

Original
Article

Radiofrequency Ablation in Patients Undergoing Mitral Valve Surgery with or without Giant Left Atria

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Purpose: We aimed to compare the efficacy of radiofrequency ablation (RFA) in patients undergoing mitral valve (MV) surgery with or without giant left atria.

Methods: This retrospective, single-center, cohort study investigated patients who underwent MV surgery and concomitant RFA from 2009 to 2019. Patients were divided into non-giant left atria (diameter ≤ 65 mm, $n = 1543$) and giant left atria (diameter >65 mm, $n = 241$) groups. Five-year freedom from atrial tachyarrhythmia recurrence and thromboembolic event (TE) rates were assessed with death as the competing risk factor with and without propensity-score matching.

Results: Patients with giant left atria had higher mortality (10.8% versus 6.2%, $P = 0.008$) and readmission rates for heart failure than those without (12.0% versus 6.8%, $P = 0.004$).

Atrial tachyarrhythmia recurrence rates were higher in patients with giant left atria than in those without (49% versus 24% at 5 years, $P < 0.001$), but the cumulative incidence of TEs before ($P = 0.944$) and after ($P = 0.695$) propensity-score matching was comparable.

Conclusions: RFA effectively prevented TEs in patients with giant left atria, despite significant atrial tachyarrhythmia recurrence. Atrial tachyarrhythmia recurrence did not increase the risk of TEs. A lower success rate should be considered when deciding whether to perform surgical ablation in patients with giant left atria.

Keywords: giant left atrium, radiofrequency ablation, outcome, competing risk, thromboembolic events

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice, affecting an estimated 2.8% of

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the general population and 10% of patients undergoing cardiac surgery.¹ Radiofrequency ablation (RFA) has been shown to reduce the burden of AF during follow-up when performed concomitantly with other indicated cardiac surgeries, especially mitral valve (MV) surgery.²

Increased left atrium (LA) size has been established as a significant risk factor for treatment failure of AF after a maze procedure. LA size itself may also influence the maintenance of sinus rhythm (SR).^{3,4} Specifically, treatment guidelines and expert consensus suggest that patients with a giant left atria (GLA; left atrial diameter [LAD] >65 mm) have significantly increased recurrence rates of AF after catheter ablation.^{5,6} However, there is no clear consensus regarding surgical ablation on the LAD line. Although several studies suggest that LAD >65 mm is an independent risk factor for AF recurrence after surgical ablation, Ad et al.⁷ maintained

that surgical ablation was an effective treatment method in patients with large LA who had acceptable SR maintenance rates when compared with those of a small LA group. However, via multivariate logistic regression, Baek et al.⁸⁾ found that a LAD >65 mm is an independent risk factor for long-term AF recurrence after surgical ablation. Furthermore, the credibility of the results was questioned due to the limited sample size and the possibility of interference of several confounding factors. Moreover, few studies have directly compared long-term thromboembolic event (TE) risk in GLA and non-giant left atria (NGLA) patients.

Therefore, this retrospective cohort study aimed to evaluate the long-term effect of RFA in patients undergoing MV surgery with GLA, and compare TE risk associated with GLA and NGLA. We present the following article in accordance with the strengthening the reporting of observational studies in epidemiology (STROBE) reporting checklist.

Materials and Methods

Patient population

From January 2009 to December 2019, 2124 patients underwent MV surgery and concomitant RFA. Patients undergoing emergency/salvage surgery with previous cardiac or maze surgery or previous incomplete RFA were excluded (n = 340). Of those initially screened, 1784 were available for analysis. These patients were treated through biatrial (n = 1483) or left atrial (n = 301) lesions. We conducted a left atrial procedure in patients with LAD ≤45 mm without tricuspid valve surgery. Subsequently, patients were divided into the following two groups according to LAD at the time of surgery: NGLA (n = 1543) and GLA (n = 241). All patients underwent conventional echocardiography by professional sonologists at our center preoperatively. Thereafter, anterior and posterior diameters of the LA were obtained. Preoperative characteristics and intraoperative data of the two groups were evaluated and compared.

Surgical methods

All procedures were performed by two experienced surgeons (Dr. Han and Dr. Li) using routine cardiopulmonary bypass with bicaval and aortic cannulation under moderate hypothermia. The procedure was carried out with the bipolar Cardioablate (Medtronic, Minneapolis, MN, USA) or AtriCure clamp (AtriCure, Mason, OH, USA). After cardioplegic arrest, a left atrial incision was

performed through the interatrial groove. The left atrial appendage was either amputated and sutured afterward or a circumferential radiofrequency lesion was created around its base and the orifice oversewn from inside the atrium. In addition to the incision in the interatrial groove, isolation of the right pulmonary veins was completed by a circular ablation line. The left pulmonary veins were encircled and a connecting line was performed between both islands of pulmonary veins on the roof, as near to the left atrial roof as possible to avoid injury to the esophagus. An ablation line from the left pulmonary veins to the posterior mitral annulus was then performed with caution so as not to injure the circumflex coronary artery. Cavotricuspid isthmus ablation was then performed to achieve a bidirectional conduction block. Division of the ligament of Marshall was performed in all patients. In the right atrial lesions, the following lesions, other than cavotricuspid isthmus ablation, were added in the right atrium: excision of right atrial appendage, superior vena cava to inferior vena cava, lateral free-wall lesion complete to anterior-medial tricuspid valve annulus, and medial free-wall lesion complete to anterior-medial tricuspid valve annulus. Details of the procedure were based primarily on our previous description.⁹⁾

Follow-up and postoperative care

Patients were followed up at 3, 6, and 12 months, and annually, thereafter. During each follow-up, patients underwent medical history, physical, and electrocardiogram (ECG) or 24-hour Holter monitoring evaluations. During the study, 77% (1374/1784) of patients underwent 24-hour monitoring during follow-up. According to the consensus statement of the United States Heart Rhythm Society in 2017, late recurrence is defined as any attack of AF, atrial flutter (AFL), or atrial tachycardia lasting more than 30 seconds after a 3-month blanking period, and expressed as AF recurrence in the subsequent text.

All patients received postoperative antiarrhythmic drugs (AADs) and anticoagulants unless contraindicated. Postoperative early AF recurrence unresponsive to AADs were cardioverted before discharge. Patients with persistent bradycardia due to junctional rhythm were closely observed for 7–14 days to allow for sinus node recovery. If symptomatic bradycardia remained, a dual-chamber pacemaker was implanted. AADs were discontinued in patients with normal SR 2–3 months postoperatively. For patients receiving bioprosthetic valve implantation or repair, warfarin was administered for 3 months if SR values were stable. Warfarin was

continued beyond this duration if AF or AFL persisted. For patients receiving a mechanical valve, warfarin was used continuously. The range of international normalized ratio was required between 2.0 and 3.0. For patients with recurrent AF with anticoagulant needs, if resistant or intolerant to warfarin, new oral anticoagulants (dabigatran) should be selected. The median follow-up time was 36.0 months (interquartile range: 13.0–48.0). At 1 and 5 years, 71% (1223/1723) and 51% (521/1022) of patients available for follow-up had documented rhythm and AAD data, respectively.

Statistical methods

Continuous variables are expressed as means \pm standard deviation or as medians and interquartile ranges (as appropriate). Student's t-test was used to compare normally distributed continuous variables, whereas the Mann–Whitney U test was used for skewed distributions. Categorical variables were compared using χ^2 analysis. Composite endpoint survival (freedom from AF recurrence and death) between subgroups delineated by LAD (≤ 65 mm and > 65 mm) was reported as a Kaplan–Meier estimate. The probability of being both alive and AF recurrence-free is equivalent to the probability of experiencing neither competing risk, as described subsequently. AF recurrence, TEs, and readmission due to congestive heart failure were evaluated using competing risk analysis. Death during the follow-up period served as the competing risk, and perioperative variables with a P value less than 0.1 served as covariates.

Propensity score (PS) matching was conducted, estimated using a logistic model, and groups were matched within a caliper of 0.1 PS standard deviations. Covariates were based on 26 clinical variables including sex; age; body mass index (BMI); mitral disease etiology; MV surgery type; combination with coronary artery bypass grafting, tricuspid valvuloplasty, or aortic valve surgery; history of preoperative pacemaker implantation, chronic lung disease, chronic kidney disease, hypertension, diabetes, smoking, and stroke; New York Heart Association (NYHA) classification $>II$; left atrial thrombosis; left ventricular ejection fraction; duration and type of AF; cardiopulmonary bypass and cross-clamp time; perioperative application of continuous renal replacement therapy, extracorporeal membrane oxygenation, or intra-aortic balloon pump; operator; and ablation energy and devices.

Data analysis was performed using SPSS version 22 (SPSS, Inc., Chicago, IL, USA) and R 3.6.1 using the

cmprsk package (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

As expected, between-group preoperative demographic differences were observed regarding BMI, AF type, NYHA class III/IV heart failure rate, rheumatic MV disease rate, preoperative pacemaker rate, and LA thrombus (**Table 1**). Compared with the GLA group, the NGLA group had a significantly lower BMI (23.6 ± 3.1 versus 25.1 ± 3.1 , $P < 0.001$) and incidence of rheumatic diseases ($589/1543$ [38.2%] versus $136/241$ [56.4%], $P < 0.001$), preoperative pacemaker ($24/1543$ [1.6%] versus $9/241$ [3.7%], $P = 0.020$), and LA thrombus ($253/1543$ [16.4%] versus $53/241$ [22.0%], $P = 0.032$). Patients in the NGLA group had elevated NYHA class III/IV heart failure rates ($1227/1543$ [79.5%] versus $176/241$ [73.0%], $P = 0.022$) and incidence of paroxysmal AF ($613/1543$ [39.7%] versus $63/241$ [26.1%], $P < 0.001$).

Perioperative outcomes

Perioperative outcomes of NGLA and GLA cohorts are also summarized in **Table 1**. NGLA patients had longer cardiopulmonary bypass (133.1 ± 46.4 minutes versus 120.7 ± 31.0 minutes, $P < 0.001$) and cross-clamp (96.3 ± 31.2 minutes versus 88.5 ± 27.2 minutes, $P < 0.001$) times, and tended to have a larger proportion of mitral valvuloplasty ($1084/1543$ [70.3%] versus $157/241$ [65.1%], $P = 0.089$) and higher incidence of concomitant coronary artery bypass grafting than those with GLA. However, GLA patients had a higher incidence of reoperation from bleeding ($27/241$ [11.2%] versus $48/1543$ [3.1%], $P = 0.089$). Five patients in the GLA group experienced a postoperative cerebrovascular accident compared with 26 (2.1% versus 1.7%, $P = 0.667$) of the NGLA group. Eleven patients received implanted permanent pacemaker after surgery, 10 in the NGLA group and 1 in the GLA group, and none of them with a documented 30-day mortality ($0/11$ [0%] vs $37/1773$ [2%], $P = 0.628$). Cerebrovascular accident was defined as stroke or other thromboembolism occurring outside the 30-day postoperative period. GLA patients tended to have greater 30-day mortality rates than NGLA patients ($8/241$ [3.3%] versus $29/1543$ [1.9%], $P = 0.145$). Causes of 30-day mortality of the cohorts were similar and included low cardiac output syndrome, septic shock, and multisystem organ failure.

Table 1 Baseline characteristics and perioperative outcomes of all patients

Variable	NGLA (1543)	GLA (241)	P value
Age, years, mean (SD)	59.0 ± 10.7	60.4 ± 8.9	0.060
Male sex, n (%)	604 (39.1)	102 (42.3)	0.348
BMI, kg/m ² , mean (SD)	23.6 ± 3.1	25.1 ± 3.1	<0.001
AF duration, median [IQR]	18.0 [12.0, 24.0]	18.0 [12.0, 24.0]	0.638
Paroxysmal AF, n (%)	613 (39.7)	63 (26.1)	<0.001
LVEF (%), mean (SD)	59.8 ± 7.2	59.7 ± 6.6	0.725
NYHA class III or IV, n (%)	1227 (79.5)	176 (73.0)	0.022
Rheumatic disease, n (%)	589 (38.2)	136 (56.4)	<0.001
Preoperative PM, n (%)	24 (1.6)	9 (3.7)	0.020
Chronic lung disease, n (%)	66 (4.3)	10 (4.1)	0.927
Diabetes, n (%)	221 (14.3)	38 (15.8)	0.554
Hypertension, n (%)	233 (15.1)	38 (15.8)	0.788
Chronic kidney disease, n (%)	45 (2.9)	5 (2.1)	0.462
LA thrombus, n (%)	253 (16.4)	53 (22.0)	0.032
Smoker, n (%)	237 (15.4)	45 (18.7)	0.190
Peripheral vascular disease, n (%)	106 (6.9)	15 (6.2)	0.711
Previous stroke, n (%)	164 (10.6)	26 (10.8)	0.940
CPB time, minutes, mean (SD)	133.1 ± 46.4	120.7 ± 31.0	<0.001
Cross-clamp time, minutes, mean (SD)	96.3 ± 31.2	88.5 ± 27.2	<0.001
MVP, n (%)	1084 (70.3)	157 (65.1)	0.089
+CABG, n (%)	85 (5.8)	4 (3.0)	0.011
+AV surgery, n (%)	459 (28.7)	68 (26.2)	0.628
+TVP, n (%)	1261 (81.7)	185 (76.8)	0.068
Operated by Dr. Han, n (%)	939 (60.9)	139 (57.7)	0.348
Medtronic devices, n (%)	469 (30.4)	61 (25.3)	0.108
Biautrial lesions, n (%)	1292 (83.7)	193 (80.1)	0.158
IABP, n (%)	36 (2.3)	5 (2.1)	0.803
ECMO, n (%)	2 (1.5)	6 (2.1)	0.734
CRRT, n (%)	73 (4.7)	10 (4.1)	0.690
Reoperation for bleeding, n (%)	48 (3.1)	27 (11.2)	<0.001
Permanent pacing, n (%)	10 (0.6)	1 (0.4)	0.667
Cerebrovascular accident, n (%)	26 (1.7)	5 (2.1)	0.667
Mediastinitis, n (%)	18 (1.2)	2 (0.8)	0.644
30-day mortality, n (%)	29 (1.9)	8 (3.3)	0.145

Bold values indicate those found to be statistically significant. AF: atrial fibrillation; AV: aortic valve; BMI: body mass index; CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation; GLA: giant left atria; IABP: intra-aortic balloon pump; IQR: interquartile range; LA: left atrium; LVEF: left ventricular ejection fraction; MVP: mitral valvuloplasty; NGLA: non-giant left atria; NYHA: New York Heart Association; PM: pacemaker; SD: standard deviation; TVP: tricuspid valvuloplasty

Late outcomes

Incidence rates of late events are shown in **Supplementary Table 1** (All supplementary files are available online.). There were 26 late deaths in the GLA group compared with 95 (26/241 [10.8%] versus 95/1543 [6.2%], $P = 0.008$) in the NGLA group. Of these, 51 were noncardiac causes of death, including malignancy, end-stage renal disease, severe lung infection, and traffic

accident. Causes of cardiac deaths included acute prosthetic valve failure, cardiogenic stroke, anticoagulation-related cerebral hemorrhage, acute heart failure due to prosthetic valve endocarditis and septic shock, and sudden cardiac death of uncertain cause. GLA patients had higher incidence of late AF recurrence (94/241 [39.0%] versus 275/1543 [17.89%], $P < 0.001$) and readmission due to congestive heart failure (29/241 [12.0%] versus

105/1543 [6.8%], $P = 0.004$) than NGLA patients. Rates of TE (15/241 [6.2%] versus 83/1543 [5.4%], $P = 0.592$) or reoperation (3/241 [1.2%] versus 24/1543 [1.6%], $P = 0.713$) in patients with GLA and NGLA did not significantly differ.

Efficacy

When examining SR maintenance off AADs at 1, 2, 3, 4, and 5 years in the NGLA group, freedom from AF recurrence was 89% (922/1036), 80% (719/899), 72% (523/727), 63% (381/605), and 60% (281/469), respectively, while in the GLA group, 82% (153/187), 73% (116/159), 68% (85/125), 61% (57/93), and 46% (24/52) of patients were free from AF and AADs at the same time points (**Fig. 1**). Freedom from AF and AADs in the GLA patients versus NGLA groups also significantly differed at postoperative years 1 ($P = 0.006$), 2 ($P = 0.045$), and 5 ($P = 0.030$). Similarly, at years 1, 2, 3, 4, and 5, the probability of remaining alive and free of AF recurrence was estimated to be 92%, 82%, 76%, 71%, and 66%, respectively, in the NGLA cohort. AF recurrence-free survival was estimated to be 80%, 69%, 59%, 52%, and 43%, respectively, at each time point for the GLA cohort. There was significant difference in AF recurrence-free survival between the two groups, shown in **Supplementary Fig. 1**.

The cumulative survival rates significantly differed between GLA and NGLA patients (**Fig. 2A**, $P < 0.001$). At years 1, 2, 3, 4, and 5, the probability of remaining alive was estimated to be 97%, 96%, 93%, 91%, and 89%, respectively, in the NGLA cohort, while cumulative survival rates were estimated to be 96%, 93%, 89%, 85%, and 82%, respectively, at each time point in the GLA cohort.

The estimated incidence of first AF recurrence at 1, 2, 3, 4, and 5 years for the NGLA patient population was 6%, 14%, 17%, 21%, and 24%, respectively, while the estimated incidence of first AF recurrence of the GLA group was 16%, 26%, 36%, 41%, and 49% at respective time points (**Fig. 2B**, $P < 0.001$). The cumulative incidence of AF recurrence was significantly higher in the GLA than in the NGLA group (subdistribution hazard ratio [SHR]: 2.286, 95% confidence interval [CI]: 1.816–2.877, $P < 0.001$).

Furthermore, the cumulative incidence of readmission due to congestive heart failure was significantly higher in the GLA versus the NGLA group (SHR: 1.621, 95% CI: 1.071–2.454, $P = 0.022$; **Fig. 2C**). However, the cumulative incidence of TE (SHR: 1.020, 95% CI:

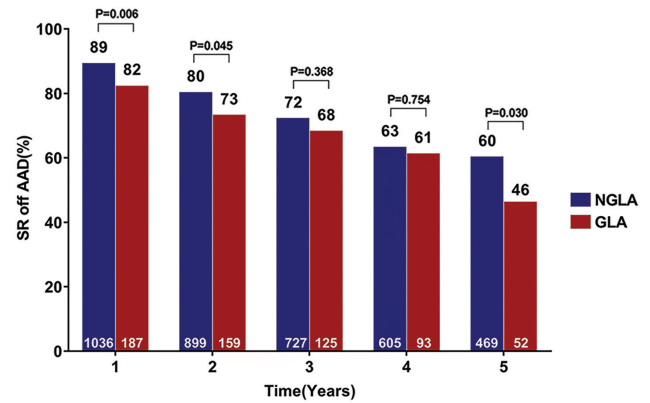


Fig. 1 Comparison of SR off AAD between the NGLA group and GLA group. AAD: antiarrhythmic drug; GLA: giant left atria; NGLA: non-giant left atria; SR: sinus rhythm

0.590–1.764, $P = 0.944$; **Fig. 2D**) of both groups did not significantly differ.

PS matching

After PS, 448 samples (224 pairs) were retained. Preoperative and perioperative variables of matched groups did not significantly differ (**Table 2**). However, mortality rates of the two matched groups differed significantly ($P < 0.001$). The cumulative incidence of AF recurrence was significantly higher in GLA than in NGLA patients (SHR: 4.801, 95% CI: 3.288–7.011, $P < 0.001$), while risks of TE (SHR: 0.873, 95% CI: 0.442–1.724, $P = 0.695$) and readmission due to congestive heart failure (SHR: 1.116, 95% CI: 0.653–1.907, $P = 0.688$) of matched groups were comparable. The results are shown in **Fig. 3**.

Late recurrence in patients with non-paroxysmal AF

To better compare the efficacy of ablation between the two groups, we conducted an analysis of patients with non-paroxysmal AF (**Supplementary Fig. 2**). The cumulative incidence of AF recurrence was significantly higher in GLA than in NGLA patients with non-paroxysmal AF (SHR: 2.562, 95% CI: 1.936–3.391, $P < 0.001$), while risks of TE (SHR: 1.104, 95% CI: 0.573–2.125, $P = 0.768$) and readmission due to congestive heart failure (SHR: 1.431, 95% CI: 0.847–2.416, $P = 0.180$) were comparable.

Subgroup analysis

To investigate the impact of AF recurrence on the incidence of TE, we conducted a subgroup analysis (**Supplementary Fig. 3**). For patients ≥ 75 years (SHR: 3.034,

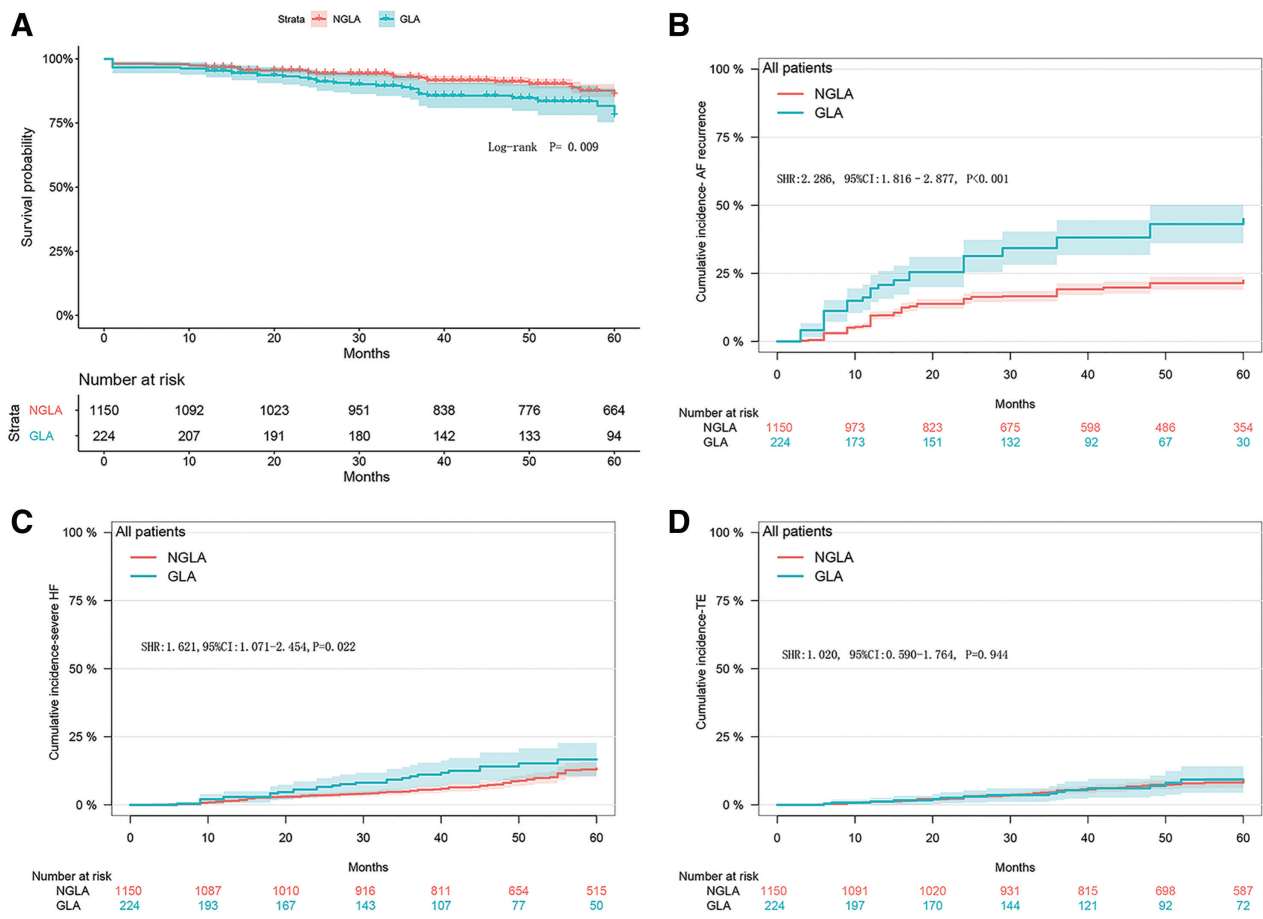


Fig. 2 (A) Kaplan–Meier curve. (B) cumulative incidence of AF recurrence. (C) cumulative incidence of readmission due to HF. (D) cumulative incidence of TE. Overall survival by Kaplan–Meier estimation and cumulative incidence of AF recurrence, TE, and readmission due to HF for NGLA and GLA patients in the first 5 years after surgery via competing risk analysis. AF: atrial fibrillation; CI: confidence interval; GLA: giant left atria; HF: heart failure; NGLA: non-giant left atria; SHR: subdistribution hazard ratio; TE: thromboembolic event

95% CI: 1.438–6.402, $P < 0.001$) and with diabetes (SHR: 1.728, 95% CI: 1.210–3.910, $P < 0.001$), AF recurrence increased TE risk. Furthermore, we divided the GLA cohort into two groups according to rhythm, as follows: AF/AFL ($n = 95$) and non-AF/AFL ($n = 146$). Baseline characteristics of the two cohorts are summarized in **Supplementary Table 2**. Patients in the AF/AFL group had larger left atrial size (72.1 ± 4.6 versus 69.5 ± 4.1 mm, $P < 0.001$) and higher rates of rheumatic MV disease (61/95 [64.2%] versus 75/146 [51.4%], $P < 0.042$), diabetes mellitus (30/95 [31.6%] versus 8/146 [5.5%], $P < 0.012$), and previous stroke (17/95 [17.9%] versus 9/146 [6.2%], $P < 0.004$) than patients in the non-AF/AFL group.

At years 1, 2, 3, 4, and 5, the probability of remaining alive was estimated to be 96%, 93%, 90%, 87%, and 79%, respectively, in the non-AF/AFL group, while the respective survival rates of the AF/AF cohorts were

estimated to be 99%, 94%, 88%, 85%, and 82%, respectively (**Supplementary Fig. 4A**).

The risk of readmission due to congestive heart failure (SHR: 1.612, 95% CI: 0.816–3.182, $P = 0.169$; **Supplementary Fig. 4B**) tended to be higher in patients with AF/AFL recurrence than in those without AF/AFL recurrence. However, the cumulative incidence of TE was comparable between the two groups (SHR: 1.493, 95% CI: 0.543–4.105, $P = 0.438$; **Supplementary Fig. 4C**).

Discussion

This is a large-sample study that evaluated outcomes of concomitant RFA in patients undergoing MV surgery. Prior literature suggests that RFA is an effective surgical method for treating AF when accompanied with other surgeries, and does not increase surgical risk in patients with GLA.^{10–13} In our study, we analyzed the follow-up

Table 2 Preoperative and perioperative characteristics of matched sample

Variable	NGLA (224)	GLA (224)	SMD	P value
Age, years, mean (SD)	59.4 ± 10.5	59.4 ± 8.5	0.006	0.974
Male sex, n (%)	89 (39.7)	91 (40.6)	0.040	0.777
BMI, kg/m ² , mean (SD)	24.4 ± 3.1	24.3 ± 3.0	0.020	0.823
AF duration, median [IQR]	18.0 [12.0, 24.0]	18.0 [12.0, 24.0]	0.004	0.820
Paroxysmal AF, n (%)	78 (34.8)	71 (32.1)	0.128	0.263
LVEF (%), mean (SD)	59.8 ± 6.9	60.1 ± 7.4	0.008	0.669
NYHA class III or IV, n (%)	169 (75.6)	171 (76.4)	0.049	0.748
Rheumatic disease, n (%)	100 (44.9)	105 (46.9)	0.128	0.134
Preoperative PM, n (%)	2 (1.2)	3 (1.7)	0.079	0.773
Chronic lung disease, n (%)	8 (3.6)	9 (4.3)	0.093	0.796
Diabetes, n (%)	33 (14.9)	40 (17.9)	0.128	0.197
Hypertension, n (%)	37 (16.9)	39 (17.6)	0.068	0.854
Chronic kidney disease, n (%)	8 (3.9)	7 (3.4)	0.013	0.853
LA thrombus, n (%)	40 (18.1)	42 (18.8)	0.091	0.811
Smoker, n (%)	29 (13.0)	34 (15.2)	0.130	0.225
Peripheral vascular disease, n (%)	15 (6.7)	15 (6.7)	0.000	1.000
Previous stroke, n (%)	29 (13.0)	36 (16.3)	0.186	0.166
CPB time, minutes, mean (SD)	124.3 ± 37.2	124.4 ± 33.9	0.005	0.952
Cross-clamp time, minutes, mean (SD)	91.3 ± 30.7	91.6 ± 28.6	0.006	0.883
MVP, n (%)	139 (62.1)	140 (62.3)	0.084	0.943
+CABG, n (%)	9 (4.3)	7 (3.4)	0.076	0.789
+AV surgery, n (%)	58 (26.2)	56 (25.7)	0.030	0.942
+TVP, n (%)	179 (80.1)	185 (82.6)	0.045	0.649
Operated by Dr. Han, n (%)	127 (56.7)	128 (57.3)	0.018	0.527
Medtronic devices, n (%)	66 (29.7)	64 (28.7)	0.046	0.595
Biatial lesions, n (%)	182 (81.3)	184 (82.1)	0.076	0.700

AF: atrial fibrillation; AV: aortic valve; BMI: body mass index; CABG: coronary artery bypass grafting; CPB: cardiopulmonary bypass; GLA: giant left atria; IQR: interquartile range; LA: left atrium; LVEF: left ventricular ejection fraction; MVP: mitral valvuloplasty; NGLA: non-giant left atria; NYHA: New York Heart Association; PM: pacemaker; SD: standard deviation; SMD: standard mean deviation; TVP: tricuspid valvuloplasty

findings of 1784 patients who underwent MV surgery with ablation. The 5-year rate of freedom from AF recurrence and the 5-year survival incidence of the total population were 73% and 88%, respectively, and the effectiveness and safety of ablation were satisfactory. Of course, because of poor follow-up rate with 5-year follow-up rate of only 51%, it may underestimate the incidence of recurrent AF. This finding is similar to that which was previously reported by Kim et al.,¹⁴ in which in patients with GLA undergoing MV surgery with concomitant surgical ablation, the 5-year AF recurrence-free survival rate was 68.9%, a value significantly higher than that of patients who did not undergo ablation ($P < 0.001$). However, RFA was less effective in maintaining SR in GLA patients, and the estimated incidence rate of first AF recurrence at 5 years was 49%. This result is similar

to that of a multicenter case-control study conducted by Baek et al.,⁸ in which 170 patients who underwent cryoablation concomitant with MV surgery for AF were followed up, and multivariate analysis showed that LAD >65 mm was an independent risk factor for long-term AF recurrence (odds ratio: 4.18, 95% CI: 1.39–12.62, $P = 0.011$). There is a lack of studies that have compared TE risk in patients with GLA versus NGLA. In the context of our study, despite the high rate of AF recurrence, patients with GLA did not have a higher TE risk than those with NGLA.

An enlarged LA is closely associated with AF recurrence post-ablation.¹⁵ AF patients with an LAD >55 mm have significantly higher recurrence rates after catheter ablation than those with a LAD <55 mm.⁵ However, no consensus has been reached regarding the cut-off value

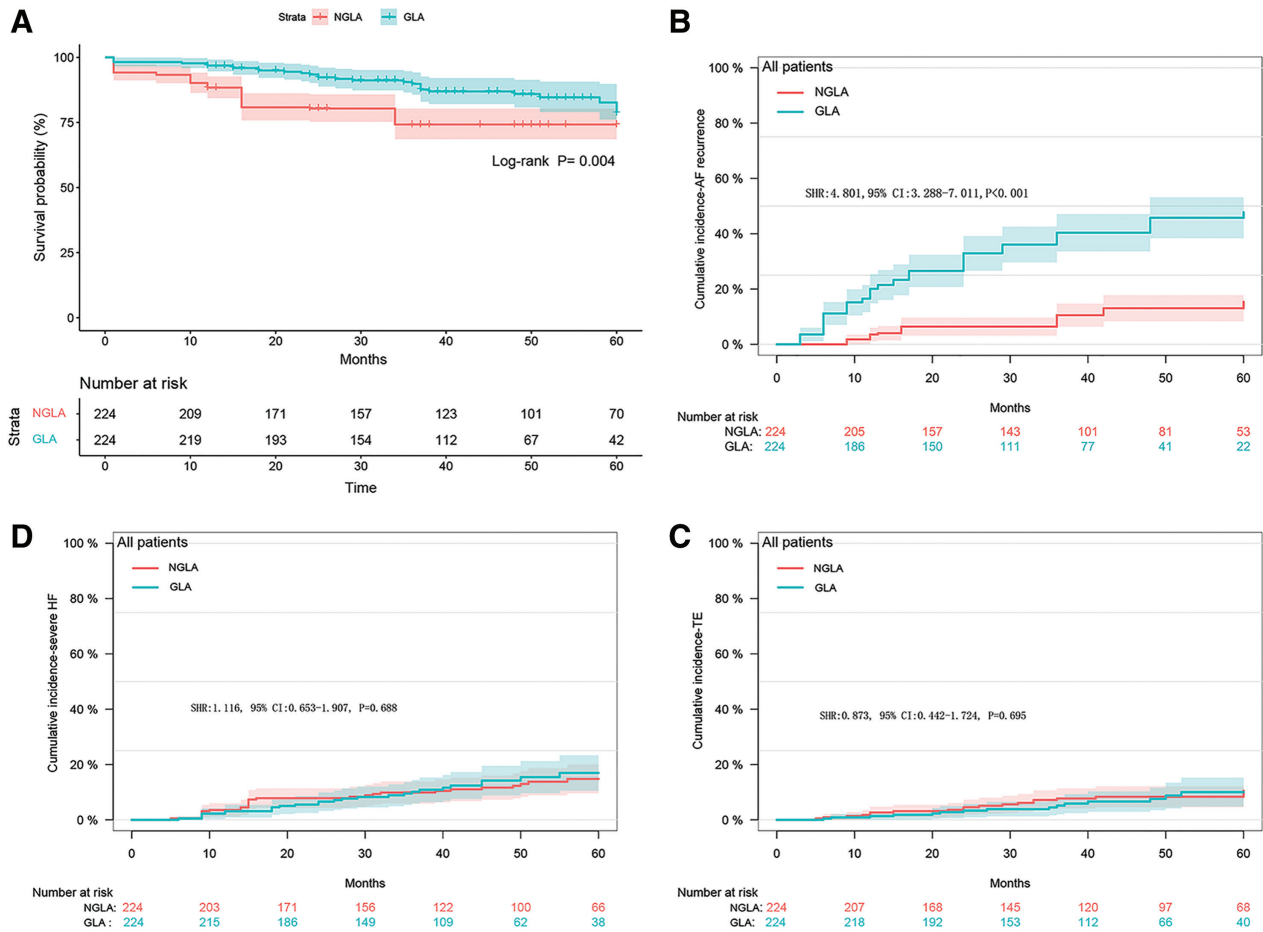


Fig. 3 (A) Kaplan–Meier curve. (B) cumulative incidence of AF recurrence. (C) cumulative incidence of TE. (D) cumulative incidence of readmission due to HF. Kaplan–Meier curve and cumulative incidence of AF recurrence, TE, and readmission due to HF for matched patients in the first 5 years after surgery via competing risk analysis. AF: atrial fibrillation; CI: confidence interval; GLA: giant left atria; HF: heart failure; NGLA: non-giant left atria; SHR: subdistribution hazard ratio; TE: thromboembolic event

for LAD indicative of increased AF recurrence risk after surgical ablation. For example, Feyrer et al.¹⁶⁾ analyzed data from 103 patients (78 with LAD <50 mm and 25 with LAD >50 mm) undergoing surgical ablation, revealing that 67% of those with LAD <50 mm were successfully converted to having SR within 3 months post-ablation, while only 48% with LAD >50 mm were successfully converted. Meanwhile, Vural et al.¹⁷⁾ found that LAD was associated with AF recurrence and that sensitivity and specificity values associated with an LAD cut-off value of 50.5 mm for the maintenance of SR were 85.7% and 70.7%, respectively. In addition, some studies have described the association between an LAD cut-off value of 60 mm and AF recurrence after surgical ablation, confirming that LAD >60 mm is a reasonable predictor of AF recurrence after surgical ablation.^{18–20)} These studies had some notable limitations. First, the sample size was small. Second, confounding factors

with potential impacts on results were not effectively eliminated. Third, the impact of death on recurrence was not considered.

However, our center is a surgical center for valvular AF, and a large quantity of data has been accumulated over the past 10 years, increasing the robustness of our findings. This study is among the first to report 5-year follow-up results in patients undergoing mitral surgery to evaluate the efficacy of RFA and compare the risk of TE in patients with or without GLA. We found that AF recurrence-free survival at 5 years post surgery was estimated to be 66% in the NGLA group and 43% in the GLA group (P <0.001); however, the cumulative incidence of TE of both groups was similar when applying before or after PS matching methods. On one hand, GLA patients had higher incidence of reoperation for postoperative bleeding, and although Armbruster et al. considered cardiac surgery induced acute-phase inflammatory

states precipitating AF, we do not believe that postoperative thoracotomy for hemostasis significantly increases the risk of AF recurrence.²¹⁾ On the other hand, it has been described that rheumatic etiology significantly decreased the success rate of RFA in patients undergoing MV surgery,²² but in our analysis, there was no significant difference in the proportion of rheumatic cause between the patients with or without giant LA after PS matching. Furthermore, AF or AFL recurrence did not increase TE risk in patients with GLA in a subgroup analysis. The incidence of TE in the AF/AFL group was comparable to that in the non-AF/AFL group ($P = 0.627$). This may be because the majority of AF/AFL patients received anticoagulants (79.6% versus 22.4%, $P < 0.001$). Meanwhile, closure of left atrial appendage significantly prevented TE among patients with AF, despite the significant recurrence of AF in patients with GLA.^{23,24)} Therefore, it remains to be investigated whether occlusion of left atrial appendage could produce comparable effect to patients with GLA compared with the RFA procedure.

This study had some notable limitations. First, this was a single-center, retrospective study. Second, surgery was performed by experienced surgeons, which may prevent the results from being generalizable to other centers. Moreover, an inherent limitation of the design of this study was the lack of continuous patient monitoring, which might lead to examination intervals and the underestimation of AF recurrence. For example, some patients did not have 24-hour Holter monitoring and were assessed via 12-lead ECG alone. Lastly, while Holter monitoring facilitates the measurement of AF recurrence, AF recurrence does not necessarily capture the clinical burden of AF. The clinical burden of AF was not examined in this study because any documented recurrence greater than 30 seconds was defined as failure.

Conclusion

Concomitant RFA is effective and feasible for the restoration of SR in patients with AF associated with MV diseases. GLA (LAD >65 mm) patients had higher rates of mortality and readmission for heart failure than those with NGLA. Furthermore, the efficacy of RFA was lower in patients with GLA versus NGLA, with an estimated 49% AF recurrence-free survival at 5 years, while effectively preventing TE. In addition, recurrence of AF or AFL did not increase the risk of TEs. Therefore, lower success rate should be considered when deciding whether to perform surgical ablation in GLA patients and whether

occlusion of the left atrial appendage produced comparable effects in these patients.

Ethical Statement

This study was approved by the Anzhen Hospital's ethics committee (Approval No. 2021150X). Consent was not required due to the retrospective nature of the study.

Data Availability Statement

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

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Disclosure Statement

The authors have no conflicts of interest to declare.

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