Catheter ablation of paroxysmal atrial fibrillation improves cardiac function: a prospective study on the impact of atrial fibrillation ablation on left ventricular function assessed by magnetic resonance imaging

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Aims Beneficial effects of atrial fibrillation (AF) ablation have been demonstrated in patients with congestive heart failure (CHF) and significantly impaired left ventricular ejection fraction (LVEF). However, the impact of pulmonary vein isolation (PVI) on cardiac function in patients with paroxysmal AF and impaired LVEF remains under discussion. This study aimed to evaluate the impact of PVI for paroxysmal AF on cardiac function in patients with impaired LVEF using cardiac magnetic resonance imaging (CMRI).

Methods and results A total number of 70 patients with paroxysmal AF and episodes ≤24 h were scanned on a 1.5-T-CMRI before and 6 months after PVI during sinus rhythm. End-diastolic volume, end-systolic volume, and LVEF were determined by epicardial and endocardial measurements. Patients were categorized into two groups regarding cardiac function as assessed by CMRI: group 1 patients (n = 18) with an LVEF < 50% and patients with an LVEF > 50% (group 2, n = 52). Group 1 patients demonstrated a significant lower success rate than patients of group 2 after a follow-up of 152 ± 40 days (50 vs. 73%, P = 0.05). Cardiac magnetic resonance imaging in group 1 patients demonstrated a significant improvement in cardiac function after AF ablation (41 ± 6 vs. 51 ± 12%, P = 0.004), whereas group 2 patients did not show significant differences (60 ± 6 vs. 59 ± 9%, P = 0.22) after a 6 months follow-up.

Conclusion Pulmonary vein isolation improves cardiac function in patients with paroxysmal AF and impaired LVEF. These data suggest that an impaired LV function can be partially attributed to AF with short-lasting paroxysms.

KEYWORDS
Atrial fibrillation;
Catheter ablation;
Pulmonary vein isolation;
Congestive heart failure;
Cardiac magnetic resonance imaging

Introduction
Atrial fibrillation (AF) is the most common sustained arrhythmia with an increasing incidence with advancing age.1 It has been shown that subjects suffering from AF have significantly reduced survival than subjects without AF.2 Mortality in patients with AF is dominantly determined by concurrent structural cardiac morbidities, e.g. ischaemic and valvular heart diseases, and thrombembolic events.1,2 However, AF is associated with about a doubling in mortality even in patients without cardiac co-morbidities.2

One of the major problems often associated with AF is the coexistence of congestive heart failure (CHF) that is predo-
mminantly seen in patients with the persistent and permanent form. Both AF and CHF have been postulated as the "two new epidemics of cardiovascular disease".3 These two interact in a self-promoting manner4 and thereby again increase mortality.3 Thus, AF occurs in ~40% of the patients with CHF, whereas its prevalence ranges between 1 and 9% in the general population, depending on age.5,6

Large studies investigating the impact of rhythm control when compared with rate control by the use of
antiarrhythmic drugs (AFFIRM, RACE) did not reveal significant differences in mortality between both groups. Moreover, mortality studies on the impact of a curative approach by catheter ablation for AF are lacking thus far. However, there are a few reports demonstrating a positive effect of AF ablation on cardiac function in patients with CHF. These studies are focused on Patients with a significantly depressed left ventricular function that was assessed by clinical validation (NYHA functional class, quality of life) and echocardiographic measurement. Nonetheless, echocardiographic assessment of LV function is of limited accuracy in terms of measuring a precise value.

Thus, the aim of the present study was to evaluate the impact of catheter ablation for paroxysmal AF on cardiac function in patients with impaired cardiac function assessed by cardiac magnetic resonance imaging (CMRI).

**Methods**

**Study population**

The study comprised 70 consecutive patients with drug-refractory paroxysmal AF. All patients had documented and symptomatic AF typically lasting <24 h and no patient had undergone prior cardioversion nor AF ablation. The patients’ baseline characteristics including failed antiarrhythmic drugs and concomitant medication are demonstrated in Table 1. The patients were divided into two groups with regard to left ventricular ejection fraction (LVEF). Amiodaron was discontinued 4 weeks prior to the ablation.

**Electrophysiological study**

Transesophageal echocardiograms for the exclusion of atrial thrombus and CMRI were performed 1 day prior to the procedure. Patients underwent electrophysiological study under sedation with propofol during continuous monitoring of blood pressure and saturation. Intracardiac electrograms were filtered in a range from 30 to 250 Hz and stored using a computer-based recording system (LabSystem Pro, BARD Electrophysiology, Murray Hill, NJ, USA). The procedure was performed following the discontinuation of all antiarrhythmic drugs for at least four half-lives with the exception of amiodaron. A standard electrode catheter was placed in the coronary sinus. After transseptal puncture, a single bolus of 50 IU/kg of heparin was administered and continued anticoagulation during the procedure was adjusted in order to maintain the activated clotting time between 250 and 300 s. Two steerable catheters were positioned in the left atrium (LA) under the guidance of transseptal sheaths (SRO™, Daig Corp., Minnetonka, MN, USA), an irrigated-tip ablation catheter (Celsius ThermoCool™, Biosense Webster Inc., Diamond Bar, CA, USA) and a circumferential decapolar catheter (Lasso™, Biosense Webster Inc., Diamond Bar, CA, USA) for pulmonary vein (PV) mapping. Prior to the ablation, selective angiography of all accessible veins was performed by hand injection of 10–15 mL contrast medium. The technique used for pulmonary vein isolation (PVI) has been previously described in detail. In brief, the PVs were electrically isolated individually or as pairs of ipsilateral veins. The circumferential PV mapping catheter was placed in an ostial position at each PV and ablation was guided by recording of the PV potentials during radiofrequency (RF) delivery. Radiofrequency energy was delivered through a Stockert generator (Biosense Webster) in a temperature controlled mode and a limit to 50°C using a maximal power of 30 W. Electrical PVI was confirmed by the abolition or dissociation of the PV potentials demonstrated by the circumferential mapping catheter.

**Cardiac magnetic resonance imaging**

All scans were performed during sinus rhythm (SR). All patients were in stable SR for at least 48 h prior to MRI scan. A 1.5 T MR tomograph (Magnetom Symphony, Siemens Medical Systems, Erlangen, Germany) with a 6-channel phased-array body surface coil was used for CMRI. The procedures were standardized to obtain the two-chamber, three-chamber, and four-chamber long axis view with cine images for orientation following an initial scouting sequence. Then, the left ventricle was scanned with 9–12 contiguous slices in short axis views covering the left ventricle from apex to base. Imaging was performed during repeated breath holds. For all image acquisitions, a prospectively triggered R-wave ECG gating was used. Image acquisition used a balanced steady state free precision (SSFP) sequence technique (TrueFISP™) with TR of 46.4 ms, a TE of 1.8 ms, a flip angle of 60°, and a slice thickness of 8 mm, with a typical voxel size 2.0 × 1.4 × 8 mm³. Left ventricular end-diastolic and end-systolic volumes (LVEDV and LVESV, respectively) were measured by an experienced radiologist (A.K.) using custom-made software (Yade, Philips Medical Systems, Hamburg, Germany) in all subsequent short axis slices by manually surrounding the endo- and epicardial surface during the appropriate heart cycle (Figure 1). Left ventricular ejection function was calculated by (LVEDV – LVESV)/LVEDV × 100 (%). Left ventricular end-systolic diameter (LVESD), end-diastolic diameter (LVEDD), and end-diastolic interventricular septum thickness (IVSD) were measured in short

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics of patients with impaired and those with normal left ventricular ejection fraction</th>
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<tr>
<td></td>
<td>Group 1 (LVEF &lt; 50%) (n = 18)</td>
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<tr>
<td>Clinical characteristics</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>56.4 ± 10.6</td>
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<tr>
<td>Male sex, no. (%)</td>
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<tr>
<td>Body mass index (kg/m²)</td>
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<tr>
<td>Arterial hypertension, no. (%)</td>
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<td>History of stroke, no. (%)</td>
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<td>Mitral regurgitation ≥ grade 1, no. (%)</td>
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<td>CHF medication, no. (%)</td>
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<tr>
<td>AT-1-receptor-inhibitor</td>
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<tr>
<td>ACE-inhibitor</td>
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<td>Antiarrhythmic drugs, no. (%)</td>
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<td>Class I</td>
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</tr>
<tr>
<td>Class II</td>
<td>12 (67)</td>
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<tr>
<td>Class III</td>
<td>7 (39)</td>
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axis slices with the previously described software. Fractional shortening (FS) was calculated by \((\text{LVEDD} - \text{LVESD}) / \text{LVEDD} \times 100\) (%). Left atrium diameter was evaluated in septal-lateral direction from the left to the right atrial margin in transversal plane and in apico-basal direction from the roof to the mitral valve plane. To reduce intra-observer variability, all parameters were measured two times and the mean value was calculated. In case of an intra-observer variability of >5%, additional measurements have been performed.

**Classification of left ventricular ejection fraction**

The patient population was divided into two groups according to the obtained left ventricular function: patients with an LVEF < 50% were assigned to group 1, whereas those with an LVEF ≥ 50% were classified as group 2 patients.

**Follow-up**

All patients discontinued antiarrhythmic drug treatment after the ablation; oral anticoagulation was continued for at least 6 months. If an AT-1-receptor or ACE-inhibitors was taken previously, e.g. due to arterial hypertension, the medication was continued. No new CHF medication was instituted after ablation. Patients were seen 3, 6 and 12 months after the procedure for routine follow-up. CMRI scans were performed at the 6 months follow-up visit in all patients.

**Tele-ECG-recording**

All patients received a Tele-ECG-recorder (RhythmCard™, Instromedix Inc., San Diego, CA, USA). The Tele-ECG follow-up protocol has been performed as previously described in detail. In brief, patients were advised to record and transmit at least one ECG per day at a relatively fixed time irrespective to the individual symptoms and an additional ECG in case of any symptoms. ECGs were transmitted to a central laboratory using a regular telephone. An AF recurrence was defined as the time to first recurrence of asymptomatic or symptomatic AF with duration of ≥30 s on trans-telephonic ECG monitoring. The initial 4 weeks after ablation were defined as a blanking period. The AF burden and ventricular heart rates were assessed 4 weeks prior to ablation and during the follow-up of 6 months. Atrial fibrillation burden was defined as the percentage of AF Tele-ECGs in all transmitted ECG.

**Statistical analysis**

Statistical evaluation was performed using custom-designed software (SPSS Inc., Cary, NC, USA). Categorical variables were analysed using \(\chi^2\) test and Fisher’s exact test. The differences between continuous variables were tested depending on distribution type with non-paired Student’s t-test and Mann-Whitney rank sum test.

**Results**

All study patients underwent CMRI scans before and 6 months after a single ablation procedure. The patient’s baseline characteristics are presented in Table 1. In 18 patients, CMRI revealed an LVEF < 50% and those patients were assigned to group 1, accordingly. A normal or slightly depressed cardiac function (LVEF ≥ 50%) was found in 52 patients who comprised group 2.

**Follow-up**

All patients completed a follow-up of 6 months. Figure 2 presents the freedom from recurrent AF during the initial 6 months as obtained by Tele-ECG monitoring. A total number of 9 (50%) group 1 patients were free of AF recurrence, whereas 38 (73%) patients of group 2 did not experience AF recurrences during a follow-up of 6 months.
The AF burden did not differ significantly between patients with an impaired LV function (group 1) and those without (group 2) during the observation period before (group 1: 13.2 ± 4.5%, group 2: 12.5 ± 4.5%; P = 0.12) and after ablation (group 1: 5.8 ± 3.4%, group 2: 4.9 ± 3.7%; P = 0.18). Furthermore, ventricular rate did also demonstrate no significant differences between before ablation (group 1: 75 ± 12 bpm, group 2: 76 ± 11 bpm; P = 0.25) and after ablation (group 1: 77 ± 14 bpm, group 2: 77 ± 12 bpm; P = 0.3) (Table 2).

Left ventricular ejection fraction and fractional shortening

In patients with an impaired cardiac function prior to ablation (group 1), mean LVEF significantly increased from 41.3 ± 6.5 to 51.5 ± 12.2% after ablation (P = 0.04) (Figure 3). The follow-up CMRI of patients without impaired LV function (group 2) did not reveal significant differences between before ablation (group 1: 75 ± 12 bpm, group 2: 76 ± 11 bpm; P = 0.25) and after ablation (group 1: 77 ± 14 bpm, group 2: 77 ± 12 bpm; P = 0.3) (Table 2).

(A) A worsening of LV function (54.3 ± 1.5 vs. 39.7 ± 11.4%) was observed in only six patients who did not have an impaired cardiac function prior to ablation (Figure 3, group 2). All these patients were characterized by AF recurrences; AF re-occurred after a mean follow-up time of 56 ± 44 days. In group 1, four patients demonstrated a reduction of LVEF after the ablation (44.2 ± 5.3 vs. 37.9 ± 11.4%; Figure 3). Of these, only one patient experienced an AF recurrence. In group 1, nine patients (50%) had AF recurrence after ablation, but only one of them had a reduction in LVEF (41.5 vs. 24.1%). In the other eight patients who still had AF episodes after PVI, the LVEF improved from 39.7 ± 6.7 to 50.5 ± 16.7% without significance (P = 0.14). However, these patients were characterized by a markedly reduced AF burden after ablation, which might explain LVEF improvement despite recurrences of AF paroxysms.

Interestingly, two patients in group 2 showed a dramatic LVEF reduction after ablation. In one patient (56.4 vs. 29.4%), AF recurrence might be one possible factor for LVEF reduction. This patient has undergone two re-ablations after the 6 months follow-up period due to AF recurrences with increasing episodes after which he is now in a stable SR. Despite a stable SR, LVEF remained impaired. Further clinical work-up revealed a dilative cardiomyopathy. The second patient showed an LVEF decrease from 54.2 to 21.8% which was also associated with AF recurrence and additional CHF risk factors (hypertension and diabetes mellitus). During follow-up, this patient required an

| Table 2 | Heart rate, AF burden, and recurrence rate before and after ablation of patients with impaired and those with normal left ventricular ejection fraction |
|---------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------|
|         | **Group 1 (LVEF < 50%)** (n = 18) | **Group 2 (LVEF ≥ 50%)** (n = 52) |                                                                                       |
|         | **Before** | **6 months FU** | **Before** | **6 months FU** |                                                                |
| Heart rate (bpm) | 75 ± 12 | 77 ± 14 | 76 ± 11 | 77 ± 12 |                                                                |
| AF Burden (%) | 13.2 ± 4.5 | 5.8 ± 3.4 | 12.5 ± 4.5 | 4.9 ± 3.7 |                                                                |
| Recurrence rate (%) | 50%* | | | 73%* |                                                                |

*P < 0.05.
intensification of antihypertensive treatment, indicating the development of CHF due to hypertensive heart disease. One patient in group 1 showed a markedly reduced LVEF from 41.5 to 24.1%. In this patient, a coronary artery disease (CAD) was newly diagnosed requiring interventions at two coronary arteries. Since this patient did not have AF recurrences, CAD is the most likely reason for LVEF deterioration in this patient.

Left ventricular volume and diameter

In patients of group 1, mean LVEDV significantly increased after ablation (104.9 ± 36.1 vs. 107.7 ± 48.7 mL, \(P = 0.006\)). However, no significant changes were observed in group 2 patients (112.8 ± 48.1 vs. 106.5 ± 47.0 mL, \(P = 0.56\)). Pre- and post-ablation comparison of the mean LVESV did not demonstrate significant differences in both groups (group 1: 61.6 ± 21.4 vs. 50.7 ± 22.8 mL; group 2: 44.9 ± 21.7 vs. 34.0 ± 16.3 mL). Furthermore, there were no significant changes in LVEDD, LVESD, and IVSD, respectively (Table 3).

Left atrial diameter

The mean LA diameters (apico-basal and septal-lateral, respectively) did not demonstrate significant changes after ablation. However, patients with an impaired cardiac function (group 1) were characterized by a significantly greater mean septal-lateral diameter when compared with group 2 patients at both baseline and 6 months after ablation (Table 3).

Discussion

The results of this study add important information on the impact of AF ablation on cardiac function in patients with paroxysmal AF and impaired left ventricular function. This study first used CMRI to evaluate cardiac chamber diameters, volumes, and functions pre- and post-AF ablation. Although all patients suffered from AF episodes ≤24 h, those with a pre-existing impaired LV function demonstrated a significant increase in left ventricular function after ablation. However, the procedural success in terms of freedom from AF was lower in patients with impaired cardiac function.

The association of AF and CHF is well recognized. A poor rate control resulting in a fast ventricular response has been suspected as one of the major determinants of heart failure in AF patients. Additionally, it has been shown that an impaired cardiac function can reverse after restoration of SR but also with the achievement of a good ventricular rate control either using antiarrhythmic drugs or by AV node ablation and consecutive pacemaker implantation. The first data on the impact of curative catheter ablation for AF has been reported by Hsu et al. The authors demonstrated that left ventricular function significantly increased after AF ablation with the greatest improvement within the first 3 months after the procedure. Interestingly, LVEF increased in most of the patients irrespective to a poor or well-regularized ventricular rate response prior to ablation, indicating the existence of other important factors than a fast ventricular rate for the development of ‘AF-heart failure’. A potential explanation for LVEF improvement might be the improvement of atrial contractility, maintenance of synchronic atrio-ventricular contraction, and prevention of high ventricular rate. However, in our study, LVEF improved irrespective to the ventricular heart rate.

Role of atrial fibrillation duration on left ventricular function

Previous studies on the impact of AF ablation on CHF included patients with paroxysmal as well as persistent and chronic AF. In all of these studies, the proportion of patients with persistent and chronic AF was at least 30% and neither of them reported on results exclusively for paroxysmal AF, e.g. in a subgroup analysis. Considering those patients with long-standing persistent AF and subsequent significant mechanical remodelling due to AF may have the greatest benefit in LV function reversal, the true impact of
AF ablation on cardiac function in paroxysmal AF patients was unclear from these studies. More recently, Reant et al.\textsuperscript{19} performed an echocardiographic study in patients with paroxysmal and chronic AF associated with LV diastolic and systolic dysfunction. This study demonstrated that left chamber diameters decreased while cardiac function improved after AF ablation even in those lone AF patients. Interestingly, the major improvement of cardiac function and regression of left chamber diameters were observed within the first 3 months in chronic AF patients, whereas patients with paroxysmal AF showed the most significant improvement during the follow-up after the initial 6 months.\textsuperscript{19} The authors subsequently hypothesized that LV diastolic dysfunction can be attributed at least in part to AF. The suspected pathophysiological mechanisms were accounted to AF-induced stretch of the LA and the PVs. However, another potentially important reason for diastolic (and systolic) dysfunction is AF\textsuperscript{þ} induced alterations in the Ca\textsuperscript{2+} regulatory proteins that are responsible for both electrical and mechanical myocyte function. Cha et al.\textsuperscript{20} reported reduced Ca\textsuperscript{2+} current density in LA and PV cells of canines after rapid atrial burst pacing. Thus, alterations of cellular Ca\textsuperscript{2+} metabolism due to AF may also contribute to impaired LV function, which may be one of the reasons for impaired cardiac function in patients with short AF paroxysms. Hence, with the elimination of frequent exposures to AF by catheter ablation, these mechanisms may occur in the opposite direction and thereby encourage the contractile properties of the myocardium.

Potential mechanisms of LVEF deterioration after ablation are alteration of atrial transport function due to AF, which may transiently persist despite the absence of AF recurrences. Furthermore, hormonal function changes due to fluid overload by the use of an externally irrigated-tip catheter might influence LV function during the initial phase after ablation. However, this explanation is rather unlikely in our series since all patients merely underwent PV isolation requiring only a limited number of RF applications. Another potential reason for LVEF deterioration is the occurrence of significant PV stenosis, which could not only cause pulmonary hypertension but also may lead to impairment of LV function. In our study, PV stenosis could be excluded by CMRI after 6 months following ablation.

In addition to the results of Reant et al.,\textsuperscript{19} our study first demonstrates that an impaired LV function may improve after AF ablation in patients with paroxysmal AF, although AF episodes in those patients are typically of a short-lasting nature that transiently intersperse SR. This makes a 'tachymyopathy' as a single reason for LVEF impairment rather unlikely. This emphasizes the fact that even in patients with paroxysmal AF a reduced LVEF may exist and can be restored/improved by ablation.

A relative low number of patients were treated with ACE-inhibitors (ACE-I; 28 vs. 25%) or angiotensin-receptor antagonists (ARB) (11 vs. 10%) (Table 1). In our study, we aimed to investigate the impact of catheter ablation on left ventricular function. Hence, we tried to avoid any concomitant influences on LVEF like new commenced pharmacological treatment for either CHF or hypertension. All patients with an ACE-I or ARB treatment prior to ablation were advised to continue this therapy during follow-up in an unchanged fashion.

**Mode of left ventricular function assessment**

In the clinical routine, assessment of cardiac chamber anatomy and cardiac function is performed by the use of transthoracic echocardiography (TTE). However, particularly the assessment of LVEF using TTE is limited in accuracy and does not measure a precise value. A study of Heuschmid et al.\textsuperscript{21} compared TTE with CMRI and revealed significantly different results in terms of the evaluation of LV volumes and function. Of note, the difference in LVEF assessment between TTE and CMRI was 14%, an inaccuracy ranging within the magnitude of LVEF improvements in the present and previous studies. Chen et al.\textsuperscript{9} did not find a significant improvement of LVEF in AF patients with impaired systolic function. These data are in contrast to other studies and the authors speculated that non-significant changes were observed because only 60% of all studied patients showed an LVEF increase after ablation. However, the limited accuracy of TTE in LVEF assessment may be another potential explanation for the controversial results of previous studies using TTE for LVEF assessment.

Hence, to accurately evaluate an improvement of LV function, particularly in an extent of 10–20%, the most reliable technique should be used, i.e. CMRI, to avoid measurements with a significant technique-related standard deviation that ranges within the expected value of improvement.

**Limitations**

One limitation of the study might be the small study sample size. However, there are several reasons for the limited number of consecutive patients who were eligible for study inclusion: (i) AF episodes should not exceed a longest duration of >24 h; (ii) patients with previous cardioversions (even within 24 h of AF onset) were excluded; and (iii) all patients had to be in SR for at least 48 h prior to MRI scan.

**Conclusions**

Assessment of cardiac function by the use of CMRI demonstrates a significant improvement of LVEF after AF ablation in patients with paroxysmal AF and impaired LV function. However, patients with an LVEF >50% did not show significant differences in LV function after AF ablation indicating that the elimination of AF by catheter ablation may influence cardiac function particularly in patients with major impaired cardiac function and less in those with mild LV function depression. Although patients with impaired LV function had a lower long-term success when compared with those without a depressed LVEF, AF ablation is a safe and feasible therapeutic option, particularly regarding the prognosis of associated CHF.

**Conflict of interest:** none declared.

**References**


