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Efficacy, Safety, and Outcomes of Catheter Ablation of Atrial Fibrillation in Patients With Heart Failure With Preserved Ejection Fraction

Tomoko Machino-Ohtsuka, MD, Yoshihiro Seo, MD, Tomoko Ishizu, MD, Akinori Sugano, MD, Akiko Atsumi, MD, Masayoshi Yamamoto, MD, Ryo Kawamura, MD, Takeshi Machino, MD, Kenji Kuroki, MD, Hiro Yamasaki, MD, Miyako Igarashi, MD, Yukio Sekiguchi, MD, Kazutaka Aonuma, MD

Tsukuba, Japan

Objectives This study sought to investigate the efficacy and safety of catheter ablation for atrial fibrillation (AF) in patients with heart failure with preserved ejection fraction (HFPEF).

Background AF is a precipitating factor for clinical deterioration of HFPEF.

Methods Catheter ablation for AF was performed in a consecutive 74 patients with compensated HFPEF (left ventricular [LV] ejection fraction >50%). AF-free probability after catheter ablation and factors relating to maintenance of sinus rhythm were investigated. LV strain and strain rate were assessed by echocardiography at baseline and over 12 months after ablation.

Results During a 34 ± 16-month follow-up period, single- and multiple-procedure drug-free success rates were 27% (n = 20) and 45% (n = 33), respectively. Multiple procedures and pharmaceutically assisted success rate was 73% (n = 54). No major complications occurred during follow-up. Multivariate Cox regression analyses revealed that AF type (other than long-standing persistent AF) and lack of hypertension were independently associated with maintenance of sinus rhythm (hazard ratio [HR]: 1.81, 95% confidence interval [CI]: 1.03 to 3.17, p = 0.04; HR: 0.49, 95% CI: 0.24 to 0.96, p = 0.04, respectively). LV systolic indices (LV ejection fraction, LV strain/strain rate at systole) and diastolic indices (E/E′, ratio of LV strain rate at diastole with early transmitral flow) were improved only in patients maintaining sinus rhythm at follow-up.

Conclusions Our results suggest that AF can be effectively and safely treated with a composite of repeat procedures and pharmaceuticals in patients with HFPEF. However, the current study was a single-arm analysis; therefore, larger randomized control studies are needed to verify the benefit of AF ablation in this cohort. (J Am Coll Cardiol 2013;62:1857–65) © 2013 by the American College of Cardiology Foundation

A substantial number of patients with symptomatic heart failure have a relatively preserved left ventricular ejection fraction (LVEF) (1,2). Such patients with heart failure with preserved ejection fraction (HFPEF) have high prevalence of atrial fibrillation (AF) ranging from 20% to 40% (1–3). HFPEF is thought to have predominant anomalies of left ventricular (LV) active relaxation and passive stiffness that lead to impaired diastolic filling (4,5); therefore, AF may facilitate the development or progression of heart failure by causing a rapid ventricular rate and short ventricular filling time that result in a reduced cardiac output. Besides LV diastolic dysfunction, recent data demonstrated a primary abnormality in left atrial (LA) function in HFPEF (6). AF exaggerates LA dysfunction through LA remodeling and loss of effective atrial contraction. Thus, AF is a consequence as well as a precipitating factor for clinical deterioration of HFPEF (3,7,8). Although prognosis of HFPEF is not better than that of heart failure with reduced LVEF (1,2), an effective management strategy for HFPEF remains to be established (9). Efficacy of catheter ablation (CA) for AF has been confirmed, and its favorable effect on patients with heart failure with reduced LVEF has been reported (10,11). However, data on the efficacy and safety of CA in patients with AF with concomitant HFPEF are lacking. Accordingly, the present study aimed to investigate whether AF elimination by CA is effective in patients with HFPEF.

From the Cardiovascular Division, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan. All the authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Abbreviations and Acronyms

AF = atrial fibrillation

CA = catheter ablation

CI = confidence interval

HFPEF = heart failure with preserved ejection fraction

HR = hazard ratio

LA = left atrial/left atrium

LV = left ventricular/left ventricle

LVEF = left ventricular ejection fraction

SR = sinus rhythm

SI_{SYS} = longitudinal left ventricular peak strain at systole

SR_E = longitudinal left ventricular peak strain rate at early diastole

SR_{IVR} = longitudinal left ventricular peak strain rate during isovolumetric relaxation period

SR_{SYS} = longitudinal left ventricular peak strain rate at systole

2DSTE = two-dimensional speckle tracking echocardiography

Methods

Study protocol. Between September 2005 and December 2011, 1,212 patients with symptomatic drug-resistant AF were candidates for CA in our institution. Of these patients, 108 presented with heart failure symptoms (pulmonary edema, leg swelling, fatigue, or dyspnea on exertion) despite preserved LVEF (>50%) and fulfilled the criteria of HFPEF according to European Society of Cardiology recommendations (12). Thirty-four patients were excluded because of significant heart valve disease, previous valve surgery, lung or renal disease (n = 20), or because follow-up data were unavailable (n = 14). Finally, this study comprised 74 patients with concomitant HFPEF and AF. All patients had at least 1 heart failure–related hospitalization and were screened for active ischemic heart disease and noncardiac causes of symptoms. Of the study population, 42 patients had sinus rhythm (SR) restored by electrical cardioversion before CA (SR pre-CA). AF continued in the remaining 32 patients until CA (AF pre-CA). All patients underwent transthoracic echocardiography just before CA. Peripheral blood samples were taken just before the CA for measurements of routine blood chemistry including estimated glomerular filtration rate (calculated as: $0.741 \times 175 \times \text{age}^{0.203} \times \text{creatinine}^{1.154}[\times 0.742 \text{ if female}]$ ml/min/1.73 m^2), N-terminal pro–B-type natriuretic peptide (Elecsys proBNP, Roche Diagnostics, Mannheim, Germany) and atrial natriuretic peptide (MI02 Shionogi ANP, Shionogi Inc., Osaka, Japan). We investigated recurrence of AF over a 12-month follow-up period after CA and then divided the patients into 2 groups based on AF recurrence (AF post-CA group) and maintenance of SR (SR post-CA group). During long-term follow-up, we investigated changes of echocardiographic parameters including LV strain/strain rate. Ethical approval of the present study was obtained from the local review committee, and all patients provided their written informed consent.

Transthoracic echocardiography. Two-dimensional images were recorded with a Vivid 9 cardiovascular ultrasound systems (GE Healthcare, Horten, Norway) equipped with a variable frequency 2.5- to 5-MHz Doppler transducer. Each parameter was determined based on American Society of Echocardiography recommendations (13,14). LV end-diastolic volume and LVEF were calculated by Teicholz methods. LV mass was estimated by area-length formula. LA volume was measured from the apical view with the biplane method of disks. LA total emptying fraction was calculated as follows: ([maximum LA volume − minimum LA volume]/maximum

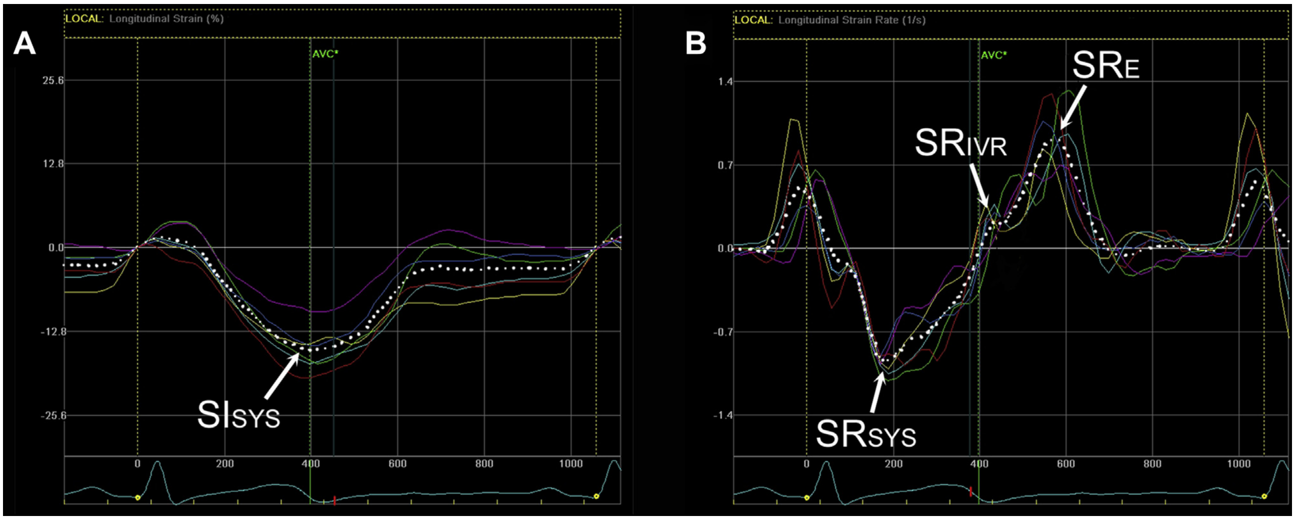

Figure 1 **Longitudinal Strain and Strain Rate of the LV**

Longitudinal left ventricular (LV) strain and strain rate of the 6 individually **colored** segments and the mean value for all segments **(dotted line)** are shown in **A** and **B,** respectively. SI_{SYS} and SR_{SYS} refer to LV peak systolic strain and strain rate, respectively, and SR_{IVR} and SR_E refer to LV peak strain rate during the isovolumetric relaxation period and early diastole, respectively. AVC = aortic valve closure.

Table 1 Follow-Up Results and Complications (N = 74)

Length of follow-up, months	34 ± 16
Mean time to first atrial arrhythmia recurrence, days	171 ± 79
Success rates	
Single procedure without AAD	20 (27)
Multiple procedures without AAD	33 (45)
Multiple procedures with AAD	54 (73)
Complication rates	
Major complications: stroke, tamponade, atrioesophageal fistula, PV stenosis	0 (0)
Minor complications	4 (5)
Groin hematoma	2 (3)
Post-procedural pulmonary edema	2 (3)

Values are mean ± SD or n (%).
AAD = antiarrhythmic drug; PV = pulmonary vein.

LA volume) × 100. The peak velocities of early (E) and late (A) transmitral flow and deceleration time of E velocity were recorded from the long-axis view by pulsed Doppler echocardiography. Tissue Doppler imaging was used to measure the mean value of early peak diastolic velocity (E′) at the mitral annular septal and lateral corners.

Grayscale images of apical views were obtained with frame rates over 80 Hz for strain analysis by 2-dimensional speckle tracking echocardiography (2DSTE). Recordings were processed with acoustic-tracking software (EchoPAC PC version 110.0.0, GE Healthcare) allowing off-line semi-automated speckle-based strain analyses. Longitudinal LV strain (Fig. 1A) and strain rate (Fig. 1B) were measured by 2DSTE as previously reported (15,16). Peak systolic strain/strain rate (SI_{SYS}, SR_{SYS}), peak strain rate during isovolumetric relaxation period (SR_{IVR}) and early diastole (SR_E) were calculated by averaging the values of each of the 18 segments, which were derived from the 6 segments of each of the 3 apical views (2-chamber, 4-chamber, and apical long-axis views). Ratios of early mitral inflow (E) and SR_{IVR} and SR_E have been shown to predict LV filling pressure (15,16) and were, therefore, used as diastolic indices.

All measurements of heart structure and performance were averaged over 3 cardiac cycles during SR. In AF rhythm, an index beat, which was the beat after the nearly equal preceding and pre-preceding intervals, was used for each measurement (17).

Catheter ablation and post-procedural follow-up. All antiarrhythmic drugs were discontinued for 5 half-lives before the procedure, except for amiodarone, which was discontinued for at least 6 weeks before. Our ablation protocol has been extensively described elsewhere (18,19). Briefly, we performed extensive encircling pulmonary vein isolation by a double-lasso technique. Two 7-F decapolar ring catheters (Lasso, Biosense Webster, Inc., Diamond Bar, California) were positioned at each pulmonary vein ostium, and an 8-mm tip 7-F deflectable catheter (Ablaze, Japan

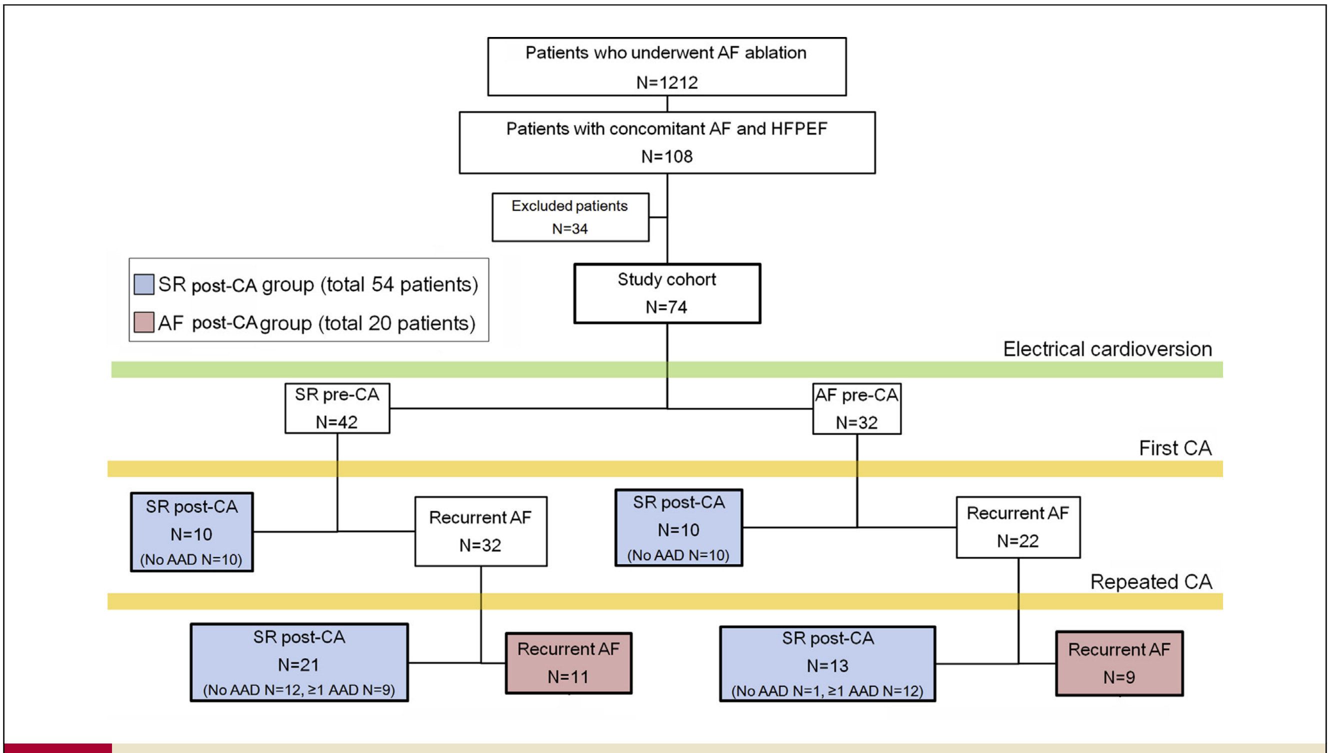

Figure 2 Flow Chart Illustrating the Study Population and Results of CA

The patients in the **blue** and **red boxes** were classified as the sinus rhythm (SR) post–catheter ablation (CA) group (n = 54) and AF post-CA group (n = 20), respectively. AAD = antiarrhythmic drug; AF = atrial fibrillation; HFPEF = heart failure preserved ejection fraction.

Table 2 Baseline Characteristics and Clinical Outcome of Study Patients

	Total (N = 74)	SR Post-CA Group (n = 54)	AF Post-CA Group (n = 20)	p Value
Age at enrollment, yrs	65 ± 7	65 ± 7	66 ± 8	0.809
Male	55 (74)	41 (76)	14 (70)	0.765
BMI, kg/m^2	26.7 ± 14.7	27.4 ± 17.0	24.8 ± 4.3	0.493
Blood pressure, mm Hg				
Systolic	126 ± 21	127 ± 22	122 ± 20	0.390
Diastolic	71 ± 12	72 ± 13	69 ± 10	0.469
NYHA class				
II	52 (70)	39 (72)	13 (65)	0.778
III	22 (30)	15 (23)	7 (35)	0.839
Hypertension	57 (77)	41 (76)	16 (80)	0.540
Diabetes mellitus	21 (28)	18 (33)	3 (15)	0.151
Dyslipidemia	42 (57)	33 (61)	9 (45)	0.292
Prior PCI or CABG	14 (19)	10 (19)	4 (20)	0.562
History of stroke	10 (14)	9 (17)	1 (5)	0.148
Obstructive sleep apnea	19 (26)	13 (24)	6 (30)	0.765
Smoking	33 (45)	24 (44)	9 (45)	1.000
Hemoglobin, g/dl	13.8 ± 1.7	13.8 ± 1.7	13.7 ± 1.9	0.811
eGFR, ml/min/1.73 m^2	64 ± 16	62 ± 14	68 ± 23	0.301
NT-proBNP, pg/ml	601 [324–936]	600 [389–871]	592 [312–1,062]	0.41
ANP, pg/ml	72 [49–95]	70 [47–81]	77 [70–118]	0.24
Medication				
ACE-I or ARB	58 (78)	41 (76)	17 (85)	0.188
Beta-blocker	53 (72)	38 (70)	15 (75)	0.779
Calcium-channel blocker	34 (46)	27 (50)	7 (35)	0.300
Diuretics	23 (31)	17 (31)	6 (30)	1.000
Digoxin	5 (7)	4 (7)	1 (5)	0.393
Statin	39 (53)	29 (53)	10 (50)	0.799
LV structure				
LV end-diastolic diameter, mm	48 ± 6	48 ± 6	46 ± 6	0.157
LV end-systolic diameter, mm	31 ± 6	31 ± 6	29 ± 5	0.221
IVST, mm	10 ± 2	10 ± 2	10 ± 2	0.721
PWT, mm	10 ± 2	10 ± 2	10 ± 2	0.758
EDVI, ml/m^2	90 ± 21	92 ± 22	85 ± 20	0.199
LV mass index, g/m^2	119 ± 33	121 ± 35	113 ± 27	0.445
RWT	0.42 ± 0.11	0.40 ± 0.08	0.44 ± 0.16	0.319

Values are mean ± SD, n (%), or median [interquartile range]. The p value indicates statistical difference between SR post-CA group and AF post-CA group.

ACE-I = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ANP = atrial natriuretic peptides; ARB = angiotensin II receptor blocker; BMI = body mass index; CA = catheter ablation; CABG = coronary artery bypass graft; EDVI = end-diastolic left ventricular volume index; eGFR = estimated glomerular filtration rate; IVST = interventricular wall thickness at end-systole; LV = left ventricular; NT-proBNP = N-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association; PCI = percutaneous coronary intervention, PWT = posterior wall thickness at end-systole; RWT = relative wall thickness; SR = sinus rhythm.

Lifeline Co., Tokyo, Japan) or a 7.5-F irrigation catheter with a 3.5-mm distal electrode (ThermoCool, Biosense Webster) was used for ablation. The endpoint of the extensive pulmonary vein isolation was creation of extensive ipsilateral bidirectional conduction block from the atrium to the pulmonary veins and vice versa. If AF was sustained after pulmonary vein isolation, additional ablation consisting of linear ablation of the LA roof, superior vena cava isolation, and/or ablation of continuous fractionated atrial electrograms was performed. If AF did not terminate after the additional ablation, SR was restored by transthoracic cardioversion (18,19). A caval-tricuspid isthmus line was also created in all patients with confirmation of bidirectional block.

After discharge, the patients were followed at 2 to 4 weeks after the CA and then every 1 to 3 months at the outpatient clinic (18,19). At each visit, the patients underwent a 12-lead electrocardiogram and questioning regarding any arrhythmia-related symptoms. At 2 weeks and 1, 3, 6, and 12 months after CA, we performed 24-h Holter monitoring and portable electrocardiographic monitoring (HCG-901, OMRON, Kyoto, Japan). These modalities were also used anytime the patients reported palpitations. If the electrocardiogram showed any episodes of AF or any other atrial tachyarrhythmias lasting >30 s during the follow-up, the patients were diagnosed as having recurrence of AF. A blanking period of 3 months was applied, and a redo procedure was recommended for recurrences after this period. If conduction gaps were present or if the pulmonary veins were not isolated during the redo procedure, ablation was performed according to the ablation scheme used during the first procedure. Successful CA was defined as the maintenance of SR without antiarrhythmic drug therapy after procedures during follow-up excluding the blanking period. All patients continued oral anticoagulation to maintain an international normalized ratio of between 2.0 to 3.0 during the entire follow-up period.

Statistical analysis. Means are expressed with 1 SD for continuous variables, and medians are presented with interquartile range for skewed variables. Differences in continuous variables were evaluated with Mann-Whitney *U* test or unpaired *t* test as appropriate. A chi-square test or Fisher exact probability test was used for comparison of categorical variables as appropriate. Cox proportional hazard regression models were used to evaluate the influence of the explanatory variables on maintenance of SR. Univariate analyses were performed with variables that might have an effect on success of CA on the basis of previous studies (18–21). Multivariate analyses were performed with variables that were statistically significant in the univariate analyses. Because of the small number of patients who did not maintain SR (n = 20), there could be up to 2 predictors without overfitting the multivariate Cox model. Therefore, to establish this multivariate model, we selected 2 variables (AF type and history of hypertension) that seemed to have significant effects on outcome compared with other variables in the univariate analysis. Reproducibility of 2DSTE was tested in 20 randomly selected patients. A value of $p < 0.05$ was considered to be statistically significant. All statistical analyses were performed using SPSS software (version 16.0, SPSS Inc., Chicago, Illinois).

Results

Study population and outcomes of AF ablation. Follow-up results and complications of CA are summarized in Table 1 and Figure 2. During a mean follow-up period of 34 ± 16 months (range: 12 to 75 months), single- and multiple-procedure drug-free success rates were 27% (n = 20) and 45% (n = 33), respectively. The multiple procedures and pharmaceutically assisted success rate was 73% (n = 54). CA was successfully performed in all patients, and no major complications occurred during follow-up. Although there were a few minor complications (groin hematoma and post-procedural pulmonary edema), all of these patients made a full recovery. General characteristics, serum markers, and LV structural parameters in patients with maintenance of SR (SR post-CA group, n = 54) and patients with AF recurrence (AF post-CA group, n = 20) are listed in Table 2. No statistically significant differences were found in any of the baseline parameters between the 2 groups. Detailed data regarding characteristics of the arrhythmia and therapies for AF are shown in Table 3. The difference of AF duration between groups did not reach statistical difference; however, the proportion of long-standing persistent AF was greater in the AF post-CA group than the SR post-CA group. The prevalence of SR

Table 3 Characteristics and Therapies of AF

	Total (N = 74)	SR Post-CA Group (n = 54)	AF Post-CA Group (n = 20)	p Value
Duration of AF before CA, yrs	7.3 ± 7.2	6.3 ± 6.3	10.0 ± 8.9	0.10
Type of AF				
Paroxysmal	23 (31)	20 (37)	3 (15)	0.09
Persistent	7 (9)	6 (11)	1 (5)	0.39
Long-standing persistent	44 (59)	28 (52)	16 (80)	0.04
AAD tried before CA, n	3 ± 1	2 ± 1	3 ± 1	0.53
AAD before CA				
Class I	57 (77)	41 (76)	16 (80)	0.49
Class III	37 (50)	26 (48)	11 (55)	0.79
Class IV	12 (16)	7 (13)	5 (25)	0.18
Restoration of SR pre-CA	42 (57)	28 (52)	14 (70)	0.56
Prevalence of additional ablation				
Roof line	44 (59)	30 (56)	14 (70)	0.19
Superior vena cava isolation	20 (27)	14 (26)	6 (30)	0.77
Complex fractionated atrial electrogram ablation	20 (27)	12 (22)	8 (40)	0.15
Repeated ablation	50 (68)	34 (63)	16 (80)	0.16
Heart rate, beats/min				
Baseline	67 ± 13	66 ± 14	70 ± 6	0.09
Follow-up	67 ± 7	65 ± 6	68 ± 9	0.13
Length of follow-up, months	34 ± 16	33 ± 7	36 ± 15	0.41

Values are mean ± SD or n (%). The p value indicates statistical difference between SR post-CA group and AF post-CA group. Abbreviations as in Tables 1 and 2.

Table 4 Factors Related to Maintenance of SR After Ablation

	Univariate Analysis			Multivariate Analysis		
Variables	HR	95% CI	p Value	HR	95% CI	p Value
Age at enrollment, per 1-yr increase	0.99	0.96–1.03	0.69			
Duration of AF before CA, per 1-yr increase	0.95	0.90–1.00	0.048			
Type of AF*	1.87	1.07–3.27	0.03	1.81	1.03–3.17	0.04
Male	0.69	0.36–1.29	0.25			
Hypertension	0.50	0.25–0.99	0.046	0.49	0.24–0.96	0.04
Obstructive sleep apnea	1.28	0.71–2.32	0.42			
NT-proBNP†‡	0.76	0.58–0.99	0.04			
LA volume index‡	0.89	0.64–1.24	0.48			
eGFR‡	1.05	0.87–1.27	0.63			

Maintenance of sinus rhythm is the dependent variable. *Other than long-standing persistent AF. †Logarithmically transformed skewed variables. ‡Per 1-SD increase.
CI = confidence interval; HR = hazard ratio; LA = left atrial; other abbreviations as in Tables 1 and 2.

restoration by electrical cardioversion before CA was comparable in the 2 groups, and it did not influence the outcome of AF ablation. The prevalence of additional ablation did not differ between the 2 groups. No significant differences in heart rate between baseline and follow-up values were noted in either group.

Prediction of patients who maintained SR. The results of the Cox proportional hazard regression analysis for maintenance of SR are summarized in Table 4. Multivariate analysis identified AF type (other than long-standing persistent AF) and lack of hypertension to be independently associated with maintenance of SR (hazard ratio [HR]; 1.81, 95% confidence interval [CI]: 1.03 to 3.17, p = 0.04; HR: 0.49, 95% CI: 0.24 to 0.96, p = 0.04, respectively).

Changes in echocardiographic parameters. Changes in conventional echocardiographic parameters are summarized in Table 5. In the SR post-CA group, LVEF increased and

Table 5 Echocardiographic Parameters in Patients With and Without Recurrence of AF

	SR Post-CA Group (n = 54)	AF Post-CA Group (n = 20)	p Value
LVEF, %			
Baseline	67 ± 7	66 ± 8	0.93
Follow-up	69 ± 7*	66 ± 7	0.10
Mitral peak E-wave velocity, cm/s			
Baseline	79 ± 20	82 ± 34	0.56
Follow-up	74 ± 22	87 ± 30	0.04
E/A ratio			
Baseline, n = 42	1.5 ± 0.6 (n = 28)	1.6 ± 0.8 (n = 14)	0.65
Follow-up, n = 54	1.3 ± 0.7 (n = 54)	NA	NA
Deceleration time of E-wave, ms			
Baseline	216 ± 52	208 ± 42	0.53
Follow-up	220 ± 51	204 ± 39	0.20
E′, cm/s			
Baseline	7.2 ± 2.6	7.6 ± 2.2	0.26
Follow-up	9.0 ± 3.5†	8.4 ± 3.0	0.40
E/E′ ratio			
Baseline	11.2 ± 3.7	13.3 ± 6.5	0.10
Follow-up	9.6 ± 3.0*	12.2 ± 4.8	0.04
LA volume index, ml/m^2			
Baseline	43 ± 14	51 ± 24	0.10
Follow-up	38 ± 16†	55 ± 25	0.008
LA total emptying fraction, %			
Baseline	27 ± 13	29 ± 10	0.65
Follow-up	36 ± 14*	25 ± 10	0.001

Values are mean ± SD. The p value indicates statistical difference between SR post-CA group and AF post-CA group. In AF post-CA group, E/A ratios at follow-up were not available because of AF rhythm. *p < 0.01 versus baseline; †p < 0.05 versus baseline.
LVEF = left ventricular ejection fraction; NA = not available; other abbreviations as in Tables 2 and 4.

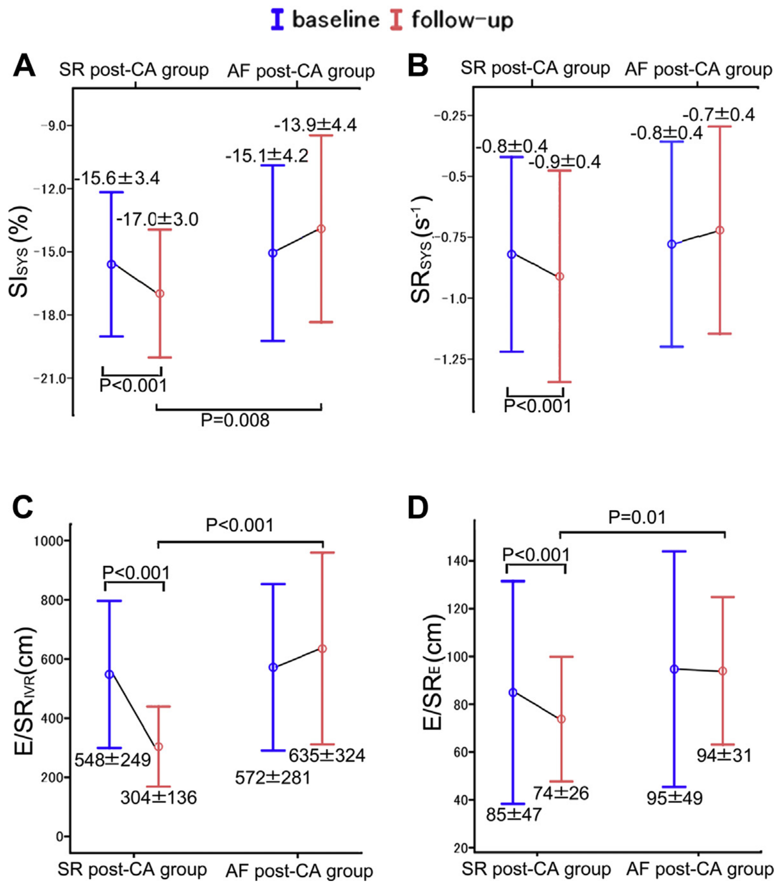

Figure 3 **Changes in LV Function**

LV strain and strain rate measurements in patients who maintained sinus rhythm (SR post-CA group) and patients with recurrence of AF (AF post-CA group). Plotted values are mean ± SD. SI_{SYS} **(A)** and SR_{SYS} **(B)** are indices of LV systolic function, and E/SR_{IVR} **(C)** and E/SR_E **(D)** are indices of LV diastolic function. Abbreviations as in Figures 1 and 2.

E/E′ ratio reduced significantly at follow-up compared with baseline values, in contrast to these parameters in the AF post-CA group, which showed no change. LA total emptying fraction improved and LA volume index was reduced only in the SR post-CA group during follow-up. Changes in LV strain and strain rate measurements are illustrated in Figure 3. Each parameter at baseline was comparable between the 2 groups. From baseline to follow-up, SI_{SYS} and SR_{SYS}, as indices of longitudinal systolic function increased, and E/SR_{IVR} and E/SR_E, which reflect LV filling pressure, significantly decreased only in the SR post-CA group.

Reproducibility. Reproducibilities of 2DSTE measurements are listed in Table 6.

Discussion

Efficacy of AF ablation in patients with HFPEF. Numerous previous studies have successfully applied AF ablation to heart failure patients with reduced LVEF (10,11). However, this is the first study, to our knowledge, to present the efficacy and safety of CA for AF in patients with HFPEF. The type of AF in this study cohort mainly consisted of persistent or long-standing persistent AF. In comparison with published outcomes of CA that targeted

Table 6 **Reproducibility of Strain and Strain Rate Measurements**

	SI_{SYS}	SR_{SYS}	SR_{IVR}	SR_E
Intraobserver				
Correlation coefficient	0.99	0.95	0.93	0.99
Mean absolute percentage error, %	7.8 ± 7.7	8.1 ± 5.6	9.6 ± 6.1	5.7 ± 5.1
Interobserver				
Correlation coefficient	0.99	0.90	0.89	0.93
Mean absolute percentage error, %	10.1 ± 13.9	10.3 ± 8.5	13.2 ± 7.9	9.9 ± 7.7

SI_{SYS} = average of peak LV strain at systole; SR_{SYS} = average of peak LV strain rate at systole; SR_{IVR} = average of peak LV strain rate during isovolumetric relaxation period; SR_E = average of peak LV strain rate at early diastole.

persistent/long-standing persistent AF, recurrence-free probability after treatment with a composite of multiple procedures and antiarrhythmic drugs was almost similar; however, drug-free success rate was relatively low in our results (22,23). LV diastolic dysfunction, which is a key feature of HFPEF, may aggravate LA remodeling and contribute to the arrhythmogenic substrate and development of AF (24,25); therefore, total AF cure without antiarrhythmic drugs in HFPEF patients may be more difficult than that in other populations. This idea might be supported by the current results that long-standing persistent AF and hypertension, which relate to diastolic dysfunction (25,26) and heart failure (3,8), could predict AF recurrence. In HFPEF patients with restrictive ventricular physiology, AF reduces diastolic filling time, and loss of effective atrial contraction adds an adverse influence on LV filling and hemodynamics. Thus, patients with HFPEF may obtain greater benefit from rhythm control, in theory. Moreover, our results showing lower complication rates than those of previous reports (22,23) suggested the safety of AF ablation in patients with HFPEF. Therefore, CA may be an effective therapeutic option for patients with AF with concomitant HFPEF, although further surveys are needed.

Improvements of cardiac function after AF elimination in HFPEF. In this study, optimal rate control was achieved before CA, and heart rate did not change significantly from baseline to follow-up in either group. Therefore, improvement in cardiac function after CA may be more related to maintenance of SR than to normalization of heart rate. In patients with AF or HFPEF, longitudinal systolic deformations are depressed as a sign of early LV systolic dysfunction despite a normal LVEF (27,28). Because the longitudinal fibers mediating long-axis deformation are located in the subendocardial region, longitudinal function may be more vulnerable to pathological changes and overload (29). Therefore, normalization of cardiac rhythm by CA might have contributed to the reduced burden within the LV and ameliorated longitudinal LV strain in the present study. As regards LV diastolic function, patients who present with isolated diastolic dysfunction but preserved LVEF are not rare in AF populations (25). The current study revealed that maintenance of SR improved diastolic indices (E/E′ ratio, E/SR_{IVR}, and E/SR_E), which correlated well with LV end-diastolic pressure in HFPEF (15). Besides improvements of LV function, long-term maintenance of SR achieved recovery of LA function, which has been recognized as a partial pathophysiology of HFPEF (6). Collectively, our results suggested that elimination of AF by CA might ameliorate cardiac function even in HFPEF as it has already been reported in heart failure with reduced EF (10,11).

Study limitations. A standard definition of HFPEF is lacking, and difficulty in diagnosing HFPEF remains a major limitation. However, our patients met widely used criteria for HFPEF (12) and had features that closely match patients with HFPEF in other published studies (1,5,7). Twenty-four–hour Holter monitoring less effectively detects asymptomatic recurrence of atrial arrhythmias than does transtelephonic daily monitoring or implantable loop recorders (30). However, follow-up strategy in our study is in line with the methodology of previous studies investigating outcomes after AF ablation in patients with heart failure (10,11).

Conclusions

Our results may suggest that AF patients with concomitant HFPEF can be effectively and safely treated with a composite of repeated CA procedures and pharmaceuticals. However, this is a single-arm study; therefore, randomized studies with larger populations and longer follow-up are warranted to confirm the efficacy of AF ablation in patients with HFPEF.

Reprint requests and correspondence: Dr. Yoshihiro Seo, Cardiovascular Division, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba 305-8575, Japan. E-mail: yo-seo@md.tsukuba.ac.jp.

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