Ventricular Flutter Induced During Electrophysiologic Studies in Patients with Old Myocardial Infarction: Clinical and Electrophysiologic Predictors, and Prognostic Significance

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Significance of Induced Ventricular Flutter. Introduction: Induction of ventricular flutter during electrophysiologic (EP) studies (similar to that of ventricular fibrillation [VF]) often is viewed as a nonspecific response with limited prognostic significance. However, data supporting this dogma originate from patients without previously documented ventricular tachyarrhythmias. We examined the significance of ventricular flutter in patients with and without spontaneous ventricular arrhythmias.

Methods and Results: We conducted a cohort study of all patients with myocardial infarction (MI) undergoing EP studies at our institution. Of 344 consecutive patients, 181 had previously documented spontaneous sustained ventricular arrhythmias, 61 had suspected ventricular arrhythmias, and 102 had neither. Ventricular flutter was induced in 65 (19%) of the patients. Left ventricular ejection fraction was highest among patients with inducible VF (35 ± 13), lowest for patients with inducible sustained monomorphic ventricular tachycardia (SMVT; 27 ± 9), and intermediate for patients with inducible ventricular flutter (30 ± 10). Similarly, the coupling intervals needed to induce the arrhythmia were shortest for VF (200 ± 28 msec), intermediate for ventricular flutter (209 ± 27 msec), and longest for SMVT (230 ± 35 msec). During 5 ± 8 years of follow-up, the risk for ventricular tachycardia/VF was high for patients with SMVT and ventricular flutter and low for patients with inducible VF and noninducible patients (46%, 34%, 17%, and 14%, P < 0.005).

Conclusion: Patients with inducible ventricular flutter appear to be “intermediate” between patients with inducible VF and patients with SMVT in terms of clinical and electrophysiologic correlates. However, the prognostic value of inducible ventricular flutter is comparable to that of SMVT. (J Cardiovasc Electrophysiol, Vol. 14, pp. 913-919, September 2003)

ventricular flutter, sustained monomorphic ventricular tachycardia, myocardial infarction

Introduction

Ventricular flutter is a sustained monomorphic ventricular tachycardia (SMVT) with a very fast rate that approximates that of ventricular fibrillation (VF) (about 300 beats/min). Because of its fast heart rate, ventricular flutter has a characteristic sinusoidal morphology that makes the distinction between its QRS and T wave complexes difficult and often impossible. For the same reason, ventricular flutter is an unstable arrhythmia that quickly deteriorates to VF. Consequently, spontaneous ventricular flutter is rarely documented. In addition, data on the value of induced ventricular flutter in patients undergoing electrophysiologic (EP) studies are limited. Two studies suggested that induction of ventricular flutter by programmed ventricular stimulation has very limited value for predicting spontaneous arrhythmic events.1,2 In both studies, the positive predictive value was lower than the predictive value of inducible SMVT1,2 and as low3 or somewhat higher than the value of inducible VF.2 Because of these studies, ventricular flutter (similarly to VF) often has been considered a nonspecific result of programmed ventricular stimulation.3 These two studies, however, included only patients without documented spontaneous ventricular arrhythmias,1,2 a patient population with relatively low pretest probability for subsequent arrhythmic events. Consequently, it is not clear if the clinical significance of induced ventricular flutter in other patient populations should be regarded like that of SMVT or like that of VF. We conducted the present study to define the clinical and electrophysiologic predictors of inducible ventricular flutter, as well as its predictive value, in patients with and patients without a history of sustained ventricular arrhythmias.

Methods

Patient Population

This was a cohort study including all patients with previous myocardial infarction (MI) who underwent EP evaluation with programmed ventricular stimulation at our center between January 1989 and June 2002. The patients were classified into one of three categories based upon the indication for EP studies. (1) Patients with documented sustained ventricular arrhythmias. This group included all post-MI patients who survived a cardiac arrest due to ventricular tachycardia

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Manuscript received 14 February 2003; Accepted for publication 30 May 2003.
Definition of Ventricular Flutter

Patients with suspected ventricular arrhythmias. This group included all post-MI patients who underwent EP studies after a syncope that was considered sufficiently atypical for vasovagal syncope to raise the suspicion of arrhythmic syncope and therefore warranted performance of programmed ventricular stimulation. (3) Patients without documented or suspected sustained ventricular arrhythmias. This group included all post-MI patients with asymptomatic high-grade ventricular arrhythmias (nonsustained VT or multiple ventricular extrasystoles) and impaired left ventricular ejection fraction (LVEF <40%) who underwent EP studies for the purpose of risk stratification.4,5

Electrophysiologic Studies

All patients underwent single and double ventricular extrastimulation at two ventricular sites (right ventricular apex and outflow tract) and two basic cycle lengths (600 and 400 msec). The extrastimuli were decreased in 10-msec steps until ventricular refractoriness was reached. Then, repetition of double ventricular extrastimulation at the shortest interval that captured the ventricle was performed 10 times. Triple ventricular extrastimulation was performed if the protocol of double extrastimulation was negative. The protocol was discontinued prematurely if SMVT requiring DC shock for termination was induced. However, if SMVT was terminated by ventricular overdrive pacing or if ventricular flutter or VF was induced, the protocol was continued. Therefore, some patients had more than one arrhythmia induced (see later).

Definition of Ventricular Flutter

As in previous studies,1,2,6 ventricular flutter was defined as a sustained VT (requiring DC shock or ventricular overdrive pacing for termination) of monomorphic configuration and ventricular rate >260 beats/min (cycle length ≤230 msec). The designation of induced arrhythmias as "monomorphic" or "polymorphic" was made at the time of EP study (before this study was contemplated).

Therapy and Follow-Up

Despite the prevailing data suggesting that induction of ventricular flutter or VF was of limited prognostic significance in some patient subgroups,1,2,6 all patients with inducible sustained ventricular arrhythmias (including ventricular flutter and VF) received antiarrhythmic therapy, which until 1991 consisted of EP-guided antiarrhythmic therapy, which until 1991 consisted of EP-guided antiarrhythmic therapy. After 1991, patients with inducible sustained ventricular arrhythmias (regardless of their clinical presentation), as well as non-inducible patients presenting with cardiac arrest, underwent placement of an implantable cardioverter defibrillator (ICD). Thus, ICDs were implanted in 71% and 14% of patients with and without inducible ventricular arrhythmias, respectively. Follow-up was performed at our arrhythmia clinic at 3- to 6-month intervals.

Statistical Analysis

Binary variables were compared between groups with Fisher’s exact test, and other categorical variables were compared with the Chi-square test. Continuous variables normally distributed were compared by t-test or analysis of variance (ANOVA). Continuous variables without a normal distribution were analyzed by the Mann-Whitney U-test or Kruskal-Wallis H-test. The endpoints were (1) arrhythmia recurrence, defined as (a) sustained VT or VF documented electrocardiographically or by ICD-stored electrograms or (b) sudden cardiac death (defined as unexpected death occurring within 1 hour from the onset of symptoms or unwatched death during sleep in an ostensibly stable patient); and (2) arrhythmia recurrence or death from any cause. Follow-up was measured from the time of EP study to death or last follow-up. Survival curves were plotted using the Kaplan-Meier method and analyzed by the log rank test. Continuous variables were analyzed by Cox hazards analysis. Multiple pairwise comparisons were corrected by the Bonferroni method. Patients undergoing cardiac transplantation (4 patients) and patients lost to follow-up (11 patients) were censored from survival curves at the time of transplant or last follow-up, respectively. All tests were two sided, and P ≤ 0.05 was considered statistically significant. All analyses were performed using GB-Stat® software, version 6.5 (Dynamic Microsystems Inc., Silver Spring, MD, USA).

Result

The study cohort consisted of 344 consecutive patients with healed MI who underwent EP studies with programmed ventricular stimulation: 181 (53%) had documented spontaneous sustained ventricular arrhythmias (91 with and 90 without cardiac arrest); 61 (18%) had suspected ventricular arrhythmias (syncope of presumed arrhythmic origin); and 102 (30%) had neither documented nor suspected spontaneous sustained ventricular arrhythmias by the time the EP study was performed (Table 1). Patients who presented with cardiac arrest were younger and had higher LVEF than patients who presented with SMVT. In addition, because of selection bias (asymptomatic patients underwent EP studies only if they were relatively young and had a very low LVEF), patients without ventricular arrhythmias were the youngest and had the lowest LVEF (Table 1). Finally, reflecting the change in accepted indications for ICD placement (and therefore for performance of EP studies), patients without spontaneous sustained ventricular arrhythmias were studied at a later stage and therefore have shorter follow-up periods than patients with documented spontaneous VT/VF (Table 1).

Clinical and Electrophysiologic Predictors of Inducible Ventricular Flutter

Sixty-five (19%) of all post-MI patients undergoing EP studies had inducible ventricular flutter (Fig. 1). The ventricular rate during ventricular flutter was 285 ± 17 beats/min (range 270–350). Induction of ventricular flutter occurred with similar frequency among patients with documented spontaneous ventricular arrhythmias, those with suspected but no documented spontaneous ventricular arrhythmias, and those who had neither (P = 0.882, Table 1). Four (6%) of the patients with inducible flutter also had inducible VF, and 9 (14%) also had SMVT (rate 208 ± 28 beats/min) induced at the same EP study. These 13 patients were counted as “ventricular flutter patients” (see Discussion).

Patients with inducible ventricular flutter were more like patients with inducible VF than patients with inducible
Table 1

Characteristics of Patients According to the Indication for Electrophysiologic Study

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Documented Sustained Ventricular Arrhythmias</th>
<th>Suspected Arrhythmias</th>
<th>No Sustained Arrhythmias</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardiac Arrest</td>
<td>Sustained VT</td>
<td>Syncope</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td></td>
<td>No. of patients 91 90 61 102</td>
<td>67 ± 13</td>
<td>62 ± 11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age (years; ±SD) 64 ± 9 68 ± 9 7 ± 13 62 ± 11</td>
<td>81 (89%) 80 (89%) 31 (11%) 98 (95%)</td>
<td>0.000</td>
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<tr>
<td></td>
<td>Males (%) 81 (89%) 80 (89%) 51 (83%) 98 (95%)</td>
<td>0.32</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>LVEF 33 ± 12 29 ± 10 31 ± 11 27 ± 12</td>
<td>0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Noninducible SVA 21 (23%) 4 (4%) 28 (46%) 40 (39%)</td>
<td>0.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inducible SMVT 45 (49%) 74 (84%)</td>
<td>11 (18%) 33 (32%)</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inducible V-Flutter 17 (19%) 10 (11%)</td>
<td>17 (28%) 21 (21%)</td>
<td>0.082</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inducible VF 8 (9%) 2 (2%)</td>
<td>5 (8%) 8 (8%)</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Follow-up (months) 65 ± 42 56 ± 36</td>
<td>41 ± 33 33 ± 40</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

LVEF = left ventricular ejection fraction; SVA = sustained ventricular arrhythmia; SMVT = sustained monomorphic ventricular tachycardia; V-Flutter = ventricular flutter; VF = ventricular fibrillation; VT = ventricular tachycardia.

SMVT in terms of both clinical characteristics and electrophysiologic correlates. For example, patients with inducible ventricular flutter and patients with inducible VF were of similar age (P = 0.56), and both groups were younger than patients with inducible SMVT (P = 0.027). In addition, LVEF was significantly different among the groups with inducible arrhythmias (P < 0.001), but this finding was related to the lower LVEF of patients with inducible SMVT compared to patients with inducible VF (P = 0.005) or noninducible arrhythmias (P < 0.001). LVEF of patients with inducible ventricular flutter appeared to be “intermediate” and was not statistically different from LVEF of patients with inducible SMVT (P = 0.13) or patients with inducible VF (P = 0.09; Table 2). Finally, ventricular flutter was induced by more aggressive ventricular extrastimulation than SMVT. For example, the number of extrastimuli was greater (2.5 ± 0.5 vs 2.1 ± 0.7, P < 0.01) and the coupling interval inducing the arrhythmia was shorter (Table 2) than those inducing SMVT.

Figure 1. Top: Induction of sustained ventricular flutter with triple ventricular extrastimulation. The ventricular rate is 3,000/min. There is no isoelectric line, and it is difficult to distinguish QRS complexes from ST-T segments. The arrhythmia eventually was terminated with DC shock. Bottom: Spontaneous ventricular flutter recorded by an implanted ICD. The ventricular rate is 310 beats/min. The arrhythmia was terminated with a 31-J ICD shock.
Follow-Up Period

Mode of Induction

LVEF 27

Males (%) 149 (91%) 55 (85%) 23 (100%) 80 (86%) 0.077

Fig. 3).

mias (syncope), or no arrhythmias, respectively (P < 0.001, P < 0.001, and P = 0.015 for the coupling of the first, second, and third extrastimuli, respectively). In fact, the coupling intervals used to induce ventricular flutter were as short as the intervals that induced VF (P = 0.87, P = 0.28, and P = 0.021 for the coupling of the first, second, and third extrastimuli, respectively; Table 2).

Prognostic Significance of Inducible Ventricular Flutter

Only 11 patients (3%) were lost to follow-up. Follow-up was complete for 98% of patients with inducible ventricular flutter and 97% patients with SMVT (Table 2). The mean follow-up period for the study cohort was 5 ± 8 years. The follow-up period was significantly different between the groups (P = 0.013), mainly because of the shorter follow-up of patients without inducible arrhythmias (P = 0.004 and P = 0.023 for noninducible vs SMVT and VF, respectively). However, the follow-up period of the patients with inducible flutter was not significantly different from that of the other three groups (Table 2). During this follow-up period, the percentage of patients who died suddenly or had sustained VT or VF was as follows: 14% of patients without inducible sustained arrhythmias, 17% of patients with inducible VF, 34% of patients with inducible ventricular flutter, and 46% of patients with inducible SMVT (P < 0.001, Fig. 2).

The positive predictive value of inducible ventricular flutter for predicting arrhythmic events depended on the indication for EP studies. It was relatively high (41%) for patients undergoing EP studies following documentation of a sustained ventricular arrhythmia, intermediate (35%) for patients undergoing EP studies because of syncope, and relatively low (19%) for patients undergoing EP studies when they were asymptomatic (P = 0.09, Fig. 3). However, this was also true for inducible SMVT, which predicted arrhythmic events in 52%, 40%, and 24% of patients undergoing EP studies for documented arrhythmias, suspected arrhythmias (syncope), or no arrhythmias, respectively (P = 0.011, Fig. 3).

Kaplan-Meier survival curves are shown in Figure 4. The long-term risk for arrhythmic events (sudden death or documented sustained arrhythmias; Fig. 4A) for patients with inducible ventricular flutter was similar to that of patients with inducible SMVT (P = 0.22) and significantly higher than the risk for patients without inducible sustained arrhythmias (P = 0.02). Similar survival curves were obtained when “freedom from all-cause death or arrhythmic events” was considered (Fig. 4B).

Induction of ventricular flutter was an independent predictor of spontaneous VT, VF, or sudden death during follow-up after adjustment for baseline parameters such as age, LVEF, functional class, antiarrhythmic drugs received during follow-up, and revascularization procedure prior to EP study. The relative risk for spontaneous VT, VF, or sudden death for patients with inducible ventricular flutter was 2.2 (95%
Figure 3. Incidence of spontaneous arrhythmic events (sudden death or sustained ventricular tachycardia [VT]/fibrillation) according to the clinical presentation and the results of electrophysiologic study. Black bars = patients who presented with documented sustained ventricular arrhythmias. Hatched bars = patients who presented with suspected ventricular arrhythmias (syncope of presumed arrhythmic origin). White bars = patients who had neither documented nor suspected ventricular arrhythmias when EP study was performed (see text).

confidence interval [CI]: 1.2–4.1, P = 0.011). Induction of SMVT was a stronger independent predictor of spontaneous VT, VF, or sudden death (relative risk: 2.97, 95% CI: 1.8–4.92, P < 0.001). In contrast, the induction of VF was not predictive of arrhythmic events.

Among the 18 patients with inducible ventricular flutter who had one or more arrhythmias documented by ICD-stored electrograms during long-term follow-up, only 3 (17%) had ventricular arrhythmias that appeared to represent spontaneous ventricular flutter (that is, VT ≥270 beats/min that appeared to be monomorphic on the single lead recorded in the stored electrogram; Fig. 1). In fact, analysis of all spontaneous arrhythmias recorded during long-term follow-up among patients with inducible flutter and patients with inducible SMVT were of similar rate. This was true for the fastest of all their spontaneous arrhythmias recorded (219 ± 43 beats/min vs 207 ± 44 beats/min for patients with inducible ventricular flutter and inducible SMVT, P = 0.64) and for their slowest spontaneous arrhythmias recorded during long-term follow-up (184 ± 34 beats/min vs 168 ± 36 beats/min for patients with inducible flutter and inducible SMVT, P = 0.32). Neither the mode of induction of ventricular flutter (single or double vs triple ventricular extrastimulation) nor the coupling intervals inducing ventricular flutter correlated with occurrence of spontaneous ventricular arrhythmias.

**Discussion**

**Main Findings**

We found that ventricular flutter was induced in 19% of patients with healed MI undergoing programmed ventricular stimulation. Patients with inducible ventricular flutter have clinical characteristics (e.g., LVEF) and electrophysiologic correlates that more resemble those of patients with inducible VF than those of patients with inducible SMVT. Specifically, the number of ventricular extrastimuli and the coupling intervals needed to induce ventricular flutter are similar to those that induce VF. Nevertheless, the prognostic value of inducible ventricular flutter is comparable to that of SMVT. The positive predictive value of inducible ventricular flutter for predicting arrhythmic events depended on the indication for EP studies, but this was also true for inducible SMVT (Fig. 4). Finally, spontaneous ventricular flutter was rarely documented, and most patients with inducible flutter who eventually developed spontaneous arrhythmias had, in fact, spontaneous SMVT. In other words, the induction of ventricular flutter was a marker for the presence of an arrhythmic substrate and predicted spontaneous monomorphic ventricular arrhythmias but not necessarily flutter.

**What is Ventricular Flutter?**

The terms “tachycardia,” “flutter,” and “fibrillation” denote distinctive arrhythmias with well-defined mechanism...
when referring to atrial arrhythmias. Specifically, atrial flutter is a macroreentrant arrhythmia, whereas atrial tachycardia generally denotes smaller reentry circuits or ectopic rhythm. It is not at all clear, however, if a similar distinction can be made between ventricular flutter and ventricular tachycardia because, to our knowledge, there are no clinical or animal studies mapping ventricular flutter. Thus, it is possible that ventricular flutter merely represents a fast, but otherwise indistinguishable, monomorphic VT, especially when (as in all clinical studies of ventricular flutter, including the present one) the definition of “flutter” is based on ventricular rate. Indeed, although ventricular flutter and SMVT have different modes of induction (flutter is induced by more aggressive extrastimulation), our study suggests that these arrhythmias do not appear to differ in terms of prognostic significance. In this regard, our report differs from previous studies of ventricular flutter.1,2,6

Previous Studies

It has long been recognized that polymorphic ventricular arrhythmias (like VF) may be accidentally induced in patients at low risk for spontaneous arrhythmias and (as opposed to induced SMVT) may represent false-positive results.7 Subsequently, data from the large Australian post-MI studies first suggested that the ventricular rate, and not only the morphology of the arrhythmias induced in the laboratory, has prognostic significance.1,3,8,9 The Australian studies were especially valuable because they were prospective, and because antiarrhythmic drug therapy was withheld even in patients with inductive arrhythmias. Thus, the Australian studies provided data bordering on the “natural history” of patients with inductive tachyarrhythmias after MI. Dennis et al.8 and subsequently Bourke et al.1,3 reported that only monomorphic VT with a ventricular rate <260 beats/min had sufficient predictive value for future spontaneous arrhythmic events. In contrast, the predictive value of VT faster than 260 beats/min (even if monomorphic) was as low as that of VF.1,3,8 It should be noted, however, that these data were collected from patients without previous spontaneous arrhythmias who had a recent uncomplicated MI, and that only a small percentage of the patients in that series had a low LVEF.1,3,8 The low pretest risk of this low-risk patient population probably contributed to their findings.10 Nevertheless, the results of the Australian studies had a tremendous impact on physicians’ attitudes to inductive ventricular flutter. For example, both MADI-T (Multicenter Automatic Defibrillator Implantation Trial) and MUSTT (Multicenter Unsustained Tachycardia Trial), two landmark studies that evaluated the role of EP studies and ICD placement in the primary prevention of arrhythmic death after MI, excluded patients with inducible ventricular flutter (and not only patients with inducible VF) when the arrhythmia was induced by more than two extrastimuli.5,11 Of note, in our study, the number of extrastimuli used to induce ventricular flutter did not affect its value for predicting arrhythmic events.

Study Limitations

Our study was a retrospective analysis of a prospectively collected database. The prognostic value of inducible ventricular flutter appeared to be intermediate (significantly higher than that of VF and nonsignificantly lower than that of SMVT) in all the survival curves. This could be related to the fact that distinguishing a very fast monomorphic flutter from a rapid polymorphic VT is not always straightforward. Thus, our flutter population could include some patients who had inducible polymorphic VT, as well as some patients with truly monomorphic flutter. It also is possible that with a larger patient population, the differences between inducible flutter and SMVT would become statistically significant. Nevertheless, the arrhythmic risk for patients with inducible flutter, regardless of their clinical presentation, appears to be sufficiently high to warrant ICD placement. In addition, 20% of our patients with inducible ventricular flutter had additional sustained arrhythmias induced at the same study. The size of the patient population does not allow for comparison of patients who had inducible flutter as their only arrhythmia to those who had more than one arrhythmia induced. It could be argued that the relatively high predictive value for inducible ventricular flutter found in our study merely reflects the other arrhythmias induced and that we should have limited our analysis to patients who only had inducible flutter. It should be noted, however, that a recent study by the Mayo Clinic (thus far published only in abstract form12), did exactly that. In that case control study, Gurevitz et al. compared 74 patients who had inducible ventricular flutter as their sole arrhythmia to patients who only had SMVT (patients who had more than one arrhythmia induced in the laboratory were excluded). Similar to our study, the Mayo Clinic also reported that inducible ventricular flutter had a predictive value that was as high as that of inducible SMVT.12

Clinical Implications

The prevailing literature reports a poor predictive value for inducible ventricular flutter.1,3,5,8,9,11 Our study, as well as the preliminary report by Gurevitz et al.12 and a recent evaluation of the predictive value of inducible ventricular flutter in post-MI patients with syncope,13 all suggest that the prognostic value of inducible ventricular flutter is not necessarily inferior to that of SMVT. In fact, it remains to be seen if ventricular flutter is fundamentally different from SMVT or merely faster.

References

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