Clinical significance of rapid ventricular tachycardia (> 270 beats per minute) provoked at programmed stimulation in patients without confirmed rapid ventricular arrhythmias

Béatrice Brembilla-Perrot, Arnaud Terrier de la Chaise, Serge Briançon, Maeva Takoordial, Christine Suty-Selton, Bernard Thiel, Jean Luc Brua

Abstract
Rapid uniform ventricular tachycardia (VT) (> 270 beats/min) or ventricular flutter induced during electrophysiological studies is thought not to be clinically significant in patients without cardiac arrest or documented rapid VT. The purpose of the study was to follow up 73 patients with inducible ventricular flutter but without confirmed rapid spontaneous VT. A long follow up (mean 3.5 years) identified two groups of patients. The first group had an excellent outcome and was characterised by a normal 24 hour Holter monitoring. In the second group, however, the risk of cardiac mortality was high (35%) and spontaneous VT was < 270 beats/min (26%) and was characterised by couplets or salvos of extrasystoles on Holter monitoring. In this group the history of syncope and decreased left ejection fraction increased the risk of mortality and VT. The presence of late potentials increased the risk of spontaneous VT. Electrophysiologicaly guided antiarrhythmic therapy reduced the risk of VT.

Ventricular flutter was a non-specific finding in patients with normal Holter monitoring. In contrast, in patients with salvos of extrasystoles, ventricular flutter was associated with a high risk of cardiac mortality and VT.

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Ventricular fibrillation (VF) induced during electrophysiological studies is believed to be a non-clinical response in patients without clinical fibrillation whereas induced multiformal ventricular tachycardia (VT) is an useful index of electrical instability in patients with cardiac arrest and haemodynamically symptomatic VT. The clinical significance of inducible rapid uniform VT or ventricular flutter in patients without a history of cardiac arrest or rapid VT is less established. Some reports claim that the induction of ventricular flutter after myocardial infarction is of no clinical significance, unlike the induction of a uniform and relatively slow arrhythmia. The significance of ventricular flutter when it is associated with another underlying heart disease is not known.

We analysed data from 73 consecutive patients who had inducible ventricular flutter and who did not have history of cardiac arrest or rapid VT and compared the results with their clinical outcome.

Patients and methods
PATIENTS
Ventricular flutter was induced by ventricular stimulation in 73 (mean (SD) age 57 (12), range 36-77) of the 1100 consecutive patients who had electrophysiological testing between January 1982 and December 1989 because of syncope, dilated cardiomyopathy, or myocardial infarction. For the purpose of this analysis, ventricular flutter was defined as having a cycle length of < 214 ms, being uniform on a 12 lead electrocardiogram, having an uniform QRS configuration and axis, having constant rate, and requiring overdrive pacing or defibrillation because of circulatory collapse and loss of consciousness. All patients with spontaneous cardiac arrest or documented rapid VT were excluded.

Sixty patients had coronary disease and a history of myocardial infarction. Five had idiopathic dilated cardiomyopathy, three had hypertrophic cardiomyopathy, two had mitral valve prolapse, and one had corrected tetralogy of Fallot. Two patients had no clinical evidence of heart disease.

The indication for ventricular stimulation was unexplained syncope or dizziness (27 patients) and systematic evaluation at least one month after myocardial infarction to identify patients at risk of ventricular tachycardia (n = 41) or for systematic evaluation of patients with idiopathic dilated cardiomyopathy (n = 5).

ELECTROPHYSIOLOGICAL STUDIES
After they had given their informed consent patients were studied in a fasting non-sedated state. Antiarrhythmic therapy was discontinued for at least four half lives before the study. Three quadripolar or bipolar electrode catheters were inserted percutaneously and were positioned in the heart under fluoroscopic guidance. The right ventricle was stimulated at the apex and infundibulum with a programmable stimulator (Explorer 2000 Ela) that delivered square wave electrical impulses of 1-8 ms duration with the amplitude set at twice the diastolic threshold.

Our protocol for ventricular premature
stimulation has been described elsewhere. Ventricular overdrive pacing was performed at cycle lengths of 500-300 ms. Ventricular programmed stimulation was then performed at three cycle lengths (sinus and 600, and 400 ms) with one and two extrastimuli. If VT, ventricular flutter, or VF was not initiated, the next ventricular site was then stimulated in a similar fashion until VT, ventricular flutter, or VF lasting ≥ 30 seconds or circulatory collapse was initiated.

SIGNAL AVERAGED ELECTROCARDIOGRAPHY

A signal-averaged electrocardiogram was obtained on the same day as programmed stimulation in 45 patients without bundle branch block. Recordings were processed and analysed according to the methods described by Simson by electrocardiograph developed by the Dr Ing Ospyka GmbH.

We measured the magnitude of the high frequency signal in the last 40 ms of the QRS complex (V40) and the total QRS duration. Late potentials were defined as a root mean square of the amplitude of the signal that was ≤ 20 μV in the last 40 ms of the filtered QRS. QRS duration was regarded as abnormal when it was > 120 ms. Signals were analysed without knowledge of the clinical status of the patient.

OTHER INVESTIGATIONS

Ambulatory electrocardiographic monitoring

Twenty four hour ambulatory electrocardiographic recordings were analysed manually. The total number of extrasystoles each hour and every 24 h was noted, as was the maximum Lown grade.

Radionuclide ventriculography

The resting left ventricular ejection fraction (LVEF) was measured during sinus rhythm by 99mTc radionuclide ventriculography and computer generated time activity curves.

FOLLOW UP

During follow up, 36 patients in whom frequent extrasystoles of Lown grade IVA or IVB were recorded during ambulatory electrocardiographic monitoring were started on antiarrhythmic drugs. Oral therapy was started with a class I drug and ambulatory electrocardiographic monitoring and serial programmed stimulation were used to determine the appropriate drug. If the class I drug was ineffective, amiodarone was tested and then a combination of β blocker and amiodarone. All 36 patients were treated with a combination of at least a class I drug and amiodarone. At electrophysiological testing protection was defined as the inability to provoke either a sustained VT or a non sustained VT (> 15 repetitive responses). In 13 patients an effective drug regimen was identified. When the VT was still inducible the patient was treated with the drug that resulted in the disappearance of ventricular extrasystoles on the Holter monitoring, increased the tachycardia cycle length, and was tolerated best.

STATISTICAL ANALYSIS

Continuous values were expressed as the

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Table 1: Clinical characteristics and outcome in patients with inducible ventricular flutter

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cardiac mortality (VT-VF) n (%)</th>
<th>SD (VT-VF excluded) n (%)</th>
<th>VT (+VF) n (%)</th>
<th>Alive (VT excluded) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) (mean (SD))</td>
<td>52 (19)</td>
<td>37 (17)</td>
<td>57 (17)</td>
<td>57 (11)</td>
</tr>
<tr>
<td>Syncope (%)</td>
<td>10/14 (71%)</td>
<td>4/6 (67%)</td>
<td>7/10 (70)</td>
<td>14/53 (26)</td>
</tr>
<tr>
<td>LVEF 31</td>
<td>31 (16)</td>
<td>35 (19)</td>
<td>29 (13)</td>
<td>46 (5)</td>
</tr>
<tr>
<td>Late potentials 5/7</td>
<td>1/2</td>
<td>6/7</td>
<td>15/35 (43%)</td>
<td></td>
</tr>
<tr>
<td>Holter monitoring (grade IVA-IVB)</td>
<td>12/14 (86%)</td>
<td>6/6</td>
<td>9/10</td>
<td>15/53 (32%)</td>
</tr>
</tbody>
</table>

SD, sudden death; VT, ventricular tachycardia; VF, ventricular fibrillation; LVEF, left ventricular ejection fraction.

*Patient was not given an antiarrhythmic drug (AA). Protected, VT induction was suppressed by AA. Not protected, patient received AA drug but the VT was still inducible.

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Figure 1: Life table analysis with survival curves for total cardiac deaths (CD) and for ventricular arrhythmic events (VT).
tricular flutter before overdrive pacing or defibrillation was 18 s. Sixty four patients required transthoracic direct current defibrillation with 200 to 400 J because of circulatory collapse and loss of consciousness. In the nine remaining patients ventricular flutter was stopped by overdrive pacing. The frequency of ventricular flutter varied from 280 to 340 CD beats/min (mean 305 beats/min).

Signal-averaged electrocardiogram—Twenty seven patients had late potentials and the remaining patients (n = 23) had a normal signal-averaging.

Ambulatory electrocardiographic monitoring—Lown grade IVA or IVB ventricular arrhythmias were seen in 36 patients. VT was non sustained. All episodes of VT with $\geq 10$ mean (ISD). Continuous variables were compared by Student’s two tailed t test. Dichotomous variables were analysed by the $\chi^2$. We used stepwise logistic regression analysis to identify the independent variables predictive of VT and death. Survival curves were calculated by the Kaplan-Meier product limit method and compared by the generalised Wilcoxon (Breslow test). We used Cox’s method to calculate the actuarial probabilities of survival, cardiac death, or VT. A p value of $< 0.05$ was considered significant.

Results

RESULTS OF INVESTIGATIONS

Ventricular premature stimulation—Seventy three patients had inducible sustained ventricular flutter. The mean duration of ventricular flutter before overdrive pacing or defibrillation was 18 s. Sixty four patients required transthoracic direct current defibrillation with 200 to 400 J because of circulatory collapse and loss of consciousness. In the nine remaining patients ventricular flutter was stopped by overdrive pacing. The frequency of ventricular flutter varied from 280 to 340 CD beats/min (mean 305 beats/min).

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1.0
0-80
Normal Holter -- VT
0-6
CD -- VT
CD

0-0
Abnormal Holter

0.0
10
20
30
40
50
60
70
80
Months

Figure 4 Life table analysis with survival curves for cardiac deaths and for ventricular arrhythmia events in patients with Lown grade IVA or IVB ventricular extrasystoles (abnormal Holter) and with Lown grade O, I, II or III activity (normal Holter). There were significant differences in total cardiac survival (p < 0.006) and VT occurrence (p < 0.004) between these two groups.

Figure 5 Life table analysis with survival curves for cardiac deaths and for ventricular arrhythmia events in patients with late potentials (LP) and without. There was no significant difference in total cardiac survival and VT occurrence between these two groups.

extrasystoles were excluded from this study.

Left ventricular ejection fraction—The mean left ventricular ejection fraction was 42 (16%) (range 12 to 70%). The ejection fraction was less than 40% in 31 patients.

FOLLOW UP
The mean follow up period was 3-5 years (up to 8 years) (table 1). During the follow up there were 13 deaths from cardiac causes (mortality 18%). One death was related to cardiac transplantation. Nine were attributable to ventricular tachycardias either confirmed (n = 3) or presumed because of instantaneous death without prodromal symptoms (n = 6). Two patients died of heart failure. Another patient died of a non-cardiac cause.

In 10 patients spontaneous relatively slow VT (< 250 beats/min) developed, in three this was complicated by ventricular fibrillation and caused death. VT developed one month to five years after the induction of ventricular flutter. One of these patients underwent cardiac transplantation and died.

Curves to show survival without cardiac death and without arrhythmic events (confirmed ventricular tachycardia or ventricular fibrillation or both) were calculated by the Kaplan- Meier product limit method (fig 1). The actuarial probability of survival without cardiac death was 90 (3)% at one year, 85 (4)% at two years, and 74 (7)% at five years and the probability of freedom from arrhythmic events was 90 (3)% at one year and 88 (4)% at two years.
The prognosis and risk of ventricular arrhythmias were compared in patients who were not treated with antiarrhythmic agents (A), those who were treated but were not protected against VT (B), and those treated with antiarrhythmic agents who were protected (C) (fig 6). Group B had a poorer prognosis than groups A and C but the differences were not significant (p < 0.08). The risk of ventricular arrhythmic events was significantly (p < 0.001) reduced in group C. Cox regression multivariate analysis showed that only syncope (p < 0.01) and a low ejection fraction (p < 0.09) were independent variables predicting cardiac death in the follow up period (table 2). Cox regression multivariate analysis showed that only Lown grades IVA or IVB for ventricular ectopic activity (p < 0.005) were independent variables predicting ventricular arrhythmic events in the follow up period (table 3).

Discussion
The results of this study suggest that ventricular flutter initiated by programmed stimulation in patients without a confirmed history of rapid VT or VF had no clinical or prognostic significance when 24 hour monitoring did not show important ventricular arrhythmias and when patients did not have dizziness and syncope. In contrast, when these findings were associated with salvos of extrasystoles or with syncope mortality was increased.

The induction of sustained uniform VT < 270 beats/min was reported to have a high diagnostic value in patients with spontaneous VT.10 11 Two studies in symptom free survivors of acute myocardial infarction showed that inducible tachycardia predicted a significant risk of death or spontaneous tachycardia or fibrillation that was related to the cycle length of inducible VT.44 An event was more likely during the follow up if cycle length of the VT was 230 ms or more and the conclusions of both studies were that the induction of a ventricular flutter or fibrillation was of no clinical significance whereas the induction of

Table 2 Predictors of cardiac death (Cox regression analysis)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>p Value</td>
</tr>
<tr>
<td>Syncope</td>
<td>27</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>EF &lt; 40%</td>
<td>31</td>
<td>p &lt; 0.03</td>
</tr>
<tr>
<td>Holter grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVA-B</td>
<td>36</td>
<td>p &lt; 0.02</td>
</tr>
</tbody>
</table>

EF, left ventricular ejection fraction.

Table 3 Predictors of ventricular arrhythmic events (VT and VF) (Cox regression analysis)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>p Value</td>
</tr>
<tr>
<td>Syncope</td>
<td>27</td>
<td>&lt; 0.15</td>
</tr>
<tr>
<td>EF &lt; 40%</td>
<td>31</td>
<td>&lt; 0.01</td>
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<tr>
<td>Holter grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVA-B</td>
<td>36</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Sex F</td>
<td>7</td>
<td>&lt; 0.06</td>
</tr>
</tbody>
</table>

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In conclusion, the clinical significance of inducible ventricular flutter depended principally on the results of 24 hour Holter monitoring. In patients without significant ventricular arrhythmia on Holter monitoring, ventricular flutter initiated by stimulation seemed to be a non-specific finding and did not mandate antiarrhythmic therapy. In contrast, in patients with salvos of extrasystoles ventricular flutter was associated with a high risk of cardiac mortality and VT and required electrophysiologically guided antiarrhythmic therapy.

8 Kim SG, Felder SD, Fagura I, Johnston DR, Mercado AD, Fisher JD. Prognostic value of the changes in the mode of ventricular tachycardia induction during therapy with amiodarone or amiodarone and a class I antiarrhythmic agent. Am J Cardiol 1987;59:1314-8.
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