Benefits of treatment with implantable cardioverter-defibrillators in patients with stable ventricular tachycardia without cardiac arrest

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Abstract

Background—The availability of implantable cardioverter-defibrillators (ICD) that are capable of antitachycardia pacing may lead to an increased use of ICDs in patients with haemodynamically tolerated ventricular tachycardia without a history of cardiac arrest. The frequency of potentially life-threatening fast ventricular tachycardias (cycle length < 250 ms) was investigated in patients who had a third generation ICD with endocardial leads implanted because they had haemodynamically tolerated ventricular tachycardia without a history of cardiac arrest.

Methods—Between January 1990 and October 1993, 50 patients (age (mean (SD)) 60 (11); ejection fraction 39 (16%); 82% with coronary artery disease and 8% with dilated cardiomyopathy) with haemodynamically tolerated ventricular tachycardia (cycle length (mean (SD)) 348 (60) ms; range 250–500 ms) and without a history of cardiac arrest were treated with third generation ICDs that were capable of antitachycardia pacing. Fast ventricular tachycardia had been induced in 14 (28%) during baseline electrophysiological study. The benefit of ICD treatment was estimated as the difference between total mortality and the occurrence of fast ventricular tachycardia that would have been fatal if it had not been terminated.

Results—During follow up of 17 (12) months, 33 patients (66%) had a total of 3861 episodes of ventricular tachycardia. 91% of these episodes were terminated by antitachycardia pacing. 11 patients (22%) had episodes of potentially life-threatening fast ventricular tachycardia and 3 of these also had inducible fast ventricular tachycardia. One patient died suddenly 27 months after implantation. The difference between survival without fast ventricular tachycardia and total mortality was 9%, 12%, 27%, and 27% at 6, 12, 18, and 24 months, respectively.

Conclusions—About a fifth of patients who had been given an ICD to treat haemodynamically tolerated ventricular tachycardia and who had no history of cardiac arrest experienced fast ventricular tachycardia during follow up requir-

ing immediate cardioversion. Prospective studies are needed to investigate whether the prognosis of patients with a history of haemodynamically tolerated ventricular tachycardia without cardiac arrest is improved by ICD therapy.

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Implantable cardioverter-defibrillators (ICD) are widely used to prevent recurrent sudden cardiac death. In several studies the incidence of recurrent sudden death was reported to be remarkably low in patients with ICDs.¹⁻³ Despite the lack of controlled trials implantation of an automatic cardioverter-defibrillator is now standard treatment for selected patients⁴⁻⁶ especially survivors of cardiac arrest.⁷ In an earlier study we showed a substantial benefit from implantation of an automatic cardioverter-defibrillator in patients with refractory ventricular tachyarrhythmia.⁸ Most of these patients, however, had ventricular fibrillation or ventricular tachycardia that was not haemodynamically tolerated.

Recently, disappointing results with antiarrhythmic drugs⁹⁻¹¹ and the introduction of automatic cardioverter-defibrillators with antitachycardia pacing modes have promoted the use of implantable cardioverter-defibrillators in patients with stable ventricular tachycardias without a history of cardiac arrest. This study was performed to analyse the potential impact of implantation of a third generation automatic cardioverter-defibrillator on mortality in patients with stable, haemodynamically tolerated ventricular tachycardia without a history of cardiac arrest.

Patients and methods

PATIENTS

We studied 50 consecutive patients with refractory, haemodynamically tolerated ventricular tachycardia without a history of cardiac arrest who had implantation of a third generation automatic defibrillator with endocardial defibrillation leads between January 1990 and October 1993 (table 1). A haemodynamically tolerated and stable ventricular tachycardia was defined as a ventricular

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Table 1 Characteristics of patients

Characteristics	Value (mean (SD)) or %
No. of patients	50
Age (y)	60 (11)
M/F (%)	86/14
Underlying disease (%):	
Coronary artery disease	82
Dilated cardiomyopathy	8
ARVC	8
Valvar heart disease	2
Ejection fraction (%)	39 (16)
NYHA class	2.3 (0.6)
VT episodes before ICD	12 (22)
Cycle length of spontaneous VT (ms)	348 (60)
VT inducible at EP study (%)	92
Fast VT inducible at EP study (%)	28
Cycle length of induced VT (ms)	298 (65)
Antiarrhythmic drugs tested before ICD	3.1 (1.6)

EP, electrophysiological; ICD, implantable cardioverter-defibrillator; VT, ventricular tachycardia; ARVC, arrhythmogenic right ventricular cardiomyopathy.

tachycardia not leading to syncope or loss of consciousness during the time taken to obtain medical attention. These tachycardias were terminated either by drugs, overdrive pacing, or cardioversion under anaesthesia. Cardiac arrest was assumed to have occurred if emergency cardioversion, defibrillation, or resuscitation was necessary to restore circulation.

There were 43 men and seven women (mean (SD) age 60 (11) years). Coronary artery disease was present in 41 patients, dilated cardiomyopathy in four, arrhythmogenic right ventricular cardiomyopathy in four, and valvar heart disease in one. The mean (SD) left ventricular ejection fraction was 39 (16)%. At the time of implantation no patient was in New York Heart Association functional class IV; the mean (SD) functional class was 2.3 (0.6).

All patients had a history of documented sustained (defined as a ventricular tachycardia lasting > 30s) haemodynamically tolerated ventricular tachycardia and none of them had required resuscitation. The mean (SD) cycle length of the spontaneous ventricular tachycardia was 348 (60) ms (range 250–500 ms). Median interval between the first spontaneous ventricular tachycardia and implantation of the device was 3.8 months (0.4–72.5 months, mean 13.7 months). Eleven patients had had only one episode of ventricular tachycardia before implantation of the device.

All patients underwent a drug free electrophysiological study. In four patients no sustained ventricular tachycardia (defined as a ventricular tachycardia lasting > 30s or requiring premature termination because of haemodynamic compromise) was inducible with up to three extrastimuli. These patients were regarded as candidates for implantation of a defibrillator. In 46 patients, a sustained ventricular tachycardia could be induced. Mean cycle length of the induced ventricular tachycardias was 298 (65) ms. In 14 patients fast ventricular tachycardias (defined as a ventricular tachycardia with a cycle length < 250 ms) were induced. Before the decision for implantation of an implantable cardioverter-defibrillator was made, a mean of 3.1 (1.6) antiarrhythmic drugs were tested during serial

electrophysiological studies. Patients were regarded as candidates for implantation of defibrillators if ventricular tachycardia continued to be inducible despite treatment with class III antiarrhythmic drugs or if arrhythmia recurred spontaneously while they were taking an antiarrhythmic drug predicted to be effective in prevention of arrhythmia recurrences. Written informed consent was obtained from all patients.

IMPLANTATION TECHNIQUE

A non-thoracotomy approach was used in all patients. The electrode system used included a transvenous lead-subcutaneous patch system in 32 patients and a transvenous lead system in 18 patients (Cardiac Pacemakers Inc (CPI) Endotak or Medtronic Transvene). The devices used included the CPI Ventak PRx in 14 patients, the CPI Ventak PRxII in 11, the Ventitrex Cadence V-100 in two, the Medtronic PCD 7217B in 17, and the Medtronic PCD 7219D in six. Because all the devices used can store the intracardiac electrograms ($n = 19$) or RR intervals before and after the delivery of therapy ($n = 31$), the treated tachycardias could be classified.

ANTIARRHYTHMIC DRUG THERAPY

In 38 patients with ventricular tachycardia that was drug refractory, all class I or III antiarrhythmic agents were stopped immediately after we decided to implant an ICD. We waited for ≥ 5 half lives of the last antiarrhythmic drug before an ICD was implanted. In patients who were taking amiodarone before implantation, a drug-free period of ≥ 10 days was required. Class I or III antiarrhythmic medication was continued to suppress frequent ventricular tachycardia in eight patients, to suppress supraventricular tachycardia that could lead to inappropriate ICD discharges in one, and to prolong tachycardia cycle length to allow antitachycardia pacing for termination of the tachycardia in three. In addition, 18 patients were treated with β blockers or digitalis to prolong atrioventricular conduction. During follow up, an antiarrhythmic regimen was changed only if frequent ventricular tachycardia could not be terminated by antitachycardia pacing or if a supraventricular tachycardia was detected.

FOLLOW UP

All patients were followed up in the pacemaker clinic of our hospital every two months. They were instructed to phone the clinic in the event of a device discharge or syncope. Treated tachycardias were classified independently by two cardiologists. In patients with CPI Ventak PRxII devices all treated tachycardias were classified according to electrograms recorded from the defibrillation leads. In all patients with a Ventitrex Cadence V-100 or Medtronic PCD 7219D device treated tachycardias were classified according to the electrograms recorded from the sensing leads. In patients with devices that could not store electrograms (CPI Ventak PRx and Medtronic PCD 7217B) tachycardias occurring

out of the hospital were classified according to the cycle lengths recorded during treated episodes. Tachycardias were classified as VT/VF if the cycle length was < 290 ms or if the RR intervals were regular and the mean cycle length was significantly shorter than the programmed detection interval. All other treatments were classified as inappropriate.

We used the following end points: perioperative mortality (defined as death from any cause within 30 days after operation), sudden death (defined as either death within 1 h after the onset of initial symptoms or unwitnessed death), cardiac death, and total death. Recorded non-fatal events included ventricular tachyarrhythmias (of any rate) and fast ventricular tachyarrhythmias, arbitrarily defined as ventricular tachyarrhythmias with a cycle length < 250 ms before the first treatment by the device. In addition, the tachycardia cycle length had to be more than 50 ms shorter than the spontaneous tachycardia leading to implantation of the device. Because the only cycle lengths used to calculate the initial rate were those that occurred before the first treatment with the device, slow tachycardias that were accelerated by antitachycardia pacing were excluded from the analysis. Because there is evidence that surgery exacerbates ventricular tachyarrhythmias,^{12,13} episodes occurring within seven days after operation were excluded from further analysis. Beyond this period, implantation of cardioverter defibrillators by itself does not exacerbate ventricular tachyarrhythmias.¹²

We estimated the benefit of implantation of an automatic defibrillator by calculating the difference between total mortality and the occurrence of fast ventricular tachyarrhythmias, which we assumed would have been fatal without termination by the implanted defibrillator.

STATISTICAL METHODS

Mean, standard deviation, and range were used as indices of dispersion of the values observed. The log rank test was used to compare survival variables. A two-tailed probability value of < 0.05 was regarded as significant. Statistical analysis was performed with the SPSS for Windows program package (version 5.01) on an IBM AT computer.

Results

OPERATIVE RESULTS

During implantation we determined the defibrillation threshold (defined as the minimal energy required for termination of

induced ventricular fibrillation) by reducing the defibrillation energy in steps of 5 J in 43 patients. The mean (SD) defibrillation threshold in these patients was 13.3 (6.4) J. In seven patients the testing procedure was stopped after the implant criterion (three consecutive episodes of ventricular fibrillation terminated with an energy ≤ 25 J) was fulfilled. In all patients the defibrillation threshold was sufficiently low to allow implantation of the device. The lead configurations we used included transvenous-subcutaneous leads (right ventricular apex, cathode; superior vena cava, anode; subcutaneous patch, anode) in 32 patients, and transvenous leads (right ventricular apex, cathode; superior vena cava, anode) in 18 patients. All PCD 7217B devices were programmed to give sequential shocks and all PCD 7219D and PRxII devices were programmed to deliver biphasic shocks.

POSTOPERATIVE COURSE

One patient died in the hospital within 30 days after operation (perioperative mortality rate 2%). This was an 81 year old woman with two vessel coronary artery disease and anterior aneurysm after myocardial infarction who had had recurrent ventricular tachycardia despite treatment with several antiarrhythmic drugs including amiodarone. She died of drug resistant shock caused by myocardial failure three days after operation. No arrhythmic events had occurred after implantation of the defibrillator.

LONG-TERM FOLLOW UP (TABLE 2)

During the follow up of 17 (12) months, there was only one death. A 64 year old patient with coronary artery disease died suddenly 27 months after implantation of the device. His symptoms began with shortness of breath, leading to cyanosis and death within a few minutes. No shocks were noted by bystanders. Interrogation of the device did not show new tachycardia episodes. Necropsy was not performed. This patient had experienced multiple episodes of slow ventricular tachycardia immediately after operation and several episodes of slow ventricular tachycardia that were always terminated by antitachycardia pacing during the following months. No shock had to be delivered by the device to terminate these tachycardias.

During the follow up period, 33 patients had a total of 3861 ventricular tachycardias (median 22, range 1 to 1035 ventricular tachycardias/patient) that were treated by the devices. Most (91%) of these tachycardias were terminated by antitachycardia pacing. 11 of the 35 patients had fast ventricular tachycardias that required immediate cardioversion by the devices. The figure shows actuarial survival curves for freedom from sudden death, total mortality, absence of ventricular tachycardia of any rate, and absence of fast ventricular tachyarrhythmia presumed to be fatal without termination by the device. The difference between total mortality and the occurrence of fast ventricular tachyarrhythmia was 9%, 12%, 27%, and 27% at 6, 12, 18, and 24 months (table 2), respectively, indicating an

Table 2 Actuarial event-free rates (%) during 18 months of follow-up

Event	6 months	12 months	18 months	24 months	P value*
Total deaths	98	98	98	98	—
Cardiac deaths	98	98	98	98	NS
Sudden deaths	100	100	100	100	NS
All VT/VF	49	43	36	23	< 0.0001
Fast VT/VF	89	86	71	71	0.0154

*Compared with total death. See table 1 for abbreviations. VF, ventricular fibrillation. One sudden death occurred after 27 months.

Survival rates for freedom from sudden death, total death, fast ventricular tachyarrhythmias (cycle length < 250 ms) and all ventricular tachyarrhythmias. VT, ventricular tachycardia; VF, ventricular fibrillation.

increasing benefit for patients with implantation of an automatic defibrillator. Neither age nor sex, ejection fraction, cycle length of spontaneous or induced ventricular tachycardia, interval between first ventricular tachycardia and implantation of the device, use of β blockers, use of antiarrhythmic agents was able to predict the occurrence of fast ventricular tachyarrhythmia. The inducibility of fast ventricular tachycardia during baseline electrophysiological study showed a tendency towards statistical significance ($P = 0.07$).

Discussion

SURGICAL MORTALITY

Perioperative mortality in our study resembled that of other studies with endocardial defibrillation electrodes and was lower than that reported for most studies with epicardial leads. Saksena *et al* reported a 0.8% surgical mortality in 123 patients treated with the Medtronic PCD and endocardial leads and 4.2% surgical mortality in 266 patients with epicardial leads.¹⁴ Mosteller *et al* reported that 29 (3.1%) of 939 patients died within 30 days after implantation of a defibrillator with epicardial patch electrodes in 15 hospitals.¹⁵

SUDDEN DEATH

There was one sudden death 27 months after implantation in our study. This resembles results reported earlier. Winkle *et al* reported an annual sudden death rate of 1.5%.¹⁶ Saksena *et al* reported two sudden deaths in 200 patients with epicardial patch electrodes during a mean follow up period of 12 months.¹⁷

TOTAL MORTALITY

There were only two deaths in our study, resulting in a very low total mortality. Kim *et al* reported non-sudden deaths that were related to arrhythmia.¹⁸ There were no deaths of this type in our study. Cardiac and total mortality were somewhat lower than reported by Fisher *et al*,¹⁹ who reported a total cardiac death rate of about 15% at 18 months, with most of the deaths occurring in patients with severe left

ventricular dysfunction. In our study there were fewer patients with extremely low ejection fraction and left ventricular dysfunction did not significantly influence outcome. Epicardial leads were used in Kim *et al*'s study whereas endocardial leads were used in our study.

BENEFIT FROM DEFIBRILLATOR IMPLANTATION

There is no consensus about the benefit from implantation of automatic defibrillators. Sweeney and Ruskin reviewed data supporting the contention that the implantable cardioverter-defibrillator prolongs survival.²⁰ Because most fast ventricular tachycardias are life threatening, the difference between total death rate and actuarial survival rate without fast ventricular tachyarrhythmia has been proposed as an estimate of the benefit of implantation of automatic defibrillators.⁸ In our study, this difference suggests a substantial benefit from implantable cardioverter-defibrillator implantation for patients with a history of haemodynamically tolerated ventricular tachycardia without cardiac arrest because about a fifth of these patients developed fast and immediately life-threatening ventricular tachyarrhythmia during follow up. As might be expected, fast ventricular tachyarrhythmias are less common in patients with a history of haemodynamically tolerated ventricular tachycardias than in the total group of patients with implantable cardioverter-defibrillators,⁸ which includes many survivors of cardiac arrests. Nevertheless, a substantial benefit from implantation of an automatic cardioverter-defibrillator was shown even in this group with a relatively low risk of sudden death. The results accord with results reported for patients who received antitachycardia pacers without a defibrillation capability. Fisher *et al* reported four sudden deaths possibly owing to primarily fast ventricular tachyarrhythmias in 20 patients who received a pacer for termination of stable ventricular tachycardias.¹⁹ Whereas Brugada *et al* found no sudden deaths at 26 months in patients without cardiac arrest at the time of the first episode ventricular tachycardia, which occurred > 2 months after myocardial infarction.²¹

In addition to this benefit in survival that can be estimated by the difference between occurrence of fast ventricular tachycardia and total mortality, the high success rate of anti-tachycardia pacing is likely to reduce the need for medical intervention to terminate recurrent ventricular tachycardias. This benefit could not be measured in this study because there was no control group. None the less, in view of the very high rate of recurrence of ventricular tachycardia in this group of patients, a substantial reduction in the use of medical resources is expected.

LIMITATIONS OF THE PRESENT STUDY

Several aspects of the present study require comment. In this retrospective analysis of the impact of implantable cardioverter-defibrillators on sudden death and total mortality,

study patients served as their own controls. All patients had third generation devices capable of storing either tachycardia cycle lengths or electrograms before initiation of device therapy. Only very fast ventricular tachycardias (cycle length < 250 ms) were included in the analysis of projected survival without the implantable defibrillator. We cannot exclude the possibility that some patients might have survived a fast ventricular tachycardia long enough to obtain medical attention. Another, less likely, source of possible overestimation of the benefit of implantable cardioverter-defibrillators is that some of the episodes of fast ventricular tachyarrhythmia might have been self terminated without the device discharging. However, patients who had self-terminating tachycardias before implantation of the device were treated with antiarrhythmic drugs to prevent this arrhythmia. In addition, in another study fast ventricular tachyarrhythmias showed no tendency to be self-terminating.

Another possibility is that the benefit of implantation of the device might have been underestimated because we included only those tachycardias that were fast from initiation in the analysis of the projected survival without the device. But many slow ventricular tachycardias degenerate into polymorphic ventricular tachycardia or ventricular fibrillation partly as a result of tachycardia induced ischaemia.²²

The possibility that the implantation of the ICD was arrhythmogenic and caused fast ventricular tachycardia in these patients who had never previously experienced a cardiac arrest is very unlikely. In an earlier study we showed that except in the immediate postoperative period the incidence of ventricular tachycardia episodes was not changed by the implantation procedure. We therefore excluded from further analysis episodes occurring within a week after implantation.

Antitachycardia pacing triggered by rapid atrial fibrillation or supraventricular tachycardia can induce ventricular tachycardia. Grimm *et al* showed that five of 241 patients received unnecessary shocks because of ventricular tachycardia induced by antitachycardia pacing during a mean follow up of 24 months.²³ In addition, antitachycardia pacing triggered by ventricular tachycardia might lead to acceleration of the tachycardia to a cycle length < 250 ms. Acceleration of ventricular tachycardias has been described in about 3% of the tachycardias.²⁴⁻²⁸ Because we used only cycle lengths recorded before the first treatment by the device to calculate the tachycardia rate we can exclude the possibility that tachycardias induced or accelerated by antitachycardia pacing have led to an overestimation of the occurrence rate of fast ventricular tachycardias in our study.

We did not find it difficult to distinguish between ventricular and supraventricular tachycardias, especially for tachycardias with a cycle length < 250 ms, because accessory pathways had been excluded in all patients during the baseline electrophysiological study.

In addition, many patients were treated with digitalis or β blockers to depress atrioventricular conduction.

Ejection fractions in our patients were higher than in earlier reports. This reflects the development of ICDs as an established form of treatment for ventricular tachyarrhythmias refractory to antiarrhythmic drugs. Moreover, ejection fractions were also higher in other studies with third generation implantable cardioverter-defibrillators. Bardy *et al* reported a mean ejection fraction of 39% for their patients treated with a Medtronic PCD and of 40% for patients with endocardial leads.²⁹ In the study reported by Fromer *et al* the mean ejection fraction in all patients treated with a Medtronic PCD was 36%.³⁰

The follow up period in our study was short, like that of other studies with second and third generation implantable cardioverter-defibrillators.¹⁷ Although a longer follow up may be desirable, we were able to show a significant benefit of implantable cardioverter-defibrillator even within this short period.

CLINICAL IMPLICATIONS

The results of our study suggest that implantation of automatic cardioverter-defibrillators should be considered not only in patients who have been resuscitated but also in patients with stable haemodynamically tolerated ventricular tachycardia without a history of cardiac arrest because many of these patients will develop fast ventricular tachyarrhythmias requiring immediate cardioversion.

Conclusions

Now that implantable cardioverter-defibrillators can have an antitachycardia pacing capability, device therapy has become a valuable alternative for the treatment of ventricular tachycardia even in patients without a history of cardiac arrest. Because some of these patients will develop primarily fast and immediately life-threatening ventricular tachycardia, they could benefit from the implantation of an automatic cardioverter-defibrillator. None the less, prospective controlled trials are needed before implantation of automatic cardioverter-defibrillators becomes an established clinical practice in patients who have not sustained a cardiac arrest.

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