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Relationship Between Left Atrial Strain Assessed by Speckle Tracking Echocardiography and New-Onset Atrial Fibrillation in Patients Undergoing Aortic Valve Surgery for Severe Aortic Stenosis

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Abstract

Aim of study: to assess the relationship between left Atrial strain and new onset atrial fibrillation in patient undergoing aortic valve surgery for severe aortic stenosis.

Methods: This prospective observational study was conducted on one hundred patients underwent elective isolated aortic valve replacement due to isolated aortic stenosis. All patients were evaluated by history taking, clinical & laboratory investigations. Echocardiographic assessment was done to assess LV ejection fraction, E, A, S`, E` and A`, E/E`, peak LA longitudinal strain (PALS) & peak atrial contraction strain (PACS). Operative details and finally post operative follow up to detect new onset post-operative atrial fibrillation was done.

Results: patients were divided into two groups, 38 patients who developed atrial fibrillation in post-operative follow up period (POAF group), and 62 patients who did not developed AF (non-POAF group). POAF group were older (P= 0.004). Pre-operative LA global PALS and PACS were significantly lower in POAF group (P=<0.001) and associated with post-operative AF. By multivariate regression analysis, age (P=0.03), LA global PALS (p=0.04) and LA global PACS (P=0.03) were independent risk factors for post-operative AF.

Conclusion: In severe aortic stenosis, left atrial dysfunction assessed by speckle tracking Echocardiography predicted the incidence of postoperative AF, suggesting that speckle-tracking echocardiography before surgery may help in risk stratification & proper management.

Keywords: Aortic stenosis; Aortic valve replacement; Atrial fibrillation; Left atrial strain

Introduction

Atrial fibrillation (AF) is one of the most common postoperative complications following cardiac surgery. Recent evidence suggests that postoperative atrial fibrillation (POAF) may be more 'malignant' than previously thought, associated with mortality and morbidity. This in turn translates into longer hospitalization, increased cost of hospitalization as well as association with thromboembolic events and mortality [1].

Identification of patients at high risk of POAF after cardiac surgery is vital for selection of the patients who might benefit from intensive prophylactic therapy or increased monitoring [2].

Neither LA volume or LA diameter were independent predictors of POAF, probably because the inclusion of atrial function gives a more comprehensive description of LA performance, given the links between chamber size, deformation, and contractile performance [3]. Two-dimensional (2D) speckle-tracking echocardiography (STE) is emerging as a powerful diagnostic tool to evaluate LA mechanics [4].

This work aimed to assess the left atrial dysfunction by speckle tracking echocardiography and find the relationship between left atrial strain and new onset atrial fibrillation in patient undergoing aortic valve surgery for severe aortic stenosis.

Material and Methods

This is a prospective observational study that included one hundred consecutive patients admitted to cardio-thoracic surgery department at Benha University Hospital and National Heart Institute, in the period from January 2020 to May 2021 for elective isolated aortic valve replacement due to isolated aortic stenosis. We included patients with preoperative sinus rhythm who were referred for elective surgical isolated aortic valve replacement. Patients with previous rhythm other than sinus, significant coronary artery disease, emergency surgery, hyper- or hypothyroidism, renal failure requiring hemodialysis, moderate to severe other valvular heart disease and valvular prosthesis,

history of congenital cardiac abnormalities or cardiac tumors, or current use of antiarrhythmic drugs were excluded from this study.

Baseline clinical variables included BMI, New York Heart Association functional class, history of systemic hypertension, diabetes mellitus, dyslipidemia, any previous episode of stroke or congestive heart failure requiring hospitalization. History of previous medications was documented. In the preoperative day conventional venous blood examination was obtained for complete blood picture, kidney, liver function tests and bleeding profile. All patients signed informed consents and this study was approved by ethical committee of Benha University Hospital.

Each patient underwent a complete standard transthoracic echocardiography study using Philips EPIC 7 ultrasound machine (Q lab, 10.8; Andover, MA, USA) with a multi frequency transducer (S-51) and conducted to 3 lead ECG. Subjects were studied in the left lateral recumbent position. Measurements of left ventricular (LV) and left atrial dimensions, LV ejection fraction (LVEF), were made in accordance with recommendations of ASE [5]. LV ejection fraction, measured using Simpson's method, was used as a standard index of global LV systolic function. The ratio between peak early (E) and late (A) diastolic LV filling velocities was used as a standard index of LV diastolic function. We measured the TDI derived systolic and diastolic velocities (S`, E` and A`) from the lateral edge of mitral annulus so we can calculate the E/E` ratio. LA volumes were measured using the area-length method, from the apical four and two chamber views. LA volumes were subsequently indexed to body surface area (BSA).

ECG guided apical 4 chamber view images were obtained using a conventional 2D grey scale echocardiography. Three consecutive heart cycles were recorded and averaged for all patients. A minimum frame rate of 60 frames per second was acquired for the reliable operation of this program. According to the definition of strain, negative strain denotes shortening of the LV, which indicates that an Increase in absolute values represents a better function. In contrast, indexes of positive LA strain denote shortening. We used to measure the atrial strain reference frame of zero strain from R-R gating. LV global longitudinal strain (LVGLS) was calculated by averaging the negative peak of longitudinal strain from 18 ventricular segments in all 3 apical views, according to the current guideline [6]. LA strain was measured using a non-foreshortened apical four and two chamber then we used software to offer adjustable endocardial contouring tool [7].

The analysis of recordings was performed off-line by a single independent and experienced echo cardiographer who had no knowledge of other clinical or echocardiographic parameters representing LV, LA and valvular structure and function, using available semi-automated two- dimensional strain software (Q lab, 10.8; Andover, MA, USA). As previously described, and as stated in the current ASE/ EAE Consensus [4], LA endocardial border was manually traced in both four- and two-chamber views, thus delineating a region of interest (ROI), composed of 6 segments.

After eventual manual adjustment of the ROI, the longitudinal strain curves were generated by the software for each atrial segment. As shown in Figure 1, peak LA longitudinal strain (PALS), measured at the end of the reservoir phase, was calculated by averaging values from all segments, and by separately averaging values from the 4- and 2-chamber views (4- and 2-chamber average PALS, respectively). In patients in whom some segments were excluded because of the difficulty in achieving adequate tracking, PALS was calculated by averaging values measured in the remaining segments.

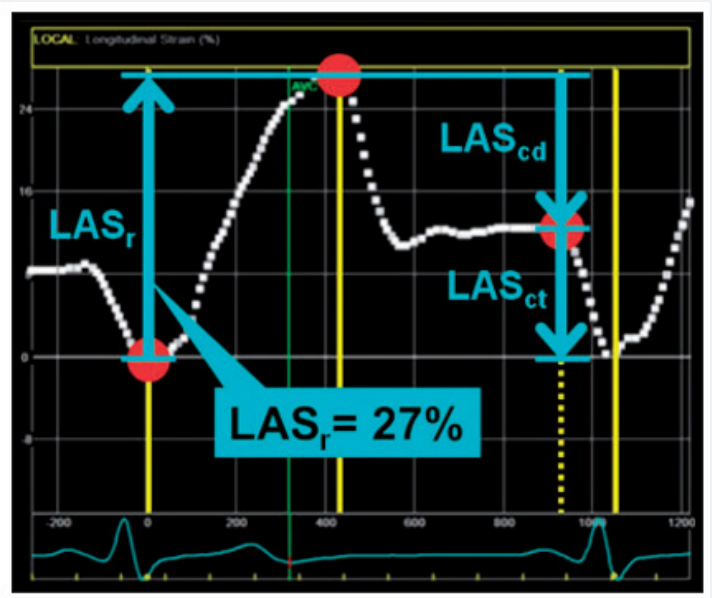

Figure 1: Measurement of left atrial strain components.
N.B. LASr=left atrial reservoir strain, LAScd=left atrial conduit strain, LASct=left atrial contractile strain.

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Continuous electrocardiography (ECG) monitoring was done throughout hospitalization in the post open intensive care. POAF was defined as episodes lasting more than 30 seconds during the postoperative hospital stay that required either pharmacologic or electrical intervention [8].

Statistical Analysis

Abstracted data were compiled and analyzed using SPSS version 21 (SPSS Inc., Chicago, IL) [9]. Continuous variables are presented as means (± standard deviation [SD]), and categorical variables are presented using relative frequency distributions and percentages. Continuous variables were compared using Student's t-test or the Mann-Whitney test, and categorical data were analyzed using the chi-square test, Fisher's exact test, and/or unadjusted odds ratios (ORs) as appropriate. Statistical significance established at $p \leq 0.05$. The diagnostic power of significant values was evaluated by the receiver operating characteristic (ROC) curve. A 2-sided P ≤0.05 considered statistically significant.

Results

In this prospective study, patients were divided into two groups. Patients who developed atrial fibrillation in post-operative follow up period (POAF group) which were 38 patients, and those who did not developed AF (non-POAF group) were 62 patients.

Analysis of demographic data revealed that POAF group patients were older than those in non-PAOF group (Table 1). Other clinical and laboratory data revealed no significant difference between study group as shown in Table 2 and Table 3.

Table 1: Demographic data in study groups.

		Non-POAF group N= 62	POAF group N= 38	P value*
Gender n (%)	female	14 (22.6%)	6 (15.8)	0.372
	male	48 (77.4 %)	32 (84.2 %)	
Age (years) mean ±SD	60.9 ±9.2	66.03 ±7.05	0.004	
BMI	32.1 ±3.9	31.9 ±3.8	0.68	

*p < 0.05 statistically significant

Table 2: Comparison between study groups regarding co-morbidities and clinical symptoms.

	Non-POAF group N= 62 N (%)	POAF group N= 38 N (%)	P value*
Current smoking	41 (66.1%)	32 (84.2%)	0.343
Hypertensive	37 (59.6%)	32 (84.2%)	0.103
Diabetic	30 (48.3%)	25 (65.7%)	0.317
NYHA class III or IV	29 (46.8%)	25 (65.9%)	0.243
Angina	14 (22.6%)	10 (26.3%)	0.939
Syncope	7 (11.2%)	5 (13.1%)	0.965

*p < 0.05 statistically significant

Table 3: Laboratory assessment of study groups.

	non-POAF group N= 62		POAF group N= 38		P value*
	Mean	±SD	Mean	±SD	
Hb (g/L)	13.33	1.65	13.27	1.91	0.873
RBS (mg/dL)	160.88	42.29	166.73	58.46	0.563
creat. (mg/dL)	1.03	0.24	1.03	0.25	0.981
ALT (U/L)	24.12	7.88	22.68	9	0.4
K pre-op (mmol/L)	4	0.38	3.95	0.32	0.499
K post-op (mmol/L)	4.31	0.38	4.25	0.33	0.431
CHOL (mg/dL)	178.61	28.42	175.2	31.55	0.574
TRIG (mg/dL)	95.08	15.18	102.98	17.25	0.088
HDL (mg/dL)	44.97	6.02	43.95	5.9	0.406
LDL (mg/dL)	114.62	29.26	110.64	32.84	0.526

*p < 0.05 statistically significant

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Regarding echocardiographic assessment by conventional 2D, Doppler and tissue Doppler parameters, there was no statistically significant difference between study groups as shown in Table 4, sections A-C. In addition, Table 4 (section D) illustrate speckle tracking data which showed significantly lower LA global PALS (21.92 ±4.28) and PACS (9.42 ±3.0) in POAF group vs. (27.60 ±3.52 and 13.56 ±2.23 for PALS and PACS respectively) in non-POAF group, with p value less than 0.001 (Figure 2).

Table 4: Echocardiographic variables in study groups.

	non-POAF group N= 62		POAF group N= 38		P value*
	Mean	±SD	Mean	±SD	
A- 2D M-mode parameters					
LVEDV (ml)	137.53	7.76	139.22	9.57	0.332
LVEF (%)	63.9	4.71	64.27	5.07	0.709
LV mass index (g/m^2)	132.92	13.46	128.97	15.18	0.174
LA volume (ml)	58.73	7.9	61.27	9.45	0.148
LA volume index (ml/m^2)	30.9	4.15	33.98	5.22	0.091
TAPSE (MM)	24.14	2.55	23.4	2.41	0.15
B- Doppler derived data					
AV peak gradient (mmHg)	88.03	6.55	88.12	6.61	0.948
AV mean gradient (mmHg)	55.42	4.91	56.08	4.28	0.486
E (cm/s)	64.92	18.75	67.93	17.41	0.419
A (cm/s)	68.96	16.7	71.04	15.16	0.527
E/A ratio	0.94	0.3	0.99	0.32	0.427
PASP (mmHg)	30.28	7.84	31.64	8.78	0.419
C- Tissue Doppler data (mitral annulus)					
mean E' (cm/sec)	6.36	1.99	6.15	2.04	0.611
mean A' (cm/sec)	8.07	1.98	8	1.96	0.863
mean S' (cm/sec)	6.65	1.42	6.94	1.24	0.283
E/E' ratio	11.15	2.55	11.67	2.43	0.316
D- 2D speckle tracking echocardiographic assessment of LV and LA					
LVGLS (%)	-25.13	2.49	-25.11	2.35	0.98
LA global PALS (%)	27.6	3.52	21.92	4.28	< 0.001
LA global PACS (%)	13.56	2.23	9.42	3	< 0.001

*p < 0.05 statistically significant.

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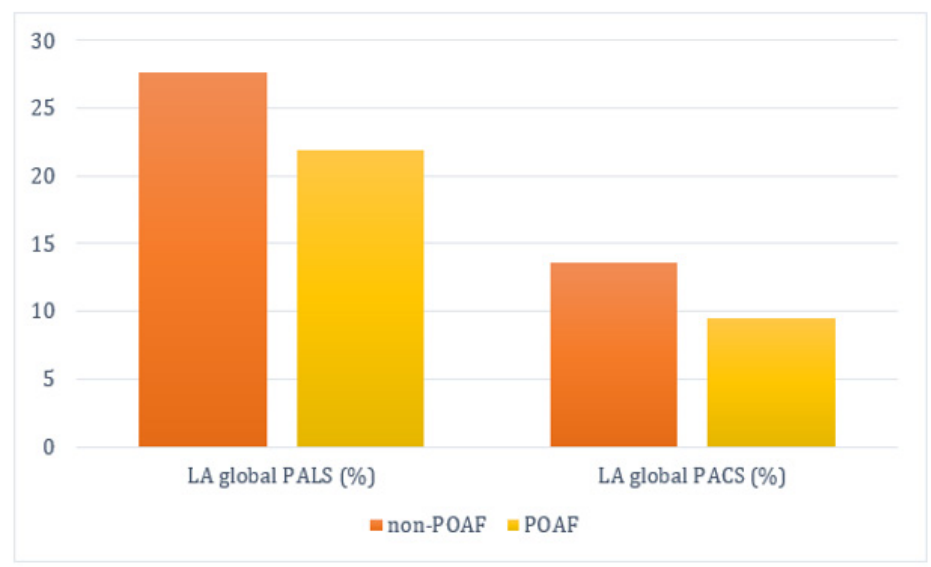

Figure 2: LA speckle tracking data in study groups.

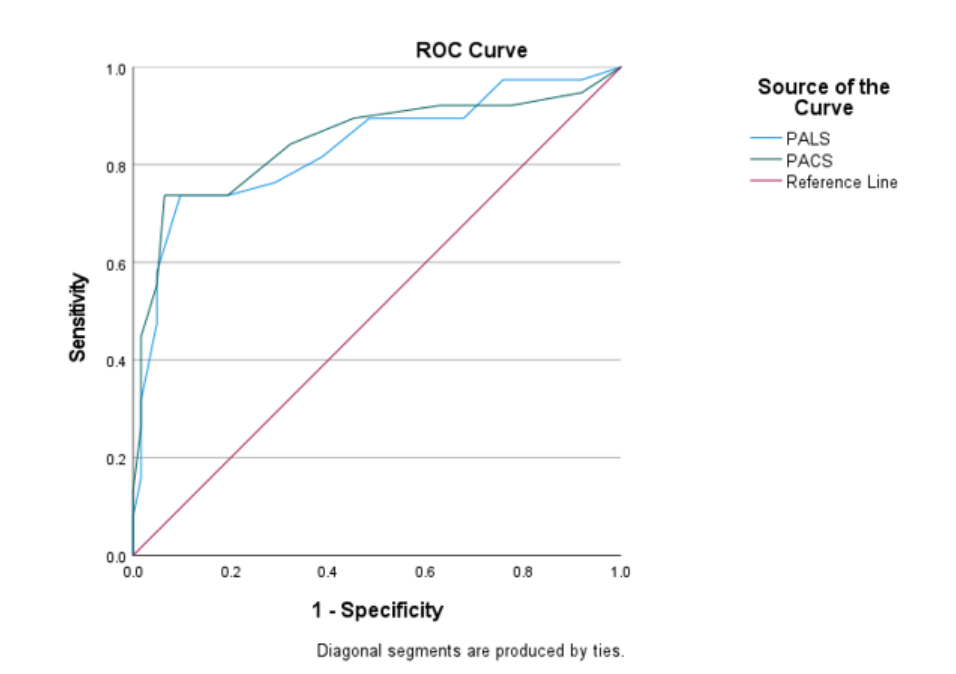

Figure 3: Receiver operating characteristic curve for LA speckle tracking data.

Receiver operating characteristic curves of LA global PALS and PACS were calculated to detect the best cut off point of Speckle tracking data that predict occurrence of postoperative AF as shown in Figure 3 and Table 5. LA global PALS of 25.5% had 76.3% sensitivity and 71% specificity in its association with development of new onset AF in post-operative periods. LA global PACS of 10.5% predicted POAF with 73.7% sensitivity and 80.6% specificity.

Table 5: ROC curve AUC values for LA speckle tracking data.

Test Result Variable(s)	Area	Asymptotic 95% Confidence Interval		
		Lower Bound	Upper Bound	P value
LA global PALS (%)	0.835	0.746	0.923	< 0.001
LA global PACS (%)	0.848	0.758	0.937	< 0.001

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Table 6: Predictors of postoperative AF by multivariate logistic regression analysis.

Variables	Odds Ratio	95% CI		P value
		Lower Bound	Upper Bound	
Age	0.94	0.88	0.99	0.03
LA global PALS	0.86	0.75	0.99	0.04
LA global PACS	0.92	0.84	0.99	0.03

In multivariate logistic regression analysis, age (P value=0.03), LA global PALS (P value=0.04) and LA global PACS (P value=0.03) were the only predictor for POAF (Table 6).

Discussion

Atrial fibrillation (AF) is one of the most common postoperative complications following cardiac surgery. This in turn translates into longer hospitalization, increased cost of hospitalization as well as association with thromboembolic events and mortality [10].

Despite new-onset postoperative atrial fibrillation occurring in 20-40% of patients following cardiac surgery, the underlying mechanisms are not well established. However, it has been traditionally thought to be transient and benign to the patients. But evidence suggests that POAF may be more 'malignant' than previously thought, associated with follow-up mortality and morbidity [11].

Previously, increased left atrial (LA) size and LA dysfunction have been shown to be related to the subsequent development of atrial fibrillation (AF), stroke, myocardial infarction, and heart failure. Therefore, as the improvement in the evaluation of LA function; preoperative LA dysfunction may emerge as an important component in the identification of patients with the risk of POAF after aortic valve replacement surgery [12].

Our study examined the relation between new onset atrial fibrillation post isolated aortic valve replacement and assessment of preoperative left atrial function by parameters of echocardiography.

The current study showed that incidence of AF was 38% (38 patients out of 100 patients). The percentage of POAF incidence varies in clinical trials, which results from different risk predictors, but it is also related to a type of cardiac surgery and the criteria for diagnosing arrhythmia, The incidence estimates of atrial fibrillation after transcatheter aortic valve implantation (TAVI) and surgical AVR have varied widely, ranging from 8% to 100% [13-15].

Saxena et. al. found that 35.1% of 2,065 patients underwent isolated first-time AVR had new onset POAF [16]. In recent population-based observational study of a total of 48 715 TAVI hospitalizations (47.4% women and 52.6% men; mean [SD] age, 81.3 [8.1] years) and 122 765 AVR hospitalizations (39.0% women and 61.0% men; mean [SD] age, 67.8 [12.0] years), a new-onset atrial fibrillation occurred in 50.4% of TAVI hospitalizations and 50.1% of AVR hospitalizations [17]. Carter-Storch et al. [18] indicated a slightly higher percentage of patients (53%) who suffered from POAF after isolated aortic valve replacement [18].

Jørgensen et al. [14] indicated a higher percentage 100% and 81.5% for patients undergoing SAVR and TAVR, respectively. Of note, their study was conducted on a small number of patients (25 and 27 patients who underwent SAVR and TAVR, respectively) [14].

In our study, patients with post-operative AF were older (66.03 ±7 years, p=0.004) (Table 1) this may be related to the anatomical and functional changes that happen with ageing and worsening of clinical conditions can contribute for this finding. Advanced age is a factor described in different studies as a risk for development of POAF in heart surgeries [19,20].

A large observational study which included 1,039 consecutive patients without a history of AF who underwent AVR with or without simultaneous coronary artery bypass graft at Baylor University Medical Center, Dallas, Texas between January 1, 1997 and December 31, 2006 done by Filardo G et al. [15] Age was one of predictor of incidence of post-operative AF with mean age (74.2 ±9.5, p= 0.001) and they conclude that The incidence of AF increases significantly with age in both the overall population and in post-aortic valve surgery patients [15].

In one study, Goette et al. [21] performed right atrial appendage biopsy on patients who underwent open-heart surgery concluded that Age > 60 years was correlated with a higher degree of fibrosis and a higher incidence of postoperative AF [21]. Another study showed also that age was the only independent predictor of the degree of atrial fibrosis in 115 patients who underwent open-heart surgery [22].

In our study, we did not observe association of other demographic variables and comorbidities with the development of POAF. Differently, results of the Framingham's study suggested an association between sex, hypertension and heart failure with development of AF in community patients. Still, there are evidences that white people have independent risk factor for POAF in isolated CABG [23]. This discrepancy may be attributed to lack of randomization and small sample size in our study.

Echocardiographic parameters

In Our study, 2D and Doppler study showed that there was no statistically significant difference between study groups as shown in Table 4. These findings were concordant with Pernigo

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et. al. which studied sixty patients (71.5 ±7.8 years, 50% men) scheduled for aortic valve replacement for severe isolated aortic stenosis [24] and Pessoa-Amorim et. al. which studied a total of 149 severe aortic stenosis patients (74 ±8.6 years, 51% men) with no prior AF by using speckle-tracking echocardiography [25].

In contrast, a post hoc analysis of a single-center prospective study that evaluate the impact of myocardial fibrosis on outcome after SAVR included a total of 96 patients with severe AS done by Carter-Storch et. al. which found POAF was associated with larger preoperative echocardiographic left atrial volume index (44 ± 12 vs 37 ± 8 ml/m2, P = 0.004) [18].

Also, Osranreek et al. [26] reported that LAVI to be a strong and independent predictor of POAF and LAVI > 32 ml/m2 was associated with a five-fold increase of risk of POAF, independent of age and other risk factor post cardiac surgery [26].

A study done also by Russo et al. [27] they found that increased left atrial volume index were significantly associated with incident AF, with LAVI in AF was (24.0 ± 6.4 vs 30.3±9.0, p <0.001) [27].

Data from the Framingham study suggested that LA enlargement is among the strongest predictors for subsequent development of AF [6]. However, standard M mode and 2-D LA measurements have many limitations in the detection of LA enlargement [28]. LAV is a more reliable index of LA enlargement and has been shown to predict AF occurrence in nonsurgical [29] and unselected cardiac surgery populations [26].

Speckle tracking parameters

Reduced LA reservoir and conduit functions, and reduced or absent booster pump function, are common in patients with AF and are able to predict CV events [30].

Our study utilizes global peak atrial longitudinal strain (PALS) and peak atrial contraction strain (PACS) to predict risk of AF post aortic valve replacement surgery.

The current study found that there was significant difference between POAF and non POAF regarding left atrial speckle tracking data which showed significantly lower LA global PALS (21.92 ±4.28) and PACS (9.42 ±3.0) in POAF group vs. (27.60 ±3.52 and 13.56 ±2.23 for PALS and PACS respectively) in non-POAF group, with p value less than 0.001 (Table 4). LA global PALS of 25.5% and LA global PACS of 10.5% were the best cut off values to predict PAOF.

These findings were consistent with that of Pernigo et. al. which found that PALS had an area under the curve (AUC) of 0.87 ±0.04 (95% CI, 0.76– 0.94), with a cutoff of ≤23% as the best predictor of the end point in the study population. PACS showed an AUC of 0.85 ±0.05 (95% CI, 0.73–0.93), with a cutoff of ≤10% as the best predictor of the end point [24].

This finding was also reported by Kawakami et al. [31] which hypothesized that detection of LA dysfunction and mechanical dispersion using strain echocardiography is useful for predicting new-onset AF. They found that patients with new-onset AF had significantly worse LA contractile strain (16.6% ± 4.3% vs 20.6% ± 4.3%; P < 0.01) and reservoir strain (31.4% ± 7.7% vs 38.0% ± 7.3%; P <.01) than those without AF. They confirmed that LA reservoir strain was independent predictor of new onset AF (AUC; 0.75; 95% CI: 0.63-0.87) [31].

The causes of AF are not fully understood, but structural remodeling with increasing fibrosis of the LA is important in the formation of a substrate for AF. Remodeling of LA is caused by several clinical conditions like hypertension, diabetes, ischemic heart disease, and heart failure. Remodeling reduces the compliance of LA, which leads to impairment of the atrial reservoir function so Atrial reservoir strain is a measure of atrial reservoir function and compliance. So, impaired reservoir strain could be a sign of remodeling of the LA [32].

Kuppahally et al. [33] found a relationship between fibrosis of LA detected by delayed enhancement magnetic resonance imaging (DE-MRI) and reduced atrial reservoir strain in patients diagnosed with AF. Additionally, they discovered that AF appears to contribute to further remodeling of the LA and therefore reservoir strain could be a sign of both the risk of developing AF and sign of damage from AF. Atrial reservoir strain has also been shown to correlate closely to LV end-diastolic pressure, which could also partly explain the association between reservoir strain and AF since elevated end-diastolic pressure is a well-known risk factor for AF [33].

Gasparovic et al. [34] showed that atria exhibiting greater fibrotic and apoptotic burdens had impaired conduit, reservoir and contractile function and suggested that atrial reservoir function might predict atrial fibrosis and apoptosis. Atrial remodeling including increase in interstitial fibrosis and decrease in atrial elasticity may lead to a decline in LA reservoir functions, all of which may contribute to electrical remodeling and POAF development [34].

So, atrial reservoir strain is a more sensitive marker of atrial dysfunction since LAV is known to reflect chronically elevated filling pressure and that enlarged LAV is a sign of more extensive remodeling.

Study Limitation

The major limitation of current study was small sample size and short period of follow up. The current software for LA strain assessed has not been validated, so we had used the software of left ventricle to analysis LA strain. Vendor differences arising from difference edge tracking may affect the cut-off of la strain values. Continuous monitoring was done only in critical care unit but in wards, ECG was done every 12 hours or symptoms appear. So, any undetected or transient episode of AF could be missed. Finally, there was no evaluation of accuracy of LA strain compared with invasive assessment or advanced noninvasive imaging such as cardiac magnetic resonance.

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Conclusion

According to our study conducted on a population of patients with severe isolated AS, the quantification of LA longitudinal strain by means of 2D-STE is feasible and reproducible in clinical practice. Reduced PALS and PACS, relative to atrial reservoir and contraction function, have an independent role in predicting POAF. These findings suggest that speckle-tracking echocardiography before surgery may help in risk stratification & proper management.

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