Sinus rhythm restoration by catheter ablation in patients with long-lasting atrial fibrillation and congestive heart failure: impact of the left ventricular ejection fraction improvement on the implantable cardioverter defibrillator insertion indication

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Aims
In the setting of congestive heart failure (CHF), atrial fibrillation (AF) ablation can improve clinical status and the left ventricular ejection fraction (LVEF) value. However, the impact of AF ablation on the implantable cardioverter defibrillator (ICD) indication has never been specifically addressed.

Methods and results
Study subject were six CHF (mean age 61.1 ± 6.9 years, mean LVEF 25.8 ± 7.3%) patients refractory to conventional medical treatment with long-lasting AF unresponsive to external cardioversion. Five patients had an idiopathic dilated cardiomyopathy (DCM) and one had an ischaemic cardiomyopathy (ICM). Their New York Heart Association (NYHA) class was III–IV. Two patients had renal insufficiency. No patient had left ventricular delay. All patients underwent AF ablation. LVEF and NYHA class were dramatically improved in the five DCM patients. New York Heart Association class, but not the LVEF, was improved in the ICM patient. A redo ablative procedure was undertaken in four of five DCM patients and in the ICM patient due to arrhythmia recurrence. Left ventricular ejection fraction and NYHA were improved again in the DCM patients (56 ± 4.4%, I–II, respectively) and led to ICD indication preclusion. The LVEF remained low in the ICM patient (30%) and led to ICD insertion. Sinus rhythm has been stable during the 18.1 ± 5.7 months follow-up period.

Conclusion
Atrial fibrillation ablation in CHF patients can improve both the clinical status of patients and their LVEF, especially among those affected by DCM. The LVEF improvement has the potential to preclude the indication for a primary prevention ICD insertion.

Keywords
Long-lasting atrial fibrillation • Catheter ablation • Congestive heart failure • Implantable • Cardioverter-defibrillator • Left ventricular ejection fraction • Outcome
Introduction

Congestive heart failure (CHF) and atrial fibrillation (AF) are two often-coexisting conditions associated with considerable morbidity and mortality. On one hand, CHF may promote initiation of AF episodes and may participate to its maintenance. On the other hand, episodes of AF, either paroxysmal or persistent, may induce clinical destabilization in CHF patients and are associated with poor outcome. Therefore, and logically, AF suppression may reverse, at least partially and transiently, the decline of the clinical status of patients affected by CHF. Accordingly, it has been established that AF ablation in CHF patients is feasible, and that it has a positive impact both in terms of quality of life and left ventricular ejection fraction (LVEF) improvement. Nevertheless, the impact of AF ablation in terms of LVEF improvement and its relationship with patients’ management has not been specifically addressed in patients with LVEF under 35%.

We report on six patients with CHF refractory to conventional medical treatment, LVEF <35%, New York Heart Association (NYHA) functional class III or IV, and long-lasting AF, for whom AF catheter ablation was undertaken before considering implantable cardioverter defibrillator (ICD) insertion (with or without associated biventricular stimulation) and subsequently and eventually atrio-ventricular junction ablation. The impact of this ablative strategy on the management of these six patients is presented.

Methods

Patient characteristics

Between January 2006 and March 2008, six consecutive patients with CHF refractory to conventional medical treatment, long-lasting AF unresponsive to external cardioversion, NYHA functional class III–IV, and LVEF <35%, underwent AF radiofrequency (RF) catheter ablation before considering ICD insertion (with or without biventricular stimulation association). Informed and written consent were obtained from all patients prior to undergoing catheter ablation procedures. The local institutional review boards approved the study.

Electrophysiological studies and ablation procedures

All patients were receiving warfarin (international normalized ratio, 2–3), which was stopped 1 week prior to the study. Patients were then started on low-molecular-weight heparin or standard heparin (when the patient presented an impaired renal function), which were held on the morning of the ablation procedure. A transoesophageal echocardiogram was done within 2 days of ablation and permitted to exclude an intra-cardiac thrombus in all patients. A spiral multi-slice computed tomography of the chest was performed prior to the study to evaluate left atrium (LA) and pulmonary vein (PV) anatomy. Electrophysiological study was performed in the post-absorptive state under general anaesthesia. The following catheters were used for mapping and ablation: a steerable 6F quadripolar catheter positioned within the coronary sinus (CS), a 7F circumferential mapping catheter (Lasso™, Biosense-Webster, Diamond Bar, CA, USA) introduced after transseptal access and stabilized with the aid of a 8.5F long sheath (SLOTM, St Jude Medical, Minnetonka, MN, USA or Preface™, Biosense-Webster) that was continuously perfused with heparinized sodium chloride 0.9% to avoid potential thrombus formation or air embolism, and a 7.5F 3.5-mm externally irrigated-tip ablation catheter (Navi-Star™, Thermo-Cool™, Biosense-Webster). After transseptal catheterization, intravenous heparin was administered to maintain an activated clotting time of 250–300 s. Surface ECG and bipolar endocardial electrograms were continuously monitored and stored on a computer-based digital amplifier/recorded system (LabSystem Pro, Bard Electrophysiology, Lowell, MA, USA or Prucka Cardiolab, General Electrics, Buckinghamshire, UK). Intra-cardiac electrograms were filtered from 30 to 500 Hz and measured with online callipers at 25–200 mm/s. Once the catheters were positioned, the AF cycle length was measured at the LA appendage (average of 30 complexes). An electro-anatomic three-dimensional map of the LA using the CARTO™ XP system (Biosense Webster) was then created and merged with data from the spiral multi-slice computed tomography. Afterwards, a stepwise ablation approach was applied during the first ablation procedure consisting in electrophysiological PV isolation, complex fractionated atrial electrograms (CFAEs) elimination (except for Patients 1 and 2, for whom CFAEs were not targeted), linear lesions deployment and cavo-tricuspid isthmus ablation (Figure 1). The AF cycle length was assessed at the onset of the procedure and after each ablative step in order to determine the impact of the ablation of each structure on the AF process.

Concerning the second ablation procedures, PV conduction and linear lesions integrity were always verified and supplementary lesions performed when needed. CFAEs where targeted according to the discretion of the electrophysiologist.

During both the first and second ablation procedures, the ultimate objective was sinus rhythm restoration achievement by ablation. Accordingly, whenever AF converted to atrial flutter, this last was always targeted and sinus rhythm restoration was attempted while ablation.

Statistical analysis

Continuous variables are expressed as mean ± SD.

Results

Population studied

The mean age of the six patients was 61.1 ± 6.9 years (range 52–73 years), three were men and three were women. One out of the six patients (Patient 1) had an ischaemic cardiomyopathy (ICM), as the consequence of an anterior myocardial infarction, which occurred in 2006. The remaining five patients presented an idiopathic dilated cardiomyopathy (DCM). None of the six patients had QRS length exceeding 125 ms. The mean ventricular rate, while in AF before the first ablative procedure, was 87.6 ± 5.3 b.p.m. (range 78–92 b.p.m.). The mean LEVF was 25.8 ± 7.3% (range 15–35%). None of the patients had significant valvulopathy, inter-ventricular, or left intra-ventricular asynchrony as assessed by trans-thoracic echocardiography. All patients were treated for at least 7 months (range 7–11 months) prior to the first ablation procedure with maximal tolerated doses of beta-blockers, spironolactone (if not contraindicated), and angiotensin-converting enzyme inhibitors. All patients underwent at least one failed external cardioversion attempt in order to try to restore sinus rhythm. Patients 1–5 were on amiodarone treatment before the first ablation procedure. Patient 6 was not on amiodarone treatment before the first ablation procedure owing to a history of amiodarone-related thyroid toxicity. Two patients (Patients 3 and 5) had NYHA
functional class III, and presented renal insufficiency defined by a glomerular filtration rate of $<60$ mL/min/1.73 m$^2$. The remaining four patients (Patients 1, 2, 4, and 6) had normal renal function but NYHA functional class IV. The mean persistent AF duration before undertaking the first ablation procedure was $27.1 \pm 16.7$ months (range 15–60 months). More epidemiological data, before the first ablative procedure, are presented in Table 1.

**Procedural observations**

Table 2 summarizes the first ablation procedures of the six patients. The mean total procedural duration of the first six procedures was $201.0 \pm 33.2$ min (range 185–271 min). The mean number of points taken for map creation purpose was $211.1 \pm 19.7$, the mean radiation exposure was $148.6 \pm 29.4$ Gy/cm$^2$, and mean total RF application time was $141.1 \pm 37.3$ min. PV isolation, CFAEs ablation, roof + mitral isthmus lines deployment, and CS isolation + cavo-tricuspid isthmus ablation increased the AF cycle length, respectively, by $7.0 \pm 1.7$ (range 4–9), $8.1 \pm 1.1$ (range 7–10), $10.1 \pm 1.1$ (range 9–12), and $6.6 \pm 2.6$ (range 4–10) ms.

Three months after the first ablation procedure, five out of six patients underwent a second ablation procedure due to arrhythmia recurrence (one left atrial flutter, four AF). The mean duration of the second five procedures was $182.0 \pm 11.8$ min (range 171–200 min). The mean number of points taken for map creation purpose was $211.1 \pm 19.7$, the mean radiation exposure was $148.6 \pm 29.4$ Gy/cm$^2$, and mean total RF application time was $141.1 \pm 37.3$ min. PV isolation, CFAEs ablation, roof + mitral isthmus lines deployment, and CS isolation + cavo-tricuspid isthmus ablation increased the AF cycle length, respectively, by $7.0 \pm 1.7$ (range 4–9), $8.1 \pm 1.1$ (range 7–10), $10.1 \pm 1.1$ (range 9–12), and $6.6 \pm 2.6$ (range 4–10) ms.

Table 1 Baseline characteristics of patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>RI</th>
<th>LVEF (%)</th>
<th>LA diameter (mm)</th>
<th>NYHA class</th>
<th>Persistent AF before ablation (months)</th>
<th>Coronary angiogram</th>
<th>AA failed</th>
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</thead>
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<tr>
<td>1</td>
<td>73</td>
<td>M</td>
<td>No</td>
<td>30</td>
<td>49</td>
<td>IV</td>
<td>15</td>
<td>Anterior inter-ventricular branch of left coronary artery occluded</td>
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<tr>
<td>2</td>
<td>58</td>
<td>M</td>
<td>No</td>
<td>35</td>
<td>51</td>
<td>III</td>
<td>19</td>
<td>Normal</td>
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<tr>
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<td>60</td>
<td>F</td>
<td>Yes</td>
<td>15</td>
<td>50</td>
<td>IV</td>
<td>29</td>
<td>Normal</td>
<td>2</td>
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<tr>
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<td>52</td>
<td>M</td>
<td>No</td>
<td>20</td>
<td>49</td>
<td>IV</td>
<td>60</td>
<td>No significant lesions</td>
<td>2</td>
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<tr>
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<td>63</td>
<td>F</td>
<td>Yes</td>
<td>25</td>
<td>50</td>
<td>III</td>
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<td>No significant lesions</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>61</td>
<td>F</td>
<td>No</td>
<td>30</td>
<td>52</td>
<td>IV</td>
<td>18</td>
<td>Normal</td>
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</tr>
</tbody>
</table>

RI, renal insufficiency defined by a glomerular filtration rate of $<60$ mL/min/1.73 m$^2$; LVEF, left ventricular ejection fraction; LA, left atrium; NYHA, New York Heart Association; AF, atrial fibrillation; AA, anti-arrhythmic drugs.
purpose was 206.3 ± 23.5, the mean radiation exposure was 112.9 ± 18.8 Gy/cm², and mean total RF application time was 92.4 ± 22.4 min. Details of the second ablation procedure are presented in Table 3.

### Adverse events

Patient 5 underwent a permanent dual-chamber pacemaker insertion 21 days after the first ablation procedure due to the unmasking, after AF cessation, of severe, symptomatic, paroxysmal sinus node disease despite amiodarone and beta-blockers cessation. The LVEF of the patient assessed 7 and 21 days, respectively, after sinus rhythm restoration, was 40 and 45%. AAI pacing mode was programmed (with the possibility to pace the right ventricle when needed) in order to avoid potential deleterious right ventricular pacing.

There were no other complications.

### Follow-up observations and patients management

The mean follow-up period was 18.1 ± 5.7 months (range 12–27 months).

All patients underwent trans-thoracic echocardiography 7 and 21 days, 1, 3 and 12 months after the first (Patient 5) and second (Patients 1–4 and 6) ablation procedures, which permitted to assess the LVEF (Figure 2).

All patients, except Patient 5, had arrhythmia recurrence episode within the 3 months after the first ablation procedure leading to a second ablation procedure in these five patients. Afterwards, 24-h Holter tracings were performed in these five patients (Patients 1–4 and 6) at 1, 3, 6, and 12 months after the second ablation procedure, and assessed the stability of sinus rhythm. Patient 1 underwent unremarkable dual-chamber ICD insertion 3 months after the second ablation procedure, owing to the fact that its LVEF remained <35% (programmed mode: AAI with the possibility to pace the right ventricle when needed). Patients 1–4 were kept on amiodarone treatment 3 months after the second procedure. Afterwards, amiodarone was ceased, but beta-blockers were continued indefinitely. Concerning Patient 6, apart from beta-blockers, which were continued indefinitely, no other anti-arrhythmic treatment was administered.

Finally, regarding Patient 5, pacemaker memories interrogation assessed the absence of arrhythmia during its 12-month follow-up period. Beta-blockers, but not amiodarone, were restarted in this patient once the pacemaker was inserted.

### Discussion

### Main findings

Our study reports on six patients with CHF refractory to conventional medical treatment, LVEF <35%, NYHA functional class III–IV, and long-lasting AF refractory to medications and resistant to external cardioversions. Out of the six patients, five were affected by a DCM and one was affected by an ICM. All patients fulfilled criteria for prophylactic ICD insertion.13 However, four out of the six patients had NYHA functional class IV and two patients presented an impaired renal function, which are both considered strong
predictors of mortality in ICD recipients. Furthermore, none of the patients had electromechanical left ventricular delay, suggesting poor response to cardiac resynchronization therapy. Atrial fibrillation catheter ablation led to a dramatic LVEF improvement after sinus rhythm restoration in the five patients with a DCM. For this reason, primary prevention ICD implantation was not performed. On the contrary, although NYHA functional class improved (explaining why two ablation procedures were undertaken), no LVEF improvement was observed in the patient presenting an ICM, in which a prophylactic ICD was inserted in accordance with current guidelines.

Current recommendations

It is currently recommended to insert a prophylactic ICD to patients, with either ischaemic- or non-ICM, LVEF ≤35%, NYHA II/III, optimal oral medication, good life expectancy, and no identifiable possibility to improve LVEF regardless of the presence or the absence of AF, since it has been demonstrated that LVEF impairment is associated with a significant risk of sudden cardiac death. In accordance, LVEF is nowadays the most powerful and reliable marker of sudden cardiac death risk available in clinical practice.

It is also currently accepted, in the setting of non-paroxysmal AF, that sinus rhythm restoration (rhythm control) or rate control obtained by medications are equivalent strategies in terms of mortality.

Study rational and clinical perspective

However, it is well established that AF episodes may promote and/or worsen CHF. In this respect, it has been shown that long-lasting AF catheter ablation has a positive impact regarding both LVEF improvement and quality of life amelioration in patients affected by CHF.

It could be, therefore, speculated that sinus rhythm restoration, which has the potential to partially or completely reverse CHF status and LVEF impairment, must be attempted before considering ICD insertion in order to achieve the best possible LVEF.
this setting, sinus rhythm restoration, when possible, could be considered as an equivalent to the need to halt alcohol consumption, or the need to perform coronary revascularization before determining the definitive LVEF value. Based on this hypothesis and because morbidity (NYHA functional class IV, renal function impairment)\textsuperscript{14,15} and the absence of electromechanical left ventricular delay of the six study subjects suggested relative contraindications for primary prevention ICD insertion and resynchronization therapy, they underwent in first intention AF catheter ablation. Moreover, a recent publication assessed the superiority of AF catheter ablation over resynchronization therapy in CHF patients, in terms of heart failure questionnaire score, 6-min walk distance, and LVEF improvement.\textsuperscript{20}

Limitations and questions

First, it can be inferred from our study, even if the number of patients is extremely limited, and from previous publications,\textsuperscript{3–6} there is a need to find the parameter(s) allowing the identification, among CHF patients with depressed LVEF, and long-lasting AF, of possible positive responders after sinus rhythm restoration in terms of LVEF and NYHA improvement. This may be of considerable prognostic value, and can avoid difficult and potentially harmful ablative procedures.

Secondly, in the context of DCM patients presenting a positive response to sinus rhythm restoration by catheter ablation, whether LVEF improvement is definitive, or LVEF will decline again, as the consequence of the progression of the cardiomyopathy, remains to be determined. Furthermore, whether the LVEF improvement will protect patients against ventricular tachycardia/ fibrillation, often presenting fibrotic ventricular islands, is unknown.

Finally, regarding ICMs, as it has been shown by others groups,\textsuperscript{14–16} there could be certain cases for which sinus rhythm restoration by catheter ablation will improve both NYHA functional class and LVEF, and render this one \textgreater{}35\% (this was not the case in Patient 1). Whether such an LVEF improvement can be sufficient to protect patients with post-necrotic ventricular scars against ventricular tachycardia/fibrillation remains to be answered.

Conclusion

Radiofrequency catheter ablation of long-lasting AF in patients with CHF and LVEF \textlessthan;35\% is, although challenging, feasible and can improve both the clinical status of patients and their LVEF. The LVEF improvement can be so dramatic that the indication for a primary prevention ICD insertion could be theoretically precluded. Nonetheless, whether this AF ablative strategy must be systematically and widely applied to symptomatic CHF patients with a depressed LVEF needs to be determined by large series studies.

Conflict of interest: A.A. is an employee of Biosense-Webster Inc.

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