or congestive heart failure.

**Statistical analysis**

Data are given as mean ± 1 standard deviation. Student’s t-test was used to assess difference in means, and \( \chi^2 \)-test for frequency data analysis. The incidence of sudden cardiac death and cardiac mortality was determined using Kaplan-Meier method. Differences between the groups and subgroups were considered statistically significant at p<0.05.
Results

Patient characteristics

According to the results of baseline electrophysiologic evaluation, 130 study patients were divided into two groups. Eighty-two (63%) patients had noninducible sustained monomorphic VT. In six of them, nonsustained polymorphic VT lasting for 6 to 12 beats was induced, but these findings were considered as nonclinical responses. The remaining 48 (37%) patients had inducible sustained monomorphic VT. Single ventricular extrastimuli were required for induction of tachycardia in four, two extrastimuli in 16, and three extrastimuli in 28 patients. The mean cycle length of the induced VT was 300 ± 50 ms.

Clinical characteristics of patients with noninducible and inducible sustained monomorphic VT are presented in Table 1. There were no differences between the groups according to gender, age, and localization of MI. Patients with noninducible VT had a slightly higher left ventricular ejection fraction, but the difference did not reach statistical significance. On electrocardiographic monitoring, there were no between-group differences according to the frequency of premature ventricular beats or mean duration of nonsustained VT.

Table 1. Clinical characteristics of 130 patients with noninducible and inducible monomorphic ventricular tachycardia

<table>
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<tr>
<th></th>
<th>Noninducible VT</th>
<th>Inducible VT</th>
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</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>61±9</td>
<td>62±10</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>83</td>
<td>82</td>
</tr>
<tr>
<td>Localization of MI (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– anteroseptal</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>– anterior</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td>– inferior</td>
<td>43</td>
<td>42</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>37 (33-39)</td>
<td>35 (30-39)</td>
</tr>
<tr>
<td>PVB (h)</td>
<td>118±26</td>
<td>124±100</td>
</tr>
<tr>
<td>Episodes of NSVT (No./24 h)</td>
<td>26±16</td>
<td>28±10</td>
</tr>
<tr>
<td>Mean number of NSVT beats</td>
<td>12</td>
<td>10</td>
</tr>
</tbody>
</table>

MI=myocardial infarction; LVEF=left ventricular ejection fraction; PVB=premature ventricular beat; NSVT=nonsustained ventricular tachycardia

Patient treatment

The treatment of patients was assigned on the basis of electropharmacologic testing (Fig. 1). Eighty-two patients with noninducible sustained monomorphic VT were randomized in two subgroups. Forty-six (56%) of them were administered no medicamentous therapy, and 36 (44%) were treated with beta-blockers. Among 48 patients with inducible sustained monomorphic VT, an effective drug was found by electrophysiologic testing in 23 (48%) patients. In this subgroup, 17 patients were treated with amiodarone, and six with sotalol. The 25 (52%) patients in whom inducible sustained monomorphic VT persisted were treated with a drug that made induced tachycardia slowest and hemodynamically more tolerable. In this subgroup, 17 patients were treated with amiodarone and eight with sotalol.

Follow-up

During a mean follow-up period of 24 ± 6 months, eight patients died suddenly, and four were successfully resuscitated from VF (Fig. 1). The overall incidence of sudden cardiac death at 2 years was 8% in patients with noninducible VT, and 21% in patients with inducible sustained monomorphic VT (p<0.05). Ten patients suffered nonsudden cardiac death (three from acute MI and seven from congestive heart failure), and two noncardiac death. The overall mortality rate at 2 years was 19% in patients with noninducible VT, and 39% in those with inducible VT (p<0.05) (Table 2).

Table 2. Cumulative survival in 130 patients with noninducible and inducible monomorphic ventricular tachycardia

<table>
<thead>
<tr>
<th></th>
<th>Noninducible VT</th>
<th>Inducible VT</th>
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<tbody>
<tr>
<td></td>
<td>(n=82)</td>
<td>(n=48)</td>
</tr>
<tr>
<td>6 months</td>
<td>95</td>
<td>91</td>
</tr>
<tr>
<td>12 months</td>
<td>89</td>
<td>80</td>
</tr>
<tr>
<td>18 months</td>
<td>82</td>
<td>74</td>
</tr>
<tr>
<td>24 months</td>
<td>81</td>
<td>61</td>
</tr>
</tbody>
</table>

p<0.05

The incidence of sudden cardiac death according to assigned therapy in the subgroups of noninducible and inducible sustained monomorphic VT is presented in Figs. 2 and 3, respectively. Among patients with noninducible sustained monomorphic VT, significant arrhythmic
events (2 VF and 1 sudden cardiac death) occurred in three of 46 patients treated with no drugs, and in two of 36 patients treated with beta-blockers, yielding a 2-year incidence of sudden cardiac death of 9% and 8%, respectively. There was a significant difference in the incidence of sudden cardiac death between the two subgroups of patients with inducible sustained monomorphic VT. Only one of 23 patients with inducible and suppressible VT (receiving amiodarone) died suddenly at 6 months of follow-up, yielding a 2-year incidence of sudden cardiac death of 7%. In contrast, six of 25 patients with inducible and nonsuppressible VT had significant arrhythmic
events (3 VF and 4 sudden cardiac death) during the follow-up, yielding a 2-year sudden cardiac death incidence of 33% (p<0.05).

Discussion

At the beginning of the new millennium, the management of patients with asymptomatic nonsustained VT and MI is still one of the continuing problems for modern physicians and cardiologists, because these patients may be at risk of sudden cardiac death due to VF. Several studies were performed to determine whether such patients might benefit from electrophysiologic testing. The rationale has been that electrophysiologic testing identifies patients at a high risk of future arrhythmic events, and that it may select those with successful drug therapy. In spite of several shortcomings, the published studies seem to demonstrate that patients with noninducible sustained VT have a low rate of sudden cardiac death and do not appear to require antiarrhythmic therapy. The risk of sudden cardiac death in these patients is even lower when they have a left ventricular ejection fraction higher than 40%. However, the ability of antiarrhythmic therapy guided by electropharmacologic testing to prevent sudden cardiac death in this population has not been proven, although some studies suggest that electrophysiologically guided antiarrhythmic therapy in this population is associated with a lower rate of sudden cardiac death compared with empirical therapy.

Our study confirmed the results of previous investigations that electrophysiologic testing may be useful in risk stratification and management of patients with MI who have asymptomatic nonsustained VT and left ventricular ejection fraction lower than 40%. The inducibility of sustained monomorphic VT during baseline electrophysiologic study was shown to be an independent predictor of future patient’s outcome. Patients with this finding had a significantly higher overall incidence of sudden cardiac death and total mortality at 2 years than those with noninducible VT (p<0.05), suggesting that such patients require a more aggressive therapeutic approach for prevention of sudden cardiac death. We examined the value of noninducibility of sustained monomorphic VT by randomization of these patients to the treatment with no antiarrhythmic drugs or with beta-blockers. The incidence of arrhythmic events in these patients at 2 years was lower (9%) than in several groups of historical controls with untreated spontaneous nonsustained VT (17%). However, there was no statistically significant difference in the incidence of sudden cardiac death between untreated patients and patients treated with beta-blockers at 2 years (9% versus 8%). It means that this patient subgroup may be followed without antiarrhythmic drug therapy. Similar data were obtained in the study of Schmitt et al., where the 2-year incidence of sudden cardiac death in patients treated mostly with beta-blockers was 8%. A positive electrophysiologic testing at baseline evaluation also appeared to be of value for the patient’s management. Patients with inducible sustained monomorphic VT that was suppressed by antiarrhythmic therapy during electropharmacologic testing had a 7% rate of sudden cardiac death, whereas those with persistently inducible VT had a 33% rate of sudden cardiac death at 2 years (p<0.05), suggesting that the results of electropharmacologic testing are predictive of outcome in these patients. The higher overall mortality in patients with inducible sustained monomorphic VT was probably associated with the higher incidence of sudden cardiac death in this group, because the incidence of nonsudden cardiac death was proportional in patients with inducible and noninducible VT.

Two recent studies contest the value of empirical and electrophysiologically guided antiarrhythmic drug therapy in populations comparable with our study population (Table 3). The Multicenter Automatic Defibrillator Implantation Trial (MADIT) evaluated the role of cardioverter-defibrillator (ICD) as prophylaxis in patients with asymptomatic nonsustained VT, prior MI, low left ventricular ejection fraction (<35%), and inducible and nonsuppressible sustained monomorphic VT. The end point of the trial was overall mortality. After a mean follow-up period of 27 months, ICD was associated with a 54% reduction of all-cause mortality compared with conventional antiarrhythmic therapy (75% amiodarone). The impact of this study was so strong that the current selection criteria for ICD therapy reflect exactly the results of the trial. The Multicenter UnSustained Tachycardia Trial (MUSST) studied a nearly identical group of patients (asymptomatic nonsustained VT, prior MI, mean left ventricular ejection fraction of 30%, and inducible and nonsuppressible sustained monomorphic VT). They were randomly assigned to receive electrophysiologically guided antiarrhythmic drug therapy, ICD, or no therapy (Table 3). The risk of cardiac arrest among patients receiving an ICD was significantly lower than that among patients on drug therapy. Moreover, the mortality reduction for all causes for patients with ICD versus patients with no drug, drugs or electrophysiologically guided drug therapy was 51%. So, MUSST has established some important clues in identifying patients with prior MI...
at high risk: high degree left ventricular dysfunction, nonsustained VT on Holter recording, and inducibility of VT at electrophysiologic study. In such a population, ICD implantation has significant benefit.

Although our study was designed in a different fashion than MUSST, there are some statements that are common to both studies. In the population presented, the electrophysiologic testing did not lose its role in risk stratification. It was definitely shown that patients without inducibility of VT had a significantly lower risk of sudden cardiac death and overall mortality than similar patients with inducible sustained monomorphic VT\textsuperscript{14}. Accordingly, the latter group of patients need a more extensive therapeutic approach such as ICD implantation. Our results of electrophysiologically guided antiarrhythmic therapy differ from those reported from the MUSST study. These differences may be explained by the smaller number of patients, shorter follow-up, and higher mean left ventricular ejection fraction (35\% versus 30\%) in our study, and lower use of amiodarone (23\% versus 74\%) in the MUSST study.

**Limitations**

A major limitation of our study was that the patients treated by electropharmacologically guided antiarrhythmic therapy had no control group administered placebo. It was therefore impossible to demonstrate that the management based on electropharmacologic testing improved the outcome in these patients. This shortcoming is even more pronounced after MUSST study, which found no benefit of electrophysiologically guided antiarrhythmic therapy. Another limitation of the present study was the relatively small number of patients in the subgroups with inducible and noninducible VT, making difficult any definite recommendations for the management of these patients. Finally, our study was terminated before the MADIT criteria for ICD implantation have been accepted. Thus, we could not offer this therapeutic option to our patients with inducible and nonsuppressible sustained monomorphic VT.

**Clinical implications**

Patients with asymptomatic nonsustained VT, prior MI, and left ventricular ejection fraction lower than 40\%, in whom active myocardial ischemia is excluded, should be considered appropriate candidates for electrophysiologic testing. Based on the results of this testing, patients with noninducible sustained monomorphic VT may be followed up without antiarrhythmic drug therapy, because their incidence of sudden cardiac death is low. In this subgroup of patients, beta-blockers did not reduce the incidence of sudden cardiac death. Patients with inducible sustained monomorphic VT which proves nonsuppressible during electropharmacologic testing, are candidates for ICD therapy. According to MUSST study, patients with inducible and suppressible sustained VT during electropharmacologic testing should also be considered for ICD implantation. However, our experience suggests that electropharmacologically guided antiarrhythmic therapy is useful in patients in whom the mean left ventricular eje-

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**Table 3. Crude survival rates in MADIT and MUSST**

<table>
<thead>
<tr>
<th></th>
<th>MADIT</th>
<th>MUSST</th>
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<tbody>
<tr>
<td></td>
<td>ICD</td>
<td>AAR</td>
<td>ICD</td>
</tr>
<tr>
<td>No. of patients</td>
<td>95</td>
<td>101</td>
<td>167</td>
</tr>
<tr>
<td>Death</td>
<td>15</td>
<td>39</td>
<td>35</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>15.8</td>
<td>38.6</td>
<td>21</td>
</tr>
<tr>
<td>p value</td>
<td>0.009</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Mean follow-up</td>
<td>27 months</td>
<td>39 months</td>
<td></td>
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\textit{pts}=patients; ICD=implantable cardioverter-defibrillator; AAR=antiarrhythmic drug therapy; EP-g=electrophysiologically guided
ction fraction is greater than in the MUSST population. Patients with left ventricular ejection fraction >40% should also be recommended for electrophysiologic evaluation and subsequent therapy, if they have another risk factor such as positive late potentials or depressed heart rate variability.

References


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Sažetak

TERAPIJSKI PRISTUP U BOLESNIKA S ASIMPTOMATSKOM NEPOSTOJANOM VENTRIKULSKOM TAHIKARDIJOM NAKON INFARKTA MIOKARDA

D. Petrač, B. Radić, H. Pintarić i D. Vukosavić

Premda asimptomatska nepostojana ventrikulska tahikardija nakon infarkta miokarda može biti povezana s rizikom od nagle srčane smrti, nema jasnih smjernica kako najdjelotvornije zbrinjavati ovu aritmiju. Prikazujemo naša iskustva u liječenju bolesnika s asimptomatskom nepostojanom ventrikulskom tahikardijom, prethodnim infarktom miokarda i ejekcijskom frakcijom lijeve klijetke <40%, koje se temelji na elektrofarmakološkom testiranju. Elektrofarmakološko testiranje provedeno je u 130 bolesnika, od kojih je 82 imalo neizazvanu, a 48 izazvanu postojanu monoformnu ventrikulsku tahikardiju. Od 82 bolesnika s neizazvanom ventrikulskom tahikardijom, 46 ih je randomizirano na terapiju bez antiaritmitika, a 36 na beta-blokatore. Od 48 bolesnika s izazvanom ventrikulskom tahikardijom, 23 ih je liječeno elektrofarmakološki vođenim lijekovima, a 25 lijekovima koji su usporavali izazvan ventrikulsku tahikardiju. Za vrijeme praćenja kroz 24 mjeseca sedmoro je bolesnika umrlo naglom srčanom smrću, petoro je preživjelo srčani arest, a 12 je umrlo nenaglom srčanom smrću. Sveukupna učestalost nagle srčane smrti i ukupna smrtnost bile su značajno više u bolesnika s izazvanom od onih u bolesnika s neizazvanom ventrikulskom tahikardijom. Dvogodišnja učestalost nagle srčane smrti bila je 33% u bolesnika s izazvanom i nesupresibilnom ventrikulskom tahikardijom, 7% u bolesnika s izazvanom ventrikulskom tahikardijom i elektrofarmakološki vođenom terapijom, 9% u bolesnika s neizazvanom ventrikulskom tahikardijom praćenim bez antiaritmitika i 8% u bolesnika s neizazvanom ventrikulskom tahikardijom liječenim beta-bloktorima. Zaključujemo da se bolesnici s asimptomatskom nepostojanom ventrikulskom tahikardijom, prethodnim infarktom miokarda, ejekcijskom frakcijom <40% i isključenom aktivnom ishemijom trebaju podvrgnuti elektrofarmakološkom testiranju. Bolesnici s neizazvanom ventrikulskom tahikardijom mogu se pratiti bez lijekova. Bolesnici s izazvanom i supresibilnom ventrikulskom tahikardijom mogu se liječiti djelotvornim lijekom, ako je njihova ejekcijska frakcija veća od one kod populacije iz studije MUSST. Zbog visokog rizika od nagle srčane smrti, bolesnici s izazvanom i nesupresibilnom ventrikulskom tahikardijom kandidati su za ugradnju kardioverter-defibrilatora.

Ključne riječi: Infarkt miokarda, komplikacije; Infarkt miokarda, terapija; Tahikardija, ventrikulska, terapija