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ORIGINAL PAPER

Atrial fibrillation ablation strategies and outcome in patients with heart failure: insights from the German ablation registry

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Abstract

Background Heart failure (HF) and atrial fibrillation (AF) often coexist, but data on the prognostic value of differing ablation strategies according to left ventricular ejection fraction (LVEF) are rare.

Methods and results From January 2007 until January 2010, 728 patients with HF were enrolled in the multi-center German ablation registry prior to AF catheter ablation. Patients were divided into three groups according to LVEF: HF with preserved LVEF (≥ 50%, HFpEF, $n = 333$), mid-range LVEF (40–49%, HFmrEF, $n = 207$), and reduced LVEF (< 40%, HFrEF, $n = 188$). Ablation strategies differed significantly between the three groups with the majority of patients with HFpEF (83.4%) and HFmrEF (78.4%) undergoing circumferential pulmonary vein isolation vs. 48.9% of patients with HFrEF. The latter underwent ablation of the atrioventricular (AV) node in 47.3%. Major complications did not differ between the groups. Kaplan–Meier survival analysis demonstrated a significant mortality increase in patients with HFrEF (6.1% in HFrEF vs. 1.5% in HFmrEF vs. 1.9% in HFpEF, $p = 0.009$) that was limited to patients undergoing ablation of the AV node.

Conclusions Catheter ablation strategies differ significantly in patients with HFpEF, HFmrEF, and HFrEF. In almost 50% of patients with HFrEF AV-node ablation was performed, going along with a significant increase in mortality rate. These results should raise efforts to further evaluate the prognostic effect of ablation strategies in HF patients.

Keywords Atrial fibrillation · Heart failure · Catheter ablation · Registry · Mortality/survival · Quality and outcomes

Introduction

Atrial fibrillation (AF) and heart failure (HF) often coexist and worsen each other [3]. This is due to a complex relationship with similar risk factors, like hypertension, diabetes mellitus, valvular, and structural heart disease on one hand going along with myocardial cellular and extracellular as well as neurohormonal and electrophysiological changes [3]. On the other hand, AF can trigger HF in consequence of rapid heart rate, loss of atrial transport function, and atrioventricular (AV) synchrony going along with reduced cardiac output [20] and HF can provoke AF through acute rise in atrial filling pressures or chronic atrial fibrosis [16].

Catheter ablation of AF is an established treatment option for patients with symptomatic AF. However, longer term outcome data on catheter ablation in patients with HF are still limited and yield controversial results. Data on catheter ablation in patients with HF and preserved LVEF are limited to small single-center or retrospective studies with lack of randomized trials [4, 12, 17]. With respect to HF

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patients with reduced LVEF, three randomized studies have just been published. In the CAMERA-MRI study, restoration of sinus rhythm with catheter ablation resulted in significant improvements in ventricular function vs. rate control in patients with idiopathic cardiomyopathy (LVEF ≤ 40%) [21]. A recent study by di Biase et al. for the first time demonstrated a reduction of mortality and hospitalizations in patients with an LVEF ≤ 40% undergoing catheter ablation of AF compared to a rhythm control approach with amiodarone [9]. These data are supported by the recently published results of the CASTLE-AF trial [18]. However, patients in these studies present a rather selected patient cohort who have been treated in highly experienced centers.

Therefore, the aim of the following analysis was to assess ablation strategies with associated outcomes and complications in a real-world cohort of patients with AF and HF included in a prospective multi-center nationwide registry and to compare results in patients with HF with preserved LVEF (≥ 50%, HFpEF), HF with mid-range LVEF (40–49%, HFmrEF), and HF with reduced LVEF (< 40%, HFrEF) [19].

Methods

Recruitment and study design

The German ablation registry is a multi-center prospective registry designed to enroll patients undergoing a catheter ablation procedure. A total of 51 German centers collected data of consecutive patients with an age of 18 years or older after written and informed consent was obtained. The registry was approved by the local ethics committees.

From January 2007 until January 2010, a total of 728 patients with structural heart disease and HF NYHA class ≥ II were enrolled in this registry prior to catheter ablation for symptomatic AF. Three patients with primary electrical disease and eight patients with chronic obstructive pulmonary disease were excluded from the present analysis to strengthen the value of NYHA-class evaluation in patients with HF. Patients were divided into three groups according to LVEF: HFpEF (LVEF ≥ 50), HEmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%) [19].

Registry data management and follow-up

The "Institut für Herzinfarktforschung" (IHF, Ludwigshafen, Germany) was responsible for project development and management, as well as data management and clinical monitoring. It also served as the central contract research organization for the study. Participation of the centers was voluntary. The overall concept of the registry and descriptive results of all collected types of supraventricular tachycardias have previously been published [5]. Documentation and data acquisition were voluntary and were carried out on an internet-based case report form system. All site information was confidential, and transmitted data were securely encrypted. The following data were obtained: patient characteristics [age, sex, and co-morbidities such as hypertension, coronary artery disease, diabetes mellitus, structural heart disease, renal insufficiency, valvular disease, stroke, and the presence of cardiac devices such as pacemakers (PMs) or implantable cardiac defibrillators (ICDs)], type of AF ablation, procedural data, and complications during index hospitalization. As data acquisition started in 2007, type of AF was defined according to the guidelines published in 2006 [11]. Therefore, the previously used term of "permanent AF" would be defined as "long-standing persistent AF" in patients undergoing a rhythm control strategy like pulmonary vein isolation (PVI), whereas "permanent AF" should be reserved to patients in whom AF has been accepted [15].

A centralized, prospective 1-year follow-up was performed by the IHF based on telephone interviews with special focus on complications, medication, AF symptoms, repeat hospitalizations, arrhythmia recurrences and 12-lead ECG documentation. Clinical symptoms were categorized as unchanged, worsened, or improved.

Definition of complications

Complications associated with the ablation procedure were categorized into major adverse cardiac events (MACE) including death and myocardial infarction, major non-fatal adverse events, moderate (reversible), and minor adverse events. MACE included death and myocardial infarction during follow-up. Severe (non-fatal) adverse events included myocardial infarction, stroke, major bleeding, pericardial tamponade, need for emergency cardiac surgery and pulmonary vein stenosis. Moderate (reversible) non-fatal adverse events included TIA, cardiopulmonary resuscitation, femoral arteriovenous fistula or pseudoaneurysm, infection of femoral access site, and phrenic nerve paresis. Besides prolonged hospitalization, any minor bleeding without intervention, new AV block types I or II, and bundle branch block were categorized as minor complications. Major adverse cardiac and cerebrovascular events (MACCE) were defined as a combination of death, myocardial infarction, or stroke.

Atrial fibrillation ablation procedure

Choice of catheter ablation strategy (PVI vs. AV-node ablation) was at the discretion of the treating center. With respect to PVI, patients underwent circumferential and/or segmental PVI with or without deployment of linear lesions, and/or ablation of complex fractionated atrial electrograms (CFAE).

Procedures and periprocedural management were performed according to the institutional standards of each participating center.

To further evaluate the influence of ablation strategy (PVI vs. AV-node ablation) and its effect on mortality in patients with impaired LVEF, subgroup analysis was performed of patients with HFrEF.

Statistical analysis

Continuous variables are presented as mean ± standard deviation. For the highly skewed length of hospital stay, median and interquartile range (IQR) are given. Categorical variables are expressed as number and percentage of patients. Differences of categorical distributions were tested for statistical significance using $\chi 2$ tests, rates of rare events using the Freeman–Halton test. The distributions of continuous variables were compared between the three patient groups with HFpEF, HFmrEF, and HFrEF using the Kruskal–Wallis test, between two groups (e.g., AV-node ablation vs. PVI) using the Mann–Whitney test. 1-year mortality after index discharge and cumulative incidence of MACE and MACCE were estimated by the Kaplan–Meier method and compared by the log-rank test. A p value ≤ 0.05 was considered statistically significant. The statistics shown should be regarded as descriptive and were based on the available cases. All analyses were performed at the Biometrics Department of the IHF using the SAS 9.3 software package (SAS Institute, Cary, NC).

Results

Patient characteristics

A total of 728 patients with structural heart disease (coronary artery disease in 47.1%, previous myocardial infarction in 14.0%, valvular disease in 25.3%, hypertensive heart disease in 28.8%, dilative cardiomyopathy in 15.9% and hypertrophic cardiomyopathy in 2.7%) and HF NYHA class ≥ II were included prior to catheter ablation for symptomatic AF. HFpEF was present in 45.7% ($n = 333$), HFmrEF in 28.4% ($n = 207$), and HFrEF in 25.8% ($n = 188$), respectively. Patients with HFpEF and HFmrEF more often had paroxysmal AF, while patients with HFrEF more often presented with permanent or long-standing persistent AF ($p < 0.001$). As expected, patients with HFrEF had a higher CHA_2DS_2-Vasc-Score and more often presented with NYHA-class III (45.2%) or IV (6.4%). Furthermore, these patients more often had an implanted device [17.0% had a PM, 30.9% an ICD and 26.6% a cardiac resynchronization therapy device (CRT)]. Patient characteristics are summarized in Table 1.

Table 1 Characteristics of patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%)

	HFpEF $n = 333$	HFmrEF $n = 207$	HFrEF $n = 188$	p value
Age (years)[a]	65.4 ± 9.6	66.1 ± 9.5	65.0 ± 10.4	0.60
Male (%)	66.1	66.7	77.7	**0.014**
Paroxysmal AF (%)	45.8	45.1	26.2	**< 0.001**
Persistent AF (%)	41.0	39.8	40.1	0.96
Permanent AF (%)	13.3	15.0	33.7	**< 0.001**
$CHADS_2$-Score[a]	1.2 ± 0.8	1.1 ± 0.9	2.4 ± 1.1	**< 0.001**
CHA_2DS_2Vasc-Score[a]	2.5 ± 1.2	2.2 ± 1.7	3.8 ± 1.7	**< 0.001**
NYHA-class II (%)	91.3	90.3	48.4	**< 0.001**
NYHA-class III/IV (%)	8.7	9.7	51.6	**< 0.001**
Diabetes mellitus (%)	10.8	19.8	21.3	**0.002**
Arterial hypertension (%)[a]	76.7	70.0	73.0	0.84
Renal insufficiency (%)[a]	4.7	4.8	18.9	0.070
Previous stroke (%)[a]	7.1	0	5.4	0.48
Coronary artery disease (%)	45.3	48.8	48.4	0.68
Valvular heart disease (%)	33.6	17.9	18.6	**< 0.001**
Pacemaker (%)	15.6	18.8	14.9	0.51
ICD (%)	2.4	5.2	18.3	**< 0.001**
CRT (%)	0.3	0.0	27.1	**< 0.001**
Anti-arrhythmic medication (classes I, III, IV) (%)	53.2	37.2	36.0	**< 0.001**
Betablocker (%)	72.1	77.8	81.7	**0.038**
ACE/ARB inhibitor (%)	62.2	70.0	76.3	**0.003**
Diuretics (%)	37.5	52.2	75.3	**< 0.001**

ACE angiotensin converting enzyme; *AF* atrial fibrillation, *ARB* Angiotensin II receptor blocker; *CRT* cardiac resynchronization therapy; *ICD* implanted cardioverter defibrillator

[a]Data available in 14% of patients due to later inclusion of the variable in the study

Procedural data and periprocedural complications

A total of 734 procedures were performed with almost half of patients with HFrEF undergoing ablation of the AV node (47.3%), but also 7.5% of patients with HFpEF and 12.6% of patients with HFmrEF. Consequently, fluoroscopy time and procedure duration were shorter in patients with HFrEF (Table 2).

Major complications prior to discharge occurred in 12 patients (1.6%) and did not differ significantly between the groups (Table 3).

Table 2 Procedural data and ablation strategies in patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%)

	HFpEF $n=338$	HFmrEF $n=208$	HFrEF $n=188$	p value
First procedure (%)	80.2	82.7	89.4	**0.025**
Ablation in sinus rhythm (%)	48.5	48.6	26.1	**< 0.001**
Circumferential PVI (%)	83.4	78.4	48.9	**< 0.001**
Segmental PVI (%)	7.4	26.0	8.5	**< 0.001**
Left atrial linear lesions (%)	7.7	9.1	5.3	0.35
Fractionated potentials (%)	13.9	5.5	4.5	**< 0.001**
AV-node ablation (%)	7.4	12.5	47.3	**< 0.001**
Radiofrequency (%)	87.0	84.6	94.7	**0.005**
Cryoballoon (%)	11.8	14.4	4.3	**0.003**
3D mapping system (%)	68.0	45.2	29.3	**< 0.001**
Fluoroscopy time (min)	30.5 ± 23.7	45.5 ± 31.6	26.6 ± 25.8	**< 0.001**
Procedure duration (min)	175.8 ± 77.8	185.7 ± 80.6	122.9 ± 81.1	**< 0.001**

Table 3 In-hospital complications in patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%)

	HFpEF	HFmrEF	HFrEF	p value
Deaths (%)	0	0	1 (0.5)	0.26*
MACE (death, myocardial infarction), *n* (%)	0	0	1 (0.5)	0.26*
MACCE (death, myocardial infarction, stroke), *n* (%)	2 (0.6)	1 (0.5)	1 (0.5)	1.00*
Stroke, *n* (%)	2 (0.6)	1 (0.5)	0	0.80*
Major bleeding (intervention), *n* (%)	7 (2.1)	2 (1.0)	0	0.11*
Transient ischemic attack, *n* (%)	2 (0.6)	0	1 (0.5)	0.62*
Cardiac tamponade, *n* (%)	2 (0.6)	2 (1.0)	2 (1.0)	1.00*
Aneurysm spurium, arteriovenous fistula, *n* (%)	8 (2.4)	3 (1.4)	0	0.085*
Atrio-esophageal fistula, *n* (%)	0	0	0	
Minor bleeding (without intervention), *n* (%)	20 (6.0)	1 (0.5)	1 (0.6)	**< 0.001***
Duration of in-hospital stay (days)	4 (3; 6)	4 (3; 7)	4 (2; 7)	0.25

*Freeman–Halton test

Ablation strategies in patients undergoing left atrial catheter ablation for treatment of atrial fibrillation

Circumferential or segmental PVI was performed in about 90% of patients in all three groups with cryoballoon ablation being performed in 12.8%, 16.5%, and 8.1% of patients with HFpEF, HFmrEF, and HFrEF, respectively ($p=0.13$). There were no significant differences with respect to placement of linear lesions (14.4% vs. 12.1% vs. 15.2%, $p=0.71$), whereas ablation of CFAEs was performed more often in patients with HFpEF (14.9% vs. 6.2% in HFmrEF vs. 8.8% in HFrEF; $p=0.018$).

Follow-up

Arrhythmia recurrence and symptoms

12-month follow-up was completed in 97.0%, 99.0%, and 97.3% of patients with HFpEF, HFmrEF and HFrEF, respectively (Table 4). Interestingly, there were no significant differences between the three groups with respect to improvement or worsening of symptoms (Fig. 1). Patients with HFpEF were more often asymptomatic ($p=0.038$) as compared to the other patients.

In patients undergoing left atrial catheter ablation, patients with HFpEF were more often treated with antiarrhythmic drugs than patients with HFrEF ($p<0.001$). Class III antiarrhythmic drugs were the main drugs used (Table 5). Documented arrhythmia recurrences in patients undergoing left atrial catheter ablation were significantly more often noted in HFpEF vs. HFmrEF and HFrEF (47.9% vs. 36.0% vs. 39.8%; $p=0.036$) (Table 5).

Adverse events and Mortality

Number of severe adverse events (myocardial infarction, stroke, and major bleeding) during follow-up did not differ between the groups. However, the mortality rate was significantly higher in patients with HFrEF as compared to patients with HFpEF and HFmrEF (10.4% vs. 2.5%

Table 4 12-month follow-up of patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%)

	HFpEF $n=322$	HFmrEF $n=205$	HFrEF $n=182$	p value
Follow-up completed, n (%)	323 (97.0)	205 (99.0)	182 (97.3)	0.23
No symptoms	61 (20.4)	21 (11.5)	22 (15.6)	**0.038**
Rehospitalization, n (%)	150 (50.0)	87 (46.8)	68 (48.2)	0.78
Re-ablation, n (%)	72 (23.1)	30 (15.4)	21 (13.0)	**0.012**
Adverse events				
1-year mortality (Kaplan–Meier estimates) (%)	1.9	1.5	6.1	**0.009**
Non-fatal myocardial infarction, n (%)	0	0	1 (0.7)	0.23*
Non-fatal stroke, n (%)	4 (1.3)	2 (1.1)	1 (0.7)	1.00*
Major bleeding (intervention), n (%)	1 (0.3)	4 (2.2)	3 (2.1)	0.081*
Transient ischemic attack, n (%)	2 (0.7)	0	0	0.71*

*Freeman–Halton test

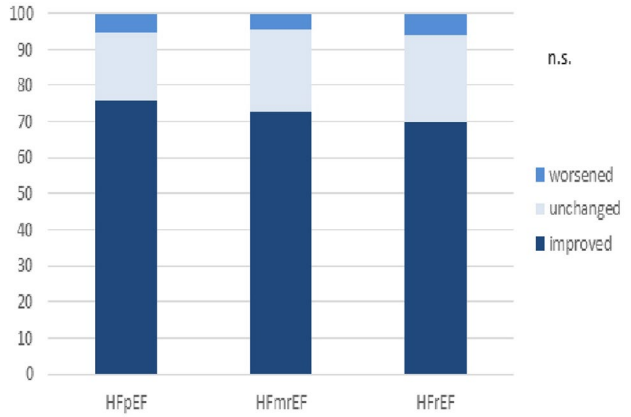

Fig. 1 Symptom assessment (percentages) as improved, worsened or unchanged at 12-month follow-up in patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%)

vs 2.2%, $p<0.001$). The cause of death was classified as sudden in 28.6% of HFpEF patients, 25.0% of HFmrEF patients, and 15.8% of HFrEF patients ($p=0.74$), non-sudden in 14.3%, 0%, and 21.1% and remained unexplained in almost two-thirds of patients (57.1% vs. 75.0% vs. 63.2%).

Kaplan–Meier survival analysis demonstrated a significant mortality increase in patients with HFrEF (1.9% in HFpEF vs. 1.5% in HFmrEF vs. 6.1% in HFrEF, $p=0.009$) (Fig. 2a). Consequently, rate of MACE (1.9% in HFpEF vs. 1.5% in HFmrEF vs. 6.6% in HFrEF, $p=0.003$) and MACCE (2.8% in HFpEF vs. 2.5% in HFmrEF vs. 6.6% in HFrEF, $p=0.046$) was significantly higher in patients with HFrEF, primarily driven by mortality. However, the higher mortality was restricted to the patient group receiving AV-node ablation. Within the two groups of patients undergoing left atrial catheter ablation (Fig. 2b) and of patients undergoing AV-node ablation (Fig. 2c), no mortality trend was observed across LVEF categories.

Subanalyses of patients with heart failure and reduced ejection fraction

Patient characteristics

Patients undergoing AV-node ablation were older (68.7 ± 8.9 vs. 61.6 ± 10.6 years, $p<0.001$), more often female (29.2% vs. 16.2%, $p=0.032$), had a lower LVEF with a highly impaired LVEF of ≤ 30% in 61.8% vs. 35.4% ($p<0.001$) and had a higher NYHA class (NYHA classes III and IV in 78.7% vs. 27.3%, $p<0.001$) as compared to patients undergoing left atrial catheter ablation. In addition, these patients more often presented with permanent or long-standing persistent AF (50.6% vs. 18.2% $p<0.001$) and an implanted device (PM in 29.2% vs. 6.1%, $p<0.001$; ICD in 39.3% vs. 23.2% and CRT in 53.9% vs. 2.0%, $p<0.001$). Patient characteristics are summarized in Table 6.

Procedural data and periprocedural complications

Fluoroscopy time [6 (3;15) vs. 33 (22,53); $p<0.001$] and procedure duration [55.2 ± 35.1 vs. 182.9 ± 60.7; $p<0.001$] were shorter in the AV-node group as compared to the PVI group. In the PVI group, 90.9% of patients underwent circumferential PVI, 16.2% segmental PVI, 15.2% placement of left atrial linear lesions, and 8.8% ablation of CFAEs. A minority of 8.1% of patients underwent cryoballoon ablation. One patient in the AV-node group died suddenly prior to discharge. Complications prior to discharge occurred only in patients undergoing left atrial ablation as follows: one transient ischemic attack (1.0%), two cardiac tamponades (2.0%), and one minor bleeding without intervention (1.0%).

Follow-Up

12-month follow-up was completed in 88/88 (100%) patients in the AV-node group and 94/99 (94.9%) in the PVI group,

Table 5 12-month follow-up of patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%) undergoing left atrial catheter ablation

	HFpEF $n=308$	HFmrEF $n=181$	HFrEF $n=99$	p value
Follow-up completed, *n* (%)	299 (97.1)	179 (98.9)	94 (94.9)	0.14
No symptoms	55 (19.8)	17 (10.6)	12 (15.0)	**0.039**
Antiarrhythmic drugs				
No antiarrhythmic drugs, *n* (%)	169 (61.7)	118 (72.8)	57 (73.1)	**0.026**
Class I antiarrhythmic drugs, *n* (%)	33 (12.0)	11 (6.8)	3 (3.8)	**0.039**
Class III antiarrhythmic drugs, *n* (%)	67 (24.5)	23 (14.2)	19 (24.4)	**0.031**
Class IV antiarrhythmic drugs, *n* (%)	11 (4.0)	11 (6.8)	1 (1.3)	0.13
Rehospitalization, *n* (%)	143 (51.3)	80 (48.8)	42 (51.9)	0.85
Documented recurrence	140 (47.9)	62 (36.0)	35 (39.8)	**0.031**
Re-ablation, *n* (%)	72 (24.7)	30 (17.3)	19 (21.3)	0.17
No re-ablation and no antiarrhythmic drugs, *n* (%)	135 (49.1)	106 (65.4)	46 (58.2)	**0.004**
Adverse events				
1-year mortality (Kaplan–Meier estimates) (%)	1,3	0	1.1	0.31
Non-fatal myocardial infarction, *n* (%)	0	0	1 (1.2)	0.15*
Non-fatal stroke, *n* (%)	3 (1.1)	2 (1.2)	0 (0)	1.00*
Major bleeding (intervention), *n* (%)	1 (0.4)	4 (2.4)	1 (1.2)	0.13*
Transient ischemic attack, *n* (%)	2 (0.7)	0	0	0.66*

*Freeman–Halton test

respectively. In the AV-node group, 16 patients (18.2%) died as compared to three (3.2%) in the PVI group. Arrhythmia recurrence was documented in 42.0% of patients undergoing left atrial ablation. Both groups did not differ with respect to AF symptoms during follow-up ($p=0.82$). However, patients undergoing AV-node ablation were more often classified as NYHA class III or IV (40.0% vs. 19.1%; $p=0.006$). Patients undergoing PVI were treated more often with antiarrhythmic drugs (54.5% vs. 14.9%, $p<0.001$). There was no difference with respect to severe adverse events (myocardial infarction, stroke, and major bleeding) or overall rehospitalizations between the groups. In patients with AV-node ablation, hospitalization for non-cardiovascular causes was more frequent (65.4% vs. 16.7%; $p<0.001$), while patients undergoing PVI were more often hospitalized for cardiovascular reasons (83.3% vs. 34.6%; $p<0.001$).

Survival analysis demonstrated a significant mortality increase in patients with HFrEF undergoing AV-node ablation as compared to patients undergoing left atrial ablation [HR 11.45 (1.47–89.48); $p=0.003$].

Discussion

Main findings of the study

Analysis of 728 patients with structural heart disease and HF NYHA class ≥ II included in the multi-center German ablation registry revealed the following major findings: (1) in patients with HFpEF and HFmrEF paroxysmal, AF was significantly more frequent as compared to patients with HFrEF, while in the latter group permanent or long-standing persistent, AF was more common. (2) About 50% of patients with HFrEF underwent AV nodal ablation as compared to only 7.4% and 12.5% in the remaining groups. (3) In patients with HFrEF undergoing AV-node ablation, a significantly higher mortality rate was observed during follow-up as compared to patients with LVEF > 40%. (4) In patients undergoing left atrial ablation, mortality rate between patients with HFpEF, HFmrEF, and HFrEF was similar.

Choice of ablation strategy in patients with heart failure

Most data on efficacy, safety, and outcome of catheter ablation strategies in patients with HF are limited to small observational studies or metaanalyses [1]. Only recently randomized trials with limited patient numbers have been published strengthening the potential benefit of PVI also in patients with HF, which had been excluded in most of the larger randomized trials. Furthermore, data of the multicentre prospective CASTLE-AF trial have just been published [18]. In this study, 363 patients with AF and HF (NYHA class ≥ II, LVEF ≤ 35% and ICD with homemonitoring function) were randomized to PVI or conventional treatment (rate or medical rhythm control). Over a follow-up of 60 months, there was a significant reduction of the primary endpoint of all-cause mortality [HR 0.53 (95% CI 0.32–0.86), $p=0.011$; log-rank test: $p=0.009$] and worsening HF

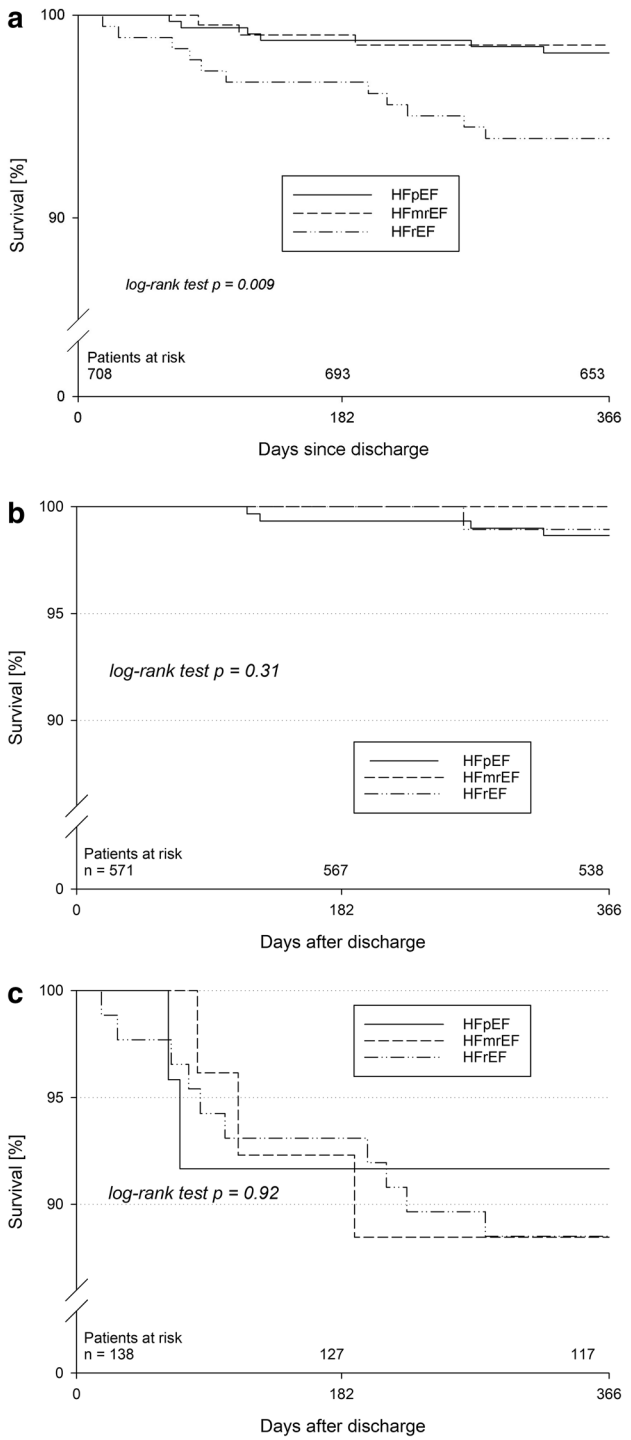

Fig. 2 **a** Kaplan–Meier survival curve analysis in patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%). **b** Kaplan–Meier survival curve analysis in patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%) undergoing left atrial ablation. **c** Kaplan–Meier survival curve analysis in patients with HFpEF (LVEF ≥ 50), HFmrEF (LVEF 40–49%), and HFrEF (LVEF < 40%) undergoing AV-node ablation

Table 6 Characteristics of patients with HFrEF undergoing AV-node ablation vs. pulmonary vein isolation

	AV-node ablation	Pulmonary vein isolation	*p* value
	n = 89	*n* = 99	
Age (years)[a]	68.7 ± 8.9	61.6 ± 10.6	< **0.001**
Male (%)	70.8	83.8	**0.032**
Paroxysmal AF (%)	18.0	33.3	**0.017**
Persistent AF (%)	31.5	48.5	**0.018**
Permanent AF (%)	50.6	18.2	< **0.001**
$CHADS_2$-Score[a]	2.9 ± 1.4	2.1 ± 0.8	0.088
CHA_2DS_2Vasc-Score[a]	4.8 ± 1.8	3.3 ± 1.5	**0.021**
NYHA-class II (%)	21.3	72.7	< **0.001**
NYHA-class III/IV (%)	78.7	27.3	< **0.001**
Diabetes mellitus (%)	24.7	18.2	0.27
Arterial hypertension (%)[a]	78.6	69.6	0.55
Renal insufficiency (%)[a]	28.6	13.0	0.24
Previous stroke (%)[a]	14.3	0	0.062
Coronary artery disease (%)	47.2	49.5	0.75
Valvular heart disease (%)	13.5	23.2	0.086
Pacemaker (%)	23.6	7.1	**0.001**
ICD (%)	14.6	22.2	0.18
CRT (%)	55.1	2.0	< **0.001**
Anti-arrhythmic medication (classes I, III, IV) (%)	14.9	54.5	< **0.001**
Betablocker (%)	78.2	84.8	**0.24**
ACE/ARB inhibitor (%)	74.7	77.8	**0.62**
Diuretics (%)	82.8	68.7	**0.026**
1-year mortality (%)	11.5	1.1	**0.003**

[a]Data available in 14% of patients due to later inclusion of the variable in the study

admissions [HR 0.56 (95% CI 0.37–0.83), $p = 0.004$; Log-rank test: $p = 0.004$] in patients undergoing PVI.

In this context, registry data like the multi-center German ablation registry can give important insight into patient characteristics, choice of ablation strategies, complications, and outcome in a real-world cohort of patients treated in clinical practice. During the inclusion period of this registry (2007–2010), almost 50% of patients with HFrEF underwent AV nodal ablation, while only 12.5% and 7.4% with HFmrEF and HFpEF underwent AV nodal ablation. In patients with HFrEF, co-morbidities seem to have influenced ablation strategy with older patients and patients with LVEF ≤ 30% and higher NYHA class being more likely to undergo AV-node ablation. Furthermore, these patients more often presented with permanent or long-standing persistent AF and implanted devices [22].

Complications

Overall major complication rates were low (1.8%) and did not differ significantly between the groups. Actually, voluntary participation might partly be responsible for the lower than expected complication rate [2, 7]. However, this should affect all patient groups. In this respect, it is reassuring that patients with impaired LVEF undergoing left atrial catheter ablation do not have an increase in complications, as might be expected due to more co-morbidities [8]. Instead, similar complication rates could be observed in patients with HFpEF, HFmrEF, and HFrEF undergoing PVI. This is also in line with data from the CASTLE-AF trial [18].

Follow-up and outcome

Documented arrhythmia recurrences were significantly more often reported in patients with HFpEF, even after exclusion of patients undergoing AV-node ablation. This might partly be explained by the fact that symptoms due to AF recurrence and HF worsening can hardly be differentiated and go along with each other. Therefore, these patients might be underreported as having symptomatic AF, but rather heart failure worsening. Consequently, patients with HFpEF significantly more often underwent re-ablation. However, there were no differences concerning rehospitalizations in patients undergoing AV-node ablation vs. PVI during follow-up. Interestingly, the reason for rehospitalization in patients with HFrEF undergoing AV-node ablation more often was classified as non-cardiovascular, while patients undergoing PVI more often were hospitalized for cardiovascular reasons.

Ablation strategy and mortality in patients with heart failure

Patients with HFrEF had a significantly higher death rate than patients with HFmrEF and HFpEF. Specifically looking at the subgroup of patients with HFrEF revealed that mortality increase was limited to patients undergoing AV-node ablation, while patients with HFrEF undergoing PVI had a similar mortality rate as patients with HFmrEF and HFpEF. Overall several factors might have contributed to the increased mortality rate in patients undergoing AV-node ablation compared to patients undergoing PVI and results have to be interpreted with caution: (1) patients selected for AV-node ablation were older and sicker with more impaired LVEF and higher NYHA class, potentially influencing these results. (2) The fact that only 53.9% of patients with HFrEF undergoing AV-node ablation had an implanted CRT might have negatively influenced mortality due to detrimental effects of right ventricular pacing in the remaining patients,[6, 13], while AV-node ablation in patients with AF and CRT facilitates effective biventricular pacing potentially going along with a reduction of mortality [10]. (3) At the same time, patients with HF undergoing PVI have been reported to benefit with respect to improvement of symptoms, longer 6-min-walk distance and higher LVEF 6 months after the intervention compared to patients undergoing AV-node ablation [14]. In this respect, our results are in line with these positive 6-month follow-up data and extend these findings to a potential mortality benefit at 12-month follow-up. Data of the multi-center prospective CASTLE-AF trial are fully in line with our data and extend the mortality benefit of patients with HF undergoing PVI to a follow-up of almost 5 years [18].

Limitations

Limitations of this analysis relate to the non-randomized study design with prospectively assessed registry data. Nevertheless, analyses of registries are of importance to assess ablation strategies and outcome in the general population managed in clinical practice. Voluntary participation might potentially go along with underreporting of procedural complications or recurrences. Recurrences might also have been missed due to lack of systematic rhythm follow-up with Holter-ECGs. Instead, follow-up care was left at the discretion of the treating center and follow-up data were assessed by telephone interview 12 months after the ablation procedure and a 12-lead ECG with all patients being independently contacted by the IHF.

Conclusion

Catheter ablation strategies differ significantly in patients with HFpEF, HFmrEF, and HFrEF. In almost 50% of patients with HFrEF, AV-node ablation was performed, going along with a significant increase in mortality rate as compared to patients undergoing left atrial ablation. In patients undergoing left atrial catheter ablation, the mortality rate was similar between patients with HFrEF, HFmrEF, and HFpEF. These results may indicate that left atrial ablation improves outcome in patients with reduced LVEF and should raise efforts to further evaluate the prognostic effect of ablation strategies in HF patients.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

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