Early- and mid-term results of cryoablation of atrial fibrillation concomitant with robotic mitral valve surgery

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Abstract

Objective: Atrial fibrillation (AF) is the most common arrhythmia, which is also associated with mitral valve disease. Surgical ablation is still known to be an important procedure in restoring sinus rhythm (SR) concomitant with mitral valve surgery (MVS). In this study, we aimed to present our early- and mid-term result of AF cryoablation during robotic MVS.

Methods: Between November 2014 and January 2020, total 34 patients who underwent robotic MVS with concomitant AF ablation were retrospectively analyzed. Ten patients had a <1 year AF history, 14 had 1–5 years, and 10 had >5 years. The primary end point of the study was postoperative AF recurrence.

Results: Total 32 and 2 patients underwent mitral valve replacement and mitral valve repair, respectively. Mean aortic cross-clamp and cardiopulmonary bypass times were 141.8±32.1 min and 196±25.6 min, respectively. The SR was restored with the removal of cross-clamp and cardiac junctional rhythm was observed in 29 (85.3%) and 5 (14.7%) patients, respectively. Two in-hospital deaths secondary to low cardiac output and hepatorenal failure were recorded. Among the rest, 24 (75%) patients were in SR, 6 (18.75%) in AF, and 2 (6.25%) in paced rhythm at discharge.

Conclusion: Robotic cryoablation of AF during MVS is a feasible method with favorable early- and mid-term results.

Keywords: atrial fibrillation, robotic cardiac surgery, cryoablation, cardiac surgery

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Introduction

Over the past two decades, minimally invasive procedures have become widespread in the field of cardiovascular surgery. With the integration of robotic techniques into cardiac surgery, the popularity of robotic cardiac interventions has increased rapidly. Previous studies have confirmed the efficacy and safety of robotic procedures, particularly for mitral valve surgery (MVS) (1, 2).

Atrial fibrillation (AF) is the most common arrhythmia worldwide, which is also strongly associated with mitral valve disease (MVD). Almost 40%–60% patients that need MVS have been reported to be in AF upon admission (3). In addition, AF has been shown to be associated with an increased incidence of thromboembolic events (TEs), morbidity, and mortality (4). Surgical ablation is the most effective way to restore sinus rhythm (SR). However, combined AF ablation and MVS enhances long-term outcomes (5). Moreover, recent guidelines, the Society of Thoracic Surgeons strongly recommends concomitant AF ablation during MVS (6).

Several studies have demonstrated the feasibility of arrhythmia ablations during MVS with minimally invasive surgery (3, 7, 8). However, studies examining the efficacy and safety of AF ablation with MVS in the robotic-assisted setting remain limited (3, 7). Therefore, we aimed to present early- and mid-term result of robotic cryoablation combined with MVSs in AF patients in the present study.

Methods

Study design and study population

In this single-center retrospective study, a total of 251 patients underwent robotic cardiac surgery between November

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HIGHLIGHTS

- Surgical cryoablation is an effective method for atrial fibrillation.
- Cryoablation is feasible in robotic cardiac surgery.
- Cryoablation of atrial fibrillation is recommended in patients who will be undergone mitral valve surgery.

2014 and January 2020, among whom 113 had robotic MVS and 48 had AF rhythm upon admission. Inclusion criterion was the cryoablation for AF secondary to MVD. Exclusion criteria were: previous ablation (percutaneous/surgical), MVD reoperations, and having a permanent pacemaker. Finally, 34 patients who had robotic MVS and concomitant cryoablation were enrolled in the study, with the primary end point being postoperative AF recurrence. Patients with isolated mitral regurgitation (MR) underwent mitral valve repair (MVrep), whereas those with mitral stenosis (MS) or mixed lesions unsuitable for repair underwent mitral valve replacement (MVR). Patient data were obtained from the hospital database. A written informed consent was obtained from each patient. The study protocol was approved by the Local Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Surgical technique

A single surgical team performed all operations, all of which were elective cases. The da Vinci® SI model (Intuitive Surgical Inc., GA, USA) was used for robotic operations. We have described our standard robotic setup and surgical technique in our previous papers (9, 10). In brief, common femoral and right jugular veins were used for inferior caval decompression and superior caval decompression, respectively. Common femoral artery was also cannulated. A 4-cm right anterolateral mini-thoracotomy was performed, and the instrument ports were also inserted as usual. If tricuspid valve intervention was planned, superior and inferior cava were clamped with two additional clamps. Vacuum-assisted venous drainage was used. After aortic cross-clamping (ACC) (Chitwood® clamp, Scanlan International Inc., MN, USA), cardiac arrest was induced with cardioplegia solution (Custodiol®, Köhler Chemie GmbH, Alsbach Hähnlein, Germany) delivered through a temporary cardioplegia catheter at the proximal part of the ascending aorta.

Following left atriotomy, cryoablation and pulmonary vein isolation were performed (detailed below) and left atrial appendage (LAA) was routinely closed using a continuous 4.0 prolene suture. In our clinical protocol, we routinely aim to repair the mitral valve if possible. Otherwise, we prefer bileaflet preservation. If anterior leaflet is seriously affected, posterior leaflet preservation is performed. In our study population, the leaflets and subvalvular apparatus were analyzed, and the mitral valve was repaired, if suitable, using standard techniques. Upon completion, ring annuloplasty was routinely performed. If the valve was not suitable for repair, MVR was planned. Bileaflet preservation was performed if possible; otherwise, at least posterior leaflet preservation was routinely done. Atrially pledgeted U-stitch sutures were inserted along the mitral annulus. Then, mitral prosthesis was introduced from the working port and the sutures were tied with the COR-KNOT® (LSI Solutions Inc., NY, USA) system. At the end of procedure, the left atrium was closed after air removal maneuvers. If third-degree tricuspid regurgitation occurred, particularly secondary to tricuspid annular dilatation, tricuspid annuloplasty was performed through right atriotomy as usual. Then, right atrium was closed.

Ablation device

We used the Cardioblate® CryoFlex™ (Medtronic Inc., MN, USA) surgical ablation console, which is basically argon-based flexible cryoablation system that has a mobile, flexible shaft covering the plastic material to prevent adjacent tissue damage. This flexible shaft allows the bedside surgeon to shape the frosting part of the system in accordance with the targeted tissue. It is inserted into the left atrium through the service port by the bedside surgeon. After placing the device in the target point, the console surgeon checks the contact of the frosting part, reshapes it if required, and releases the system before initiating freezing. Cryoablation begins after confirming the full contact and releasing the robotic instruments from the frosting part.

Ablation technique

We performed ablation first, before other concomitant procedures. Only left atrial cryoablation was performed on the patients to prevent sinus node dysfunction, which might further damage right-side ablation procedures. Ablation was started with a longitudinal incision to the interatrial groove from the margin of the superior right pulmonary vein to the inferior right pulmonary vein. Then, a box lesion, described briefly as a two-sided (left and right) approach to the left pulmonary veins merging with each other on the posterior left atrial wall, was made to isolate the pulmonary veins. The margin of the box was lying down with an extension lesion toward the interatrial incision on both sides. After creating a box lesion, two additional ablation lines were made from the box lesion to the LAA and mitral annulus (Fig. 1). All ablation lines were created using a 120-sec endocardial approach and an average temperature of –137.9°C±5.1°C.

Postoperative course

AF was defined as new-onset AF, which presents the ECG characteristics of AF, lasts at least 30 seconds on a rhythm strip by telemetry/monitor and/or ECG according to the European Society of Cardiology guideline that also declared that postoperative AF was mostly seen between 2 to 4 days (11). Gillinov et al. (12) also reported that the average time for the onset of postoperative AF was 2.4 days. Therefore, follow up for all patients was done using a 24-hour event recorder telemetry (Infinity® M300, Draeger Medical Systems Inc, USA) in the intensive care unit and

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also during clinical course for minimum 3 days. Pace-dependent patients and patients with AF recurrence at the early postoperative course (within the first 3 days) were followed with 24-hour event recorder telemetry throughout the postoperative course, even if SR was restored. Other patients without diagnosed AF recurrence throughout the hospital stay underwent ECG daily. They were also informed about the new-onset AF symptoms.

All patients underwent warfarin treatment with a target international normalized ratio between 2.5 and 3.5. Lifelong anticoagulant treatment was prescribed for patients with mechanical heart valves, permanent AF rhythm, and pacemaker dependency. Patients with biological heart valves and MVrep were advised to use anticoagulant therapy for 3 months only.

AF protocol

Intravenous (IV) amiodarone treatment was prescribed for all patients at an initial dose of 300 mg, followed by 900 mg maintenance dose for the first 24 hours. Afterward, oral amiodarone treatment was given at a dose of 450 mg/day if the patient was in SR. If the patient was in AF or had AF within the previous 6 hours, IV infusion was continued till 6 hours of SR restoration. Oral amiodarone treatment was continued for 3 months and tapered-off during the last month.

For patients who were not converted to SR with amiodarone treatment, cardioversion electrically was attempted after 36 hours of IV treatment. If initial cardioversion failed, IV amiodarone was continued and another electrical cardioversion was attempted after 24 hours. If the patient was still in AF despite this protocol, then the patient was accepted as a permanent AF. In these patients, amiodarone was discontinued and anti-tachycardia medications, such as beta-blockers, calcium channel blockers, or digoxin, were initiated if necessary.

Follow-up

After discharge, the patients were scheduled for follow-up visits in the outpatient setting at Day 10, 1 month, and 3 months. During follow-up, functional status, rhythm status, and echocardiographic variables were evaluated. The rhythm status was recorded using a 24-hour Holter monitoring. All patients were followed up by the operating surgeon until the third month and then referred to their cardiologists, who were contacted to collect relevant patient data and postoperative complications.

During the follow-up period, if any rhythm abnormalities were confirmed by ECG or 24-hour event recorder telemetry or any suspicion of palpitations, the patients were informed to contact their operating surgeon as soon as possible with their ECG recordings. If an AF recurrence was noted, the patients were hospitalized again and AF protocol was reapplied. If the SR was restored once again, amiodarone treatment was continued for at least three more months. In such cases, the operating surgeon planned follow-up visits more frequently. If SR was not restored, the patients were accepted as permanent AF cases and their treatment was modified according to our AF protocol.

Statistical analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), version 17.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed as mean±standard deviation for continuous variables, whereas categorical variables were presented as number and percentage. Overall AF free survival was analyzed using the Kaplan–Meier method.

Results

Baseline demographic and clinical characteristics

Table 1 summarizes baseline demographic and clinical characteristics of the patients. Although majority of them were overweight, which made them difficult candidates for robotic surgery, they were operated with robotic settings.

Since most MVDs depend on rheumatic MVD in Turkey, majority of our patients had rheumatic MS with concomitant MR. More than two-thirds of the patients had greater than or equal to third-degree MR with >15 mm Hg mean mitral systolic gradient. Table 2 outlines echocardiographic variables.

Operative data

MVR was the most common procedure as most of the patients had rheumatic MVD. Eight patients underwent concomitant tricuspid valve annuloplasty. Left atriotomy was the only access to the mitral valve, and transseptal approach was not used in any of the patients. The Medtronic Open Pivot™ mechanical heart valve (Medtronic Inc., MN, USA) was used as the mechanical valve,

Table 1. Baseline demographic and clinical characteristics of patients

Variable	Total (n=34)
Age (year)	58.1±9.8 (34-75)
Sex (Male/Female)	10/24
Body mass index (kg/m^2)	28.4±5 (18-39.9)
Hypertension	9 (26.5%)
Hyperlipidemia	7 (20.6%)
Diabetes mellitus	6 (17.6%)
Chronic obstructive pulmonary disease	2 (5.88%)
Chronic renal disease	1 (2.94%)
Coronary artery disease	1 (2.94%)
Smoking	7 (20.6%)
Atrial fibrillation profiles	
Paroxysmal	1 (2.94%)
<6 months	1 (2.94%)
6 months – 1 year	8 (23.5%)
1-5 year	14 (41.2%)
>5 year	10 (29.4%)

Data are given in mean±standard deviation, median (min-max), or number and frequency, where applicable

Table 2. Preoperative echocardiographic data

Variable	Total (n=34)
Ejection fraction (%)	55±11.9 (20-68)
Left atrial diameter (mm)	64.2±10.7 (49-85)
LV end-diastolic diameter (mm)	50.5±8.8 (31-77)
LV end-systolic diameter (mm)	39.3±9.9 (27-60)
Systolic pulmonary artery pressure (mm Hg)	46.4±10.1 (25-75)
Mitral gradient (mm Hg)	16.7±5.25 (5-32)
Mitral regurgitation, degree	
1	2 (5.88%)
2	11 (32.4%)
≥3	21 (61.8%)
Tricuspid regurgitation, degree	
1	17 (50%)
2	8 (23.5%)
≥3	8 (23.5%)

Data are given in mean±standard deviation, median (min-max), or number and frequency, where applicable. LV - left ventricle

while the Medtronic Hancock II™ bioprosthetic valve (Medtronic Inc., MN, USA) was implanted as the bioprosthesis. The Medtronic Profile 3D® annuloplasty ring (Medtronic Inc., MN, USA) and the Medtronic Contour 3D® annuloplasty ring (Medtronic Inc., MN, USA) were used for mitral and tricuspid annuloplasty, respectively. Two patients underwent bileaflet preservation, whereas the remaining patients with MVR (n=30) underwent posterior leaflet preservation. One patient required sternotomy conversion due to bleeding in the left ventricular posterior wall. All patients underwent LAA closure. Table 3 details the operative data.

Postoperative outcomes

There were two in-hospital deaths associated with low cardiac output syndrome and hepatorenal syndrome. One patient underwent emergent sternotomy due to left ventricular posterior wall rupture that was repaired without a serious complication. The patient had an uneventful postoperative course and was discharged on postoperative Day 10.

Another major postoperative complication was myocardial ischemia (n=1) treated with stenting of circumflex artery, and two patients (5.9%) underwent pacemaker implantation for third-de-

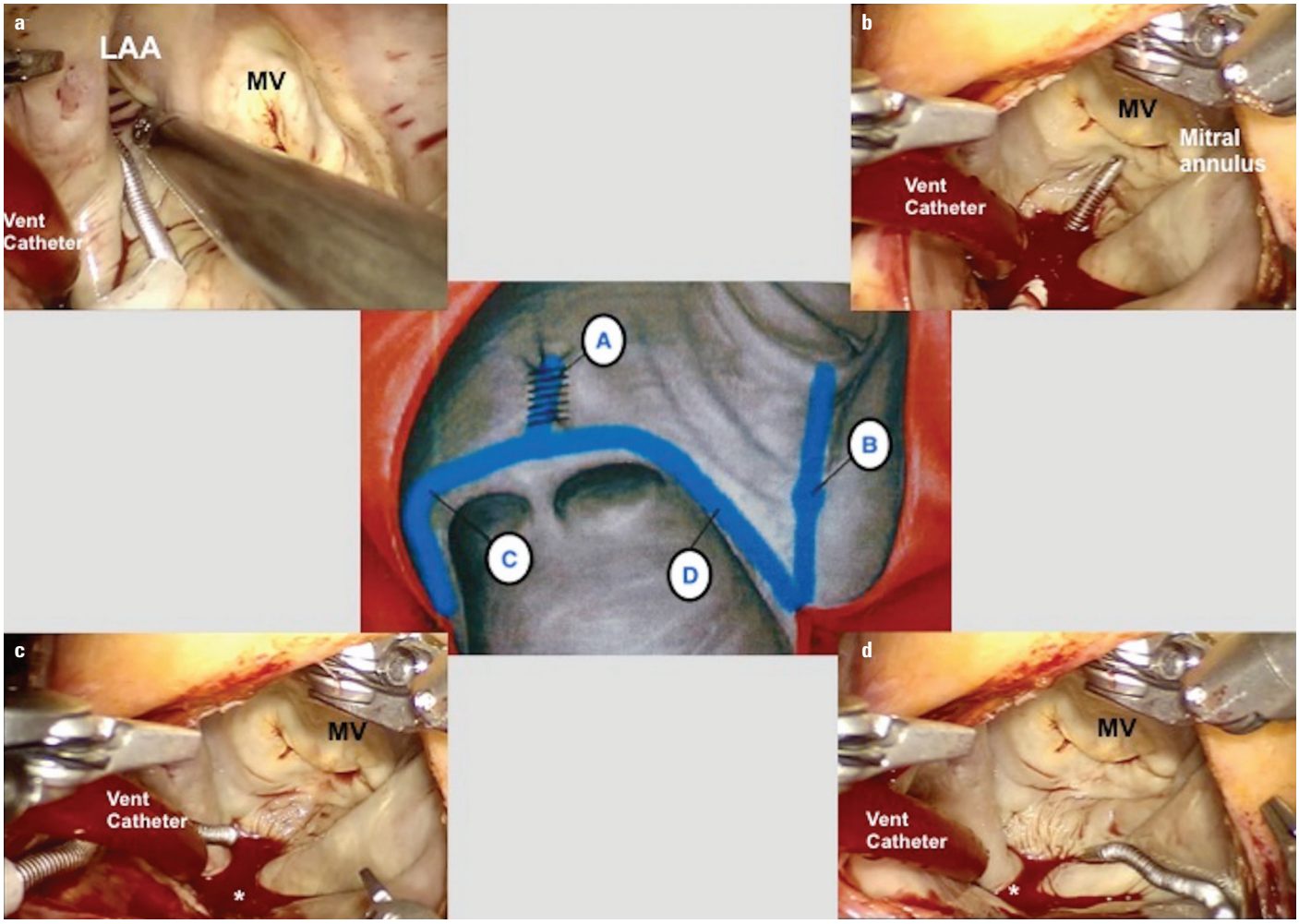

Figure 1. Schematic illustrations and surgical view of ablation technique and ablation lines
MV - mitral valve; LAA - left atrial appendage. *Ostium of left pulmonary veins

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Table 3. Operative data

Variable	Total (n=34)
Type of operation	
MV replacement+mechanical valve	21 (61.7%)
MV replacement+biological valve	3 (8.8%)
MV repair	2 (5.88%)
Additional tricuspid repair	8 (23.5%)
Concomitant procedures	
Papillary muscle resuspension	2 (5.88%)
PFO closure	3 (8.8%)
LV free-wall repair	1 (2.94%)
Left atrial volume reduction	5 (14.7%)
Femoral embolectomy	2 (5.88%)
LAA closure	34 (100%)
Sternotomy conversion	1 (2.94%)
Aortic cross-clamp (min)	141.8±32.1
Cardiopulmonary bypass (min)	196±25.6
Cardioplegia amount (mL)	1614.1±425.6

Data are given in mean±standard deviation, median (min-max), or number and frequency, where applicable. MV - mitral valve; PFO - patent foramen ovale; LV - left ventricle; LAA - left atrial appendage

Table 4. Postoperative data

Variable	Total (n=34)
ICU stay (day)	2.5±2.7 (1-15)
Mechanical ventilation (hour)	11.2±9.7 (2-46)
Drainage amount (mL)	255.2±142.9 (75-725)
Inotropic support	25 (74%)
Hospital stay (day)	8.4±3 (3-19)
Mortality	2 (5.88%)
Complications	
Prolonged mechanical ventilation (>24 hours)	5 (14.7%)
Revision for bleeding	0
Pneumonia	2 (5.88%)
First-degree atrioventricular block	4 (11.8%)
Lymphorrhea	3 (8.8%)
Delayed chest tube removal (>48 hours)	2 (5.88%)
Pacemaker implantation	2 (5.88%)

Data are given in mean±standard deviation, median (min-max), or number and frequency, where applicable. ICU - intensive care unit

gree atrioventricular (AV) block. The patients did not experience any cerebrovascular event (CVE) and embolic event, nor did they require revision surgery. Table 4 shows postoperative data.

Rhythm data

Residual AF was not detected in the operating room. Seventeen patients showed SR without any defibrillation necessity after ACC removal. Three patients needed one, four patients needed two, and five patients needed three or more defibrillations to maintain the SR. Five patients were in the junctional rhythm with ACC removal, three of whom were spontaneously returned to AF, while the remaining two had third-degree AV block and needed a permanent pacemaker.

During the hospital stay, no recurrent AF episode was seen in 22 patients (64.7%). Recurrent AF episodes were seen in seven patients, two of whom were converted to SR with one or two attempts of electrical cardioversion. Three patients, who were spontaneously returned to AF from junctional rhythm within the first 3 days, underwent IV amiodarone treatment and electrical cardioversion as per AF protocol. But despite these maneuvers, SR was not restored in these patients, three of whom were also recorded as AF. Overall, 24 patients (75%) were discharged with SR, six (18.75%) with AF, and two (6.25%) patients remained pacemaker-dependent. Figure 2 shows a diagram of postoperative rhythm data.

Follow-up data

The mean follow-up was 23.3±19.4 (range, 6.5–66.8) months. During follow-up, 32 patients were still alive. None of the patients experienced any CVE or anticoagulation and/or antiarrhythmic treatment-related complications. There was no need for a new pacemaker insertion, 22 patients were still in SR. Three patients had new-onset AF. The AF rhythm occurred within the first month in one patient, on Day 41 in another patient who was discharged with a permanent pacemaker, and 3 months in the remaining patient. Kaplan–Meier analysis revealed an overall AF free survival rate of 64.7% at 6 months, depicted by the Kaplan–Meier curve in Figure 3. Except for those with MVrep and biological heart valve,

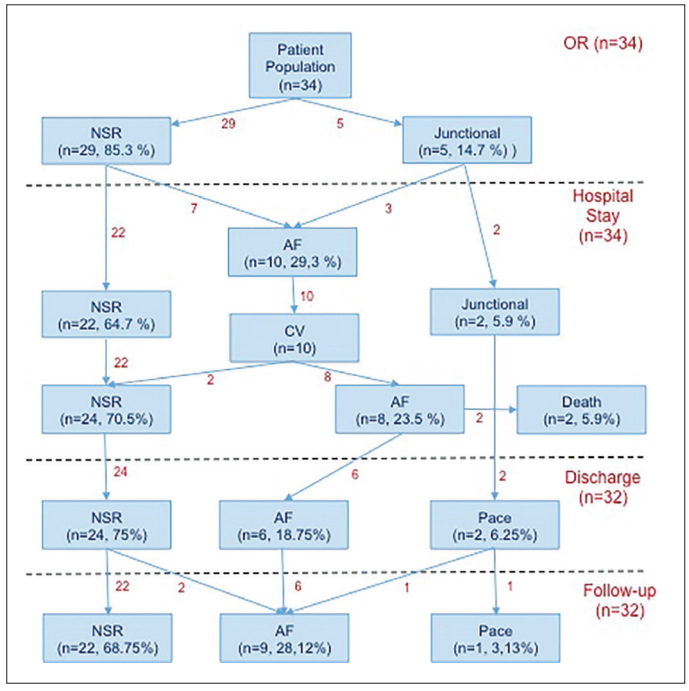

Figure 2. Diagram of postoperative rhythm data. Data are given in number and frequency, unless otherwise stated

AF - atrial fibrillation; CV - cardioversion; NSR - normal sinus rhythm; OR - operating room

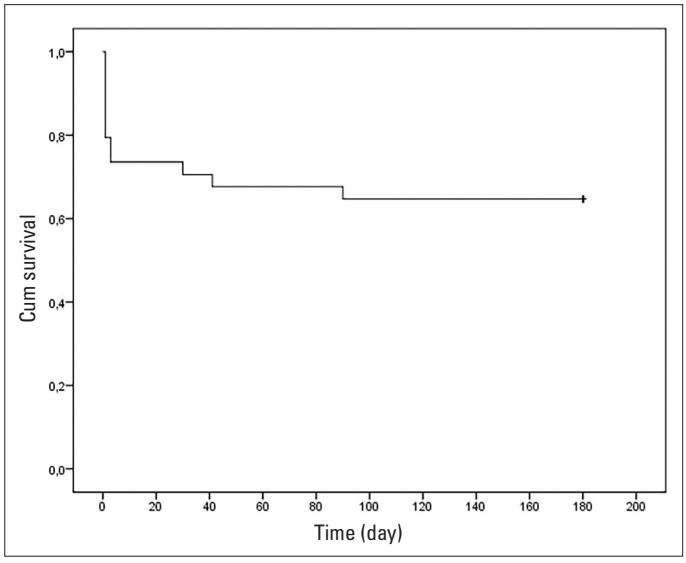

Figure 3. Overall AF free survival in the Kaplan–Meier curve. Overall AF free survival was 64.7% at 6 months

all patients were still on warfarin treatment. Except for the patients with permanent AF rhythm and a permanent pacemaker, all patients were given amiodarone treatment for 3 months. No amiodarone-related complications were recorded.

Discussion

AF is the most common arrhythmia associated with various cardiac disorders and increased cardiovascular mortality and morbidity rates (3). Previous studies have demonstrated that SR restoration during MVS significantly reduces AF-related complications and improves left ventricular outcomes (13). MVS without ablation procedures has been associated with only 20%–50% SR restoration at the ti me of surgery and during long-term follow-up (3, 7). Therefore, ablation strategies with MVS should be preferred. Despite these proven advantages, concomitant ablation strategies were not routinely performed for MVD in the early 2000s. As many centers avoided using ablation surgery due to its complexity and invasiveness, alternative techniques for AF ablation were developed. In recent years, various devices have been introduced for AF ablation by creating endocardial injury using different energy types, such as radiofrequency, cryotherapy, microwave energy, and high-intensity focused ultrasound (3, 4, 7). The overall results of are comparable; however, radiofrequency and cryoablation systems are the most preferred devices with similar outcomes (3, 7). Studies about the advantages of these two techniques over each other remain limited. The choice of the ablation systems mainly depends on the surgeon's experience. In our center, we routinely use cryoablation system.

Independent from the technique, ablation procedures mainly depend on the isolation of the pulmonary veins from the left atrium, which is called the box lesion. In one study, ionic characteristics of the left atrial myocytes and pulmonary veins were found to be different, resulting in a shorter refractory period in the left atrial tissue and favoring re-entry (3). Therefore, creating a box lesion around the pulmonary veins is a well-known crucial step of ablation surgery with additional ablation lines toward mitral annulus and LAA. In recent studies, biatrial ablation is associated with a high incidence of sinus node dysfunction (3). Therefore, we routinely prefer using left atrial ablation only. Our institution first started AF ablation in the 2000s, and cryoablation has been routinely performed on patients undergoing MVS over the last seven years. With our satisfactory results, we consider robotic cryoablation procedures to be feasible with acceptable results when combined with robotic MVS.

Since minimally invasive surgeries have become increasingly widespread, a paradigm shift has occurred in the field of cardiac surgery. With a progressive increase in the number of minimally invasive cardiac surgeries, robotic surgery has also found its place in daily practice. Since the end of 2014, we routinely perform robotic-assisted MVS in our center, which enables the surgeon to visualize the mitral valve and subvalvular apparatus in detail with three-dimensional, 10-times magnified high-definition visualization and provide perfect mobility for endoscopic instruments. Therefore, more complex procedures can be simply performed with a robotic approach.

Furthermore, the number of studies on AF ablation and MVS via minimally invasive cardiac surgery has been rapidly increasing. Marchetto et al. (8) reported their results on video-assisted MVS with concomitant cryoablation in 68 patients. Similarly, Aydin et al. (7) reported their results on radiofrequency AF ablation combined with MVS in 11 patients. In another study, Ju et al. (3) assessed robotic MVS combined with cryoablation in 94 patients. All aforementioned studies confirmed the usability of minimally invasive cardiac surgery on arrhythmia ablation, and almost all of them reported higher ACC and Cardiopulmonary bypass (CPB) times when MVS was combined with additional AF ablation. Indeed, robotic cardiac surgery is associated with prolonged ACC and CPB times compared to conventional approaches, although mortality and morbidity rates are similar (14). In a systematic review of robotic MVS alone, Seco et al. (1) reported that the mean ACC and CPB times varied from 79±16 to 140±40 min and 106±22 to 188.5±53.8 min, respectively. With the addition of ablation techniques, Aydin et al. (7) reported their mean ACC and CPB times as 105.75±20.03 min and 147.88±19.12 min, respectively. In our study, the mean ACC and CPB times were comparable with the previous studies. According to our experiences, an additional 20 min was necessary for ACC using the robotic-assisted AF ablation, which could easily be ignored.

Literature review reveals many studies demonstrating the efficacy and feasibility of minimally invasive AF ablation combined with MVS; however, only few studies have investigated robotic AF ablation (3, 7). In a recent study, Ju et al. (3) performed robotic MVS combined with cryoablation on 94 patients. In their study, they did not use postoperative antiarrhythmic medication (AAM) routinely; however, postoperative AF was seen in 30 patients (14 during hospital stay, 10 within the first 3 months, six after the 3

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months) (3). We consider these episodes to be secondary to the lack of AAM. In our study, we routinely used amiodarone in the postoperative period on patients with SR, except for certain contraindications. Similarly, Jeong et al. (15) recommended amiodarone treatment after a successful ablation. In our opinion, AAM should be used for at least 3 months after successful ablation in all patients without contraindications.

In the current study, we performed LAA closure in all patients. In their study including 75.782 patients, Yao et al. (16) reported LAA closure to be associated with a lower thromboembolism risk. The authors also concluded that LAA should be closed routinely in patients with AF. On the other hand, in another study, Ju et al. (3) suggested LAA occlusion only in patients with previous CVE, left atrial thrombi, or a shape of LAA having a high risk of TEs. However, in their study, approximately 30% of the patients had a new-onset AF episode during postoperative course, which might be a risk factor for TEs. Therefore, we believe that LAA closure strongly prevents CVEs secondary to possible new clot formations during unobserved AF. In addition, LAA closure does not prolong the ACC time by >5 min.

Study limitations

This is a retrospective study, so it has potential designing limitations. It is also a single-center study with a small-sized study population; therefore, it is difficult to generalize the results. In-hospital continuous rhythm follow-up was restricted to within 3 days in patients without rhythm anomaly, which may cause the paroxysmal AF attacks to be overlooked after 3 days. Another major limitation of the study was the type of follow-up after 3 months. Although patients were followed up by their cardiologist, who were aware of the potential complications, our results may overestimate the actual rate of possible complications during the late follow-up period. We used one-sided ablation only, which may be another limitation. Finally, the relatively short follow-up period may have impeded the statistical significance.

Conclusion

In conclusion, our study results suggest that robotic cryoablation with concomitant MVS is a feasible method with satisfactory results at the early- and mid-term follow-up. The combined method complication rates are also comparable with the standard surgical procedures or minimally invasive surgery. However, further large-scale, long-term studies are necessary to establish a definite conclusion.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

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