Retrospective investigation of postoperative mid-term results of cryoablation and radiofrequency ablation methods used in atrial fibrillation surgery treatment

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ABSTRACT

Objectives: Atrial fibrillation (AF) is the most common arrhythmia encountered and is usually seen in patients scheduled for coronary artery bypass and mitral valve surgery. Radiofrequency ablation and cryoablation are two methods used in AF surgery and proven efficacy. In this study, cryoablation and radiofrequency ablation methods were compared in terms of clinical outcomes, efficacy and safety.

Methods: Between November 2011 and September 2017; 99 patients with AF who underwent radiofrequency ablation or cryoablation during open heart surgery were included in this study with 2 groups. The patients who underwent cryoablation were defined as Group I (n = 40), and the patients who underwent radiofrequency ablation as Group II (n = 59). Preoperative, perioperative, early and mid (1 year) postoperative period characteristics of the groups were analyzed.

Results: The mean age was 60.6 ± 9 years in Group I and 60.7 ± 9.1 years in Group II (p = 0.960). When the operative values were examined, ablation time and cross-clamp time was found to be low in Group II and a statistically significant difference was found (p < 0.001 and p = 0.043; respectively). When the rhythms of the postoperative first year controls are examined, sinus rhythm was observed in 34 (85%) patients in Group I and 50 (84.7%) patients in Group II. There was no statistically significant difference in return to sinus rhythm in the first year (p = 0.975).

Conclusions: The success rates of these two methods used in AF surgery are effective but they are not superior to each other.

Keywords: Atrial fibrillation, cryoablation, radiofrequency ablation, surgical ablation

Atrial fibrillation (AF) is a common arrhythmia in the society. It was first described in 1909 by Thomas Lewis. While the incidence in the general population is between 0.4% and 2%, this rate reaches 10% over the age of 60. This rate was reported to be 30% and 84% in patients scheduled for surgery for mitral valve, and 5% in patients scheduled for surgery for coronary heart disease [1].

AF has been perceived as a benign arrhythmia for many years; therefore, treatment options have been...
limited. However, several previous studies showed that AF increases the probability of stroke by six times, doubling the mortality due to cardiovascular causes. Even in the absence of stroke, it was shown that AF probably causes cognitive impairment as a result of silent lacunar and cortical infarctions or hypoperfusion. Persistent AF was associated with doubled mortality due to all causes and cardiovascular disease-related [2-4].

Approaches in surgical treatment targeted to stop uncontrolled electrical triggers in the atrium and to ensure atrial contraction function. For this purpose, left atrial isolation procedure, catheter ablation of sense node, corridor procedure, pulmonary button isolation, atrial compartment operations were applied, respectively throughout the history. Finally, the surgery that was called “Maze III Procedure”, which was developed by Cox and which was modified twice, became the gold standard for AF treatment with 99% success. Today, radiofrequency (RF) ablation and cryoablation methods are used widely in the surgical treatment of AF [5]. Success of AF treatment with isolated left atrial RF ablation and cryoablation has been reported to be 70–85% [6-8].

The purpose of this study was to determine the efficacy and reliability, and early and mid-term clinical results after RF ablation and cryoablation methods used for AF therapy in patients who have AF rhythm in the preoperative period and have undergone open heart surgery.

METHODS

A total of 99 patients at the University of Health Sciences, Bursa Yıktıp Ihtisas Training and Research Hospital, Bursa, Turkey, between November 2011 and September 2017, who underwent open heart surgery with cardiopulmonary bypass (CPB), who had AF in the preoperative period, and who underwent RF ablation or cryoablation during the surgery were included in the study in 2 groups (Group I: Cryoablation, Group II: RF ablation). The study was designed retrospectively based on the database, and was approved with the decision of Uludag University Faculty of Medicine Clinical Research Ethics Committee on 21.11.2017 with the number 2017-17/3.

The preoperative, perioperative, early and mid (1 year) postoperative period features of patients were recorded. Patients with endocarditis, sick sinus syndrome, calcification in the left atrium wall, who did not admit to our hospital for routine outpatient follow-ups after discharge, and who did not complete their first 1-year follow-ups were excluded from the study. All patients were examined with transthoracic echocardiography (TTE) in the preoperative period. In the echocardiography unit of our hospital, left atrium (LA) diameter and ejection fraction (EF) were calculated using the Teichholz formula from two-dimensional parasternal long axis images with the G.E Electronics Vivid 7 Echocardiography device. The pulmonary artery pressure (PAP) was measured with continuous wave (CW) method through the tricuspid valve in patients who had tricuspid insufficiency. In patients who did not have tricuspid insufficiency, it was measured with pulmonary flow acceleration time.

Surgical Technique

Aorta-bicastral cannulation was performed after median sternotomy, and CPB was started after the ACT (activated clotting time) was > 400. After cross-clamping, if there was coronary bypass grafting (CABG) in the surgical procedure to be performed, distal anastomosis of saphena grafts was performed firstly. If the surgery to be performed was valve surgery, left atriotomy was performed.

After left atriotomy, firstly, left atrium and appendix were evaluated. The first thing to do was thrombectomy in cases with thrombus in the left atrial appendix, and the left atrial appendix was ligated internally with 4/0 prolene suture. If valve replacement was planned, the mitral valve was excised (if possible, posterior leaflet was preserved). The right pulmonary veins were circled starting from the incision made from the interatrial groove, then the left pulmonary veins were circled in one single circle to form a set of lesions. Then another set of lesions was created to combine the two candidates that included the right and left pulmonary veins from the superior segment. This line was positioned towards the left atrium ceiling as much as possible to avoid possible esophageal damage. Another ablation line was created to combine the left pulmonary veins and the mitral valve posterior anulus after the ablation line extending from the left atrial appendix to the left superior pulmonary vein was created. Another line that started exactly in the middle
of this line was extended towards the atrium base to prevent “re-entry” waves that might occur between atriums through the coronary sinus.

As the precaution for this, ablation was performed before additional surgical procedure in order not to damage the suture lines. In addition, wet gauze was placed in the LA posterior before the ablation to prevent possible esophageal damage, and the trans-esophageal echocardiography (TEE) probe was withdrawn (if any). The ablation line was directed towards P2-P3 to avoid damage to the circumflex artery during the ablation process. The Cardioblate CryoFlex Surgical Ablation Probe (Medtronic Inc., Minneapolis, MN, USA) was used in Group I, and the Irrigated Unipolar Cardioblate Surgical Ablation Pen was used in Group II (Medtronic Inc., Minneapolis, MN, USA).

The concomitant surgery procedure was performed after the ablation procedure was completed. The cross-clamp was removed after the surgical procedure was completed, and CPB was terminated. Temporary epicardial “pacemaker” wires were placed in patients at the end of the surgery against AV block risk.

**Postoperative Medical Treatment and Follow-up**

In our clinic, our medical treatment protocol for patients who undergo surgical ablation is administering intravenous Amiodaron (1200 mg) in the first 24 hours postoperatively, to every patient without discrimination. Half of this treatment dose (600 mg) is given in the form of loading dose after the cross-clamping, and the rest is given in the form of maintenance dose. Amiodaron oral tablet is initiated (600 mg/day), and is used as 200 mg/day for at least 3 months after the discharge.

Amiodaron infusion was started without discrimination in the groups of patients included in our study at the loading dose (600 mg) after cross-clamping, and maintenance Amiodaron infusion (600 mg) was initiated after the loading dose. Following decannulation, internal cardioversion was applied to patients who had AF. Patients were taken to the intensive care unit and followed up with full monitoring. Rhythm follow-up was carried out with 12-derivation electrocardiography (ECG). In the intensive care unit, patients were re-evaluated in terms of rhythm, and patients without hemodynamic problems were taken to the ward. Patients were discharged with planned anticoagulant and antiarrhythmic treatment. The ECG data and postoperative 6th month TTE follow-up results were recorded in routine follow-ups of patients after the discharge (3rd month, 6th month, and 1st year).

**Statistical Analysis**

The SPSS 21.0. (IBM Corp. Armonk, NY: USA. Released 2012) program was used to analyze the data obtained in the study, and $p < 0.05$ was taken statistically significant. While analyzing the study data, besides descriptive statistical methods (Mean ± standard deviation); Student t-test or Mann-Whitney U-test was used in cross-group comparisons of parameters that showed normal distribution or not in the comparison of the quantitative data; Chi-Square Test was used to compare the qualitative data.

**RESULTS**

There were 40 patients in Group I, and Group II included 59 patients in our study. Isolated left atrial ablation was applied to all patients. The mean age of the patients was $60.6 \pm 9$ years in Group I; and the mean age of the patients in Group II was $60.7 \pm 9.1$ ($p = 0.960$). Among the patients in Group I, 26 (65%) were females, and 14 (35%) were males; and in Group II, 35 (59.4%) were female, and 24 (40.6%) were male ($p = 0.569$). When the preoperative patient characteristics were evaluated, no statistically significant differences were detected between the groups in terms of chronic obstructive pulmonary disease, diabetes mellitus, hypertension, and coronary artery disease. The demographic characteristics of patients are presented in Table 1.

When the groups were compared in terms of preoperative EF, EF values of patients in Group II were lower than patients in Group I and statistically significant differences were found (Group I: $54 \pm 7.5$ vs Group II: $50.25 \pm 6.1$, $p = 0.014$). There were no statistically significant differences between the other TTE parameters that were evaluated; preoperative LA diameter and PAP values ($p = 0.327$ and $p = 0.947$; respectively) (Table 1).

Considering the surgical procedures applied to the patients; Mitral valve replacement in 48 (48.5%) patients, mitral valve replacement with aortic valve replacement in 13 (13.1%) patients, tricuspid ring annuloplasty with mitral valve replacement in 12 patients.
(12.1%) patients and mitral ring annuloplasty in 11 (11.1%) patients. In addition, CABG was applied as an additional surgical procedure in 10 (10.1%) patients. Surgical procedures applied to patients are shown in Table 2.

Both groups were compared in terms of perioperative total perfusion times (TPT), cross-clamp times (CCt) and ablation times. Mean TPT was 113.5 ± 11 minutes in Group I, 109.6 ± 10.1 minutes in Group II; mean CCt was 76.8 ± 7.3 minutes in Group I and 74.1 ± 10.4 minutes in Group II. While no statistically significant difference was found between the groups in terms of TPT, CCt was significantly lower in Group II (p = 0.101 and p = 0.043; respectively). When the mean ablation times were examined, it was found that it was 13.7 ± 1 minutes in Group I and 8.6 ± 1 minutes in Group II, and this difference was statistically significant (p < 0.001) (Table 3).

When the operation output rhythms of the patients were evaluated, Sinus rhythm was achieved at a rate of 80% in Group I and 79.7% in Group II, and no significant difference was found (p = 0.967). In routine follow-ups of the groups after the discharge, 1 patient in Group I and 2 patients in Group II returned to AF rhythm during the follow-ups in the 3rd month. During the follow-ups in the 6th month, it was seen that 3 patients in Group I and 5 patients in Group II returned to sinus rhythm. In statistical terms, no statistical differences were detected between the groups compared to the 3rd and 6th month sinus rhythm rates (p = 0.961)

### Table 1. Demographic and preoperative features of the patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I (n = 40)</th>
<th>Group II (n = 59)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.6 ± 9 (40-80)</td>
<td>60.7 ± 9.1 (36-82)</td>
<td>0.960</td>
</tr>
<tr>
<td>Gender (Male/Female)</td>
<td>26/14</td>
<td>35/24</td>
<td>0.569</td>
</tr>
<tr>
<td>COPD</td>
<td>10 (25%)</td>
<td>15 (25.4%)</td>
<td>0.962</td>
</tr>
<tr>
<td>DM</td>
<td>7 (17.5%)</td>
<td>13 (22%)</td>
<td>0.581</td>
</tr>
<tr>
<td>HT</td>
<td>13 (32.5%)</td>
<td>14 (23.7%)</td>
<td>0.336</td>
</tr>
<tr>
<td>CAD</td>
<td>7 (17.5%)</td>
<td>10 (16.9%)</td>
<td>0.943</td>
</tr>
<tr>
<td>EF (%)</td>
<td>54 ± 7.5 (40-65)</td>
<td>50.25 ± 6.1 (35-65)</td>
<td><strong>0.014</strong></td>
</tr>
<tr>
<td>PAP (mmHg)</td>
<td>48.1 ± 9.3 (30-70)</td>
<td>48.2 ± 8.4 (30-70)</td>
<td>0.947</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
<td>56.2 ± 6.7 (43-70)</td>
<td>55.1 ± 6.8 (44-77)</td>
<td>0.327</td>
</tr>
</tbody>
</table>

Data are shown as mean ± standard deviation (minimum-maximum) or number (%). COPD = Chronic obstructive pulmonary disease, DM = Diabetes mellitus, HT = Hypertension, CAD = Coronary artery disease, EF = Ejection fraction, PAP = Pulmonary artery pressure, LA = Left atrium

### Table 2. Surgical procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Group I (n = 40)</th>
<th>Group II (n = 59)</th>
<th>Total (n = 99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVR + MVR</td>
<td>5 (12.5%)</td>
<td>8 (13.5%)</td>
<td>13 (13.1%)</td>
</tr>
<tr>
<td>MVR</td>
<td>20 (50%)</td>
<td>28 (47.4%)</td>
<td>48 (48.5%)</td>
</tr>
<tr>
<td>MRA</td>
<td>4 (10%)</td>
<td>7 (11.8%)</td>
<td>11 (11.1%)</td>
</tr>
<tr>
<td>MVR + CABG</td>
<td>3 (7.5%)</td>
<td>3 (5.1%)</td>
<td>6 (6.1%)</td>
</tr>
<tr>
<td>MRA + CABG</td>
<td>1 (2.5%)</td>
<td>2 (3.4%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>AVR + MRA</td>
<td>0</td>
<td>2 (3.4%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>AVR + MVR + TRA</td>
<td>1 (2.5%)</td>
<td>1 (1.7%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>MVR + TRA</td>
<td>6 (15%)</td>
<td>6 (10.2%)</td>
<td>12 (12.1%)</td>
</tr>
<tr>
<td>MVR + TRA + CABG</td>
<td>0</td>
<td>1 (1.7%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>MRA + TRA</td>
<td>0</td>
<td>1 (1.7%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

Data are shown as number (%). AVR = Aortic valve replacement, MVR = Mitral valve replacement, MRA = Mitral ring annuloplasty, CABG = Coronary artery bypass grafting, TRA = Tricuspid ring annuloplasty
In the 1st year of follow-ups, it was determined that sinus rhythm continued at a rate of 85% in Group I and 84.7% in Group II, and no statistically significant difference was found ($p = 0.975$). In line with the data obtained, no return to sinus rhythm was observed after the 6th month follow-ups (Table 4).

When the 6th month TTE results were evaluated, it was seen that there were statistically weakly significant differences between the groups compared in EF values ($p = 0.013$); and there were similar values with EF values in the preoperative period. In the 6th month, no statistically significant differences were detected between the groups in terms of LA diameter and PAP values ($p = 0.633$ and $p = 0.117$, respectively) (Table 5).

### DISCUSSION

AF increases mortality and morbidity at significant levels, as well as significantly impairs the quality of life of patients and imposes a significant socioeconomic burden on patients. Arrhythmia is the cause of approximately 10% of hospitalizations related to the circulatory system. Most of this is composed of AF and atrial flutter [3, 6]. In patients who undergo cardiac surgery, the achieving sinus rhythm in the postoperative period is very important for healing process [9, 10].

The groups in our study were those who underwent irrigated unipolar RF ablation and cryoablation, and all of them had pathology in the mitral valve. In the literature, the presence of AF rhythm was reported in 30-79% of patients who undergo valve surgery and the rate of spontaneous return to postoperative sinus rhythm was less than 10% [11, 12]. However, Forlani et al.’s [13] study argued that the return to sinus rhythm increased the survival rates of patients and reduces morbidity significantly. For this purpose, the application of ablation therapy together with mitral intervention will be beneficial in patients with persistent AF rhythm in the preoperative period.

Several complications might develop due to this
process. The complications reported so far in the literature consist of endocardial applications. Regardless of the probe used, bleeding due to esophageal damage or left atrium perforation may develop especially in left atrial RF ablation. Phrenic nerve damage may occur during cryoablation. However, cryoablation has low thrombogenicity compared with RF ablation, with a low perioperative bleeding and atrial wall perforation risk [14]. The most fatal complication in endocardial practice is esophageal damage [15]. During the circling of the right and left pulmonary vein mouths in two separate islets and the combination of these two, the esophageal may be damaged due to its neighboring localization to left atrium posterior wall. In our clinical applications, to avoid such complications and minimize the possibility of damage, the TEE probe and nasogastric catheter are removed (if any) during the ablation process, and gauze is placed in the oblique sinus. Also, attention must be paid not to intersect the left atrial circles because applying energy to the same tissue for a second time increases the risk of perforation [16]. Doll et al. [15] applied RF ablation to 387 patients, and reported that esophageal perforation developed in four patients (1%). Also, circumflex artery injury during Maze Operation combined with cryoablation, left main bronchial injury because of its proximity to the posterior wall of the left atrium, and pulmonary vein stenosis can also be named among related complications [17, 18]. No complications were detected in our patients in our study, including esophageal damage and left atrial wall perforation.

In the present study, it was observed that TPt was shorter in patients who underwent RF ablation compared to those who underwent cryoablation. In his study, Güden et al. [19] reported that the endocardial procedure lasted between 9 and 12 minutes for left atrial ablation. In our study, cryoablation lasted 12-15 minutes, and RF ablation process lasted 7-10 minutes. It was observed in our study that RF ablation process was significantly shorter, when the ablation application times were compared between both groups ($p < 0.001$). When TPt and CCt, which included ablation and surgical procedure, were compared, no statistically significant difference was found between the two groups in terms of TPt. In terms of CCt, CCt was found to be significantly shorter in the RF ablation group ($p = 0.043$).

The amputation of atrial appendices, especially the left atrial appendix, is still controversial today. However, with the risk of thromboembolic events, it is still considered as a logical approach to perform atrial amputation, or at least applying ablation to the base, then sewing it from the inside, or by inserting a pouch suture from the outside, closing the mouth completely [20]. We also think in line with this approach in our clinic, and apply internal ligation to the left atrial appendix in the framework of our surgical ablation protocol.

One important point that stands out in all studies reporting RF ablation results was that although the rates of recovering from Af after surgery were always close to 100%, a significant decrease also occurred, especially in the first week, followed by a re-increase in six months to one year. In our study, it was found that there was a return from sinus rhythm to AF rhythm in the first 3 months (1 patient in Group I, and 2 patients in Group II). After 1st year follow-up, it was found that 3 patients in cryoablation group and 5 patients in RF ablation group returned to sinus rhythm in the last nine months. This condition is explained with temporary shortening of the refractory period of atrium because of edema, inflammation and high catecholamine levels in circulation as a result of surgical trauma in the postoperative period [21]. However, AF can also be seen in early postoperative period because of advanced age, increased sympathetic activity, ischemia and electrolyte disorder, atrial factors, and other underlying cardiac diseases. This period lasts about 3 months, and patients are advised to continue their antiarrhythmic treatments. For this reason, Geidel et al. [22] recommended using “Amiodaron” in the first 3 months. Antiarrhythmic treatment (Amiodaron) is applied to all patients in the first 3 months of postoperative period according to the medical treatment protocol of our clinic after cryoablation and radio-frequency ablation. For this reason, six-month, even one year and above follow-up times should be considered in the evaluation of surgical treatment results of AF. In terms of clinical applications, it must also be noted that AF attacks in early postoperative period may be temporary. It should be known that the actual result will be determined in a longer period.

There are numerous studies in the literature that compare cryoablation and RF ablation methods in terms of clinical outcomes, efficacy and safety. In the case control study of Linhart et al. [23] with 40 pa-
patients with paroxysmal AF, they found that cryoablation and RF ablation had similar success rates. Kojodjojo et al. [24] compared cryoablation and RF ablation in 124 patients with persistent and paroxysmal AF. The success rate at the end of one year follow-up was reported to be 77% in cryoablation group, and 72% in RF ablation group. Kühne et al. [25] conducted a study and compared cryoablation and RF ablation procedures, 88% success rate was reported in cryoablation group, and 92% success rate in RF ablation group in one year follow-up. In the “Fire and Ice” study published by Kuck et al. [26], 762 patients who underwent cryoablation and RF ablation were followed-up in two groups for approximately 18 months, and had no significant differences when the effectiveness and reliability of the two methods were compared. Also, a large-scale meta-analysis study compiled by Hachem et al. [27] consisting of 247 randomized controlled trials found similar results with “Fire and Ice” study. In our study, at the end of the 1st year, 85% success rate was reported in cryoablation group, and 84.7% in RF ablation group with no statistically significant differences between the groups ($p = 0.975$). The success rates we achieved in our study showed similar results with these studies in terms of the comparison of cryoablation and RF ablation methods, and suggested that both methods are not superior to each other, and their efficacy is similar.

Limitations

The fact that the number of patients was low in our study, its retrospective design, high diversity of patients, and lack of a long follow-up period were the limitations of our study. In this respect, we believe that large-scale studies should be conducted with larger patient series and longer follow-up periods.

CONCLUSION

As a conclusion, sinus rhythm was achieved at a high rate with cryoablation and irrigated unipolar RF ablation applied to patients in preoperative AF rhythm scheduled for open heart surgery. When they were compared in terms of postoperative morbidity, mortality, rhythm control and echocardiographic values, it was observed that both methods were effective and reliable; however, at the same time they had no superiority over each other.

Authors' Contribution

Study Conception: ABT; Study Design: ABT, AAP; Supervision: YA; Funding: ABT; Materials: ABT, AAP, ME; Data Collection and/or Processing: ABT, ME, TT; Statistical Analysis and/or Data Interpretation: AAP, YA; Literature Review: ABT, ME, TT; Manuscript Preparation: ABT, AAP, TT and Critical Review: YA.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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