

Original research-Orijinal araştırma

The efficiency of radiofrequency ablation therapy for the treatment of atrial fibrillation during concomitant mitral valve surgery; short and midterm results

Mitral kapak replasmanı yapılan olgularda atriyal fibrilasyon nedeni ile uygulanan radyofrekans ablasyon tedavisinin etkinliği; kısa ve orta dönem sonuçları

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Abstract

Aim. The aim of this study is to evaluate the efficiency of intraoperative endocardial Radiofrequency Ablation (RFA) treatment at short and mid-term in patients with mitral valve disorders and chronic atrial fibrillation (CAF) during mitral valve operation in the light of the literature. **Methods.** Between June 2004 and April 2009, 25 patients with mitral valve diseases associated with chronic atrial fibrillation underwent valve replacement and endocardial RFA with Medtronic cardioblade ablation pen at our clinic. There were 12 (%48) male and 13 (%52) female patients ranging in age from 23 to 67 years, with a mean age of 43.2 ± 10.6 years. The functional capacity of the patients were Class II in 6 (%24), Class III in 16 (%64), Class IV in 3 (%12) according the NYHA functional classification. At the preoperative period all patients were evaluated by 12 lead electrocardiography (ECG) and transthoracic echocardiography (TTE). For the patients over 40 years old, coronary angiography was performed to rule out concomitant coronary artery disease. The patients were evaluated at the 1st, 3rd, 6th, 9th months and annually by 12 lead ECG, TTE and as needed Holter monitoring after discharging. **Results.** There was not any complication related with the ablation technique. There were no operative or early postoperative deaths (within 30 days). Thirteen patients reverted to sinus rhythm postoperatively. But SVT was seen in 3 patients, and they were treated with antiarrhythmic drugs. The remaining 9 patients were in AF. The mean follow up period is 9 months. During the follow up period, 16 patients were noted to be in normal sinus rhythm. **Conclusion.** RFA can be a useful and efficient technique for restoring normal sinus rhythm and atrial functions after mitral valve surgery performed in patients who have mitral valve disease associated with chronic atrial fibrillation. But further studies with larger number of patients are needed to confirm our results.

Key words: Radiofrequency catheter ablation, atrial fibrillation, mitral valve

Özet

Amaç. Kronik Atriyal Fibrilasyonlu, mitral kapak hastalığı bulunan ve kliniğimizde mitral kapak replasmanı yapılan hastalarda intraoperatif uyguladığımız Radyofrekans ablasyonunun (RF) etkinliğinin belirlenmesi, kısa ve orta dönem sonuçlarının literatür ile karşılaştırılarak değerlendirilmesi amaçlanmıştır. **Yöntem.** Haziran 2004 ve Nisan 2009 tarihleri arasında kliniğimizde kronik atriyal fibrilasyonlu 25 hastaya Medtronic cardioblade cerrahi ablasyon kalem ile radyofrekans ablasyon tedavisi uygulandı. Hastaların 12'si (%48) erkek 13'ü (%52) bayandı. Ortalama yaş $43,2 \pm 10,6$ (23-67) idi. Hastaların fonksiyonel kapasiteleri NYHA sınıflamasına göre 6'sı (%24) sınıf II, 16'sı (%64) sınıf III, 3'ü (12) ise sınıf IV idi. Bütün

hastalara standart 12 derivasyonlu EKG ve ekokardiyografi yapıldı. Kırk yaş üzeri hastalara muhtemel bir koroner arter hastalığını saptayabilmek amacı ile koroner anjiyografi yapıldı. Hastalar taburcu edildiklerinden itibaren 1.ay, 3.ay, 6.ay ve 9.aylarda standart 12 Derivasyonlu EKG, Transtorasik Ekokardiyografi ile ve gereğinde Holter monitarizasyonu ile takip edildi. **Bulgular.** Uygulanan yöntemden kaynaklanan herhangi bir komplikasyon gözlenmedi. Ameliyat sırasında ve hastanede ölüm olmadı. Ameliyat sonrası 13 hastada sinüs ritmi sağlandı. Hastaların 3 ünde postoperatif dönemde SVT gelişti. Antiaritmik tedavi sonrası hastalarda sinüs ritmi tesis edildi. Hastalarımızın 16'sı sinüs ritmi ile taburcu edildi. Ortalama takip süresi 9 aydı. 9 aylık takip sonunda 16 hastamız sinüs ritminde kaldı. **Sonuç.** AF'nin eşlik ettiği romatizmal mitral kapak hastalarında mitral kapak cerrahisi sonrası radyofrekans ablasyon tedavisi sinüs ritminin ve atriyal fonksiyonların geri dönmesinde etkili ve yararlı bir yöntem olabilir ancak sonuçların doğrulanması için daha geniş vaka sayılı çalışmalar gerekmektedir..

Anahtar Sözcükler: Radyofrekans katater ablasyon, atriyal fibrilasyon, mitral kapak

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Introduction

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia revealing with atrial depolarization above 300/min without concomitant atrial contraction [1]. It is more common in men than in women. It's incidence is about 0.4% in general population and increases with the age [1]. AF is the most common consistent cardiac rhythm disorder and its incidence rises with the increase of elderly population. In Framingham study, AF incidence was found as 2% in people over 22 years old [2]. Stasis developed due to disappearing of the atrium contraction in AF leads to thrombosis in the atrium and this may cause to systemic thromboembolic events [2]. Furthermore, since the absence of atrial contraction eliminates the contribution of atriums in late filling phase to the ventricle volume, hemodynamia is also impaired. These negative effects accounts for the morbidity and mortality of atrial fibrillation [3]. Purpose of the medical treatment is to control the ventricle rate, provide rhythm control and reduce the risk for thromboembolism with anticoagulation [4]. Embolic events develop in 20% of the patients with mitral stenosis (MS) and AF and these more frequently affect the cerebral circulation. AF increases the risk for stroke and thromboembolism by 3-7 times in the patients with MS [5]. In cases having coexistence of mitral valve disease and chronic atrial fibrillation, AF has been seen to be persisted in more than 80% of the cases after only surgical intervention. In a conducted study, the rate for returning to spontaneous sinus rhythm was reported as 8% [7]. Both of the studies demonstrate us that improving of the mitral valve functions with operation is not enough for the AF treatment, and an additional attempt should be performed [8, 9]. Elimination of the cause may not be sufficient alone for returning to the sinus rhythm as there is an enlarged atrium with an altered electrical structure. Although many operations had been performed in historical development for this necessity, the most successful results have been obtained through Maze III operation developed by Cox et al.[10] Performing of the additional procedures such as valve and bypass together with Maze operation, makes this operation more complex. However, when considering significant success rates of the procedure, the idea of creating the conduction blocks in same localizations with different energy sources instead using the surgical incision and sutures has been suggested. Today the most successful method for these purposes is RFA [11]. Radiofrequency ablation with serum irrigated tip has been used first by Wittkamp et al. [12] in 1988. In our study, RFA was performed in our patients with unipolar endocardial irrigated radiofrequency pen (Cardioblate, Medtronic Inc., 2006, USA). Nagakawa et al. [13] investigated the efficiency of various catheters, compared dry and serum irrigated catheters, and

consequently, they observed that, carbonization was occurred in the given energy level to reach the desired depth of the lesion in the dry system, carbonized surface was resistant to the transmission of heat to the other layers, and as a result of this, creating of a full-thickness lesion was difficult. Furthermore, this carbonized surface produced a focus for thromboembolism and the widest and deepest lesions were realized through serum irrigated catheter . In the recently developed bipolar system, this disadvantage is eliminated by creating a controlled and fully transmural lesion. Several lesion types were created for RFA. All of these lesion types include complete or almost complete isolation of the pulmonary veins and excision or ruling out of left atrial appendix. Left atrial applications include prevention of the conduction by creating of the lesions between the left pulmonary veins and left atrium appendix and again between the left pulmonary veins and mitral valve annulus. Objective of this study is to evaluate the short and midterm result of RFA procedure that we performed due to concomitant AF in the cases with mitral valve replacement.

Materials and methods

Patient selection and the study protocol: Attention was paid to criteria such as CAF in the cases and surgical indication due to mitral valve replacement. RFA was performed intraoperatively in 25 patients with mitral planned valve surgery and CAF. 12-lead ECG and transthoracic ECO were taken in all patients. The patients were followed-up in the postoperative period for 9 months and evaluated with ECG and Echocardiography.

Exclusion criteria: The patients who had endocarditis, sick sinus syndrome, calcification in the left arterial wall, improper cardiac functions (EF less than 25%), who were cachectic and had a highly degree large atrium diameter (case with the left atrium diameter larger than 7.2 cm) and the patients with coronary artery diseases were excluded from the study.

Application technique

Standard aortic arterial bicaval and venous cannulation was performed following the median sternotomy. Left atriotomy was performed after the cross-clamp. A serum irrigated ablation pen (Cardiobale, Medtronic Inc.,2006, USA) was used for the endocardial ablation. Radiofrequency energy of 25-30 Watt was used with average duration of 10-15 seconds. Thrombectomy was done in the cases who had thrombus in the left atrium. First, right pulmonary veins were isolated by creating a lunar lesion as to be connected to left atriotomy incision from the both ends. Next, left arterial veins were isolated by creating an elliptical lesion. These two isolated islets were connected with a straight line. Then the procedure was completed by creating a lesion with a straight line from the left pulmonary vein islet to the left atrium appendix and mitral valve posterior annulus. Next, left atrial appendix was excised and sutured. Since the suture material might be damaged before the ablation operation, the procedure for mitral valve was introduced.

Statistical comparisons

All of the statistical evaluations were done by using Statistical Package For Social Sciences (SPSS) 13.0 (Microsoft, 2008, USA) software running under Windows XP. P values between 0.05 and 0.01 were considered as significant, between 0.01 and 0.001 as very significant and less than 0.001 were considered as highly significant.

Chi-square test of independence was used to check whether there was a dependency between two or more directional cross categories. There was no statistical correlation between the other three variables (gender, age and EF) and rhythm.

Mann-Whitney U test was used to test whether two independent samples with volume of N1 and N2 taken from the population with the same median were random samples or not. Although the number of samples was small as to the rhythm variable according to Mann

Whitney U test, there was statistically highly significant difference ($p=0.001$) between left atrium diameters of AF and sinus groups. While average number and standard deviation of the patients with continuing AF rhythm were 7.0429 and 0.25071 respectively, these values of the patients with a rhythm had returned to sinus were 5.3294 and 0.49971.

Results

In this study, RFA was performed on 13 female and 12 male, totally 25 patients. All the cases were those with the operation decision made by common council of cardiology and cardiovascular surgery. All patients had rheumatic mitral valve disease. Three of the patients had undergone previously mitral valve replacement operation. Mitral valve replacement alone was performed in 17 patients, while mitral valve replacement and aortic valve replacement in 2 patients, mitral valve replacement and tricuspid annuloplasty in 3 patients, mitral valve replacement and DeVega annuloplasty in 1 patient and mitral valve replacement and left atrial thrombectomy in 2 patients. While AF was paroxysmal in 4 patients, there was chronic AF in 21 patients. Eleven of the patients were using antiarrhythmic drugs preoperatively. Three of our patients had low ejection fraction ($EF < 40\%$). Four of our patients were taken to revision due to bleeding. RFA was performed with unipolar endocardial irrigated radiofrequency pen (Cardioblate, Medtronic Inc., 2006, USA) in all patients. There was sinus rhythm in 13 of the 25 patients in the postoperative period. Three patients had supraventricular tachycardia, and normal sinus rhythm was provided with medical treatment. AF had continued in 9 patients. There was not any patient with nodal rhythm and permanent pace maker was needed. AF with a high ventricular response was observed in three of the patients who were taken to the intensive care. Their heart rates were controlled with medical treatment. Treatment continued for six months in the patients with antiarrhythmic medicine introduced. Electrical cardioversion was not applied in any of our patients.

We had no mortality and operation related complications. AF was detected again in 3 patients who were taken to the intensive care with normal sinus rhythm and were discharged also with sinus rhythm. These patients were interned and returned to the sinus rhythm after the medical treatment. First follow-up of the patients was at the end of the first week of discharging and second was in the range of 1st to 9th month. In our 3 patients who came with high heart rates at the first follow-up, the rate was controlled with additional beta blocker medication. In the second follow-up (6th month) high heart rate was detected in another patient and beta blocker treatment was introduced in that patient also. Our operation success rate was 64% at the end of the 9th month. When the left atrium diameter was evaluated, our success rate for 5.5 cm and less was 76%.

Cerebrovascular event developed in a patient who was discharged with AF and this patient is followed-up with the right hemiparesis. Probable cause of this was considered to be irregular use of anticoagulants. Patients using warfarin sodium were controlled with frequent INR follow-up and hospitalized when necessary. Pleural efusion was identified in one case following posterior-anterior (PA) lung graphy in the first month. INR of the patient was checked, thoracentesis was performed and effusion was discharged. Spontaneous echo contrast (SEC) was observed in our 3 patients with echocardiographic controls in the postoperative period. SEC detected in the left atrial appendix was seen to be completely resolved at the end of 3rd month providing the protection of sinus rhythm. In echocardiographic controls at the postoperative 6th month, a significant increase was defined in ejection fractions of the patients compared to the preoperative period. Also a significant decrease ($p < 0.001$) was observed in the values of left ventricular end-diastolic and end-systolic diameters, left atrium diameter and pulmonary arterial pressure in the posoperative 6th month period.

Table1: Preoperative data of study population.

Male: Female	12:13 (48% / 52 %)
Mean age (year)	43.2 ± 10,6 (23–67)
Mean functional capacity (NYHA Class)	3.1 ± 0.64 (2–4)
Mean AF duration (year)	2.5 ± 1.01 (1–5)
EF (%)	52.6 ± 4,9 (35–65)
Mitral valve lesion	MD 12 (48%) MF 9 (36%) Mixt 4 (16%)
LVEDD (cm)	4.13 ±0.44 (3,8–5,7)
LVESD (cm)	3.02 ± 0.37 (2,1–4,1)
Left atrium diameter (cm)	3.98 ± 0.87 (3,9–6,5)
Pulmonary artery pressure	48.7 ± 7.7 (35–90)

NYHA: New York Heart Association, EF: Ejection fraction,
MD: Mitral stenosis, MF: Mitral failure, LVEDD: Left
ventricle end-diastolic diameter, LVESD: Left
ventricle end-sistolic diameter

Table2: Operative data of study population.

Applied procedure	MVR 25 (100%)
Additional procedure	AVR 2 (8%) Left atrial thrombectomy 2 (8%) Tricuspid val ve ring annuloplasty 3 (12%)
ACC (min)	73.2 ± 19.8 (42–158)
TBPT (min)	123.7± 24,6 (83–216)
CPB output rhythm	NSR 13 (52%) SVT 3 (9%) AF 9 (36%)
Drainage quantity (ml)	457 ± 187
Length of stay in intensive care (day)	3.2 ±1.4 (1–7)
Length of stay in hospital (gün)	13.3±2.6 (9–25)

MVR: Mitral valve replacament, AVR: Aortic valve replacement, ACC: Aortic cross clamp,
TBPT: Total by-pss time, CPB: Cardio pulmonary by-pass

Table 3: Postoperative 6.Month Echocardiography Contol

EF (%)	54.1±6,2 (35–65)
LVEDD (cm)	3.88± 0.5 (3–5.3)
LVESD (cm)	2.35 ±0.5 (2.0–4.4)
Left atrium diameter (cm)	3.67 ±0.7 (3.1–6.8)
Pulmonary artery pressure (mmHg)	43.3 ±8.7 (30–75)

EF: Ejection fraction, LVEDD: Left ventricle end
diastolic diameter, LVESD: Left ventricle end systolis diameter

Discussion

RFA performing in the surgical treatment of AF has recently gained quite popularity with ease of application, efficiency and reliability. Adjustability of the energy quantity applied on the tissue and creating of the linear lesions in tissue in depth is the superiority of the radiofrequency energy on the other methods. Isolation of the abnormal discharge foci by this way leads to provide again the spectral atrial conduction beginning from the physiological sinoatrial node toward atrioventricular node. However, the most important point here is that the regular rhythm is able to provide the effective atrial contraction. There are several publications demonstrating RFA is much more successful in providing

atrial contractions compared to Cox-maze procedure changing the atrial geometry [13]. In our study, in the follow-up at the end of 9th month, atrial contraction was echocardiographically identified in 78% of our patients who had returned to sinus rhythm. When compared with the cut and suture technique of Maze method, RFA had an obviously less risk for bleeding, a shorter surgery time and more success rate to make the return to sinus rhythm [14]. Rate for returning to the sinus rhythm in patients who had undergone mitral valve surgery and RFA procedure has been reported as 68 to 92% [15]. In the study conducted in our clinic, rate of returning to sinus rhythm was found as 64% and the reason of that rate to be lower compared to literature may be the increased left atrium diameters due to late admission of the patients. Results of our study have supported the view obtained from the important studies up today that low atrium diameter increases the success in RF ablation. In the study, we conducted with 25 patients, while the rate of returning to sinus rhythm was 64% in the follow-up of 9 months, this rate was found as 76% in the cases who had a left atrium diameter less than 5.5 cm. When considering that left atrium diameter increases with the duration and degree of the disease, this result might suggest an expected result [16]. We preferred serum irrigated RFA in this study. We think the transmuralty of the lesion created is one of the most important factors for success of ablation. Chance of the operation is quite low if the lesion created with RFA does not hold all layers of the wall. Some clinical studies have reported that even isolation and amputation of the left atrium appendix will lead the foci causing AF to be limited and re-entry foci to be broken [17]. Left atrial appendix was routinely ligatured in our RFA applied patients. There are numerous studies suggesting that the ligation of left atrial appendix decreases the risk for increased thromboembolism related to atrioventricular asynchronous contractions [18]. Specially, in cases of mitral insufficiency, the risk of left atrial thrombus may increase following mitral valve replacement [19]. Therefore, we think that RFA is even more important in AF cases accompanied by mitral insufficiency. One of the most important goals to make the patients who had preoperative AF return to sinus rhythm is to provide atrial contraction and Atrio-Ventricular electromechanical synchronization and thus to reduce the risk for cardiac thromboembolism. Since cut and suture procedures changing the atrial geometry as like in Maze operations was not performed, AF ablation performed with radiofrequency was seen to cause fewer thromboembolic events [20]. In our study, cerebrovascular event has developed in one patient, and the patient is currently followed-up with right hemiparesis. This event has been considered to result from the irregular use of the anticoagulants. Some studies suggest the use of diuretics in the postoperative early period in the RFA applied patients [21] and protection of the atrial appendix [22]. In echocardiographic controls of the first postoperative year, a significant difference was found in the ejection fraction compared to the preoperative period and thus the method applied was seen to positively affect the ejection fraction of the patients in the medium term. In our serie, a significant decrease was detected in the diameters of the left ventricle end-diastolic and end-systolic, left atrium diameter and pulmonary artery pressure values compared to the preoperative period ($p < 0.001$), and we think this situation is mainly an indicator for the positive effects of returning to the normal sinus rhythm on left ventricle functions by providing the mitral valve function. Even if the sinus rhythm is provided by either macroscopic and microscopic structural changes in enlargement of the left atrium that is notably particularly in the pathophysiology of the mitral valve diseases, atrial contraction function may not be provided [23]. In one study maintenance of sinus rhythm provided a positive effect on pulmonary circulation in short and mid term, improved the left ventricle functions and positively affected the functional capacity as a result. A significant reduction is seen in pulmonary arterial pressure without a significant change in mitral valve gradient in the long term by providing the sinus rhythm [24]. Our study is in concordance with the current literature. Although success rate of the treatment has been reported to be low in patients over 60 years old depending on sinoatrial node fibrosis, increased fat tissue, atrial dilatation and regional accumulation of amyloid [25], in our study age was not statistically significant for the success of

treatment. AF has been demonstrated to result from the left atrium and particularly from pulmonary vein mouths. Therefore, limitation of the RFA procedure with left atrium and particularly ablation around the pulmonary veins has gained importance. While bilateral ablation has superiority in the presence of the atrial flutter, in the cases except this, there is no significant difference between left atrial and bilateral application in returning to sinus rhythm [26]. Although we had performed left atrial ablation on all patients in our study, we also think bilateral ablation is proper for the cases, in particular those had atrial flutter. Radiofrequency energy has found widespread use in surgical treatment of AF, because both the procedure time is short and complication rates are low. This method with proven efficiency can be used both as bipolar and often as unipolar in the patients who had undergone open heart surgery for the valve operation [27]. Some researchers have reported that the rate of returning to sinus rhythm is higher in the patients with RF ablation performed for repairing the mitral valves than in the patients with RF ablation performed for mitral valve replacement [28]. Since all patients in our study had rheumatic mitral valve disease, and their heart valves were highly calcific, repair was disapproved and mitral valve replacement was performed in all of them. When compared with the patient profile of the other studies conducted with AF, since all our patients had mitral valve disease with rheumatic etiology, RFA success was decreased a little compared to the literature. Maintenance of the sinus rhythm in a patient provides atrial contractions and these contractions can prevent congestive heart failure in the cases at the limits. AF that develops in the postoperative early period is the result of recovery processes of the atrial lesions, inflammatory processes related to the operation and macro-reentries which give well response to the antiarrhythmic treatment [29]. Therefore, in the postoperative period we administered to all of our patients amiodarone for 6 months by 200 mg/day and after one week, 6 months again by 200-400 mg/day. In one study plasma BNP level and decreasing quantity in BNP level following a successful cardioversion have reported to predict AF recurrence in patients with persistent AF [29]. Increased risk for AF was reported in women using zoledronic acid and alendronate [30]. For this reason, we inform our female patients in the postmenopausal period not to use these medicines. Treatment of atrial fibrillation by using minimally invasive methods is one of the most important developments recently. Akpınar et al. [28] published combined ablation and mitral valve procedures by using port access technique. In this technique, cardiopulmonary bypass (CPB) is provided through the femoral artery and femoral vein, and the heart is reached by right thoracotomy. Akpınar et al. [28] observed that the patients operated with this method returned to the sinus rhythm by 80% at the end of the first year. We also think to take advantage of this technique in the future. In AF, in the dilated left atrium, erythrocytes take a roll formation as a result of the decreased velocity of blood movement and appearance of the image in the form of cigarette smoke that shows the tendency to coagulation on the echocardiography is called SEC. Left atrial SEC is seen in 84% of the patients who had MS and embolism history and in 48% of the patients who had no embolism history. SEC with mitral stenosis reflects hypercoagulation [31]. SEC was observed in our 3 patients on echocardiographic controls in the postoperative period. All these patients were operated due to mitral stenosis. SEC detected in left atrial appendix, was not observed on echocardiography taken at the end of 3rd month. Sönmez et al. [32] have reported atrio esophageal fistula in one case whom RFA was performed. They have stated that bipolar and epicardial radiofrequency ablation is the more appropriate method to avoid this very rarely encountered complication. At all patients in our study, mitral valve replacement was performed, and unipolar endocardial radiofrequency ablation pen was used from the left atriotomy incision. However, any complication was not encountered. Careful technique and continuously retrograde cardioplegia may play a role in this. Bipolar epicardial radiofrequency can be preferred in the operations that don't require left atriotomy (like coronary bypass).

In conclusion; currently, the most frequently applied method for returning AF that is seen more common with mitral valve disease to sinus rhythm is RFA. It seems to be the most

superior and promising technique among other methods. Its most important advantage compared to cox-maze method is the ease of application and shortness of duration. Consequently, we think that, RFA which is also performed in our clinic has ease of application, reliability and satisfactory results in rheumatic mitral diseases. It improves the prognosis of the disease and treatment of the atrial fibrillation that negatively affects the clinical presentation. Accompanying of RFA to mitral valve surgical procedure in this patient group has a positive effect on the risk for hemodynamics and thromboembolism. Perhaps a prospective randomized study on this subject would be more appropriate.

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