Review Article

Journal of Kathmandu Medical College, Vol. 8, No. 2, Issue 28, Apr.-Jun., 2019

Radiofrequency ablation as a concomitant procedure for the treatment of atrial fibrillation during cardiac surgery

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Abstract

Atrial fibrillation is the most common type of arrhythmia with increasing burden for stroke and thromboembolic events. Medical treatment of atrial fibrillation hasn't shown promising results, so alternative method of treatment is emerging out. Cox-Maze procedure has been used for decades for the treatment of atrial fibrillation. Surgical treatment of atrial fibrillation with traditional Cox-Maze procedure is a complex and technically challenging procedure limiting its use in clinical practice. Recently, radiofrequency ablation is being used as a modification of Cox-Maze procedure. However, its effect in the treatment of atrial fibrillation in not reported uniformly and in large number of patients. Therefore, our aim of study was to assess the impact of concomitant radiofrequency ablation in the treatment of atrial fibrillation during cardiac surgery. We performed literature review on PubMed Central to evaluate effect of concomitant radiofrequency ablation for atrial fibrillation treatment. About 303 papers were found using the reported search, of which 15 represented suitable to fulfill our query. The authors, date, patient group, study type, relevant outcomes and results of these papers are tabulated. We conclude that radiofrequency ablation surgery of left atrium at the time of other cardiac procedures is a comparatively straight forward procedure with satisfactory freedom from atrial fibrillation, acceptable morbidity, mortality, and minor procedure related complications. Careful patients selection by sticking to the "Rule of 5", i.e. left atrial diameter less than 55 mm and atrial fibrillation duration no more than five years, is recommended to optimize the result of atrial fibrillation surgery.

Key words: Atrial fibrillation; Radiofrequency ablation; Surgery.

DOI: https://doi.org/10.3126/jkmc.v8i2.28174

INTRODUCTION

Atrial fibrillation (AF) is the most common type of arrhythmia presenting in the clinical practice. It is estimated that 2.2 million people suffer from AF in the United States alone and that this number will increase steadily over the next few decades, exceeding 10 million by 2050[1]. About 40-60% of the patients undergoing mitral valve surgery will have one or either form of AF[2,3]. Symptoms of AF include palpitations, chest pain, dyspnoea and fatigue. Stroke is a frequent life threatening complication of AF accounting for 5% in non-coagulated patients every year. The risk of stroke increases substantially with age, from 1.5% in individual ages 50-59 years to 23.5% for those aged 80-89 years[4, 5]. Medical treatment and electric conversion are the first line treatment options. However, medical therapy has its limitation with failure rates as high as 60%. Furthermore, during cardiac surgery it is frequently encountered as a concomitant disease in patients undergoing surgery for other reason[2]. In patients with permanent and persistent AF and large left atrium, mitral valve surgery alone is associated with a low rate of conversion to sinus rhythm during early and long-term follow-up[6]. Considering all these data and the high burden of AF in the general population led to search for a better treatment option by developing interventional and surgical method of treatment.

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Cox-Maze III procedure proposed by Prof James Cox became a gold standard for the surgical treatment of AF with an efficacy of 97% freedom from symptomatic AF[7]. However, use of Cox-Maze procedure was restricted due to its complexity, invasiveness and postoperative complications[8]. Cox-Maze IV, a modified version of original Cox-Maze procedure using radiofrequency and cryo energy was proposed to simplify and shorten the surgical procedure[9]. The decision to perform concomitant radiofrequency ablation for AF during open cardiac surgery depends mainly on a risk/benefit assessment of the procedure and the ambition of the individual patient[10]. Furthermore, effect of RF ablation during cardiac surgery is not reported uniformly as well as in a large series of patient populations.

In this scenario, aim of our study is to review the role of concomitant RF ablation during cardiac surgery for the treatment of AF. Additionally, to establish clearly results of such treatment in terms of freedom from arrhythmia and mortality during long term follow up.

METHODS

We performed a literature review to search for evidence of concomitant radiofrequency ablation (RFA) therapy in patients undergoing cardiac surgeries for other reasons. The search was performed in the PubMed interface from 1950 till May 2018 for English language literatures using following terms: atrial fibrillation, concomitant RF surgical ablation.

RESULTS

303 papers were found using the reported search. From these 15 papers were identified based on their relevance in regards to higher number of patients enrolled, longer follow-up time and study design (prospective randomized control trials were preferred to retrospective series). All the articles were evaluated first by studying the abstracts. Most relevant studies were selected and distributed among the authors to evaluate their strength and quality of publication. After discussion among the authors, ultimately fifteen studies fulfilling our selection criteria were selected to be included in the review. We have excluded non randomized studies, studies with small number of patients, case reports, short communication and paper published in other than English language journals. If articles from same author were repeated, most recent publication from that author was selected as most of the repeated articles are continuation of the previous study with more number of patients. Selected papers are presented in table 1.

DISCUSSION

In 2011, Geidel and coauthors[10] studied 325 patients undergoing isolated mitral valve surgery (n= 201), Coronary Artery Bypass Grafting (CABG) and/or Aortic Valve Replacement (AVR) (n=124) and concomitant radiofrequency ablation. All patients had persistent AF. The lesion set include bipolar RF pulmonary vein isolation using AtriCure device (ArticureInc, Cincinnati, OH) plus two connecting lesions using monopolar Cobra device (Boston Scientific Corp, San Jose, Calif). Three year survival was 94.4% with freedom from AF 72.1% at discharge and 75.6% at 3 year follow-up. Moreover, in the subgroup of patients undergoing only CABG and AVR surgery conversion to stable sinus rhythm was better, 78.3% and 81.8% respectively, probably due to small Left atrium (LA) size and shorter duration of AF. In fact, they found using univariate logistic regression analysis, preoperative LA size (less than 55 mm) and duration of atrial fibrillation (less than 5 years) as independent factors for successful ablation surgery. Cut off value of 55 mm LA size and AF duration of less than 5 years were correlated to stable SR at follow-up. Patients in stable sinus rhythm showed a significant improvement in post operative NYHA functional class (from 3.1±0.4 to 1.7±0.4; p< .0001).

Halkos et al.[11] retrospectively analyzed 54 patients undergoing left atrial (42 patients) or biatrial (12 patients) monopolar RF ablation using Cardioblate probe (Medtronic, Minneapolis, MN). Seventy percent of patients were free from AF at discharge, while 77.3% were free from AF at a median follow up about 9 months. In spite of the low statistical power related to the small population, the authors suggested that isolated mitral valve surgery with RF ablation had better freedom from AF rate than other procedures plus RF ablation (88.0% vs 63.2%; p=0.07).

In a prospective cohort study, Beukema & colleagues[12] enrolled 258 patients, with longstanding persistent AF having at least 12 months duration, for LA radiofrequency ablation during surgery for structural heart disease. In their cohort of patients, 3.9% patients died during hospital stay, whereas 28.2% mortality was observed during the follow-up of 43 months. At a follow-up of 9 years they observed conversion to stable sinus rhythm in 57% patients. In support of other studies, authors have also found preoperative LA size, duration of AF and F wave amplitude as a prognostic factor for recurrence of AF or sustained AF. Ironically, they have concluded that conversion to sinus rhythm is not related to reduction in mortality and stroke rate.

Table 1: Findings of elected Papers

Author	Type of study	Number of patients	AF pattern	AF duration (mo)	Left atrial diameter (mm)	Isolated PVI	PVI + left atrial lines	Biatrial	Associated procedure	Hospital Mortality	F-U length (M)
Geidel et al, 2011	Prospective cohort study (level 2b)	325	Persistent AF 100%	69,6±72,0	53±7	-	325 (100%)	-	MV surgery (isolated or combined) 201 (61,8%) Other 124 (38,2%)	7 (2,2%)	36
Halkos et al, 2005	Retrospective observational study (level 2b)	54	Continous AF 59,3% Non continous 40,7%	46,3±44,0	51±9,4	-	42 (78%)	12 (22%)	MV surgery (isolated or combined) 47(87%) Other 7 (13%)	7 (12,9%)	46,3±44
Beukema et al, 2008	Prospective cohort study (level 2b)	258	Continous AF 100%	66,6±69,8	52,7±9,8	-	-	258 (100%)	MV surgery (isolated or combined) 222 (86%) Other 36 (14%)	10 (3,9%)	60
Akpinar et al, 2003	Prospective randomized study (Level 1b)	67 GroupA (RF) 33 GroupB (no RF) 34	Persistent AF 100%	GroupA 19,9±10,6 GroupB 22,0±13,9	GroupA 62,5±10,5 GroupB 66,7±9,0	-	GroupA 24(72,7%) GroupB -	GroupA 9(27,3%) GroupB -	MV surgery (isolated or combined) 67(100%)	2 (2,9%) GroupA 1(3%) GroupB 1(2,9%)	12
Bevilacqua et al, 2009	Retrospective study (Level 2b)	12	Paroxysmal 3(2559 Persistent 3(25%) LS Persistent 6(50%)	33,5±33,2	50,1±7,4	12(100%)	-	-	MV surgery (isolated or combined) 12(100%)	-	8,8±1
Melo et al, 2008	Retrospective multicenterstudy (level 2b)	1723	Paroxysmal 11,8% Persistent 11,6% Permanent 76,6%	79,2±72	57±22	N/A	N/A	604(35,5%)	MV surgery (isolated or combined) 1723(100%)	45(2,6%)	12
Jeanmart H et al, 2006	Retrospective study (Level 2b)	103	Continous 58,5% Non continous 41,2%	30,3±28,9	52,4±7,8	-	103 (100%)	-	MV surgery (isolated or combined) 103(100%)	1(1%)	17,4±14,1
Abreu Filho et al, 2005	Randomized multicenter study (Level 1b)	70 Group A(RF) 42(60%) Group B (no RF) 28(40%)	Permanent 70 (100%)	GroupA 66,1±57,4 GroupB 43,8±28,5	GroupA 61,1±11,2 GroupB 58,8±4,7	-	-	GroupA 42 (100%) GroupB -	MV surgery (isolated or combined) 70(100%)	1(1,4%) GroupeA 1(2,4%) GroupB -	12
Veasey et al, 2011	Retrospective Study (Level 2b)	100	Paroxysmal 47 (47%) Persistent 53(53%)	49,2±57,6	48±11	-	100(100%)	-	MV surgery (isolated or combined) 27(27%) Other 73(73%)	N/A	6

Chevalier et al, 2009	Randomized multicenter study (Level 1b)	43 Group A (RF) 21 (48,8%) Group B (noRF) 22 (51,2%)	Persistent 43(100%)	Group A 161 GroupB 89,2	Group A 54,6±10,9 GroupB 52,6±11	-	Group A 21(100%) GroupB -	-	MV surgery (isolated or combined) 43(100%)	N/A	12
Maltais et al, 2010	Retrospective study (Level 2b)	293	Paroxysmal 151(51,5%) Permanent 129(44%) Undetermined 13(4,5%)	108±71	53±10	-	293(100%)	-	MV surgery (isolated or combined) 293(100%)	3(1,2%)	39,6±14,4
Doukas et al, 2005	Randomized study (Level 1b)	97 GroupA(RF) 49(50,5%) GroupB(noRF) 48(49,55)	Continous 97(100%)	Group A 57±55,1 Group B 46,7±64,3	Group A 58±7 Group B 60±11	-	Group A 49 (100%) GroupB -	-	MV surgery (isolated or combined) 97 (100%)	GroupA 3(6,1%) GroupB 4(8,3%)	12
Benussi et al, 2005	Retrospective study (Level 2b)	90	Continous 74(82%) Non continous 16(18%)	15(9-49)	54(49-59)	-	90(100%)	-	MV surgery (isolated or combined) 67(84%) Other 23(16%)	1(1,1%)	12
Khargi et al, 2005	Prospective Cohort study (Level 2b)	128 pts Group 1 – 65 Mitral valve surgery Group 2 – 63 Non-Mitral surgery	Permanent AF	Group 1 – 60.1±49 months Group 2 – 68.0±74.7 months	Group 1 – 52.4±9.7 mm Group 2 – 45.9±7.4 mm	-	128 (100%)	-	Group 1 – Only Mitral surgery Group 2 – CABG or Aortic surgery	30 days mortality Group 1 – 4.6% Group 2 – 3.2%	12
Budera et al. 2012	Multicenter Randomized trial (Level 1b)	224 pts Group A (Surgical Ablation – 117) Group B (No Ablation – 107)	Group A Parox – 22.2% Persis – 25.6% Longstand – 52.1% Group B Parox – 30.8% Persis – 23.4% Longstand – 45.8%	Group A – 15 months Group B – 16 months	Group A – 48.7±7.3 mm Group B – 47.7±7.1 mm	-	117 (100% of group A)	-	Group A – With Mitral valve surgery – 58 pts Without Mitral valve Surgery – 59 pts Group B – With Mitral valve surgery – 45 Without Mitral valve surgery - 60	Group A – 5.1% Group B – 4.7%	12
Tiwari et al, 2016	Retrospective study (Level 2b)	75 patients underwent RF ablation by minithoracotomy approach	Persistent AF 100%	25.1±22.7	63.1±9.8	75 (100%)	22 (29.3%)	1 (1.3%)	Mitral valve 65 (86.7%) Aortic 10 (13.3%)	1 (1.3%)	21.6±10.1

In a study by Khargi et al.[13] evaluated role of anti-arrythmic procedure for permanent AF in a group of patients undergoing mitral valve surgery and another group of patients undergoing non-mitral valve surgery, i.e. CABG and/or Aortic valve surgery using unipolar RFA. They have achieved a cumulative postoperative SR in 71% and 79% of patients in Group 1 and Group 2 respectively. They conclude that RFA during CABG and Aortic valve surgery is as effective as in Mitral valve surgery.

Furthermore, in prospective randomized study, Akpinar et al.[14] studied chronic AF patients undergoing minithoracotomy port access mitral valve surgery. The study included 33 patients (Group A) undergoing mitral valve surgery combined with irrigated RF ablation using monopolar ablation device, while 34 patients undergoing only mitral valve surgery as control group (Group B). At the discharge 81% of the group A patients were free of AF, whereas only 15.2% of the patients in group B. Most importantly, at a follow-up of 1 year most of the patients in group A (93.6%) were free from AF vs. 9.4% in group B. Anti-arrhythmic drugs were discontinued earlier in group A patients (3 months vs. 1 year).

In our own experience of concomitant RF ablation for AF during minimally invasive port access mitral valve surgery using an epicardial vacuum assisted monopolar Cobra Adhere XL probe (Estech, San Ramon, CA), we observed 91.7% freedom from AF at a follow up of 9 months. No major cardiac and cerebro-vascular events occurred during follow-up[15]. We have also observed better cosmetic result with less post operative pain in the patients treated with this approach.

Melo and colleagues[16] reported a multicenter study enrolling 1723 patients, with different type of AF and mean AF duration of 6.6±6 years, from 10 European and American hospitals in a period of three years. Three percent of the patients underwent cut-and-sew surgery, while 97% underwent ablation with different types of energy. 65% of the patients were ablated with unipolar and bipolar RF energy, 27% microwave, 4% Argon cryoablation and 4 % other type of energy. Fifty nine percentages of the patients were in sinus rhythm at the discharge, while 66% were in stable sinus rhythm (sSR) after one year of follow-up. Before discharge 3% of patients required pacemaker implantation. On log rank analysis they found that stable SR was associated with higher early and late survival (p=.01) and lower thromboembolic events (p=.010). Left atrial dimension (>55mm) and concomitant coronary revascularization was found to be independent negative predictor of sSR. Use of cut-and-sew technique and isolated left atrial procedure for AF treatment were reported to be independent predictors for in-hospital mortality.

Jeanmart et al.[17] studied hundred and three patients with intermittent (41.2%) and continuous (58.8%) AF, undergoing minimally invasive mitral valve surgery and concomitant pulmonary veins isolation with monopolar radiofrequency using Cardioblate® irrigated RF ablation probe (Medtronic, Inc, USA). At a follow-up of 18 months 69.7% of patients were in sinus rhythm, while 28.3% were in atrial fibrillation, 2% patients were pacemaker dependent, and 81.2% of treated were still taking anti-arrhythmic drugs (AAD) in comparison to 76.5% on AAD at discharge.

Seventy patients with permanent AF lasting for more than 1 year and rheumatic mitral valve disease were randomized by Abreu Filho and colleagues[18] in two groups. The RF ablation group (n=42 patients) underwent RF ablation of right and left atrium using monopolar probe plus mitral valve surgery, while the control group underwent only mitral valve surgery. There was no in-hospital mortality in the control group, whereas one death (2.3%) was in RFA group, which was not related to ablation procedure. A significant difference in conversion to SR among the two groups at the time of discharge (75.6% in RFA group vs. 17.9% in control group) as well as at the end of 12 months follow-up (79.4% vs. 26.9%) was evident.

For the first time, Veasey et al[19], evaluated heart rhythm for 7 days by Holter monitoring in one hundred patients with paroxysmal and persistent AF undergoing RF ablation of left atrium at the time of concomitant cardiac surgery. Pulmonary veins were isolated as pairs with a connecting line to the left atrial appendage using Articure bipolar RF probe (ArticureInc, Cincinnati, OH). In their cohort of patients, they observed slight decrease in freedom from AF at 12 months follow-up, from 86% at the discharge to 62% at the follow-up. However, they have found a reduction of AF burden from 56.2% to 27.5% in patients with RF ablation. In addition, they also confirmed the duration of AF, persistent AF and mitral valve surgery as significant predictors of AF recurrence.

A multicenter, double-blinded randomized study conducted by Chevalier et al[20], enrolled 43 patients with persistent AF for more than 6 months either to undergo RF ablation plus mitral valve surgery or mitral valve surgery alone. They isolated pulmonary veins and created additional lesions toward the mitral annulus. There was a significant difference in conversion to sinus

rhythm at discharge (72.73% in RFA group vs. 4.76% in control group). This trend of significance remained constant at the end of follow-up. Although pacemaker implantation were frequent in RFA group (14.3% vs. 9.1%), need of electric cardioversion at 12 months follow-up was less in RFA group (9.52% vs. 50%).

Another important and large multicentre RCT, PRAGUE-12,by Budera et al[21]has divided overall 224 patients in two groups. Group A undergoing cardiac surgery with RFA and Group B without ablation. In group A patients they have created a complete lesion of ablation. Authors have analyzed ECGs in regular follow up of 1, 3, 6 and 2 months. At a follow up of 1 year, 60.3% of group A and 35.5% of group B patients were in SR. Additionally, they have observed a remarkable, but non-significant, difference in stroke rate in favor of ablated patients at 1 year follow up.

Maltais and co-authors[22] retrospectively studied results of 293 patients, who underwent cardiac surgery with concomitant RF ablation of left atrium using monopolar probe. They observed a mortality of 1.2% not related to RF ablation procedure. Furthermore, authors also noticed a trend in increasing conversion to sinus rhythm at the end of 40 months follow-up (52% vs. 71% at follow-up).

Doukas and colleagues[23] had studied 97 patients with continuous AF for at least 6 months, who were undergoing surgery for mitral valve plus left atrium RF ablation and mitral valve surgery only. In their randomized study, in hospital mortality was not different in both groups. Conversion to sinus rhythm at discharge (53.3% vs. 4.5%) and at a 12 months follow-up (44.5% vs. 4.5%, P<.001) was significantly higher in RF ablation group in compared to mitral valve surgery only. Furthermore, authors have stressed on the importance of conversion to SR, which had significantly greater improvement in Shuttle-walk test.

In a cohort of 90 patients with continuous and intermittent AF, Benussi and coauthors[24] has shown 89% freedom from AF at one year follow-up using a bipolar complete left atrial RF ablation. Moreover, they emphasize that use of bipolar RF grants acute transmurality of the lesionswith no major complications related to the AF procedure. Furthermore, they advise addition of an extra lesion to the mitral annulus to prevent left atrial flutter.

Overall freedom from AF in the reported studies using RF ablation during concomitant cardiac surgery is satisfactory at the discharge, although highly variable. A trend towards higher freedom from AF at the end of follow up period was observed in various studies. It could be due to a transient phase of pro-arrhythmic state in the early postoperative period. Importantly, symptomatic relief in the patients treated with RF ablation was evident, including improved shuttle-walk test. In addition, some authors reported decrease in use of anti-arrhythmic drugs after the ablation, which could contribute to a better outcome in terms of patient's survival. Besides, in all randomized study it has been well demonstrated a net benefit of RF ablation in terms of SR restoration in patients with concomitant AF surgery, which is associated with clinically symptom's improvement, decrease in thromboembolic events and better functional outcome. No mortality was directly related to the AF ablation procedure. However, RF ablation treatment has not demonstrated any superiority in term of mortality reduction in AF patients. But, conversion to stable SR is associated with higher early and late survival.

Minimally invasive approaches for RF ablation have been used in few studies. In our own study, we have performed ablation in 75 for AF in patients undergoing different valvular surgeries through right sided minithoracotomy. All of the patients were ablated with radiofrequency energy. In the majority of cases, i.e. in 82.7% of cases, monopolar energy was implemented. After a mean follow-up of 21.6 ± 10.1 months (range: 5 - 45 months), 98.6% of patients completed the follow up, 46 (63%) were in a stable sinus rhythm, and 27 (37%) remained in AF. However, out of 17 patients with paroxysmal AF, 14 (82.4%) converted into SR. While 70% of patients with persistence AF converted into SR. We observed minithoracotomy approach to be as safe as conventional sternotomy, with better cosmetics and less pain[25]. Further studies with larger population might need to draw a conclusion about the use of minimal invasive approach.

LIMITATIONS OF REPORTED STUDIES

Before making any conclusion, we must underline obvious limitations of studies being performed. First of all, in several studies low statistical power due to the small sample size was evident. With the relentless evolution and advancement of new technology for ablation, different type of devices and lesion set were used throughout these studies. Furthermore, selection criteria, definition of AF, end points (freedom from AF, freedom from symptomatic or asymptomatic AF), AF burden, follow-up criteria (duration, and method of ECG registration), use of anti-arrhythmic drugs and its

duration were not standardized. Such non-standardized evaluation of the results generated variability and difficulty in the elaboration and presentation of the outcomes. In future, a better compliance is needed to standardize definition, recommendations and evaluation criteria as proposed by HRS/EHRA/ECAS expert consensus conference on catheter and surgical ablation of AF[26].

CONCLUSION

On the basis of our review, we conclude that overall freedom from AF in patients undergoing concomitant RF ablation during other cardiac procedures is satisfactory. Restoration of sinus rhythm after RF ablation is associated with symptomatic relief and improved functional capacity of treated patients as well as decreased use of anti-arrhythmic drugs in post operative period. Importantly, concomitant RF ablation is not associated with higher mortality.

Finally, "Rule of 5", i.e. a cut off value for left atrial diameter less than 55 mm and AF duration less than 5 years, could be implemented in clinical practice to achieve better result in terms of freedom from AF and stable sinus rhythm at the long term follow-up.

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