Low recurrence of syncope in patients with inducible sustained ventricular tachyarrhythmias treated with an implantable cardioverter-defibrillator

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Aims To determine the effectiveness of the implantable cardioverter defibrillator (ICD) in preventing recurrence of syncope in patients with structural heart disease, previously unexplained syncope and inducible ventricular arrhythmias.

Methods Thirty-eight patients with syncope, structural heart disease and inducible arrhythmias had an ICD implanted. All ICDs delivered antitachycardia pacing and shocks of adjusted energy. Detection and therapy were programmed according to uniform criteria.

Results The mean age of the patients was 63 ± 11 years and most of them were male (36/38). After a mean follow-up of 28 ± 15 (4–61) months, six patients died and one underwent heart transplantation. Syncope recurred in three patients, but in none of them was it caused by an arrhythmic event. In 18 patients, 113 episodes of ventricular tachycardia/ventricular fibrillation were detected and appropriately treated by the ICD. The mean time from implant until first appropriate therapy was 18 ± 14 months. The actuarial probability of receiving appropriate therapy was 20% and 42% at 12 and 24 months, respectively.

Conclusions In patients with unexplained syncope, structural heart disease and inducible arrhythmias, ICD prevents syncope associated with arrhythmic events. Frequent effective use of antitachycardia pacing and shocks of adjusted energy seem essential to this aim.

Key Words: Implantable cardioverter defibrillator, syncope, ventricular arrhythmias.

Introduction

The ICD was initially introduced as a therapeutic tool to prevent sudden death caused by ventricular tachyarrhythmias\[1,2\]. It has proven its efficacy in the secondary prevention of sudden death\[3\] and also in the primary prevention of sudden death in specific subgroups\[4,5\]. The implantation of an ICD in patients with unexplained syncope, structural heart disease and inducible sustained ventricular tachycardia or ventricular fibrillation is an accepted indication\[6\]. This is based on the rationale that syncope may have been caused by a non-sustained arrhythmia which may be the harbinger of sudden death. Therefore, induction of a ventricular arrhythmia is considered as a specific finding that deserves therapeutic action\[7–9\]. These patients seem to have a similar profile to those with documented ventricular tachycardia/ventricular fibrillation\[9,10\].

Syncope is known to be associated with arrhythmic episodes appropriately treated by ICDs. The occurrence of syncope or pre-syncope associated with shock therapy was considered as a marker of appropriate therapy in early devices without electrogram storage. Episodes of ventricular tachycardia that cause loss of consciousness may seriously threaten personal and public safety\[11–13\]. Therefore, the prevention of syncopal episodes during arrhythmia recurrence is important. Currently, the so-called third generation ICDs provide antitachycardia pacing and shocks of adjusted energy. The incidence of syncope in patients treated with this type of ICD is not known.

The objective of this study is to assess the recurrence of syncope after ICD implantation in a group of patients with structural heart disease, unexplained syncope of unknown origin and inducible ventricular tachycardia/ventricular fibrillation at electrophysiological study.
Methods

Patient population

From March 1994 until December 1999, 531 patients were referred to our unit for electrophysiological study for unexplained syncope. Structural heart disease was present in 182 patients. Of these, electrophysiological study was normal in 98 patients. Based on the results of the electrophysiological study, 41 patients received a pacemaker. In 43 patients ventricular stimulation elicited sustained ventricular tachycardia/ventricular fibrillation, four of them received antiarrhythmic therapy guided by non-inducibility after a second electrophysiological study, one patient underwent successful radiofrequency ablation and 38 received an ICD with antitachycardia pacing, adjusted energy shocks and electrogram storage capabilities. These 38 patients formed the study group. In these patients ventricular tachycardia, although not documented, remained as the plausible cause of their syncope after ruling out structural causes such as left ventricular outflow tract obstruction, or electrical diseases such as long QT or Brugada syndrome.

Electrophysiological study

Electrophysiological study was performed in a non-sedated postabsorbic state. No other antiarrhythmic drugs were present at the time of the electrophysiological study. Stimulation was delivered from the right ventricular apex with up to three extrastimuli on sinus rhythm and on basic eight-beat trains at 600, 500 and 430 ms. Coupling intervals were progressively shortened until induction was achieved, or refractoriness was encountered. Inducibility of ventricular arrhythmias was considered to be present when a ventricular rhythm faster than 100 beats.min⁻¹ was sustained for more than 30 s or required immediate termination due to severe haemodynamic compromise. This definition of inducibility comprises both regular monomorphic rhythms along with fast, irregular tachycardias and ventricular fibrillation.

ICD implantation

All devices were implanted under deep sedation in the subpectoral position through transvenous subclavian puncture or dissection of the cephalic vein.

ICD programming

Devices were systematically programmed with two zones of heart rate for detection and therapy. The lower heart rate zone (ventricular tachycardia zone) was set with a cut-off rate between 180–200 beats.min⁻¹ or 10 beats.min⁻¹ below the rate of the induced monomorphic tachycardia. In this zone, additional detection criteria of ‘sudden onset’ (9%) and stability (40 ms) were enabled. If the tachycardia persisted longer than 1 min inhibition of therapy by these additional detection criteria was stopped. The efficacy of this programming has been previously reported\cite{14}. In the ventricular tachycardia zone, the antitachycardia pacing algorithm was also empirically programmed. It comprised two schemes of antitachycardia therapy. The first scheme (antitachycardia pacing — ATP) ATP1 used a maximum of eight bursts, consisting of sequences of ventricular impulses initiated by four in the first burst up to a maximum of eight (with a step increment of one impulse in each burst), starting at 81% of the tachycardia cycle length, and with a decrement of 4 ms in the coupling interval from burst to burst (minimal interval of 200 ms). The second scheme (ATP2) was delivered if tachycardia was not terminated by ATP1. It consisted of a maximum of eight ramps with the same number of ventricular impulses (from four to eight) and the same decrement in coupling interval (4 ms) as in ATP1, but with a decrement of 4 ms between the impulses within the ramp and a decrement of 6 ms in the initial cycle length from one ramp to the next. The antitachycardia pacing attempts were delivered until tachycardia was reverted, or to sustained duration of the tachycardia of up to 60–120 s. If antitachycardia pacing was unsuccessful, low energy cardioversion was attempted by successive shocks of progressively increasing energy. The upper heart rate zone was established for ventricular fibrillation or fast ventricular tachycardia above a cut-off rate of 200–210 beats.min⁻¹. In this zone, therapy consisted only of shocks of increasing energy. The energy for shocks was programmed if the energy was considered effective in defibrillating at implant. Advantage was taken of an additional third heart rate window for monitoring or therapeutic purposes in individual cases.

Follow-up

The patients were seen at 1 and 3 months after discharge and then every 6 months. Additional visits, off-the-schedule, were recommended if there were symptoms presumably related to rhythm disorders such as palpitations, syncope or discharges from the ICD.

Follow-up assessment comprised a brief clinical interview, including specific questions on the occurrence of syncope. A full interrogation of the device in order to determine the status of the ICD generator and leads was done. Afterwards, retrieval of available information from the ICD memory, on detection and therapy of tachycardia episodes, was performed. This information was set aside in floppy disks, if available, for later review.

Review and interpretation of stored data

A systematic and complete review of all the episodes detected during follow-up in these patients was done by
two observers independently. If there was a disagree-
ment on the character of the episode or outcome of the
therapy a consensus was reached. For every episode,
information on the parameters of detection and therapy
was collected as follows.

Detection
Date and time of the episode, onset and stability when
available. The diagnosis of the episode was established
bearing in mind the following categories:

Ventricular tachycardia was diagnosed in cases of fast
monomorphic rhythms falling either in the ventricular
tachycardia or ventricular fibrillation zone, following
analysis of changes in the stored electrograms with
respect to baseline morphology and in response to
antitachycardia therapy.

Ventricular fibrillation was diagnosed when the rhythm
was detected in the ventricular fibrillation zone and was
unstable in cycle length and morphology, unless spuri-
ous detection due to electrical noise or electromagnetic
interference could account for the episode.

Supraventricular tachycardia was suggested by fast
rhythms of gradual onset or irregular RR intervals in
the case of atrial fibrillation, without changes in the
morphology electrograms.

Electrical noise was recognized by the characteristic
features of stored electrograms.

Therapy
The mode of delivered therapy (shocks or antitachy-
cardia pacing) was recorded for every episode as well as
and the number of therapeutic attempts of each mode.
Combining the diagnosis and therapy a judgement was
made on the appropriateness and effectiveness of
therapy.

Inappropriate therapy was declared if antitachycardia
pacing or shocks were given for a rhythm other than
ventricular tachycardia or ventricular fibrillation. Appropriate therapy was divided into effective or ineffective, according to the success in converting the tachycardia.

Antiarrhythmic drug therapy
Antiarrhythmic drug therapy was prescribed either
before or after the implant by the attending physicians.
During follow-up, frequent recurrence of ventricular
tachycardia or the intention to control other arrhyth-
mias such as atrial fibrillation caused initiation of
antiarrhythmic drug therapy.

Statistical methods
Numerical variables were expressed as mean ± standard
deviation. The survival curves to illustrate actuarial
probability of events during follow-up were computed
using the product-limit (Kaplan–Meier) method. The
length of follow-up for survival analysis was established
censoring observations at the time of the last visit, death
or heart transplantation when this was the case.

Results

Patient characteristics
The mean age of patients was 63 ± 11 years. Most
patients were male (36/38; 95%). The distribution of
types of structural heart disease is shown in Table 1.
Syncopal episodes before referral had occurred on more
than one occasion in 24 (63%) patients. The rhythm at
the time of electrophysiological study was atrial fibril-
lation in five (13%) patients. The mean ejection fraction
was 37 ± 13. In 29 (76%) patients ejection fraction was
less than 0.4.

Electrophysiological study
Electrophysiological study was performed without com-
plications in all cases. Details on the type and mode of
induction of ventricular tachycardias is shown in
Table 2. In eight of the 31 patients with inducible
monomorphic ventricular tachycardia more than one
morphology was observed. The mean cycle length of
the tachycardias was 256 ± 51.4 ms. The mode of

Table 1 Type of structural heart disease

<table>
<thead>
<tr>
<th>Absolute number</th>
<th>Percent from total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>26</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>5</td>
</tr>
<tr>
<td>HOCM</td>
<td>4</td>
</tr>
<tr>
<td>ARVD</td>
<td>1</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
</tr>
</tbody>
</table>

HOCM=hypertrophic cardiomyopathy; ARVD=arrhythmogenic right ventricular dysplasia.

Table 2 Electrophysiological study. Mode and type of induction of ventricular tachycardia

<table>
<thead>
<tr>
<th>SMVT n=31</th>
<th>PVT/VF n=7</th>
<th>Total n=38</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Extrastimulus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2 Extrastimuli</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>3 Extrastimuli</td>
<td>18</td>
<td>4</td>
</tr>
</tbody>
</table>

SMVT=sustained monomorphic ventricular tachycardia; PVT/ VF=polymorphic ventricular tachycardia/ventricular fibrillation.
termination of the tachycardia at the electrophysiological study was external cardioversion in 21/38 and overdrive pacing in 17/38.

Follow-up

Mean follow-up duration was 28 ± 15 (4–61) months. During this time six patients died of non-arrhythmic causes. Two of them died of malignant neoplasies, another patient died of sepsis of urinary origin and the remaining three patients died because of end stage heart failure. Heart transplantation was performed in one case 38 months after ICD implantation.

Three patients suffered syncopal episodes during follow-up. In none of them were these episodes related to tachycardia, as demonstrated by the absence of coincident detected episodes by the ICD. Evidence for this mechanism was suggested by electrocardiographic monitoring during an episode. A second patient had frequent drop attacks because of transient cerebrovascular ischaemia. In these two patients the possibility of a slow ventricular tachycardia as the cause of syncope was excluded by the addition of a monitoring window at a low heart rate cutoff of 140 beats min⁻¹. The third patient suffered frequent syncopal episodes with prodromal vasovagal symptoms and syncope was positively reproduced by tilt test. None of these patients ever presented sustained or non-sustained ventricular tachycardia/ventricular fibrillation detected by the ICD during follow-up.

Arrhythmia recurrences

A third heart rate monitoring window was enabled in six patients at some time during follow-up. In four of them it was used to investigate the cause of palpitations and disclosed supraventricular tachycardia. In the other two it was used to rule out slow ventricular tachycardia as the cause for syncope, as previously mentioned.

Table 3 Detection and treatment of arrhythmias by ICDs during follow-up

<table>
<thead>
<tr>
<th>Diagnosis of the episode</th>
<th>No. of episodes</th>
<th>No. of patients (% from total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT/VF</td>
<td>278</td>
<td>22 (58)</td>
</tr>
<tr>
<td>Supraventricular rhythm</td>
<td>193</td>
<td>17 (45)</td>
</tr>
<tr>
<td>Electrical noise</td>
<td>7</td>
<td>4 (10)</td>
</tr>
<tr>
<td>VT/VF appropriately treated</td>
<td>113</td>
<td>17 (45)</td>
</tr>
</tbody>
</table>

Mode of therapy

<table>
<thead>
<tr>
<th>ATP</th>
<th>No. (percent) successfully terminated</th>
</tr>
</thead>
<tbody>
<tr>
<td>51</td>
<td>48 (94)</td>
</tr>
<tr>
<td>52</td>
<td>50 (96)</td>
</tr>
<tr>
<td>10</td>
<td>8 (80)</td>
</tr>
</tbody>
</table>

No. of episodes: 474
No. of patients: 28 (74)

Table 2 Detection and treatment of ventricular tachycardia/ventricular fibrillation by ICDs during follow-up

- The average programmed detection rate for the ‘ventricular tachycardia zone’ was 173-4 ± 12 beats min⁻¹ (150–200) and for the ‘ventricular fibrillation zone’ it was 200-8 ± 7-8 beats min⁻¹ (190–210). The figures concerning the number of detected episodes grouped by diagnostic categories and mode of therapy delivered by the ICDs are shown in Table 3. The difference between the number of detected episodes of ventricular tachycardia/ventricular fibrillation (278) and the number appropriately treated by the ICD (113), namely 165 episodes, corresponded to runs of ventricular tachycardia/ventricular fibrillation which did not last long enough to require therapy. These non-sustained episodes were found in 14 patients, of whom all but three required appropriate therapy on other occasions. Most of these non-sustained episodes (126/165) were monomorphic ventricular tachycardia, although 60 of 126 were fast enough to fall in the ventricular fibrillation detection zone. Some episodes (39/165) corresponded to self-limited polymorphic ventricular tachycardia. The average number of shocks per episode when at least one shock was delivered was 1-15 ± 0-6. The mean energy of discharge for effective shocks was 20-9 ± 8-49 Joule. The mean number of antitachycardia pacing bursts in episodes successfully treated by antitachycardia pacing was 1-85 ± 1-7. Inappropriate antitachycardia pacing was delivered for 22 episodes in 10 patients. Acceleration due to antitachycardia pacing was observed in 7/113 episodes. Inappropriate shocks were administrated for four episodes in three patients. Evidence of ventricular tachycardia undetected by the ICD was found in only one patient who presented at the emergency room with a slow ventricular tachycardia (150 beats min⁻¹), below
the detection heart rate cutoff (180 beats \cdot \text{min}^{-1}). This patient underwent successful radiofrequency ablation during subsequent hospital admission.

The mean interval of time from implant until first appropriate therapy was $18.7 \pm 14.5$ months. The actuarial probability of receiving appropriate therapy was 20% and 42% after 12 and 24 months, respectively. (Fig. 1)

**Antiarrhythmic drugs**

Six patients were on amiodarone at the time of electrophysiological study because of previous documentation of non-sustained ventricular tachycardia and another one patient because of a prior history of atrial flutter. In another six, the treatment was added because of documentation of ventricular tachycardia by the ICD during follow-up. In the remaining 12 patients, antiarrhythmic drug therapy was added shortly after ICD implantation, before the first outpatient follow-up. This was done mostly by attending physicians at hospital discharge after ICD implantation. Two patients who had amiodarone started during follow-up developed thyroid analytical disorders and so the drug had to be withheld. In one patient mexilene was added to amiodarone because of frequent recurrences of ventricular arrhythmias. Two others received sotalol, which achieved complete suppression of arrhythmias for more than 1 year in one of the two. In summary, at the time of the last follow-up, 20 patients were receiving antiarrhythmic therapy, as a back-up to ICD therapy.

**Discussion**

**Syncope recurrence**

The most remarkable findings in our study is that patients who present with syncope and in whom ventricular tachycardia can be induced have a high probability of receiving appropriate therapy from an ICD. Despite the high frequency of recurrent ventricular tachycardia, recurrent syncope is avoided presumably due to the rapid delivery of effective ICD therapy. Although specific references to the rate of recurrence of syncope in ICD recipients are scarce\cite{15-18}, data from other authors suggest a higher incidence of syncope as compared to our patients. The main reason to explain this difference is the improvement in the detection and therapy in late generation ICDs. Bänisch et al. reported an actuarial incidence of syncope in the recipients of ICDs of 15% at 2 years. Their population included 52% of patients with ICDs that did not allow antitachycardia therapy and discharges were initially adjusted to maximum energy\cite{16,18}. Kou et al. found a 9% recurrence of syncope at a mean follow-up of 16 months and 16% at 35 months, respectively, in a series of 180 patients who received an ICD after aborted sudden death or a history of syncope/pre-syncope and documented ventricular tachycardia. In all of these reports, high energy shocks were the only or predominant mode of therapy. Our therapeutic approach shows that a sizeable portion of ventricular tachycardia episodes could be successfully treated by antitachycardia pacing alone (48/113). Furthermore, failure of antitachycardia pacing or
acceleration secondary to antitachycardia pacing was infrequent. Back-up shock therapy was necessary in only 10/113 episodes (8.8%). In our series, patients suffered no arrhythmic episodes and no recurrences of syncope were due to arrhythmic events. This suggests that previous syncopal episodes were probably misclassified as being of arrhythmic origin in spite of inducibility at the electrophysiological study. This observation, along with the strong need for appropriate antiarrhythmic therapy for the whole series, illustrates how adequate sensitivity has to be gained at the expense of losing some specificity.

The actuarial probability of arrhythmia recurrence, as detected by the ICD, is similar in our patients to that in studies that found a higher incidence of syncope. This supports our view, that our results of absence of arrhythmic syncope after ICD implantation compared with a previously reported incidence of 10–15%, should be put down to a better treatment of arrhythmias by third generation devices rather than significant differences in ICD-recipient populations.

**Antitachycardia therapy**

Antitachycardia pacing is a useful tool for terminating monomorphic reentrant tachycardia. An important advantage for the tolerability of this therapy is that it can be promptly delivered, since charging the capacitors for shock therapy can be avoided. Furthermore, it avoids the discomfort of the shock. Our practice, of systematically enabling antitachycardia pacing, is in line with previous reports on the efficacy of antitachycardia pacing independent from clinical presentation or induced tachycardia. Additional support for this attitude in our patients is given by the efficacy of this therapy during follow-up. As shown in Table 3, antitachycardia pacing was the only necessary therapy to terminate 48 out of 113 episodes of ventricular tachycardia (42.4%), and only in 10/113 was antitachycardia pacing (8.8%) ineffective and had to be followed by shocks. A drawback of this therapy is that tachycardia acceleration may happen as a result of antitachycardia pacing. Several mechanisms for this phenomenon have been described. The incidence of this event is variable and unpredictable. Our results of efficacy and acceleration in response to antitachycardia pacing agree well with other previous recent reports. Nonetheless, avoiding treating very fast tachycardias with antitachycardia pacing and limiting the aggressiveness of the pacing protocol seem advisable measures.

**Shock therapy**

The time necessary for the ICD to charge its capacitors before a shock means a delay in delivering therapy once the detection criteria have been met. During that time the patient is suffering the adverse consequences of the ventricular arrhythmia. A shortening of this delay can only be achieved by programming shocks of lower, adjusted, energy and improvement of ICD technology. Major breakthroughs have been made in the reduction of the threshold for effective defibrillation, such as improved defibrillation waveforms, non-thoracotomy leads, and the use of the pulse generator case as the anode (hot can devices). All our patients profited from these advantages, and so the low energy charge of effective shocks mentioned in the results may explain the successful prevention of arrhythmic syncope.

**Limitations of the study**

The patients in this study include only those who presented with syncope, had structural heart disease and inducible arrhythmia. Therefore, conclusions made about these patients cannot be readily extended to the whole population of patients with ICD. However, some features in our patients, such as the depressed ejection fraction, the presence of structural heart disease, syncope as the presenting symptom and the high incidence of arrhythmia recurrence during follow-up, mean that our patients were suitable for testing whether ICD implantation was effective in preventing arrhythmic syncope.

The small size of the study group, however, means that our figures about incidence of events (recurrence of syncope and need of therapy) are not as reliable as those from a larger population. However, the main message of this article, namely the absence of recurrence of arrhythmic syncope in ICD recipients, contrasts enough sharply with previously reported data to support our conclusions.

**Implications of the study**

Syncope consists of a sudden loss of consciousness that abruptly prevents an individual from maintaining postural tone and effectively interacting with the environment. The obvious consequences of this untoward and unpredictable situation can be a dangerous fall or a fatal crash while driving a motor vehicle. Therefore, patients at risk of having a syncope suffer from restrictions in their lifestyle, either imposed by themselves or by law, in order to preserve personal and public safety. In this regard, current restrictions on activities, such as driving, would no longer be valid for patients receiving third generation ICDs.

**References**


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