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Original Article

Left atrial diameter in estimating success rates of radio-frequency ablation treating atrial fibrillation

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Abstract

Background: In treating atrial fibrillation with radio-frequency ablation, few studies seek to define a cut-off value for left atrial diameter size beyond which the intervention risks outweigh chance of sinus recovery. This study aims to identify a cut-off value for pre-operative left atrial diameter to assess the efficacy of surgical radio-frequency ablation for treatment of chronic atrial fibrillation in patients undergoing mitral valve surgery.

Methods: A prospective 6-month follow-up cohort study was conducted, in which 40 patients were recruited during the period from May 2016 till April 2018 at the Academy of Cardiothoracic Surgery, Ain Shams University. All patients had either isolated mitral valve replacements or mitral valve replacements combined with other valve surgeries. A mono-polar saline-irrigated cooled tip Radio-frequency ablation (SICTRA) was performed using the Medtronic Radiofrequency Generator Model 68000 as an energy source. A voltage of 25-30 watts was adjusted according to effectiveness of ablation. Oscillatory and to-and-fro motions were employed on the atrial endocardium using the Cardioblate pen until proper blanching or whitening was achieved. Receiver operator characteristic (ROC) curves were used to calculate the area under the curve and cut-off value for left atrial diameter. The efficacy of the overall survival time was estimated using the Kaplan-Meier method.

Results: Pre-operatively left atrial diameter of 59 mm was significantly associated with decrease in the possibility of reverting to sinus rhythm after surgery (OR 0.292, p-value = 0.001). The cut-off value for left atrial diameter was 59mm (sensitivity = 93.3%, specificity = 96.1%). Kaplan-Meier survival estimates were 175.07 days (156.3 - 193.9) for patients with left atrial diameter < 59mm and 62.64 days (26.6-98.7) for patients with left atrial diameter > 59mm.

Conclusion: In patients undergoing mitral valve, we have experienced a significant higher degree of success associated with smaller left atrial diameter (less than 59.0 mm) in terms of conservation of the sinus rhythm post operatively.

KEYWORDS

Atrial fibrillation; Radio-frequency; Ablation; Left atrial diameter; Mitral valve

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia and a significant cause of morbidity such as stroke, thromboembolisms, and heart failure [1 – 4]. Extensive research was done in the field of methods and techniques treating atrial fibrillation. Nowadays, ablation devices are being utilized in surgical procedures. Maze procedure modifications involved new surgical ablation devices using various energy sources. In addition to radio-frequency and Cryo-ablation, energy sources have included microwave, laser, and high-frequency ultrasound [5 – 10].

Despite evidence highlighting preoperative left atrial diameter (LAD) as a risk factor for maze failure, relatively few studies seek to define a definitive cut-off value for LAD size beyond which the risks of the procedure (such as bleeding, infection or stroke) outweigh the chance of sinus rhythm (SR) recovery. Some studies have reported that, enlarged LAD could be a risk factor for failure of a maze procedure. Various models of AF suggest that reducing atrial mass and/or diameter may help to abolish the re-entry circuits underlying AF [10]. However, the evidence is not strong since papers available were not readily comparable owing to substantial variations in the populations and procedures involved [11].

This study aims to identify a cut-off value for the pre-operative LAD to assess the efficacy of surgical radio-frequency ablation using unipolar pen for the treatment of chronic atrial fibrillation in patients undergoing mitral valve surgery (either replacement or repair) with or without other valvular surgeries.

Patients and Methods:

The study was conducted at the Academy of cardiothoracic surgery at Ain Shams University, Wady El-Nile hospital, Air force specialized hospital and Dar El-Salam hospital. Patients were recruited during the period from May 2016 till April 2018. Demographics and baseline measurements were recorded for each patient. All patients had rheumatic mitral valve disease with or without other valvular disease and permanent atrial fibrillation. Permanent AF was defined as continuous long-standing AF that lasts for a period of more than 12 months and that does not respond to electrical or medical cardioversion. Routine preoperative investigations were preformed which consisted of standard preoperative lab work (CBC, coagulation profile, and liver and kidney function tests), 12-lead ECG strip, transthoracic echocardiography (TTE), transesophageal echocardiography (TEE) and chest X-Ray. Moreover, anterior-posterior diameter was used for measuring the left atrial diameter through echocardiography. Other inclusion criteria were: both male and female with age between 18 and 60 years who underwent cardiac surgery of the mitral valve (replacement or repair) with or without other valve surgery (aortic, tricuspid or combined lesions). Patients with chronic kidney failure (CKD) were excluded as CKD is often associated with hypertension and high atrial pressure, both of which may lead to AF [12]. Moreover, patients with chronic liver dysfunction, defined as increased circulating levels of γ glutamyl transpeptidase and liver transaminase markers, increase the risk of new-onset atrial fibrillation, thus will be excluded. Ischemic stroke patients or patients who had to redo the surgery were excluded. Finally, emergency cases were also excluded[13,14].

Surgical technique

All patients had either isolated mitral valve replacements or mitral valve replacements combined with other valve surgeries. A median sternotomy was employed in all cases after which pericardium was then opened using cautery. Aortic purse was taken using 3/0 prolene followed by atrial purse using 3/0 or 4/0 prolene. In cases involving tricuspid valve, tapes were taken around SVC and IVC for the right atrial opening Cardiopulmonary by-pass was established. The conventional approach was used to gain access to the mitral valve via left atriotomy [14, 15]. After the left atriotomy was done the 4 pulmonary veins, the left atrial appendage and the mitral valve were clearly defined then the ablation procedure started. Then the mitral valve was replaced using interrupted sutures on Teflon pledges using 2/0 Ethibond. All patients had a left atrial maze procedure using radiofrequency ablation as an energy source. The procedure was performed on the endocardial surface of the heart before the actual mitral valve surgery. As shown in

Figure 1, monopolar saline-irrigated cooled tip RF ablation (SICTRA) was performed using the Medtronic Radiofrequency Generator Model 68000 as an energy source [16]. A voltage of 25-30 watts was adjusted according to effectiveness of ablation. Oscillatory and to-and-fro motions were employed on the atrial endocardium using the Cardioblate pen until proper blanching or whitening was achieved. Prolonged or repeated application was done when necessary in order to achieve a complete transmural lesion. After the maze procedure was performed closure of the left atrial appendage was achieved using a 3-0 polypropylene purse string suture or the left atrial appendage were included in the ablation lines. After completion of surgery and as soon as the patient was weaned off cardiopulmonary bypass IV Cordarone therapy was administered in the operative theatre and in the ICU; first loading dose of 300 mg over 1 hour followed by a maintenance dose of 900 mg over 24 hours. Oral amiodarone administration was continued as soon as IV therapy ended through the oral route if patient was extubated or through a nasogastric tube until extubation. The dose was 200 mg once daily for 3 months after surgery [9, 13 – 16]. It was important to note that none of the patients had excision of the left atrial appendage (LAA).

Post-operative follow-up

A 12-lead ECG Rhythm strip was done at 1 week post-operatively and at 3 months while at 6 months a 24 h Holter was done to view the sinus conversion rate. As outlined in the Heart Rhythm Society consensus document on AF ablation, 'success' should be defined as freedom from symptomatic or 'asymptomatic' AF, atrial tachycardia, or atrial flutter lasting 30 s or longer 12 months following AF ablation [16]. A trans-thoracic echocardiography was performed at 6 months post-operatively to assess left atrial size, ejection fraction and confirm sinus rhythm. The incidence of stroke was recorded as well as any need for pacemaker implantation. 12-lead ECG was recorded on all 4 predetermined times using the SCHILLER CARDIOVIT AT-101 ECG. Echocardiography was performed by two experienced investigators using the GE VIVID 3 (General Electric) ultrasound device. Values were obtained from a mean of 3-5 beats.

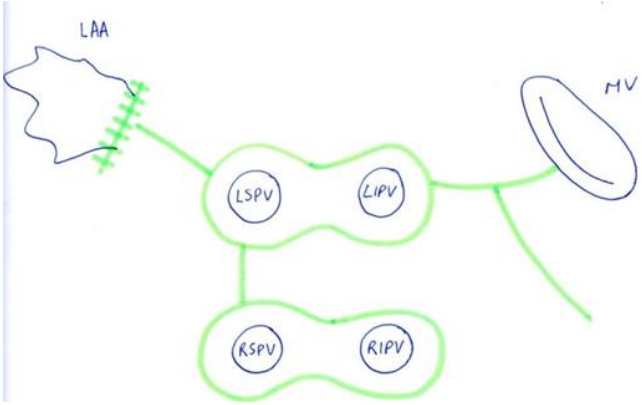

Figure 1: Diagram of the maze lines performed in the left atrium. It included pulmonary vein isolation where both left pulmonary veins and both right pulmonary veins were isolated separately. A roofing line between the 2 superior pulmonary veins was done as well two lines extending from the left pulmonary vein island, one going towards the base of the left atrial appendage and the other towards the annulus of the mitral valve at a point corresponding to the middle of the posterior mitral leaflet. Another blind-ended line was drawn perpendicular to the line running from the left pulmonary vein island towards the mitral annulus. It ran across the isthmus and towards the area of the inferior vena cava and stopping just short of the atriotomy incision.

Statistical analysis

Baseline data were expressed as means with standard deviations (SD) or numbers and percentages. Evaluation of baseline characteristics was done using independent t-tests or Mann-Whitney U test for continuous variables. Fisher's exact test or chi-square test were used to test the significance of association of qualitative variables. Univariate logistic regression models were used to assess the influence of the measured variables on the study outcome. ROC analysis was used to detect a cut-off value for the left atrial diameter associated with failure to revert to sinus rhythm. The Kaplan-Meier method will be used to present time to reversion to AF between patients with left atrial diameter < 59 mm (Group A) and those with higher diameter (Group B), the significance of the difference was tested. SPSS software, version 23 (SPSS Inc., Chicago, Illinois, USA) was used for data entry and analysis. All analyses were carried out at a 5% two-sided significance level.

Results

A total of 40 patients were selected and recruited in this prospective cohort study. With no

loss to follow-up, all patients successfully completed the 3- and 6-month follow-up period of the study. Table 1 illustrates baseline characteristics for the study cohort. The mitral valve was replaced using a metallic prosthesis in all cases except two cases were replaced by biological valve. Eight cases had Tricuspid valve (TV) repair which was done by conventional Devega annuloplasty. One case had TV repair by Medtronic ring and another case had TV replacement. The aortic valve was replaced using a metallic prosthesis in all cases. We did not experience any of the described procedure-related complications except for 1 patient who presented with a 1st degree heart block for 3 days after the procedure and then reverted back to sinus rhythm.

Table 1: Baseline Characteristics

Baseline Characteristics (n=40)		
Age (mean, SD) in years		47.55 ±7.89
Duration of Atrial Fibrillation in months (mean, SD)		45.60 ±17.25
Sex (%)	Male	12 (30.0)
	Female	28 (70.0)
Diabetes (%)	Negative	36 (90.0)
	Positive	4 (10.0)
Hypertension (%)	Negative	36 (90.0)
	Positive	4 (10.0)
Caffeine Intake (%)	Negative	6 (15.0)
	Positive	34 (85.0)
Smoking (%)	Negative	30 (75.0)
	Positive	10 (25.0)
NYHA[a] (%)	2	14 (35.0)
	3	25 (62.5)
	4	1 (2.5)

a: New York Heart Association heart failure Classification

The mean pre-operative LAD in patients who reverted back to sinus rhythm was 50.32 ± 7.22 while for those who were AF was 64.13 ± 7.11. Immediately after surgery, 28 (70%) patients returned to sinus rhythm. After 6 month, three patients developed AF, leaving a total of 25 (62.5%) patients with a stable sinus rhythm. The results show that pre-operatively LAD (OR 0.292, 95%CI 0.110 – 0.484, p-value = 0.001) and duration of the AF (OR 0.286, 95%CI 0.096 – 0.476, p-value = 0.003) was identified to be significantly associated with post-operative AF status (Table 2).

Receiver operating characteristic (ROC) curves were estimated, along with the area under the curve (AUC), for the LAD (Figure 2). LAD had an AUC of 0.925 (95% CI 0.83 - 0.97, p-value<0.0001). At this level, the cut-off value for LAD was identified to be 59mm with a corresponding Youden index of 0.91, sensitivity was 93.3% (95% CI 0.91 - 0.98); specificity was 96.1% (95%CI 0.89 - 0.98).

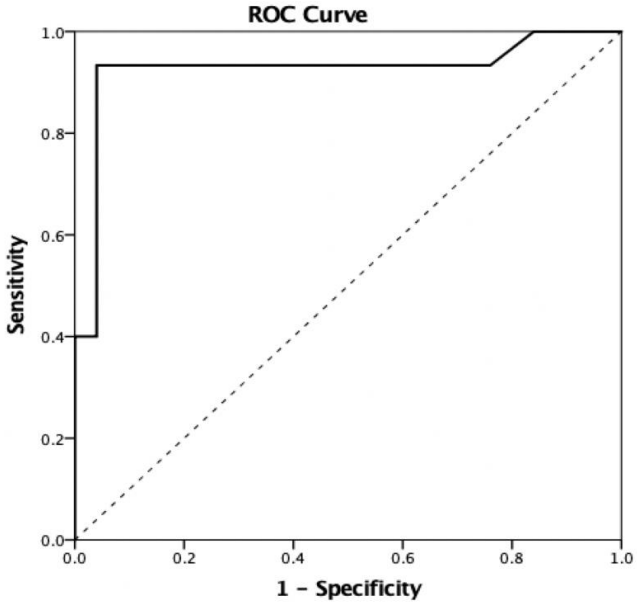

Figure 2: Receiver Operating Characteristics (ROC) curve for the left atrial diameter cut-off point.

For the survival analysis, we experienced right censoring in which participants did not have the event of interest during the study period (180 days) and thus their last observed follow-up time was less than their time to event. Kaplan-Meier survival curves were estimated after using the previously selected LAD cut-off value (59.0mm) to distribute the study cohort into two groups. Group A were patients having a LAD < 59.0mm, while group B were patients with a LAD ≥ 59.0mm. Figure 3 shows the two survival curves, in which, visually, the survival distribution appears to be

Table 2: Univariate logistic regression with post-operative AF status as the dependent variable

Parameter	OR [a]	OR 95% Confidence Interval		P-value
		Lower	Upper	
LAD	0.292	0.110	0.484	0.001*
Duration of Atrial Fibrillation	0.286	0.096	0.476	0.003*
Gender	0.811	-0.695	2.317	0.291
Diabetes	-0.571	-2.645	1.504	0.591
Hypertension	-0.571	-2.645	1.504	0.592
Smoking	-0.141	-1.608	1.326	0.855
Age	-0.021	-0.102	0.06	0.613
Ejection Fraction	0.079	-0.052	0.209	0.237
Other surgeries	0.118	-1.231	1.467	0.864
Cross Lamp Time	0.06	-0.037	0.158	0.224
Bypass Time	0.091	-0.031	0.212	0.143
NYHA *(reference group: Class 4)*				
Class 2	1.293	-8.24	8.451	0.931
Class 3	0.541	-10.24	4.428	0.721
Surgeries *(reference group: Aortic valve replacement)*				
Aortic valve replacement	0.377	-1.189	1.944	0.637
Aortic valve replacement + Tricuspid valve replacement	-2.446	-5.83	8.261	0.999
Tricuspid valve repair	2.178	-5.93	9.402	0.999

a: Odds ratio for logistic regression models used.
All hypothesis testing was carried out at the 5% (2-sided) significance level. All p-values were presented with at least 3 decimal places. Significant p-values were noted with an asterisk (*)

much higher in the Group A (LAD < 59.0mm) compared to the Group B (LAD ≥ 59.0mm). There was a significant difference in survival times between the Group A and Group B (log rank test P-value = 0.0001). The Kaplan-Meier survival probability estimates at 180 Days were about 175.07 (95% CI 156.26 – 193.89) for Group A and 62.64 (95% CI 26.59 – 98.69) for Group B (Table 3).

Discussion

Patients with mitral valve disease are usually diagnosed with concomitant atrial fibrillation (AF) which results in a variety of morbidities including hemodynamic compromise, syncope, dizziness, fatigue, palpitations, chest pain and an increased probability of a thromboembolic event [17 – 20]. Surgery for treatment of atrial fibrillation culminated in the development of Cox-Maze III, the Gold standard, which is the procedure with the highest success rates [20, 21]. However, it has not been widely adopted due to its complexity, its need for cardiopulmonary by-pass and its significant prolongation of by-pass time. Efforts have focused on developing a potentially less invasive and less time-consuming operation by simplifying the pattern of atrial lesions and using alternative energy sources that can create them quickly, without a cut-and-sew technique. Intra-operative endocardial radiofrequency ablation to the pulmonary veins for atrial fibrillation is a

promising new treatment option for patients with atrial fibrillation undergoing cardiac surgery or patients with highly symptomatic atrial fibrillation not responding to other therapies [22]. The evidence suggests that patients with an enlarged (≥55.0 mm) or giant (≥75.0 mm) LA who were at risk of failing to obtain sinus conversion after a standard maze procedure may derive benefit from concomitant atrial reduction surgery using either a tissue excision or a tissue plication technique [11, 13 – 16].

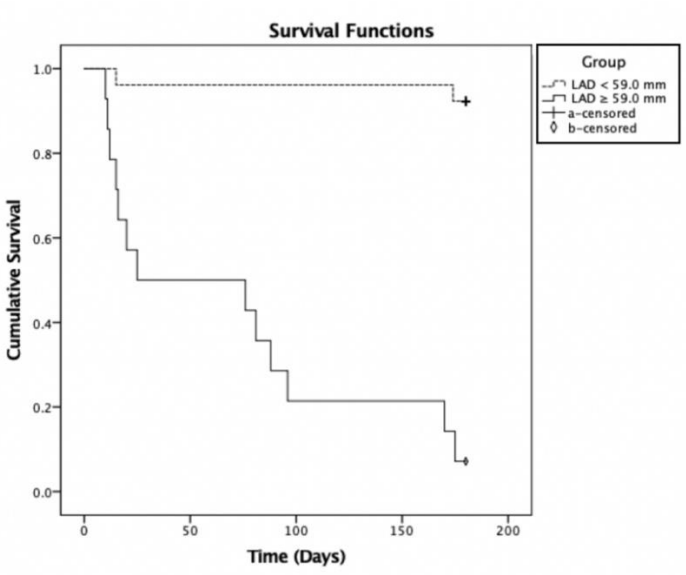

Figure 3: Kaplan-Meier Survival curves. Dashes line: Group (A) survival curve for Left after diameter < 59.0mm. Solid line: Group (B) survival curve for Left after diameter ≥ 59.0mm.

In our study, the surgical technique was safe with no reported complications such as oesophageal perforation, the need for permanent pacemaker implantation or PV stenosis. Since our mono-polar probe was saline-irrigated atrial wall injury, perforation or charring was not observed in spite of prolonged ablation time over the same areas and the creation of a trans-mural scar was much more easily achieved than with dry or temperature-controlled RF energy. This further affirms safety of the procedure [22, 23]. Also, patients in our study had a mean age of 47.55 ± 7.98; this was largely attributed to the fact that the pathology of mitral valve disease in our cases was exclusively rheumatic.

In our study, after 6-month follow-up period, 25 (62.5%) patients had restored sinus rhythm despite rheumatic etiology, large left atrial diameters and long AF duration. We employed a simple and relatively short procedure that focused exclusively on the left atrium taking into account the main lines of the maze operation. This finding was close to a previous study, were the percentage of patients in SR was 59% [24]. On the other hand, Williams and colleagues observed sinus rhythm restoration in 78% of patients at 9 months following surgery; however, the study included patients that had AF not lasting more than 6 months [25]. We could conclude in our study that sinus conversion rate was significantly lower in patients with a left atrial diameter over 59mm.

These findings were similar to most studies, in a study on 99 patients, Chen and collaborators claimed that sinus conversion rate was significantly lower in patients with a left atrial diameter over 56.8 mm [15]. In another study, a left atrial dimension of 51-60 mm was not associated with a lower rate of sinus conversion if compared to left atrial diameters below 50 mm, but atrial dimensions of more than 60 mm were associated with a 9-fold higher risk of failure at 1-year follow-up [16].

There was a statistical significance between pre-operative AF duration and SR restoration. In the sinus group, mean AF duration in patients that regained SR at 6 months was 35.24 ± 11.47 months and in patients who were still in AF was 82.87 ± 9.61 months. These findings suggest that post-operative atrial fibrillation is also most likely affected by the duration of disease, as patients with shorter pre-operative disease duration are less vulnerable in retuning to atrial fibrillation post operatively. Yet, further investigation is recommended to investigate this finding.

New York Heart Association heart failure Classification (NYHA) class did not seem to be a strong predictor of success or failure as. We did not experience any of the described procedure-related complications except for one patient who presented with a first-degree heart block for 3 days after the procedure and then reverted back to sinus rhythm. In our study, we reported a number of patients presenting with first-degree atrioventricular block or nodal rhythm in the immediate and early post-operative period, but

Table 3: Kaplan-Meier Survival function estimates

Group	Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Group A LAD < 59 mm	175.077	9.601	156.26	193.894
Group B LAD ≥ 59 mm	62.643	18.392	26.594	98.692

they all transitioned into sinus rhythm upon assessment at one week and/or at one month post-operatively.

There were no reported cases of stroke or mortality in our study, which could be explained by the relatively young mean age of patients. However, in a study on 285 patients, in-hospital mortality was 4.2% (12 patients) and post-operative stroke was reported 6 patients (2.1%) [26]. Ad and colleagues reported a low incidence of embolic stroke (6 patients out of 373) despite cessation of oral anticoagulation at 12 months in the majority of them [27].

Reviewing study limitations

We had limitations in our study, one of them was the small sample size, and that was due to the limited number of resources (probes). The other limitation was to judge whether we have reached the accurate trans-mural ablation, as it was somehow based on subjective judgment which varies from surgeon to another. For future studies, we recommend increasing the sample size, increasing the follow-up period and introducing a comparative group, while further investigating confounding risk factors, to have a more controlled environment in accessing the incidence rates of AF.

Conclusion

A significant higher rate of success was associated in treating patients with paroxysmal or persistent atrial fibrillation patients using radio frequency ablation, who have left atrial diameter less than 59.0 mm. This can potentially allow mitral valve repair patients to stop taking oral anticoagulation in the future as all benefits of elimination of AF will be achieved (improved hemodynamics, no palpitations, improvement of symptoms and avoiding complications of anticoagulation).

Conflict of interest: None declared

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