Safety and effectiveness of catheter ablation of atrial fibrillation in patients with mitral valve replacement mechanical versus bioprosthetic valves

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Abstract

Introduction: The safety and effectiveness of catheter ablation in patients with atrial fibrillation (AF) who underwent mechanical mitral valve replacement (MVR) have been reported. However, the impacts of different types of mitral valves on the safety and effectiveness of catheter ablation in patients with AF who underwent MVR have not been elucidated. **Methods and results:** From 2015 to 2021, 17,496 patients underwent catheter ablation of AF for the first time in Beijing Anzhen Hospital were screened. The inclusion criteria were (1) aged 18 years or older; (2) diagnosed with AF; (3) history of mitral valve replacement. The exclusion criteria were a history of catheter ablation, surgical maze procedure, left atrial appendage closure or resection. A total of 68 patients were enrolled in the study. The patients were divided into two groups: the bioprosthetic MVR group (n=12) and the mechanical MVR group(n=58). The size of the left atrial was larger (49.5mm vs. 46.0mm, p<0.05), the thickness of the left interventricular septum was larger (11.0mm vs. 10.0mm, p<0.05), and the mitral ring area was smaller (2.3mm2 vs. 2.6mm2, p<0.05) for the bioprosthetic MVR group than the mechanical MVR group. During 23.4 (6.1, 36.5) months of follow-up, the incidence of the endpoint events was not significantly different between the two groups (33.3% vs. 30.4%, log-rank p=0.48). There were 2 cases (3.4%) of pseudoaneurysm and 1 case of acute cerebral infarction in the mechanical MVR group. No complication was observed in the bioprosthetic MVR group. No significant clinical bleeding events were observed in the bioprosthetic group while eight patients in the mechanical MVR groups had bleeding events (p=0.368) during the follow-up. **Conclusion:** The safety and effectiveness of catheter ablation of AF were comparable between the patients with mechanical MVR and bioprosthetic MVR.

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Conclusion: The safety and effectiveness of catheter ablation of AF were comparable between the patients with mechanical MVR and bioprosthetic MVR.

Keywords: atrial fibrillation; mechanical mitral valve replacement; bioprosthetic mitral valve replacement; catheter ablation; safety and effectiveness

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia with a prevalence of approximately 2% to 4% in adults[1]. Mitral valve diseases are strongly associated with the development of AF, which occurs in 30% – 40% of the patients with rheumatic mitral valve disease[2-4]. During long-term follow-up, about 41% – 47% of patients with mitral valve disease had AF[5]. Mitral valve diseases may contribute to the occurrence of AF by inducing volume overload and left atrial (LA) enlargement[6]. However, the high prevalence of persistent AF in these patients remained even after hemodynamic abnormity was corrected by mitral valve surgery in previous study[7].

Catheter ablation is an effective treatment for AF. It was shown that catheter ablation of AF was safe and effective in patients with mechanical mitral valve replacement (MVR)[8]. However, the study about the safety and efficacy of catheter ablation of AF in patients with bioprosthetic MVR was limited. This study aims to investigate whether there is a difference in the safety and efficacy of catheter ablation of AF in patients with mechanical MVR versus bioprosthetic MVR.

Method

A total of 17,496 patients who underwent catheter ablation of AF for the first time in Beijing Anzhen Hospital from January 2015 to December 2021 were screened. The inclusion criteria were (1) aged 18 years or older; (2) diagnosed with AF; (3) history of mitral valve replacement. The exclusion criteria were a history of catheter ablation, surgical maze procedure, left atrial appendage closure or resection. A total of 68 patients who met the inclusion and exclusion criteria were enrolled in the study. According to the type of MVR, the patients were divided into two groups: the bioprosthetic MVR group and the mechanical MVR group. Totally, 12 patients were enrolled in the bioprosthetic MVR group and 56 patients in the mechanical MVR group. Written inform consents were obtained in all the patients prior to the ablation procedure. The study was approved by the institute ethics committee.

Catheter ablation of AF

All anti-arrhythmic drugs except amiodarone were discontinued for at least 5 half-lives before catheter ablation. The procedure was performed under fasting, conscious sedation and uninterrupted anticoagulation. During the procedure, heparin was injected intravenously to maintain the activated clotting time at 300-400s. AF ablation strategy was described previously[9]. The left atrium geometry was reconstructed in the CARTO system, with a 3.5 mm tip ablation catheter point by point (Navi-Star Thermocool, or Thermocool-Smart-touch Biosenes Webster, USA) (2015-2018) or PentRay Nav eco tip catheter (Biosenes Webster, USA) with fast anatomy mapping (Since 2018). The patients with paroxysmal AF were treated with circumferential pulmonary vein ablation (CPVA), the ablation endpoint is all pulmonary veins isolation (PVI). After CPVA in patients with persistent AF, LA roofline, mitral isthmus (MI), and cavotricuspid isthmus (CTI) was routinely targeted. If AF was still persistent, 200 J direct current cardioversion was performed to convert AF to sinus rhythm. Additional ablation was applied, if needed, to achieve PVI and linear block in sinus rhythm. Coronary sinus (CS), superior vena cava (SVC), fractionated potentials (CFAEs), and ligament of Marshall (LOM) were targeted at the physician's discretion.

Data collection and follow-up

Antiarrhythmic drugs were routinely taken orally for 3 months after the procedure. The patients in the bioprosthetic MVR group were given new oral anticoagulants. The patients in the mechanical MVR group were given warfarin, targeting the international normalized ratio range of 2.0–3.0. 24h-Holter was performed monthly in the first 3 months, which was followed by 24h-Holter 6 months after the procedure and every 6 months thenceforth. Scheduled follow-up was implemented by telephone interview or outpatient follow-up to collect the occurrence of endpoint events at 3, 6, months and every 6 months thereafter. The follow-up information was collected by professionally trained follow-up personnel. If the patient had palpitations or other symptoms suggestive of arrhythmia, ECG examination was performed in the local hospital at any time.

The study endpoint was AF recurrence which was defined as any recurrence of atrial arrhythmias with a duration of [?] 30 seconds. AF recurrence occurring within 3 months after the procedure was defined as early recurrence, and recurrence after 3 months of procedure was defined as late recurrence. If a patient underwent AF ablation again during the follow-up, the patient would not be counted in the survival analysis after the redo procedure.

Statistical analysis

SPSS 26.0 software was used for statistical analysis. All continuous variables with normal distribution were presented as mean ± standard deviation, and Independent-Samples t -test was used for comparison. Medians and quartiles were used for continuous variables with non-normal distribution, and non-parametric Mann-Whitney U -test was used for comparison. Categorical variables were presented as numbers and proportions and compared by χ^2 or Fisher's exact test. Kaplan-Meier analysis with log-rank test was used to calculate AF recurrence-free survival between the groups. COX univariate and multivariate regression analyses were used to assess independent predictors of AF recurrence after the catheter ablation. A p -value < 0.05 was considered statistically significant.

Results

Baseline characteristics

The baseline data of the patients were shown in Table 1. Compared with the mechanical MVR group, the bioprosthetic MVR group had a larger left atrium (49.5 [IQR, 46.0-55.5]mm vs. 46.0 [IQR, 40.3-48.9]mm, $p<0.05$), a larger thickness of the left interventricular septum (11.0 [IQR, 10.0-11.8]mm vs. 10.0 [IQR, 9.0-10.8]mm in the mechanical MVR group, $p<0.05$), and a smaller mitral ring area (2.3 [IQR, 2.0-2.6]mm^2vs. 2.6[IQR, 2.4-2.9]mm^2, $p<0.05$). There were no significant differences in left ventricular ejection fraction, left ventricular end-diastolic diameter and left ventricular end-systolic diameter between the two groups. There were no statistically significant differences in gender, age, blood pressure, BMI, laboratory parameters and co-morbidities between the two groups.

Electrophysiology study and ablation

The ablation strategies and results of the two groups were shown in Table 2. In the bioprosthetic MVR group, all the 12 patients underwent CPVA. The bilateral PVI rate was 100%. Seven patients underwent MI ablation with bidirectional MI block in 5 of the 7 patients (71.4%). Nine patients underwent CTI ablation with a 100% CTI block rate. In the mechanical MVR group, all the 58 patients underwent CPVA. Bilateral PVI was achieved in all the patients. MI ablation was performed in 36 cases (64.3%). Bidirectional MI block was achieved in 21 of the 36 cases (58.3%). Unidirectional mitral block was achieved in one case, and MI block was not verified in one case. Forty-seven patients (83.9%) underwent CTI ablation, bidirectional CTI line block was achieved in 44/47 (93.6%) patients. CTI block was not verified in one case. The prevalence of ethanol infusion in vein of Marshall was significantly higher in the bioprosthetic MVR group than in the mechanical MVR group (33.3%vs.0.0%, $p<0.001$). There was no significant difference of MI block rate between the two groups. There were 2 cases (3.4%) of pseudoaneurysm and 1 case of acute cerebral infarction in the mechanical MVR group. No complication was observed in the bioprosthetic MVR group.

Follow-up results

After a follow-up of median 23.4 (6.1, 36.5) months, the incidence of the endpoint events (33.3% vs. 30.4%) was not significantly different between the two groups (log-rank $p = 0.48$, Fig.1). One case (8.3%) had early recurrence in the bioprosthetic MVR group, and two cases (3.4%) had early recurrence in the mechanical MVR group ($p = 0.964$). As shown in Table 3, Cox univariate and multivariate regressions were used to identify risk factors for AF recurrence. Univariate analysis showed that blood glucose level was related to the recurrence of AF after catheter ablation ($p = 0.039$). However, there was no significant risk factor related to the endpoint event in multivariate analysis.

Eight patients had bleeding events with clinical symptoms in the mechanical MVR group, mainly manifested as hematuria and nasal hemorrhage, all of which used warfarin. The INR values were between 2.37 and 4.0 at occurrence of the bleeding events. No significant clinical bleeding events were observed in the bioprosthetic MVR group ($p = 0.368$).

Discussion

Mitral valve disease is one of the major pathophysiological causes of AF. Up to 50% of patients undergoing mitral valve surgery had atrial fibrillation[10]. On the other hand, AF is also a common complication after mitral valve surgery, with an incidence as high as 25%[11]. Concomitant valvular surgery at the time of maze procedure is usually recommended for patients with AF and mitral valve disease. However, previous studies have suggested that the proportion of surgical AF ablation in complex mitral valve surgery was only about 64.6%[10]. Catheter ablation may be considered for patients without surgical ablation in mitral valve replacement surgery or with new-onset AF after mitral valve surgery. Several studies have investigated the efficacy and safety of catheter ablation of AF with mitral mechanical valve replacement or mitral valvuloplasty[12-14]. There is no evidence for the safety and efficacy of catheter ablation of AF with mitral bioprosthetic valve replacement. Considering the problems such as structural valve deterioration, patients under 50 years old were recommended to use mechanical valves, patients over 65 years of age were recommended to use bioprosthetic

valves, and either type was optional for patients in the intermediate age range according to guidelines[15,16]. The median age of this study population was 59 years with mechanical valve replacement and 61 years with bioprosthetic valve replacement. Considering the interval between valve replacement surgery and catheter ablation for AF, which was from 10 months to 29 years, this study population followed the recommendations by guidelines in the choice of valve type. During the follow-up period, no procedure-related adverse events were observed after catheter ablation in the patients after bioprosthetic MVR. The recurrence rate of AF after catheter ablation did not differ between mechanical and bioprosthetic MVR. Catheter ablation may be safe and effective in patients with AF with bioprosthetic MVR.

The STAR AF II study reported that linear ablation performed in addition to pulmonary vein isolation in patients with non-valvular persistent AF did not change the outcomes of AF recurrence[17]. However, it is unclear whether additional linear ablation is required in patients with rheumatic heart disease. In addition, atrial flutter was also frequent in patients after mitral valve surgery[18,19]. In this study, 67.6% of patients had rheumatic heart disease and 82% of patients with paroxysmal AF had atrial flutter at the time of the ablation procedure. Therefore, PVI plus linear ablation was performed in these patients. At the time of MI line ablation, the physician will cautiously approach the mechanical mitral ring to avoid mitral valve entrapment. Sometimes, it is difficult to reach the anatomical boundary of the ablation line to achieve MI block. In the patients with bioprosthetic MVR, the ablation line anatomical boundary can be more easily reached without worrying about valve entrapment. Therefore, we assumed that the MI linear block rate in the patients with bioprosthetic MVR might be higher than the patients with mechanical valve replacement. However, there was no statistical difference in the success rate of bidirectional MI linear block between the two groups in this study, even though a large proportion of patients with bioprosthetic MVR underwent Marshall ligament alcohol ablation. This result is different from our hypothesis. Possible reasons: (1) The pouch structure existed in the isthmus of the mitral valve after valve replacement, which was the main reason affecting the MI linear block. Long et al. and Deng et al.[20,21] both reported that the isthmus of the mitral valve in patients with mechanical MVR may have pouched MI, which might result in significantly increasing the difficulty in the achievement of block across MI line. (2) Statistical Class II errors might be caused by the small sample size of this study.

Lang et al.[14] observed that sinus rhythm was maintained in 73% of patients with AF and mechanical MVR 1 year after catheter ablation. The study by Liu et al.[22] indicated that the recurrence-free survival rate of AF in patients with persistent AF 6 months after rheumatic valve surgery who underwent catheter ablation was 55.2%. Almorad et al. (2022) reported a recurrence-free survival rate of 31.7% after the first catheter ablation of AF after mitral valve surgery[23]. In this study, the overall sinus rhythm was maintained at 69.1% after catheter ablation, which may be related to the correction of hemodynamic abnormalities after mitral valve surgery. Similarly, Kim et al.[12] also demonstrated that there was no significant difference in recurrence rate after catheter ablation of valvular AF after hemodynamic correction compared with non-valvular AF (38.7% vs. 30.6%, p=0.366).

Compared with the mechanical MVR group, the incidence of bleeding events after AF catheter ablation was reduced in the bioprosthetic MVR group. Non-vitamin K antagonist oral anticoagulations were used for anticoagulation after catheter ablation in the bioprosthetic MVR group, while warfarin was used in the mechanical MVR group. The INRs of patients in the mechanical MVR group ranged from 2.37 to 4.0 when bleeding events occurred. Previous studies have shown that NOACs were associated with lower rates of intracranial hemorrhage, major hemorrhage, fatal bleeding events, and cardiovascular death than warfarin, and were noninferior to warfarin in preventing stroke or systemic embolism [24,25].

Some studies have shown that left atrial size was a predictor of the recurrence of AF after catheter ablation for non-valvular AF and valvular AF[12,26]. However, Kim et al. (2018) did not report a correlation between left atrial size and recurrence after catheter ablation of valvular AF[12]. Meanwhile, no relationship between left atrial size and AF recurrence after catheter ablation was observed in this study, which may be related to the generally large atria in the patients included in the study. In addition, Cox regression models showed no predictors of outcome.

Study limitations

The small sample size in single center was the main limitation of this study. However, we screened the study population from 17,496 patients, and the incidence of valvular disease combined with AF in China was higher than that in developed countries. To the best of our knowledge, this study was still the first and the largest study to explore catheter ablation of AF in the patients with bioprosthetic MVR. Due to the retrospective study, the study did not clearly distinguish the order between receiving valve surgery and diagnosis of AF. It may be related to the differences in the mechanism of postoperative AF recurrence in patients who underwent MVR, and future studies will improve on this problem.

Conclusion

In conclusion, this study demonstrated the rate of AF recurrence after catheter ablation was not significantly different between the patients with bioprosthetic MVR and mechanical MVR. Compared to the patients with mechanical mitral valves, bleeding events occurred non-significantly less frequently in the patients with bioprosthetic MVR replacement during the follow-up.

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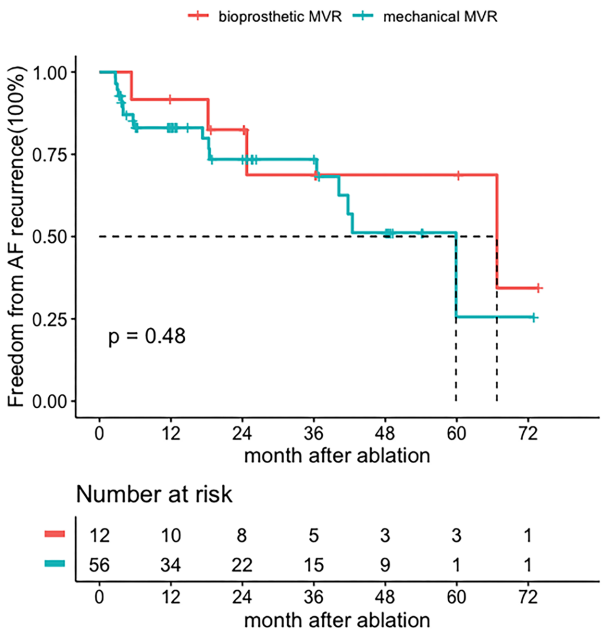

Figure1. Kaplan–Meier curve of freedom from AF recurrent for both groups. Log-rank test, P=0.48.

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