Impact of single atrial fibrillation catheter ablation on implantable cardioverter defibrillator therapies in patients with ischaemic and non-ischaemic cardiomyopathies

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Aims

Atrial fibrillation (AF) is associated with frequent appropriate and inappropriate implantable cardioverter defibrillator (ICD) therapies. Catheter ablation of AF has been shown to reduce AF burden and improve left ventricular function in heart failure patients but the impact on ICD therapies has not yet been studied. The aim of this study was to test the hypothesis that AF ablation reduces ICD therapies in patients with cardiomyopathies.

Methods and results

In 73 consecutive patients (mean age 59 ± 10 years, 85% male) with previously implanted ICD due to ischaemic (n = 30) or dilated cardiomyopathy (n = 43) undergoing AF ablation, the prevalence and frequency of ICD therapies before and after AF ablation were compared. During the total follow-up of 3.3 ± 3 years prior to AF ablation, 5.1 ± 14.7 therapies per patient-year were delivered as opposed to 1.8 ± 10.9 in a period of 1.1 ± 0.9 years after ablation (P = 0.002). Prior to AF ablation, 39 patients (53%) received at least one ICD therapy when compared with 15 patients (21%) after ablation. Atrial fibrillation ablation was associated with freedom from any therapy regardless of appropriateness (odds ratio, OR, 0.366, CI 0.164–0.816, P = 0.014, adjusted for follow-up). Appropriate shocks significantly decreased from 0.3 ± 1.3 to 0.1 ± 0.5 per patient-year (P = 0.030). While heart failure medication and use of antiarrhythmic drugs were comparable during the entire follow-up, a statistically significant improvement of left ventricular ejection fraction (LVEF) from 36.9 ± 12.3% to 40.7 ± 6.7% (P = 0.008) was observed after AF ablation.

Conclusions

In patients with ischaemic or dilated cardiomyopathy, catheter ablation of AF is associated with the reduction of inappropriate and appropriate ICD therapies and improvement of LVEF.

Keywords

Atrial fibrillation • Ablation • ICD • Shocks

Introduction

With the increasing number of patients with implantable cardioverter defibrillators (ICDs), the topic of frequent appropriate and inappropriate therapies becomes more and more clinically important. Inappropriate shocks account for ~12–30% of these cases and result in patient discomfort, chronic anxiety, additional cost or hospitalizations, and increased mortality.1–4 The majority of inappropriate shocks are secondary to supraventricular tachycardias, mainly atrial fibrillation (AF).5,6 Despite technical improvements and advanced detection algorithms,1 the incidence of spurious shocks or antitachycardia pacing (ATP) due to AF remains a significant clinical
What’s new?

- The impact of catheter ablation on the frequency of implantable cardioverter defibrillator therapies has not yet been studied.
- Our study shows for the first time an association between atrial fibrillation ablation and subsequent reduction of appropriate and inappropriate therapies.

Methods

Patients

Seventy-three consecutive patients with AF and previously implanted ICD with ischaemic or non-ischaemic cardiomyopathy included prospectively between September 2006 and 2011 in our institutional AF catheter ablation registry were analysed. Table 1 shows the baseline characteristics of the patients. Paroxysmal and persistent AF were defined according to the current guidelines.10 Informed consent was obtained from all patients concerning data acquisition and analysis.

Ablation procedure and follow-up

Left atrial catheter ablation was performed using a previously described approach.11 In brief, patients were studied under deep propofol sedation with continuous invasive monitoring of arterial blood pressure and oxygen saturation. Non-fluoroscopic 3D catheter orientation, computed tomography image integration, and tagging of the ablation sites were performed using Ensite NavX, Ensite Velocity (St. Jude Medical) or CARTO 3 (Biosense Webster). Trans-septal access and catheter navigation were performed with a steerable sheath (Agilis, St. Jude Medical). In all patients, circumferential left atrial ablation lines were placed around the antrum of the ipsilateral pulmonary veins (irrigated tip catheter, pre-selected tip temperature of 48°C, and power of 30–45 W). In patients with persistent AF, additional linear lesions were added at the left atrial roof, the basal posterior wall, and the left atrial isthmus. Ablation of complex fractionated electrograms was not performed.

After circumferential line placement, voltage and pace mapping along the ablation line were used to identify and close gaps. The isolation of all pulmonary veins with bidirectional block was verified with a multipolar circular mapping catheter and was defined as the procedural endpoint.

Rhythm follow-up was performed with repeated continuous 7-day-holter electrocardiogram (ECG) recordings (Lifecard CF, Delmar-Reynolds Medical, Inc.) immediately after the procedure and during 6 and 12 months of follow-up. Patients with symptomatic AF episodes were encouraged to refer to a physician and undergo ECG or device interrogation. Recurrence of AF was defined as any atrial arrhythmia > 30 s documented in 7-day Holter ECG or mode switch or atrial high-frequency episodes detected during device interrogation without the use of a 3-month blanking period after ablation.

After ablation, Class I and III antiarrhythmic drugs were routinely discontinued. In the event of an early AF recurrence, cardioversion was performed for symptomatic persistent AF episodes. In case of late AF recurrence, the medication was adapted on an individual basis and when indicated, reablation was performed.

Implantable cardioverter defibrillator therapies

For the purpose of ICD therapy analysis, the total follow-up time (4.4 ± 3.3 years) was divided into a period from ICD implantation until the first catheter ablation of AF (3.3 ± 3 years) and into a period from the AF ablation to the most recent follow-up, to the next AF ablation procedure (in 22 cases) or to a ventricular tachycardia ablation (in 2 cases) (1.1 ± 0.9 years). Device interrogation was performed regularly (every 4–6 months) or on demand after ICD shocks in an outpatient clinic. Two physicians, experienced with ICDs and EGM interpretation, performed rhythm adjudication. Implantable cardioverter defibrillators were programmed according to the current manufacturer recommendations for the optimal arrhythmia detection and therapy. No changes in device programming were performed after the ablation procedure. Detailed device and programming characteristics are included in the Appendix.

The ICD therapy was defined as either ATP or ICD shock. Any ICD therapy delivered for VT or VF was defined as appropriate. All other episodes were deemed as inappropriate.

Table 1 Characteristics of the study population (n = 73)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>59 ± 10</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>62 (85)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33 ± 28</td>
</tr>
<tr>
<td>Coronary artery disease, no. (%)</td>
<td>30 (41)</td>
</tr>
<tr>
<td>Dilated cardiomyopathy, no. (%)</td>
<td>43 (59)</td>
</tr>
<tr>
<td>Persistent AF, no. (%)</td>
<td>51 (68)</td>
</tr>
<tr>
<td>Hypertension, no. (%)</td>
<td>59 (79)</td>
</tr>
<tr>
<td>Diabetes mellitus, no. (%)</td>
<td>15 (20)</td>
</tr>
<tr>
<td>Mean CHADS-score</td>
<td>2.1 ± 1</td>
</tr>
<tr>
<td>Mean CHADS risk-factor, no. (%)</td>
<td>3.1 ± 1</td>
</tr>
<tr>
<td>ACEI/ARB, no. (%)</td>
<td>67 (93)</td>
</tr>
<tr>
<td>Beta-blocker, no. (%)</td>
<td>71 (97)</td>
</tr>
<tr>
<td>Diuretics, no. (%)</td>
<td>66 (90)</td>
</tr>
<tr>
<td>Cardiac glycolide, no. (%)</td>
<td>17 (24)</td>
</tr>
<tr>
<td>Amiodaron, no. (%)</td>
<td>12 (17)</td>
</tr>
<tr>
<td>Other antiarrhythmics, no. (%)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Primary SCD prevention, no. (%)</td>
<td>53 (73)</td>
</tr>
<tr>
<td>Secondary SCD prevention, no. (%)</td>
<td>20 (27)</td>
</tr>
<tr>
<td>Single chamber ICD, no. (%)</td>
<td>36 (50)</td>
</tr>
<tr>
<td>Dual chamber ICD, no. (%)</td>
<td>19 (27)</td>
</tr>
<tr>
<td>CRT-D, no. (%)</td>
<td>17 (23)</td>
</tr>
</tbody>
</table>

ACEIs, angiotensin-converting enzyme inhibitors; AF, atrial fibrillation; ARB, angiotensin II receptor antagonists; BMI, body mass index; CRT-D, cardiac resynchronization therapy defibrillator; ICD, implantable defibrillator; SCD, sudden cardiac death.
Echocardiography
Transthoracic echocardiography data were analysed directly before the ICD implantation, at baseline and at 6, 12 and 24 months after the procedure, regardless of heart rhythm. The most recent echocardiographic examination recorded in the medical record before and after ablation was used for statistical analysis. The echocardiographic studies were conducted according to the recommendations of the American Society of Echocardiography.12

Statistical analysis
Continuous variables are expressed as mean and standard deviation. Categorical variables are reported as frequencies and percentage. The Kolmogorov–Smirnoff test was used to analyse the distribution of continuous variables. The frequency of ICD therapies was adjusted by follow-up duration, presented in patient-year manner and compared by means of Student’s t-test. Paired parametric variables were compared by means of paired Student’s t-test and non-parametric by the Wilcoxon test. The alterations in nominal and ordinal data were analysed by means of McNemar’s- and marginal homogeneity-model, respectively. For the calculation of odds ratio (OR) adjusted for unequal follow-up, a logistic regression model using patients as their own controls was used. Correlation between alteration in continuous parameters and reduction of ICD therapies was analysed with a linear regression model.

Results
Outcome of atrial fibrillation ablation
Complete pulmonary vein isolation as procedural endpoint was achieved in all patients. Recurrence of tachyarrhythmias within 90 days occurred in 11 patients (15%). After 6 and 12 months of follow-up, a recurrence was observed in 20 (30%) and 46 (63%) patients, respectively. In 22% of patients with AF before ablation, atrial tachycardias occurred after ablation. After a mean period of 11.4 ± 6.6 months, a reablation of AF was performed in 22 patients (30%). Complications occurred in eight patients: in four patients post-procedural oesophagoscopy, which is performed routinely in patients with a pseudoaneurysm was surgically treated and one patient had to be transiently non-invasively ventilated due to post-procedural pulmonary oedema.

After AF ablation, a statistically significant improvement of the left ventricular ejection fraction (LVEF) from 36.9 ± 12.3% to 40.7 ± 6.7% (P = 0.008) was observed. Furthermore, patients with worse baseline LVEF were more likely to show a LVEF improvement after ablation (OR 0.729 per 5%, CI 0.576–0.921, P = 0.014, adjusted for follow-up). In an additional model including also the use of beta-blockers and antiarrhythmic drugs, ablation remains a strong protective factor (OR 0.378, CI 0.164–0.816, P = 0.019). Furthermore, considering the total number of device therapies applied, a significant reduction of ICD therapies was observed. During follow-up prior to AF ablation, 5.1 ± 14.7 therapies per patient-year were administrated as opposed to 1.8 ± 10.9 during 1.1 ± 0.9 years after ablation (P = 0.002).

In particular, there was a significant reduction of appropriate and inappropriate shocks (Figure 1).

Predictors of implantable cardioverter defibrillator therapies reduction
Catheter ablation of AF was associated with a significant reduction in the frequencies of ICD therapies in the whole study population regardless of baseline characteristics, such as sex, age, aetiology of cardiomyopathy, or type and brand of devices.

Recurrence of AF after ablation did not influence the reduction of therapies during the follow-up.

Impact of atrial fibrillation ablation on implantable cardioverter defibrillator therapies
Atrial fibrillation ablation was significantly associated with freedom from any therapy regardless of appropriateness (OR 0.366, CI 0.164–0.816, P = 0.014, adjusted for follow-up). In an additional model including also the use of beta-blockers and antiarrhythmic drugs, ablation remains a strong protective factor (OR 0.378, CI 0.168–0.856, P = 0.019). Furthermore, considering the total number of device therapies applied, a significant reduction of ICD therapies was observed. During follow-up prior to AF ablation, 5.1 ± 14.7 therapies per patient-year were administrated as opposed to 1.8 ± 10.9 during 1.1 ± 0.9 years after ablation (P = 0.002).

In particular, there was a significant reduction of appropriate and inappropriate shocks (Figure 1).

Table 2 Echocardiographic variables before and after ablation

<table>
<thead>
<tr>
<th>Variables</th>
<th>Ablation</th>
<th>Last follow-up</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV-EF (%)</td>
<td>36.9 ± 12.3</td>
<td>40.7 ± 6.7</td>
<td>0.008</td>
</tr>
<tr>
<td>LV-EDD (mm)</td>
<td>60.4 ± 9.9</td>
<td>60.3 ± 8.7</td>
<td>0.671</td>
</tr>
<tr>
<td>IVSD (mm)</td>
<td>11.6 ± 2.2</td>
<td>11.6 ± 2.1</td>
<td>0.885</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>47.6 ± 7.2</td>
<td>47.3 ± 6.9</td>
<td>0.421</td>
</tr>
</tbody>
</table>

IVSD, interventricular septum dimension; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; LV-EDD, left ventricular end-diastolic diameter; LV-EF, left ventricular ejection fraction; LVEDD, left ventricular end-systolic diameter.

Figure 1 Number of ICD therapies per patient year prior to AF ablation, in comparison to the period after ablation.
Alterations of NYHA class after ablation were not correlated with decreased therapy.

Regression analysis showed that reduction of the total frequency of therapies was not related to the LVEF improvement ($P = 0.605$).

**Discussion**

**Main findings**
To the best of our knowledge, this is the first study describing the impact of catheter ablation of AF on the prevalence and frequency of ICD therapies and should be seen as hypothesis generating. In a cohort of 73 patients with ischaemic and non-ischaemic cardiomyopathy, with a mean follow-up of 1.1 ± 0.9 years, a significant reduction of total ICD therapies and statistically significant improvement of LVEF following ablation of AF was observed.

**Influence of catheter ablation on implantable cardioverter defibrillator therapies**

Our analysis revealed the association of AF ablation and subsequent reduction of appropriate and inappropriate therapies and improved the clinical outcome. Our study not only suggested an effective approach to reduce ICD therapies, but also demonstrated a low rate of adverse events giving us a promise of a new, safe, and powerful therapeutic avenue.

Interestingly, a total elimination of AF which proved to be especially challenging in a single procedure in those particular patients did not determine the aimed goal. Very recently, similar results have been observed in a small series of patients with Brugada syndrome, showing a reduction of inappropriate shocks after the first ablation despite the AF recurrence.13,14 It can be hypothesized that the expected reduction of AF burden alone ensured clinical benefits but this has not been assessed.

Concerning appropriate therapies, it is interesting to note that it is a common clinical observation that ventricular episodes in ICD recipients frequently occur during, or are preceded by AF. Stein et al.9 noted that in 20% of patients such dual chamber tachycardia might be documented. Mechanisms discussed to be responsible for this phenomenon include (i) a shortened ventricular refractoriness secondary to a rapid ventricular rate; (ii) a high incidence of short–long–short sequences; (iii) an aggravated heart failure; (iv) increased sympathetic tone; (v) tachycardia-mediated induction of ischaemia.15

Our data mirror that concept, showing a significant reduction of appropriate shocks reflecting a decreased frequency of ventricular arrhythmias and inhibition of pro-arrhythmic components independently of antiarrhythmic drugs, heart failure medication, or echocardiographic alteration.

Previous studies reported noticeable changes in systolic function in patients with normal or mildly reduced LVEF.16,17 In our cohort, the AF ablation resulted in a statistically significant LVEF improvement. Most interestingly, the subgroup analysis identified patients with severely depleted LVEF being favoured to benefit mostly.

**Limitations**

The present study is a non-randomized study with the inherent limitations of a retrospective analysis. Our observations are restricted to homogeneous group of patients with symptomatic AF that reflect in our opinion the common clinical cohort of patients. Due to incomplete data, from interrogation of devices, which were not implanted in our facility, an unknown percentage of ICD therapies prior to AF ablation remained unclassified but, statistically, it rather favours the therapy reduction.

Furthermore, the follow-up time was abridged due to strict criteria of follow-up ending, including reablation of AF or a VT ablation, leading to a reduced follow-up period and to high standard variation. Although this excludes bias due to reablation and simplifies statistical analysis, it cannot be surely extrapolated to a longer follow-up period. Further data are needed to clarify the long-term effect of AF ablation.

The reduction of AF burden in patients experiencing AF recurrence has not been assessed as it would require a continuous monitoring of all patients with dual or CRT devices through the whole study period. However, numerous studies documented such reduction as a partial success of the interventional AF treatment.18

Although a statistically significant LVEF improvement of ~5% (relative improvement of 10%) was observed which is an acknowledged endpoint in heart failure studies, the resulting clinical difference is difficult to determine in this cohort.

Due to the wide variation of different manufactures, types of devices and discriminating algorithms, a direct comparison of programming within the cohort was not possible. Therefore, the current study design in which every individual patient served as own control may have minimized that kind of bias.

**Conclusions**

In patients with ischaemic or dilated cardiomyopathy, catheter ablation of AF is associated with the reduction of inappropriate and appropriate ICD therapies and improvement of LVEF.

**Conflict of interest:** none declared.

**Appendix**

**Devices**

Most devices (50, 68%) were implanted between 2005 and 2010, 13 (18%) were implanted before 2005 and 10 (14%) were implanted after 2010. There were a variety of devices used in this study, from the following manufacturers (and device families):

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>n (%)</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>St. Jude Medical</td>
<td>26 (35)</td>
<td>14 Atlas, 4 Promote, 3 Epic, 2 Fortify, 1 Unify, 2 Current</td>
</tr>
<tr>
<td>Medtronic</td>
<td>21 (29)</td>
<td>13 Marquis, 4 GEM, 3 Maximo, 1 EnTrust</td>
</tr>
<tr>
<td>Biotronik</td>
<td>19 (26)</td>
<td>12 Lumax, 5 Lexos, 1 Lumos, 1 Belos</td>
</tr>
<tr>
<td>Guidant</td>
<td>5 (7)</td>
<td>3 Vitality, 2 Contak Renewa</td>
</tr>
<tr>
<td>Boston Scientific</td>
<td>2 (3)</td>
<td>1 Cognis, 1 Teligen</td>
</tr>
</tbody>
</table>

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Baseline device programming

According to the manufacturer recommendations and device specification, the detection zones were programmed as follows:

- Depending on the company and ICD model specific arrhythmia discriminating algorithms were used: Morphology Discrimination plus AV Rate Branch (St. Jude Medical), PR logic and Wavelet (Medtronic), SMART (Biotronic), Rhythm ID (Boston Scientific and Guidant).

- All devices were programmed with at least three trains of ATP in the VT zones prior to shock while in the fast VT/VF zone 82% of devices were set to ATP prior to shocks. No committed therapies were programmed.

References

12. Lang RM, Biering M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography’s Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2006;18:1440–63.