

Impact of the Cox-Maze IV Procedure on Left Atrial Mechanical Function



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Background	The Cox-Maze IV procedure is a proven surgical treatment for atrial fibrillation (AF). Previous studies on the procedure and its effect on left atrial mechanical function have yielded mixed results.
Methods	Sixty-four (64) patients underwent Cox-Maze IV at St Vincent's Hospital, Melbourne between March 2010 and May 2016. Baseline characteristics were collected and outcomes assessed including rhythm analysis. Preoperative and postoperative transthoracic echocardiograms were reviewed.
Results	Fifty-seven (57) patients had complete follow-up with all clinical measures collected. The mean age was 71.1 ± 10.2 years, 63% being male. Fifty-eight per cent (58%) (33/57) of patients were in AF and 42% (24/57) in sinus rhythm (SR) at preoperative transthoracic echocardiography. Follow-up postoperative transthoracic echocardiography was performed at a mean of 2.3 ± 1.9 years. Nineteen (19) patients with a history of paroxysmal AF were in SR both preoperatively and postoperatively. In these patients, there was a significant decrease in Mitral A wave 0.63 ± 0.28 m/s (pre-op) vs 0.47 ± 0.29 m/s (post-op), $p = 0.044$. There was a significant decrease in left ventricular ejection fraction (LVEF) postoperatively $64.2 \pm 9.7\%$ vs $55.0 \pm 12.9\%$, $p = 0.005$. At follow-up, 28% (16/57) were in AF, 61% (35/57) in SR, and 11% (6/57) in a paced rhythm. In a multivariate analysis, predictors of AF recurrence included higher LA volumes ($p = 0.042$) and younger age at surgery $p = 0.030$. Preoperative AF, sex and LVEF had no impact on AF recurrence.
Conclusions	The Cox-Maze IV procedure, while effective in converting patients to sinus rhythm, may reduce left atrial mechanical function in patients with paroxysmal AF.
Keywords	Cox-Maze IV • Atrial fibrillation • Left atrium • Left atrial appendage

Introduction

The Cox-Maze procedure was first introduced in 1987 [1] as a surgical treatment for atrial fibrillation (AF). The procedure was performed as a bi-atrial 'cut and sew' to block all macro-reentrant circuits, and guide the native sinus impulse to both atria and the atrioventricular node. The aim of the procedure was to restore sinus rhythm, and reduce the risk of stroke and left ventricular dysfunction [2–4].

The original Cox-Maze procedure had issues with chronic incompetence causing high numbers of permanent

pacemaker insertions [3]. Modifications of the Cox-Maze I were made to overcome these issues and the Cox-Maze III became the gold standard surgical treatment for AF. However, this procedure did not have a high uptake amongst surgeons due to longer cardiopulmonary bypass times. The Cox-Maze IV was introduced in 2002, with bipolar radio-frequency and cryothermal ablation replacing the original 'cut and sew' technique. This resulted in a dramatic increase in the popularity of the procedure [5].

The Cox-Maze IV demonstrated equivalent rates of freedom from AF with reduced cardiopulmonary bypass times,

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and less perioperative morbidity [6–8]. It has been shown to be equally effective in patients undergoing ablation for lone AF, and those undergoing concomitant procedures such as coronary artery bypass grafting and valvular surgery [3,9,10]. In studies at high volume institutions, long-term results (follow-up >5 years) have shown freedom from AF in a majority of patients [11,12]. There is evidence to suggest no difference in the late success of the procedure for patients with paroxysmal versus persistent permanent AF [12]. In addition, the duration of preoperative AF is not a predictor of late failure post-procedure [12].

Left Atrial Function

The left atrium (LA) serves multiple functions in the cardiac cycle, acting as a conduit for the passage of blood from the pulmonary veins to the left ventricle. When in sinus rhythm, the LA contracts providing additional left ventricular (LV) filling [13], and can contribute up to 30% of the LV stroke volume [14]. Left atrial mechanical function, is estimated by non-invasive techniques, including pulse wave Doppler across the mitral valve. This can be calculated during diastole in patients in sinus rhythm with the transmitral 'A wave' corresponding to late diastolic filling of the left ventricle, associated with atrial contraction [15].

Older versions of the Cox-Maze procedure and its effect on left atrial mechanical function were previously studied with mixed results. Patients with chronic AF, who are converted to sinus rhythm have improved transport function (as A waves are absent in patients in AF). However, the effect of the procedure is not known for people in SR before and after surgery.

Lönnnerholm *et al.* [16] looked at a small cohort of Cox-Maze III patients in sinus rhythm before and after surgery. They found left atrial contractility, measured as fractional area change, was significantly reduced at 6 and 56 months of follow-up (0.20 ± 0.09 and 0.19 ± 0.07 vs baseline 0.36 ± 0.09), as was the transmitral A-wave velocity (30 ± 12 and 28 ± 8 cm/s vs baseline 40 ± 15).

If left atrial function is preserved before the operation, a decrease in the atrial mechanical function postoperatively may have significant clinical implications including risk of thrombus formation [16,17]. Buber *et al.* evaluated the risk of thromboembolic stroke in patients post Cox-Maze III, concluding that 31% of patients in sinus rhythm pre and postoperatively had no evidence of LA mechanical contraction, leading to a five-fold increase in thromboembolic stroke [17]. To the authors' knowledge, there have been no such studies looking at left atrial mechanical function in Cox-Maze IV patients.

Material and Methods

Ethics approval was obtained through St Vincent's Health Ethics committee. After consent, all patient information was de-identified. All patients undergoing the Cox-Maze IV procedure at St Vincent's Hospital Melbourne between March 2010 and May 2016 were evaluated. Operative information and preoperative baseline characteristics were sought from

the Australian and New Zealand Society of Cardiothoracic Surgeons database.

Sixty-four (64) patients were enrolled in the study, two patients died in the early postoperative phase and five patients had incomplete preoperative or postoperative echocardiography results, and thus were excluded. Fifty-seven (57) patients had complete follow-up. Three surgeons were involved in the series with the majority 47/57 (82%) being performed by a single surgeon. The Cox-Maze IV procedure was performed as a concomitant procedure to valvular or coronary artery bypass surgery in all cases. Fifty-three (53) patients (93%) had bipolar radiofrequency ablation and four patients (7%) underwent cryothermal ablation depending on individual surgeon preference. The standard procedure involved blunt dissection of the left and right pulmonary veins, with ablation used to isolate both pulmonary veins. Roof and floor lesions were then created, with ablation used to isolate the left atrial appendage. From this a line was made to the encircling block on the left pulmonary veins, and across the isthmus to the AV annulus. A purse string was placed in the midpoint of the right atrium and from this a line was made to the superior vena cava (SVC) superiorly, inferior vena cava (IVC) inferiorly, tricuspid annulus anteriorly and to the tip of the right atrial appendage. The left atrial appendage was opened and a line of block was made down to the encircling block of the left pulmonary veins, after which the left atrial appendage was stapled and then ligated.

Results from their preoperative transthoracic echocardiograms were obtained and compared with the most recent postoperative transthoracic echocardiogram sought from the medical record or referring cardiologist. Continuous data and categorical data were compared with Student's two-tailed paired *t* tests and Fisher's exact test respectively. A binominal regression was used to identify potential predictors of AF recurrence postoperatively. Significant covariates on univariate analysis $p < 0.10$ or clinically relevant covariates were entered into a multivariate binary logistic regression. Four preoperative and perioperative variables were evaluated in a univariate analysis; age, sex, preoperative AF and left atrial area. Significance was determined by $p < 0.05$. Data were coded using Microsoft Excel 2016 and analysed using SPSS v22 (IBM Inc., SPSS, Armonk, NY, USA).

Results

Fifty-seven (57) patients had complete follow-up with the mean age 71.1 ± 10.2 years, 63% male. Full demographics are illustrated in Table 1. Preoperatively, 58% (33/57) patients were in AF and 42% (24/57) in SR. Postoperative echocardiography performed at a mean of 2.3 ± 1.9 years after the index procedure, found 28% (16/57) of patients in AF, 61% (35/57) in SR and 11% (6/57) in a permanently paced rhythm (see Table 2). Of those patients in SR

Table 1 Demographics n = 57.

Age	71.1 ± 10.2
Gender (male)	63% (36)
Hypertension	67% (38)
Hypercholesterolaemia	54% (31)
Previous AMI	14% (8)
Diabetes	16% (9)
Smoking History	53% (30)
BMI	27.4 ± 5.0
Concomitant procedures	
CABG	40% (23)
MV repair	63% (36)
MV replacement	12% (7)
AV procedure	23% (13)
TV procedure	33% (19)

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index, kg/m²; CABG, coronary artery bypass grafting surgery; MV, mitral valve; AV, aortic valve; TV, tricuspid valve.

postoperatively, 5/35 (14%) had no significant left atrial mechanical function defined as a velocity of <0.2 m/s of the transmitral A wave. There was no evidence of LA thrombus in any of the postoperative transthoracic echocardiograms.

Transthoracic echocardiography was compared in 19 patients who were in SR both preoperatively and postoperatively. At follow-up there was a significant reduction in mitral A wave 0.63 ± 0.28 m/s vs 0.47 ± 0.29 m/s, $p = 0.044$ along with a significant decrease in LVEF $64.2 \pm 9.7\%$ vs $55.0 \pm 12.9\%$, $p = 0.005$. There was no significant difference between the measures of LA area, RA area or right ventricular end systolic pressure (RVSP) (Table 3).

The remaining patients (n = 38) had no significant change in LVEF $58.3 \pm 9.7\%$ vs $56.0 \pm 7.6\%$, $p = 0.129$ pre and post procedure, however there was a significant decrease in LA area 34.5 ± 7.6 cm² vs 28.1 ± 6.6 cm² $p = 0.000$ and RA area 26.3 ± 6.5 cm² vs 22.0 ± 5.3 cm² $p = 0.005$. Interestingly, there was no significant change in RVSP (Table 4).

There were 12 patients with preoperative AF that were converted to SR postoperatively. Their mean A wave velocity was 0.39 ± 0.24 m/s. There was no change in LVEF in this group $58.4 \pm 8.9\%$ vs $57.2 \pm 5.5\%$ $p = 0.6$.

In a multivariate analysis the predictors of AF recurrence post Cox Maze IV included higher LA volumes $p = 0.027$, and younger age at surgery $p = 0.038$. There was no difference in preoperative AF or sex of the individual (Table 5). One-way ANOVA analysis revealed a larger LA area preoperatively which was associated with a higher percentage of AF postoperatively $p = 0.042$ (Figure 1).

The SR pre and post group (n = 19) was closely matched to the rest of the cohort (n = 38) in terms of baseline demographics (Table 6).

Table 2 Heart rhythm at echocardiography n = 57.

Rhythm	Preoperative	Postoperative
AF	33 (58%)	16 (28%)
SR	24 (42%)	35 (61%)
PACED	0	6 (11%)

Abbreviations: AF, atrial fibrillation; SR, sinus rhythm.

Table 3 Echocardiography results—patients in sinus rhythm pre and postoperatively, n = 19.

	Preoperative	Postoperative	P
MITRAL A	0.63 ± 0.28	0.47 ± 0.29	0.044
LVEF	64.2 ± 9.7	55.0 ± 12.9	0.005
LA area	29.7 ± 8.6	27.2 ± 65.9	0.234
RA area	22.2 ± 7.0	22.0 ± 7.1	0.941
RVSP	33.8 ± 9.8	36.8 ± 11.4	0.293

Abbreviations: MITRAL A, transmitral A wave, m/s; LVEF, left ventricular ejection fraction %; LA area, left atrial area, cm²; RA area, right atrial area, cm²; RVSP, right ventricular systolic pressure, mmHg.

Table 4 Echocardiography results, remaining cohort, n = 38.

	Preoperative	Postoperative	P
LVEF	58.3 ± 9.7	56.0 ± 7.6	0.129
LA area	34.5 ± 7.6	28.1 ± 6.6	0.000
RA area	26.3 ± 6.5	22.0 ± 5.3	0.005
RVSP	45.2 ± 14.0	42.5 ± 16.7	0.431

Abbreviations: LVEF, left ventricular ejection fraction, %; LA area, left atrial area, cm²; RA area, right atrial area, cm²; RVSP, right ventricular systolic pressure, mmHg.

Discussion

Left Atrial Mechanical Function

In patients in SR both pre and postoperatively there was a significant reduction in postoperative mitral A wave 0.63 ± 0.28 m/s vs 0.47 ± 0.29 m/s, $p = 0.044$. With 14% of these patients having no significant left atrial mechanical function (transmitral A wave <0.2 m/s). To the authors' knowledge, this is the first data to compare left atrial mechanical function pre and postoperatively in Cox Maze IV patients. However, it must be noted this finding is congruent with other studies reporting similar findings on earlier versions of the procedure, namely the Cox-Maze III [2,17]. The benefits of this operation in those patients with permanent or longstanding AF are well described. However, in those

Table 5 Multivariate analysis—predictors of AF postoperatively, n = 57.

Variable	Odds ratio	95% CI	P-value
LA area	1.12	1.01–1.22	0.027
Age	0.91	0.84–0.98	0.038
AF preoperative	4.65	0.88–24.3	0.069
Sex (male)	2.013	0.45–9.0	0.362

Abbreviations: LA area, left atrial area, cm²; AF, atrial fibrillation.

patients with paroxysmal AF, further investigation may be indicated. If these patients are found to be in AF for only brief periods of time, medical management of their AF may maintain their atrial transport function when compared with a Cox Maze IV operation. Those who have had a Cox-Maze IV operation should be carefully followed up with serial echocardiography. If they have been found to lose their atrial transport function (mitral A wave velocity <0.2 m/s) they would be theoretically at higher risk of a thrombus forming in the left atrium/cerebrovascular event as previously described in the literature [17]. It is unknown if the left atrial mechanical function (transmitral A wave) in these patients will increase over time—and is an interesting area of further research.

Left Ventricular Ejection Fraction

Thirty-three per cent (33%) of patients were in SR at pre and postoperative echocardiography. These patients had a significantly higher LVEF at baseline compared to the remainder of the cohort. In the sinus rhythm group, there was a significant decrease in LVEF postoperatively. The remainder of the cohort had no significant drop in LVEF. The 'atrial kick' contribution to cardiac output can account for up to 30% of LV stroke volume [14]. This becomes increasingly important in the preservation of cardiovascular performance in patients

with reduced LV compliance. This result was unexpected and needs to be viewed carefully, as the Cox-Maze IV procedure was performed as a concomitant procedure in all subjects in this series. The major confounding factor to this finding is the heterogeneity of procedures performed in this cohort of patients. In particular, the high rates of mitral valve surgery would have played a large role in LV function and haemodynamics postoperatively. The short follow-up period must also be taken into account. A further area of research would be to investigate if the LVEF increases over time in this group of patients.

Freedom From Atrial Fibrillation

The prevalence of AF dropped from 58% preoperatively to 28% postoperatively, with 16/33 of patients in AF preoperatively in SR at long-term follow-up. The effectiveness of the Cox-Maze IV procedure in treating AF has been widely documented, with freedom from AF postoperatively noted as high as 80–90% in high volume experienced centres [8,12]. One explanation for the relatively lower success rate in this cohort may be the very high rate of concomitant procedures (in all patients) and the large preoperative LA area (mean = 33.5 cm²). The mean age of the cohort (77.1 years) along with a high mean body mass index (BMI) (27.4 kg/m²) classified as overweight are both known independent risk factors for AF and may have contributed [18].

Predictors of Late Atrial Fibrillation Recurrence

The two preoperative risk factors for predicting late AF recurrence included LA size and younger age at surgery. Greater LA size increases the surface area leading to atrial fibrillation occurrence previously well reported in the literature [12,19,20]. The one way ANOVA demonstrated a significant increase in postoperative AF with increasing preoperative LA area. In these patients, due to the high failure rate, either a more aggressive atrial reduction,

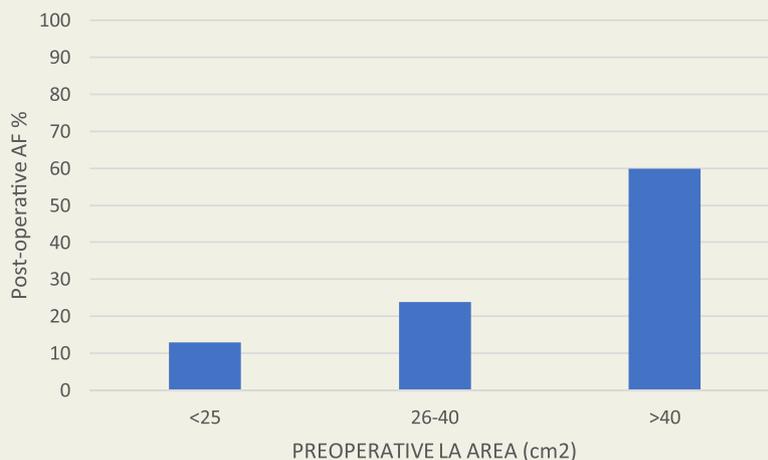


Figure 1 Preoperative left atrial area v incidence of postoperative AF, n = 57. ANOVA p = 0.042.

Table 6 Demographic differences between patients in sinus rhythm pre and postoperative and remaining cohort, n = 57.

	SR pre/post (n = 19)	Rest of cohort (n = 38)	P
Age	73.1 ± 8.3	70.0 ± 11.0	0.285
Male	12 (63%)	24 (63%)	0.999
Diabetes	2 (11%)	7 (18%)	0.450
Smoking History	9 (47%)	21 (55%)	0.582
Hypertension	11 (58%)	27 (71%)	0.329
Hypercholesterolaemia	11 (58%)	20 (53%)	0.713
BMI	26.7 ± 4.8	27.8 ± 5.2	0.446
AMI	3 (16%)	5 (13%)	0.792
CAGS	6 (32%)	17 (45%)	0.349
MV procedure	14 (74%)	29 (76%)	0.619
TV Procedure	4 (21%)	15 (39%)	0.077
AV Procedure	5 (26%)	9 (24%)	0.222
LVEF (pre-op)	64.2 ± 9.7	58.2 ± 9.7	0.033
LVEF (post-op)	55.0 ± 12.9	56.0 ± 7.6	0.721

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index, kg/m²; CABG, coronary artery bypass grafting surgery; MV, mitral valve; AV, aortic valve; TV, tricuspid valve; LVEF, left ventricular ejection fraction, %.

extensive ablation lesion set or reconsideration of the procedure may be considered. The younger age at surgery was an interesting finding, with previous literature conversely reporting that older age at surgery was associated with late failure [19]. One explanation is that a proportion of the older patients had a paced rhythm postoperatively likely influencing the data.

Limitations

This was a single centre retrospective analysis of a small patient cohort, with a heterogeneous group of concomitant procedures performed. Similarly, there was a significant heterogeneity in antiarrhythmics used pre and postoperative in both the community and intensive care setting.

Evaluation of pre and postoperative rhythm was based solely on patient's rhythm at time of echocardiogram, whereas previous analyses have aggressively monitored for AF with regular 24 hour Holter monitoring or regular electrocardiograms.

The echocardiograms were performed at a variety of centres, which may have resulted in inter-observer variability. This also influences the ability to utilise more comprehensive LA volume measurements such as biplane area length, biplane modified Simpson or the prolate ellipse methods [21]. Perhaps the greatest limitation of this study is the absence of atrial strain measurements, which is an emerging modality for assessment of left atrial function [22]. This has grounds for future study. The mean follow-up of 2.3 years is not adequate in assessing the long-term freedom of atrial fibrillation and performance of left atrial function.

In conclusion, the Cox-Maze IV procedure may cause a decrease in left atrial mechanical function in patients with a history of paroxysmal AF who are in sinus rhythm pre-

procedure at short-term follow-up. This may have significant clinical implications including risk of thrombus formation. High LA area preoperatively and younger age at surgery are associated with late AF recurrence. Further larger cohort studies are required to confirm these findings.

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References

- [1] Cox JL, Schuessler RB, Lappas DG, Boineau JP. An 8 1/2-year clinical experience with surgery for atrial fibrillation. *Ann Surg* 1996;224(3):267–73. discussion 73–5.
- [2] Feinberg MS, Waggoner AD, Kater KM, Cox JL, Lindsay BD, Perez JE. Restoration of atrial function after the maze procedure for patients with atrial fibrillation. Assessment by Doppler echocardiography. *Circulation* 1994;5(Pt 2):ii285–92.
- [3] Prasad SM, Maniar HS, Camillo CJ, Schuessler RB, Boineau JP, Sundt 3rd TM, et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. *J Thorac Cardiovasc Surg* 2003;126(6):1822–8.
- [4] Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. *J Thorac Cardiovasc Surg* 1999;118(5):833–40.
- [5] Yii M, Yap CH, Nixon I, Chao V. Modification of the Cox-Maze III procedure using bipolar radiofrequency ablation. *Heart Lung Circ* 2007;16(1):37–49.
- [6] Gaynor SL, Diodato MD, Prasad SM, Ishii Y, Schuessler RB, Bailey MS, et al. A prospective, single-center clinical trial of a modified Cox maze procedure with bipolar radiofrequency ablation. *J Thorac Cardiovasc Surg* 2004;128(4):535–42.
- [7] Robertson JO, Saint LL, Leidenfrost JE, Damiano Jr RJ. Illustrated techniques for performing the Cox-Maze IV procedure through a right mini-thoracotomy. *Ann Cardiothorac Surg* 2014;3(1):105–16.

- [8] Weimar T, Schena S, Bailey MS, Maniar HS, Schuessler RB, Cox JL, et al. The Cox-Maze procedure for lone atrial fibrillation: a single-center experience over 2 decades. *Circ Arrhythm Electrophysiol* 2012;5(1):8–14.
- [9] Henn MC, Lawrance CP, Sinn LA, Miller JR, Schuessler RB, Moon MR, et al. The effectiveness of surgical ablation in patients with atrial fibrillation and aortic valve disease. *Ann Thorac Surg* 2015;100(4):1253–60.
- [10] Damiano Jr RJ, Gaynor SL, Bailey M, Prasad S, Cox JL, Boineau JP, et al. The long-term outcome of patients with coronary disease and atrial fibrillation undergoing the Cox maze procedure. *J Thorac Cardiovasc Surg* 2003;126(6):2016–21.
- [11] Henn MC, Lancaster TS, Miller JR, Sinn LA, Schuessler RB, Moon MR, et al. Late outcomes following the Cox-Maze IV procedure for atrial fibrillation. *J Thorac Cardiovasc Surg* 2015;150(5):1168–78. e2.
- [12] Damiano RJ, Schwartz FH, Bailey MS, Maniar HS, Munfakh NA, Moon MR, et al. The Cox-Maze IV procedure: predictors of late recurrence. *J Thorac Cardiovasc Surg* 2011;141(1):113–21.
- [13] Pagel PS, Kehl F, Gare M, Hettrick DA, Kersten JR, Warltier DC. Mechanical function of the left atrium: new insights based on analysis of pressure-volume relations and Doppler echocardiography. *Anesthesiology* 2003;98(4):975–94.
- [14] Delgado V, Di Biase L, Leung M, Romero J, Tops LF, Casadei B, et al. Structure and function of the left atrium and left atrial appendage. *AF Stroke Implic* 2017;70(25):3157–72.
- [15] Mottram PM, Marwick TH. Assessment of diastolic function: what the general cardiologist needs to know. *Heart* 2005;91(5):681–95.
- [16] Lönnerholm S, Blomström P, Nilsson L, Blomström-Lundqvist C. Long-term effects of the maze procedure on atrial size and mechanical function. *Ann Thorac Surg* 2016;85(3):916–20.
- [17] Buber J, Luria D, Sternik L, Raanani E, Feinberg MS, Goldenberg I, et al. Left atrial contractile function following a successful modified maze procedure at surgery and the risk for subsequent thromboembolic stroke. *J Am Coll Cardiol* 2011;58(15):1614–21.
- [18] Lau DH, Nattel S, Kalman JM, Sanders P. Modifiable risk factors and atrial fibrillation. *Circulation* 2017;136(6):583.
- [19] Gillinov AM, Sirak J, Blackstone EH, McCarthy PM, Rajeswaran J, Pettersson G, et al. The Cox maze procedure in mitral valve disease: predictors of recurrent atrial fibrillation. *J Thorac Cardiovasc Surg* 2005;130(6):1653–60.
- [20] Kamata J, Kawazoe K, Izumoto H, Kitahara H, Shiina Y, Sato Y, et al. Predictors of sinus rhythm restoration after Cox maze procedure concomitant with other cardiac operations. *Ann Thorac Surg* 1997;64(2):394–8.
- [21] Jiamsripong P, Honda T, Reuss CS, Hurst RT, Chaliki HP, Grill DE, et al. Three methods for evaluation of left atrial volume. *Eur J Echocardiogr* 2008;9(3):351–5.
- [22] Pathan F, Sivaraj E, Negishi K, Rafiudeen R, Pathan S, D'Elia N, et al. Use of atrial strain to predict atrial fibrillation after cerebral ischemia. *JACC Cardiovasc Imaging* 2018;11(November (11)):1557–65. <http://dx.doi.org/10.1016/j.jcmg.2017.07.027>. Epub 2017 Nov 15.