Outcomes of a single centre registry of patients with ischaemic heart disease, qualified for an RF ablation of ventricular arrhythmia after ICD intervention

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Abstract

Background and aim: Reduction of ICD interventions improves the quality of life and possibly reduces mortality. Ablation reduces ICD interventions in patients with ablatable arrhythmia, but its effectiveness needs to be proven for patients with coronary artery disease (CAD) regardless of the type of arrhythmia. Our study was designed to address this issue, but it had to be terminated due to recruitment problems. The reasons for early termination are described in this paper.

Methods: Patients with CAD and implanted ICD, who within the past three months survived an episode of VT/VF, were selected for this study. Patients were to be randomised for ablation or pharmacotherapy. A group of 209 patients was screened between June and December of 2007.

Results: Out of 209 patients, 39 (18.7%) had appropriate ICD therapy during the last three months and were potentially eligible for the trial. Out of 39 patients, 34 could not be randomised, due to the presence of exclusion criteria (n-25) or consent refusal (n-9). Previous ablation (n-10), left ventricular thrombus (n-3) or presence of mitral or aortic artificial valve (n-3) were the most frequent exclusion criteria. During follow-up of 12 months one patient required ablation due to frequent ICD discharges. From the five randomised patients, two were randomised to ablation and three to the pharmacotherapy arm.

Conclusions: 1. Ablation might not be suitable as a routine treatment for all patients with ICD interventions, as a significant group prefers not to undergo RF ablation as a routine treatment or there are contraindications for the ablation. 2. There are obstacles in prospective and randomised evaluation of the role of ablation in patients with CAD and ICD interventions, which are related both to patients' medical conditions and to patients' will. These limitations should be taken into account when designing further studies.

Key words: ventricular tachycardia, radiofrequency ablation, implantable cardioverter defibrillator

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Introduction

Patients who have survived acute ischaemic events and have implantable cardioverter defibrillators (ICD) suffer from ventricular arrhythmia that may cause ICD discharges despite optimal pharmacological therapy [1-3]. Frequent ICD discharges might significantly influence the quality of life and possibly lead to post-traumatic stress disorder [4, 5]. It is known that ICD does not provide absolute protection against sudden cardiac death. Unsuccessful ICD therapy has been recorded for up to 5% of the population of patients [6]. Therefore reduction of ICD interventions should improve the quality of life and possibly reduce mortality. Ablation reduces ICD interventions in some patients with post myocardial infarction and ablatable arrhythmia, such as stable ventricular tachycardia, as well as in patients with unstable arrhythmia, such as polymorphic VT and electrical storm [7-12], but needs to be proven for the general population of patients with coronary artery disease (CAD) regardless of the type of arrhythmia [13]. A study was designed to address this problem. Unfortunately the study had to be terminated due to recruitment problems. The reasons for early termination are described in this paper.

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Methods

Study Design

The ABLATION 4 ICD trial was a prospective, unblinded, randomised, controlled study (www.clinicaltrials.gov, NCT 00481377). It was planned as a single centre study performed in our hospital, that is a tertiary referral centre and one of the leading hospitals in the field of electrophysiology in Poland, where ICDs have been implanted since 1995. In recent years, the average annual ICD implantation number has exceeded 250.

The study protocol and informed consent form was approved by the local Ethics Committee. Patients were deemed eligible for the study if they were at least 18 years old, gave written informed consent, had previously implanted ICD for secondary or primary prophylaxis of SCD, had CAD (documented by coronary angiography) and survived at least one episode of ventricular tachycardia (VT) or ventricular fibrillation (VF) terminated by the ICD during the past three months. They had to be randomised within three months after index arrhythmia.

The exclusion criteria included: pregnancy, active participation in another trial, severe, refractory heart failure (NYHA class IV), acute ischaemia, contraindication for catheter ablation (left ventricular thrombus, artificial aortic or mitral valve, no vascular access), previous catheter ablation of ventricular arrhythmias, incessant VT or electrical storm necessitating immediate treatment, refusal or inability to participate in the trial and life expectancy <1 year. Coronary angiography had to be performed within 6 months prior to enrolment and revascularisation was performed if necessary to exclude active ischaemia as a trigger of arrhythmia.

Baseline ICD programming was performed at the discretion of the cardiologist in a follow-up clinic.

After giving their written informed consent, the patients were randomised, in a 1:1 ratio, into two therapy groups: ablation or conventional treatment. There were no limitations on using antiarrhythmic drugs in either group.

The primary end point was the number of ICD therapies (both shocks and anti-tachycardia pacing). The secondary end points were overall and cardiac mortality, hospitalisation due to heart failure or cardiac arrhythmia and quality of life assessment.

Table I. Baseline characteristics of the patients

Parameters	
Age [years]	65.2±9.8
Male gender (%)	38 (97.4)
LVEF (%)	28±7.3
NYHA functional class I or II (%)	31 (77.5)
NYHA functional class II or III (%)	9 (22.5)
Previous myocardial infarction – n (%)	38 (97.4)
Previous PTCA (%)	15 (38.5)
Previous CABG or (and) valve replacement (%)	7 (17.5)
Interval between recent myocardial infarction and index arrhythmia [years]	11.6±9.5
AF – n (%)	9 (23)
Indications for ICD implantation – n (%)	
sVT/VF	36 (89.8)
Primary prevention	4 (10.2)
Type of ICD – n (%)	
Single chamber	11 (28.2)
Dual chamber	26 (66.7)
Biventricular	2 (5.1)
Medication – n (%)	
Class I or III antiarrhythmic drugs	0
Amiodarone	12 (12.7)
Sotalol	2 (5)
Beta-blockers	35 (89.8)
ACEI or ARB	38 (97.4)
Statins	39 (100)
Aspirin or (and) other antiplatelet drugs	36 (92.3)
Diuretics	23 (59)
Aldosterone receptor blockers	21 (53.8)

Abbreviations: ACEI – angiotensin-converting enzyme inhibitors, AF – atrial fibrillation, ARB – angiotensin receptor blockers, CABG – coronary artery bypass grafting, ICD – implantable cardioverter defibrillator, NYHA – New York Heart Association, PTCA – percutaneous transluminal coronary angioplasty, VF – ventricular fibrillation, VT – ventricular tachycardia

Results

Between June 2007 and December 2007, 293 consecutive patients were screened; among them, there were 209 patients with coronary artery disease. In this group, 39 (18.7%) patients had had appropriate ICD therapy during the last three months and were potentially eligible for the trial. Their characteristics are presented in Table I. Arrhythmia was detected in the VT zone in 29 (74.4%) patients, and in the VF zone in 11 (28.2%). Two patients had both VT and VF. Two hundred and eighty-one episodes of ventricular tachyarrhythmias were recorded in the ICD memory during the last three months [if multiple antitachycardia pacing (ATP) or shocks were necessary to terminate the arrhythmia, it was considered as one episode]. In 279 (96%) instances, arrhythmia was detected and treated as VT using ATP as the first therapy in all but one case. In twelve episodes of arrhythmia detected in the VF zone, shock therapy was required as initial therapy (Table II). Nine patients received only shock therapy, whereas in 19 patients all arrhythmias were terminated by ATP alone. Eleven patients received both types of therapy. Although some patients had multiple ICD interventions, none of them met the criteria of VT storm (≥3 episodes of ventricular tachyarrhythmias separated by >5 minutes during a 24-hour period) [14-16].

Out of 39 patients who met the inclusion criteria and were potentially eligible for the study, only 5 of them were not excluded based on the exclusion criteria and gave informed consent for participation in this trial. The two main reasons for exclusion were previous ablation (29%)

and consent refusal (26%), along with factors increasing procedure risk, such as left ventricular thrombus, or presence of mitral or aortic artificial valve (Table III).

The study was terminated after six months because of the low randomisation rate, which was substantially lower than the target calculated for the sample size.

Out of the 39 patients that were eligible for the study, two were randomised for the ablation procedure, which was performed according to the protocol. The thirty-four patients that did not match the inclusion criteria were followed up for 12 months and one of them required ablation due to frequent ICD discharges. A summary of patient recruitment is presented in Figure 1.

Discussion

This study was designed to objectively answer the question whether ablation is an efficient method of reducing ICD interventions for a cohort of patients with CAD. The inclusion and exclusion criteria were similar as in the previous studies on pharmacological treatment in ICD patients [2, 3]. In order to answer this question the study had to be a prospective, randomised trial. There is no consensus on the number of ICD shocks that are sufficient to refer a patient for ablation. Moreover, a VF episode registered in the ICD memory is not a classical ablation indication [13]. On the other hand, in many CAD patients who receive ICD shocks very fast, electrically unstable (VF type) arrhythmias are observed [17]. Therefore we wanted to include all ICD appropriate shock patients regardless of the type of arrhythmia. In such trials severe precautions needed to be taken and therefore patients with a higher procedure related risk (left ventricular thrombus, mitral or aortic artificial valve) had to be excluded from the study. Previous ablation constituted another exclusion criterion, for we wanted to address the question of the efficacy of a single procedure as a treatment option in patients with ICD interventions. Also patients who had multiple ICD interventions were excluded, as they had indications for an ablation attempt and therefore could not be randomised [12, 13, 18].

The inclusion criteria of ICD therapy – ATP or shock – were similar to the SMASH-VT trial [19], which included patients selected for an ICD implantation regardless of the reason for implantation or type of arrhythmia.

The study presented here had to be terminated due to recruitment problems. Similar problems were probably encountered in the SMASH VT study, where the recruitment of 128 patients (64 in the ablation group) in 3 large centres lasted 4 years [19]. Moreover, during the SMASH VT study in an effort to foster enrolment, a further qualifying criterion was implemented after the study had commenced. This criterion allowed the enrolment of patients who had received an ICD for primary prophylaxis and subsequently received appropriate ICD therapy for a single event.

This suggests that recruitment for studies investigating cohorts of post-MI patients might be challenging. It is important to note that nine out of thirty-nine patients refused to undergo randomisation. In this group of patients ICD therapy did not diminish the quality of life to a degree that would justify a procedure with potential severe complications.

Table II. Electrophysiological characteristics of the study patients

Parameters		
Time from ICD implantation [months]	38.9±38.6	
Time from last ablation [months] n-10	29.9±20.5	
Tachyarrhythmia detected in the VT zone	Number of patients 29 (74.4%)	Number of episodes 279 (range 1-52, mean 9±14.6)
Tachyarrhythmia detected in the VF zone* ICD therapy n [%]	Number of patients 11 (28.2)* ATP alone	Number of episodes 12 (range 1-2) 19 (48.8)
Only shock therapy	9 (23)	
ATP and shock	11 (28.2)	

** In two patients tachyarrhythmias were detected both in VF and in VT zone*

Table III. Reasons for exclusion from the study

Cause of exclusion	n-34 (%)
Previous ablation	10 (29)
Consent refusal	9 (26)
Artificial aortic or mitral valve	4 (12)
No vascular access	3 (9)
Left ventricular thrombus	3 (9)
Inability to participate in the study	2 (6)
VT storm between follow-up visit and randomisation	1 (3)
End stage neoplastic disease	1 (3)
Active participation in another trial	1 (3)

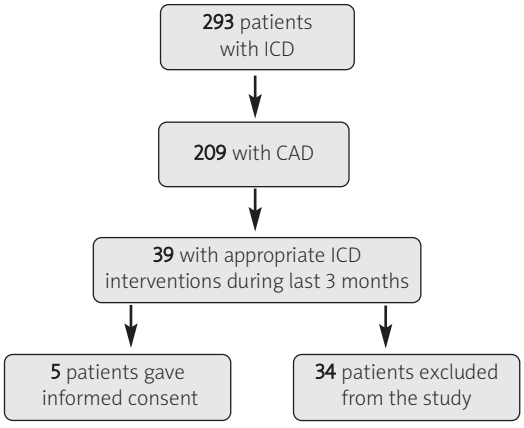

Figure 1. Study design and randomisation results

Due to recruitment problems, a group undergoing randomisation and analysis might not be representative for post-MI patients and therefore the conclusions might be misleading.

Conclusions

1. This early terminated study shows that ablation might not be suitable as a routine treatment for all patients with ICD interventions. A significant group of patients with ICD interventions prefers not to undergo RF ablation.
2. There are several obstacles in prospective and randomised evaluation of the role of ablation in patients with CAD and ICD interventions. These obstacles are related both to patients' medical conditions and to patients' will. These limitations should be taken into account when designing further studies.

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Wyniki jednoośrodkowego rejestru pacjentów z chorobą wieńcową kwalifikowanych do ablacji arytmii komorowych po interwencji ICD

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Streszczenie

Wstęp: Zmniejszenie liczby tachyarytmii komorowych wymagających interwencji implantowanego kardiowertera-defibrylatora (ICD) poprawia jakość życia, a prawdopodobnie również zmniejsza śmiertelność. Możliwe jest usunięcie części arytmii komorowych za pomocą ablacji (np. monomorficznych częstoskurczów komorowych). Nie jest znana natomiast rola ablacji u osób z chorobą wieńcową i różnymi rodzajami arytmii komorowych. Rozpoczęto badanie mające na celu ocenę roli ablacji u osób z chorobą wieńcową i tachyarytmiami komorowymi przerywanymi przez ICD. Badanie zostało przedwcześnie przerwane z powodu trudności z randomizacją odpowiedniej liczby chorych.

Cel: Przedstawienie przyczyn przedwczesnego zakończenia badania.

Metody: Badaniem objęto osoby z chorobą wieńcową i wszczepionym ICD, u których w ciągu ostatnich 3 miesięcy wystąpił częstoskurcz komorowy lub migotanie komór przerwane przez ICD. Chorzy mieli być randomizowani do grupy ablacji lub leczenia farmakologicznego. Badaniem objęto 209 osób z chorobą wieńcową zgłaszających się na kontrole ICD w okresie od czerwca do grudnia 2007 r.

Wyniki: W obserwowanej grupie 209 chorych w ciągu ostatnich 3 miesięcy interwencje ICD spowodowane tachyarytmiami komorowymi wystąpiły u 39 (18,7%) chorych. Chorzy ci stanowili więc grupę spełniającą kryteria włączenia do badania. Z tej grupy nie było możliwe włączenie do badania 34 chorych z powodu obecności kryteriów wykluczających (n=25) lub braku zgody chorego (n=9). Najczęstszymi kryteriami wykluczającymi z udziału w badaniu były wcześniej wykonana ablacja arytmii komorowych (n=10), wszczepiona sztuczna zastawka w ujściu mitralnym lub aortalnym (n=3) oraz obecność skrzepliny w lewej komorze (n=3). W tej grupie w czasie 12-miesięcznej obserwacji wykonano ablację u jednego chorego. Wskazaniem do zabiegu były częste nawroty arytmii powodujące interwencje ICD. Z pozostałych 5 chorych 2 zostało przydzielonych do grupy ablacji i 3 do grupy farmakoterapii.

Wnioski:

1. Rutynowe zastosowanie ablacji u wszystkich chorych, u których miały miejsce interwencje ICD, może być niemożliwe, gdyż duża część chorych nie wyraża zgody na takie postępowanie, a część ma przeciwwskazania do przeprowadzenia ablacji.
2. Istnieje szereg ograniczeń w przeprowadzeniu prospektywnego badania z randomizacją dotyczącego znaczenia ablacji w grupie osób z chorobą wieńcową i wszczepionym ICD. Wynikają one zarówno z przyczyn medycznych, jak i z decyzji chorego. Ograniczenia te należy brać pod uwagę przy opracowywaniu kolejnych badań.

Słowa kluczowe: częstoskurcz komorowy, ablacja prądem o częstotliwości radiowej, wszczepialne kardiowertery-defibrylatory

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