Catheter ablation of nonparoxysmal atrial fibrillation in patients with heart failure with reduced ejection fraction and functional mitral regurgitation

Teng Li (gdmc99@163.com)
Fuwai Hospital Chinese Academy of Medical Sciense, Shenzhen https://orcid.org/0000-0002-3502-2758

Jun Huang
Fuwai Hospital Chinese Academy of Medical Sciences, Shenzhen

Jian Liang
Fuwai Hospital Chinese Academy of Medical Sciences, Shenzhen

Wenjie Peng
Fuwai Hospital Chinese Academy of Medical Sciences, Shenzhen

Ligang Ding
Fuwai Hospital Chinese Academy of Medical Sciences, Shenzhen

Yifu Li
Fuwai Hospital Chinese Academy of Medical Sciences, Shenzhen

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Abstract

Background

The optimal treatment for patients with nonparoxysmal atrial fibrillation (AF) and heart failure with reduced ejection fraction (HFrEF) has been a subject of debate for years. We aimed to evaluate the efficacy and safety of catheter ablation (CA) of nonparoxysmal AF in patients with HFrEF and functional mitral regurgitation (MR).

Methods

This single-center, retrospective, and observational study enrolled 21 consecutive patients with nonparoxysmal AF, HFrEF and functional MR underwent CA The ablation strategy consisted of bilateral circumferential pulmonary vein isolation and empirical linear ablations.

Results

After a mean follow-up of 18.2 ± 8.5 months, stable sinus rhythm (SR) was achieved in 15 patients (71.4%) after the initial procedure and 17 patients (81%) after the final procedure. The NYHA class improved from 2.7 ± 0.7 before ablation to 1.2 ± 0.4 during follow-up ($p < 0.001$). Left ventricular ejection fraction increased from 36.5 ± 6.3% to 54.9 ± 6.6% ($p < 0.001$). Among 17 patients in continuous SR after the final procedure, MR severity decreased to mild or none,and 10 patients with decreased ventricular wall motion was completely restored to normal after the procedure. No serious complications occurred.

Conclusion

CA may be a safe and effective method for treating nonparoxysmal AF in patients with HFrEF and functional MR. It can significantly improve HF symptoms, functional MR and left ventricular function..

Background

Atrial fibrillation (AF) and heart failure (HF) are predominantly cardiovascular diseases [1–3]. Their combination is associated with increased morbidity and mortality. Catheter ablation (CA) has played an increasingly important role in treating symptomatic patients with AF. For patients with nonparoxysmal (persistent or long-standing persistent) AF and HF, CA is more effective than antiarrhythmic drugs (AADs) therapy in achieving freedom from AF at long-term follow-up, and improved left ventricular (LV) function[4–8]. 2017 HRS expert consensus[9] and 2016 ESC Guidelines[10] recommend that CA should be considered in symptomatic patients with AF and HF with reduced ejection fraction (HFrEF) to improve symptoms and cardiac function.

AF, HF and Mitral regurgitation (MR) often coexist, and one leads to the others. Functional MR (FMR) has been described as a result of atrial enlargement and annular dilatation. Severe FMR was successfully treated with medication in only 40% of the patients with HFrEF [11]. A Case Report demonstrated that a significant reduction in MR severity after maintenance of sinus rhythm (SR) was achieved by Pulmonary vein isolation (PVI) [12]. Fewer data are available regarding the effectiveness and safety of CA in patients with drug-refractory nonparoxysmal AF, HFrEF and FMR, especially in patients with moderate or severe MR. The purpose of this study was to evaluate the impact of rhythm control strategy using CA among nonparoxysmal AF patients complicated with HFrEF and FMR.

Methods

Study population

The single-center study was an observational, retrospective cohort study performed within the Fuwai Hospital Chinese Academy of Medical Sciences, Shenzhen. Consecutive patients with nonparoxysmal AF undergoing index AF ablation between January 2017 and July 2019 were retrospectively enrolled. Nonparoxysmal AF was defined as continuous AF of > 7 days, and included long-standing persistent AF, which lasted > 1 year. The inclusion criteria were: (1) nonparoxysmal AF was symptomatic and refractory to at least one AAD; (2) age ≥ 18 years; (3) New York Heart Association (NYHA) class II, III, or IV HF and a left ventricular ejection fraction (LVEF) of 45% or less; (4) functional MR. The exclusion criteria were: (1) previous AF ablation; (2) rheumatic heart disease or heart valve replacement; (3) left atrial (LA) thrombus; (4)coronary artery bypass graft surgery in the past year; and (5)stroke or myocardial infarction within last 3 months. The local ethics committee approved the study protocol that complied with the provisions of the Declaration of Helsinki. All patients provided written informed consent before the procedure.

Transthoracic Echocardiography

MR severity was diagnosed by transthoracic echocardiography and was graded to non-MR, mild MR, moderate MR, and severe MR in accordance with the guidelines of the American Society of Echocardiography [13]. Left atrium anterior-posterior diameter (LAD) was measured in the parasternal long-axis view. The assessment of the evolution of the MR was based on the comparison of the baseline echocardiography and the last available echocardiography at follow-up.

Electrophysiological Study And Ablation

Procedures were performed in the fasted state and under conscious sedation using intravenous fentanyl or sufentanil. After transseptal puncture, electroanatomic mapping was performed using a three-dimensional system (CARTO3, Biosense Webster, Inc. or Ensite NavX Velocity, St. Jude Medical) with either a Lasso or Pentaray catheter (Biosense Webster, Inc.). A 3.5 mm irrigated ablation catheter

(SmartTouch, Biosense Webster, Diamond Bar, CA, USA, or Cool flex, St. Jude Medical, Irvine, CA, USA) was advanced to the LA for subsequent ablation.

Ablation strategy included PVI and linear ablations across the LA roof, the mitral isthmus (MI) and the cavo-tricuspid isthmus (CTI)[14]. Synchronized, biphasic direct current shocks (200J) were delivered externally to restore SR after PVI and linear ablations. If cardioversion was unsuccessful, additional ablation was made at the discretion of operators (Fig. 1B). If AF organized into an AT (atrial tachycardia), activation and entrainment mapping was performed to identify the mechanism of AT and optimal site for ablation. Procedural endpoint was isolation of PV antrum and completed conduction block across the three ablation lines. Radiofrequency energy was delivered with 43 °C, 35W as the maximum temperature and power, and 17 mL/min as the flow rate. Contact force was recommended within a range of 5 to 20 g. Along the posterior wall, the maximum power was limited to 30W. At each site, the ablation time was restricted to 30–60 s, but no more than 30 s when ablating on the LA posterior wall and inside Coronary Sinus.

Follow-up

After the procedure, continuous ECG monitoring was performed for 48 hours. Follow-up was performed at 3, 6, and 12 months and comprised a clinical examination, eechocardiography, 12-lead ECG, and 24-hour Holter ECG. Additional ECG was initiated in patients with symptoms suggestive of arrhythmia recurrence. Success in terms of maintaining SR was defined as freedom from documented atrial arrhythmia lasting ≥ 30 seconds after the 3-month blanking period [10].

Statistical Analysis

Continuous variables (expressed as mean ± SD) were compared with Student's t-test (or Wilcoxon when necessary). Categorical variables are presented as counts and percentages. Categorical variables were compared with chi-squared or Fisher exact test, as appropriate. A probability value < 0.05 was considered statistically significant. Non-normally distributed continuous variables are expressed as median (interquartile range).

Results

Patient characteristics

From January 2017 to July 2019, only 21 nonparoxysmal AF patients (13 males, mean age 59 ± 14 years) with HFrEF and MR were included in the study, and their baseline data are shown in Table 1. Median (Q1, Q3) AF duration was 36 months (33, 49). The baseline NYHA class function and echocardiographic data were summarized in Table 2 and Fig. 3. Five patients (23.8%) had moderate MR and 5 patients (23.8%) had severe MR, respectively. Three patients (14.3%) had severe MR with severe tricuspid regurgitation

(TR) spontaneously. Patients with severe FMR were more likely to be female, had a lower LVEF and larger left cardiac dimensions. Decreased ventricular wall motion (VWM) was found in 13 patients (61.9%).

Table 1
Baseline Characteristics

Patients	**21**
Age (years)	59 ± 14
Male, n (%)	13(61.9)
AF duration, months	36
Average ventricular rate (bpm)	90 ± 11
BMI (kg/m2)	23.6 ± 3.0
CAD, n (%)	5(23.8)
Hypertension, n (%)	8(38.1)
Diabetes mellitus, n (%)	6(28.6)
Stroke, n (%)	2(9.5)
AF Atrial fibrillation, BMI Body mass index, CAD Coronary artery disease	

Table 2
Differences in baseline and during follow-up of 21 patients

Characteristic	Baseline	Follow-up	*P value*
NYHA class, n (%)			
I	0	16(76.2)	-
II	8(38.1)	5(23.8)	0.51
III	10(47.6)	0	-
IV	3(14.3)	0	-
Degree of MR, n (%)			
Mild	11(52.4)	9(42.9)	0.76
Moderate	5(23.8)	0	-
Severe	5(23.8)	1(4.8)	0.18
TR, n (%)	13 (61.9)	4(19.0)	< 0.05
Decreased VWM, n (%)	13 (61.9)	3(14.3)	< 0.05
NYHA New York Heart Association, MR Mitral Regurgitation, TR Tricuspid Regurgitation, VWM Ventricular wall motion			

Procedural Parameters And Complications

All 21 patients had cardioversion after PVI and linear ablations. The total procedure time, ablation time and radiofrequency time were 118.9 ± 18.1, 47.0 ± 10.0 and 11.2 ± 1.9 minutes, respectively. Temporary cardiac pacemaker was implanted due to persistent and slow atrioventricular junctional escape rhythm after cardioversion in one patient with obvious symptoms, whose SR could not spontaneous restored in 36 hours, while AF recurred and maintained in a long term. No major complications occurred in this study. One patient had femoral pseudoaneurysm and femoral arteriovenous fistula simultaneously, and it was cured by conservative therapy. There was no procedure-related death or acute left heart failure attack.

Freedom From Atrial Fibrillation

During a mean follow-up of 18.2 ± 8.5 (7□32) months from the initial ablation, AF recurred in 3 of 21 (14.3%) patients and AT occurred in 3 patients. Two patients (9.5%) underwent repeat ablations (1 repeat procedure in 1 and 2 repeat procedures in 1) during follow-up, other four patients refused to repeat procedure. The freedom from AF/AT off ADDs after the initial ablation procedure and after the final procedure was 71.4% (15/21) and 81% (17/21), respectively. The Kaplan-Meier curve for the effectiveness outcomes was shown in Fig. 2.

Clinical And Echocardiographic Outcomes

The NYHA class of 21 patients improved from a mean of 2.7 ± 0.7 before ablation to 1.2 ± 0.4 during follow-up ($p < 0.001$). Among 17 patients in continuous SR after final procedure, the NYHA class of 16 patients restored to normal (class I). No changes were observed among the 4 patients in whom arrhythmia recurred despite the use of drugs. The average ventricular rate of 24 hour Holter before initial procedure was greater in those who maintained SR (93.0 ± 7.4 bpm) compared with those with recurrent AF/AT (73.2 ± 10.2 bpm, p□0.05).

On follow-up echocardiogram, marked improvement of the LVEF,LAD and left ventricular end diastolic dimension(LVEDD) were observed in 21 patients after final ablation procedure(Fig. 3). One case example was shown in Fig. 1. LVEF increased from 36.5 ± 6.3% before ablation to 54.9 ± 6.6% during follow-up ($p < 0.001$) also decrease significantly. A significant decline in LAD ($p < 0.001$) and LVEDD was experienced in 17 patients with maintained SR after final ablation.

Marked improvement of the MR, TR and decreased ventricular wall motion were also found in 21 patients after final ablation procedure(Table 2), the percentage of MR decreased from 100% before ablation to 47.6% during follow-up ($p < 0.001$). Only 35.3% of (6/17) patients in this study had no more than mild residual MR at follow-up with successful restoration of SR. No significant improvement of the MR was observed in the four patients who recurred after the final procedure. Among 17 patients in continuous SR, decreased ventricular wall motion (VWM) of 10 patients before procedure was completely restored to normal after the final procedure.

Discussion

Major Findings

This retrospective, observational study showed that CA was a safe and effective method for treating nonparoxysmal AF in patients with HFrEF and FMR. The single procedure success rate off AADs was 71.4% at long term follow-up, increased to 81% in patients who allowed to repeat the procedure. HF symptoms, FMR and LV function were significantly improved by CA. Restoration and long-term maintenance of SR may be associated with rapid ventricular rate of AF before ablation procedure.

Safety And Efficacy Of AF Ablation

For patients with AF and HF, AADs maintenance of SR is incomplete or unsatisfactory with significant adverse side effects and drug interaction, and AF ablation became more and more widely used as a rhythm control strategy without the adverse effects of AADs. Restoration and maintenance of normal SR following treatment directly correlates with improved quality of life in patients with AF and HF. Several studies [4–8, 15] have reported that CA is effective in restoring SR in selected patients with persistent AF and HF, and can reduce unplanned hospitalization and mortality. In this study, stable SR was achieved in

15 patients (71.4%) after the initial procedure and 17 patients (81%) after multiple procedures. Following treatment, CA has been shown to improve HF symptoms and NYHA class. Moreover, we observed significant improvements in echocardiographic parameters including MR, LVEF, LAD and LVEDD in our patients with restoration of SR. However, there is no significant change in LV function in patients without maintenance of SR, and long-term medical treatment is still required. There were no serious procedural complications and adverse events such as pericardial effusion, acute left heart failure and even death.

AF And Functional MR

Severe FMR was present in 23.8% of our study population. MR is reported to decrease the outcome of CA for AF patients, and the degree of MR is significantly higher among patients with recurrence [16, 17]. Previous studies [12, 17, 18]suggest that patients with AF and an enlarged mitral annulus may be at risk of developing FMR, and patients with a moderate or greater degree of FMR showed significant improvement in valve function with restoration of SR or great reduction of AF episodes after CA. The results of this study are similar to previous studies [12]. Despite having a moderate or greater degree of MR before ablation procedure, patients with successful ablations experienced significant reductions in LAD, mitral annular dimension and LVEDD. In contrast, among patients who had recurrence of AF, there was no significant improvement in the MR and LAD after procedure.

For symptomatic patients with AF and severe FMR, the treatment mainly depends on the clinical and echocardiographic findings together to prevent unnecessary mitral valve replacement or valvular intervention [13, 19]. Therefore, the presence of significant MR should not necessarily preclude CA of nonparoxysmal AF in appropriately selected patients. In our study, a significant improvement in HF symptoms, LVEF and MR severity was showed after CA, which made additional mitral valve surgery unnecessary for patients with AF and severe FMR symptoms.

AF-mediated Cardiomyopathy

This study also found that the average ventricular rate before initial procedure in patients with stable SR was significantly faster than that in patients with recurrence. AF with failed ventricular rate control may be the sole cause for ventricular dysfunction or exacerbating ventricular dysfunction. In this study, after SR restoration and ventricular rate control, HR symptoms and LV function were significantly improved, dilated LA and LV were completely reversed to normal, and there was no need to take AADs and anti-HF treatment. This may be associated with tachycardia cardiomyopathy or AF-mediated cardiomyopathy (AMC), but it should be distinguished from other cardiomyopathies complicated with AF [3].Once the tachyarrhythmia is controlled, its cardiac function is partially or completely reversible. Although significant improvement was achieved in our patients, we could not determine whether the mean rapid ventricular rate before procedure was a risk factor for the successful ablation of nonparoxysmal AF in patients with HFrEF and FMR.

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Study Limitations

This is a single-center observational and retrospectively study including a small number of patients (n = 21) with nonparoxysmal AF in patients with HFrEF and MR. In this study, atrial arrhythmia recurrence was only assessed with 24 hour Holter monitoring and not with implantable loop recorders or 7 day Holter monitoring before ablation and during follow-up, overall success rate might have been overestimated, particularly in patients with asymptomatic AF. The results of this study do not represent that CA is safe and effective for all patients with nonparoxysmal AF complicated with HF and MR, especially primary MR. Therefore, its results and conclusions require further confirmation in larger randomized controlled trials.

Conclusions

CA may be a safe and effective method for treating nonparoxysmal AF in patients with HFrEF and FMR. It can significantly improve HF symptoms, FMR and LV function. We found that restoration and long-term maintenance of SR maybe associated with rapid ventricular rate of AF before ablation procedure. For patients with nonparoxysmal AF combined with HFrEF and FMR without specific catheter ablation contraindications, CA should be recommended to improve the prognosis of patients.

Abbreviations

AF: atrial fibrillation; AT: atrial tachycardia; HF: heart failure; HFrEF: heart failure with reduced ejection fraction; CA: catheter ablation; MR: mitral regurgitation; FMR: functional mitral regurgitation; TR: Tricuspid Regurgitation; AADs: antiarrhythmic drugs; SR: sinus rhythm;LA: left atrial; LV: left ventricular; LVEF: Left ventricular ejection fraction; NYHA: New York Heart Association; LAD: Left atrium anterior-posterior diameter; VWM: ventricular wall motion; LVEDD: left ventricular end diastolic dimension;

Declarations

Ethics approval and consent to participate

This retrospective study was approved and supervised by the Ethics Committee of Fuwai Hospital Chinese Academy of Medical Science. Written informed consent was obtained from all individual participants included in the study. A copy of the written consent is available for review by the Editor of this journal.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors' contributions

TL and JH have done the patient's follow-up and drafted the manuscript. TL, YFL and LGD have done the ablation and provided the photographs of the ablation. JL and WJP have helped on the manuscript drafting and revision. All authors read and approved the final manuscript.

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Not Applicable

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Figures

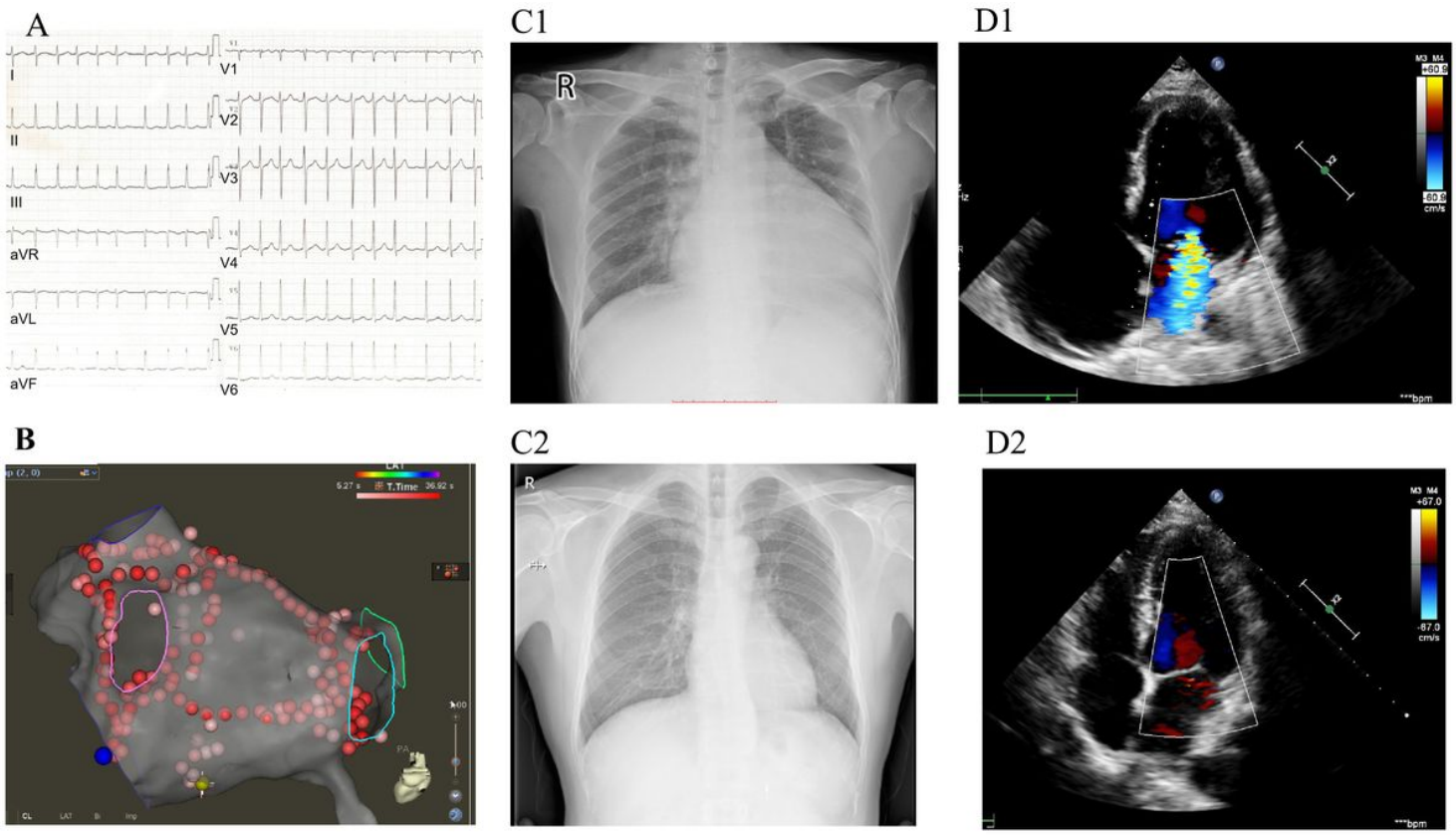

Figure 1

Case example of catheter ablation in a patient with persistent atrial fibrillation, HFrEF and severe MR. A Native ECG B, Ablation strategy Radiograph before (C1) and 12 months after (C2)ablation procedure. Apical four chamber view showing severe mitral regurgitation (MR) before ablation procedure (D1); and only mild MR 3 months afterwards (D2). HFrEF, Heart failure with reduced ejection fraction.

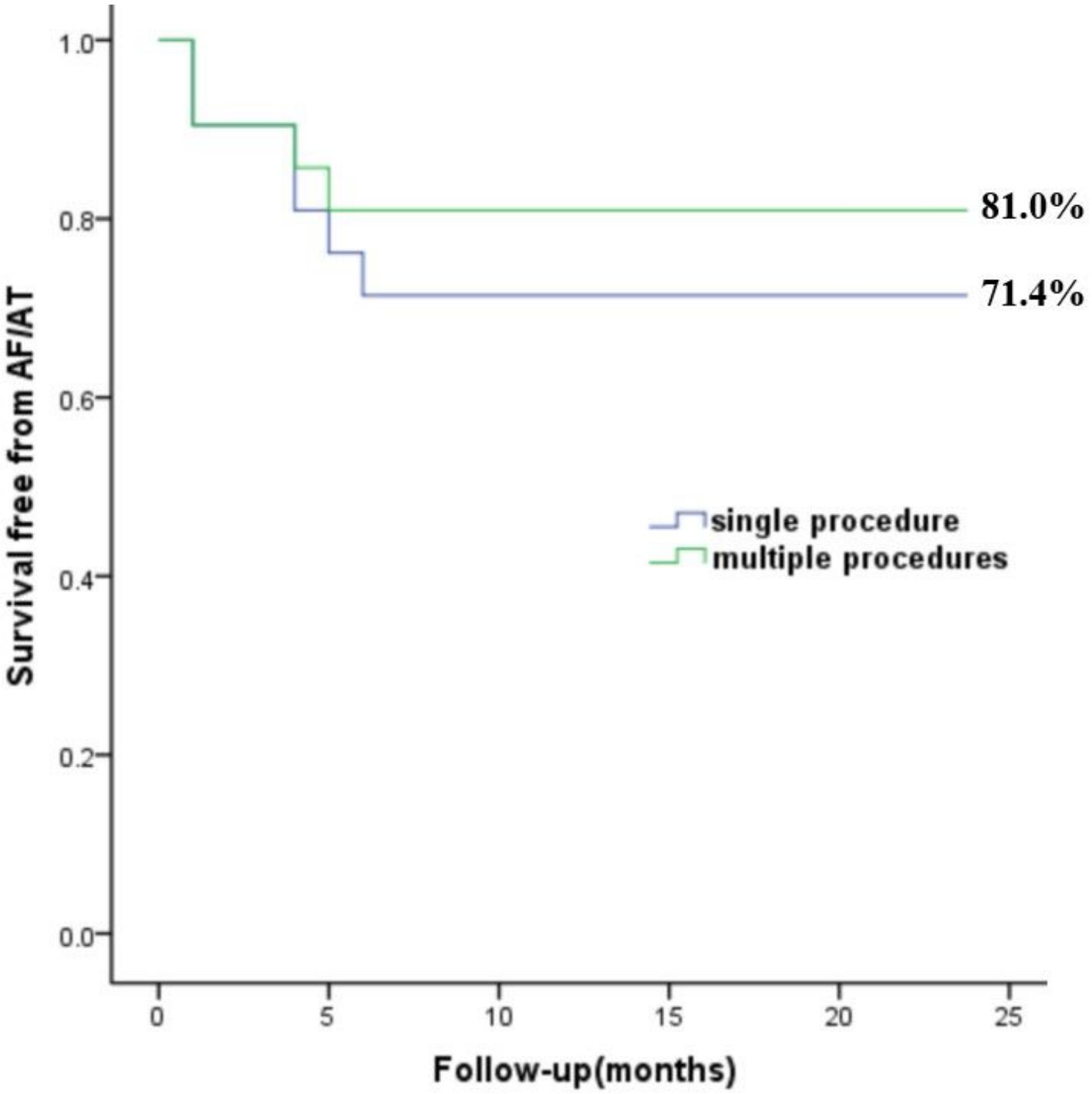

Figure 2

Freedom from AF/AT. The Kaplan-Meier curve showing freedom from AF/AT following the primary and last procedure for patients.

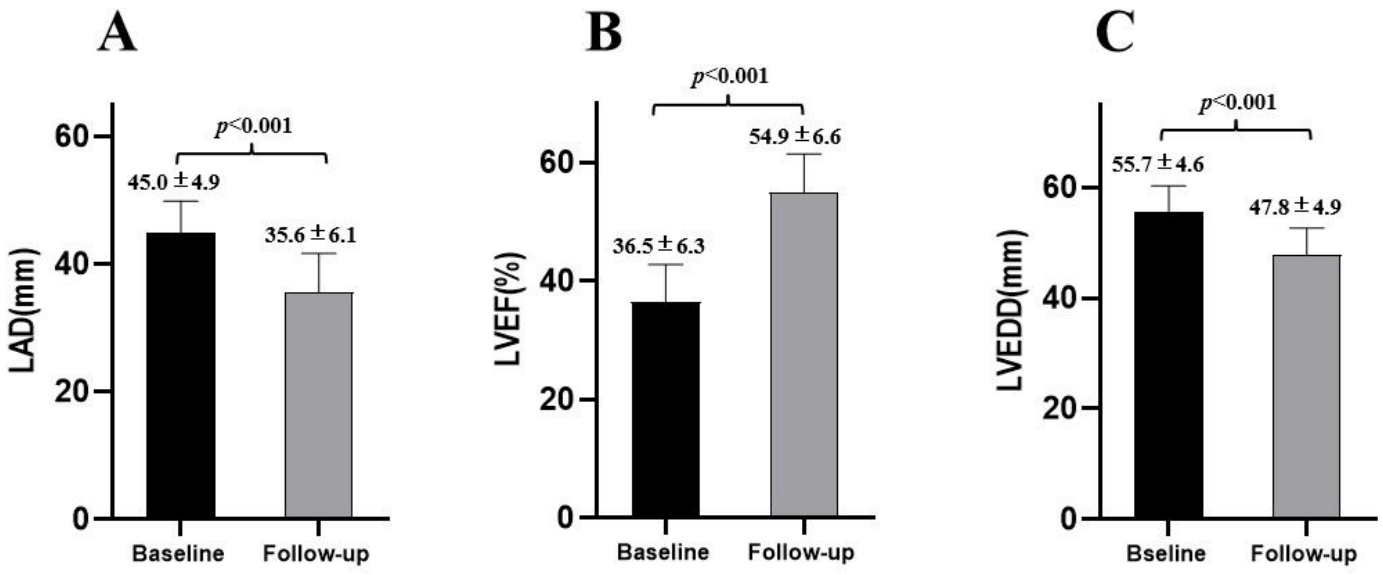

Figure 3

Comparison of echocardiographic parameters between preoperative and postoperative follow-up. Figures A, B and C show the preoperative and postoperative comparison of LAD, LVEF and LVEDD, respectively. LAD, left atrial dimension; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic dimension.