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PREDICTION OF POST OPERATIVE ATRIAL FIBRILLATION (POAF) IN PATIENTS UNDERGOING OFF-PUMP CORONARY ARTERY BYPASS GRAFTING (OP-CABG) SURGERY BY LEFT ATRIAL STRAIN ANALYSIS; A TRANSESOPHAGEAL ECHOCARDIOGRAPHIC STUDY.

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Abstract;

Introduction; Atrial fibrillation is a common arrhythmia seen after cardiac surgery particularly coronary artery bypass graft surgery. It has significant implications on patient morbidity and mortality. Left atrial contractile dysfunction was one of the major inciting factors in the development of postoperative atrial fibrillation (POAF). Two-dimensional speckle track echocardiography (2-D STE) emerges as a Nobel tool to assess the LA function.

Aim of study; To evaluate the relationship between Peak Atrial Longitudinal Strain (PALS), measured by 2-D STE Analysis through Trans-Esophageal Echocardiography (TEE) with POAF.

Methods; In this study, 50 patients with coronary artery disease (CAD) undergoing off-pump coronary artery bypass graft (OP-CABG) surgery were randomly selected after matching baseline characteristics. Left atrial strain analyses by 2-D STE in Deep Transgastric 5-Chamber view by transesophageal echocardiography (TEE). Peak atrial longitudinal strain (PALS) was calculated. The patient was continuously monitored for 3 consecutive days postoperatively for the development of newly diagnosed atrial fibrillation.

Results; POAF occurs in 16 out of 50 patients (32%). Patients with POAF were older and had lower ejection fraction than those patients who had sinus rhythm after OPCABG surgery. Patients with a decreased value of PALS <28% have a higher incidence of POAF, reduction in PALS reflects impaired atrial function either due to fibrosis or remodelling, which are known contributors to POAF. The odds ratio of POAF with PALS < 28%, is 35.2 which shows a strong correlation between the two.

Conclusion; Perioperative reduced PALS measured by 2D STE analysis is associated with POAF after OPCABG surgery.

Keywords; Atrial Fibrillation, Postoperative Atrial Fibrillation, Speckle Track Echocardiography, Peak Atrial Longitudinal Strain, Peak Atrial Contraction Strain, Conduit Strain.

Introduction;

Cardiac arrhythmia is one of the most common complications after cardiac surgery, particularly atrial fibrillation & supra ventricular tachycardia[1]. The incidence of Post Operative Atrial Fibrillation (POAF) is about 15-40% after cardiac surgery[2].
POAF has a significant impact on hemodynamic instability, ionotropic support, and recovery from ICU. It also causes thromboembolic complications[3] like transient ischemic stroke, which increases morbidity and mortality[4-5]. Structural and functional changes in the left atrium, caused by age, hypertension, volume overload, or pressure overload, lead to increased left atrial volume or fibrosis, significantly raising the risk of developing postoperative atrial fibrillation (POAF). Structural and functional changes in the left atrium, caused by age, hypertension, volume overload, or pressure overload, lead to increased left atrial volume and subsequently atrial fibrosis, significantly raising the risk of developing postoperative atrial fibrillation (POAF)[6-7]. The proposed inciting factor that precipitates POAF following cardiac surgery includes intraoperative ischemia, electrolyte imbalance, increased post-operative sympathetic activity, etc.
Structural and functional changes which lead to significant risk of POAF can be quantified by different parameters like LA diameter, LA volume index, doppler echocardiography, trans-mitral inflow velocity, tissue Doppler imaging, left atrial function index (LAFI), LA strain analysis, etc.[8-9].
Two-dimensional speckle track echocardiography (2-D STE) has evolved as a Nobel tool for assessing LA function, which is angle independent, and free of myocardial tethering[10]. It evaluates myocardial function by analyzing speckles (echogenic spots on myocardium) on the 2-D grayscale ultrasound image of the myocardium. It produces reliable and reproducible results which correspond with Doppler parameters.
The aim of this study was to evaluate the relationship between PALS, measured by 2-D STE Analysis through trans-esophageal echocardiography (TEE) with POAF in patients with CAD undergoing OP-CABG surgery.
We here present a study of 50 patients with coronary artery disease (CAD), undergoing Off-pump coronary artery bypass graft (OP- CABG) surgery, whose LA is assessed peri-operatively by TEE, through LA strain analysis by speckle tracking echocardiography (STE). Which is considered as an independent predictor of POAF. These patients were monitored for the development of POAF after the surgery.

Method;

This prospective, observational, cohort study was done on patients with coronary artery disease (CAD), undergoing off-pump coronary artery bypass graft surgery (OP-CABG) in ABVIMS, Dr RML Hospital, New Delhi, India. 56 patients with CAD planned for OPCABG

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surgery, aged between 20-75 years were randomly enrolled in this study. Patients with ages <20 years and >75 years, previous history of arrhythmia, atrial fibrillation, current use of anti-arrhythmic drugs, concomitant valvular heart disease, low left ventricular ejection fraction < 40%, previous history of cardiac surgery, operation on ascending aorta, history of renal impairment, known hepatic disease, thyroid abnormality, allergy with the local anaesthetic agent were excluded from the study. Also, patients with unfeasible STE Analysis due to poor acoustic window, inadequate tracking of Left atrial border and oesophageal anomaly, prior history of oesophageal surgery, space-occupying lesion in Oro-pharyngeal or oesophageal area, and the patients with any known contraindication for transesophageal echocardiography (TEE) were excluded from this study. 6 patients were excluded from the study due to unfeasible STE analysis because of poor acoustic window.
All study procedures complied with the Declaration of Helsinki protocol for clinical studies.

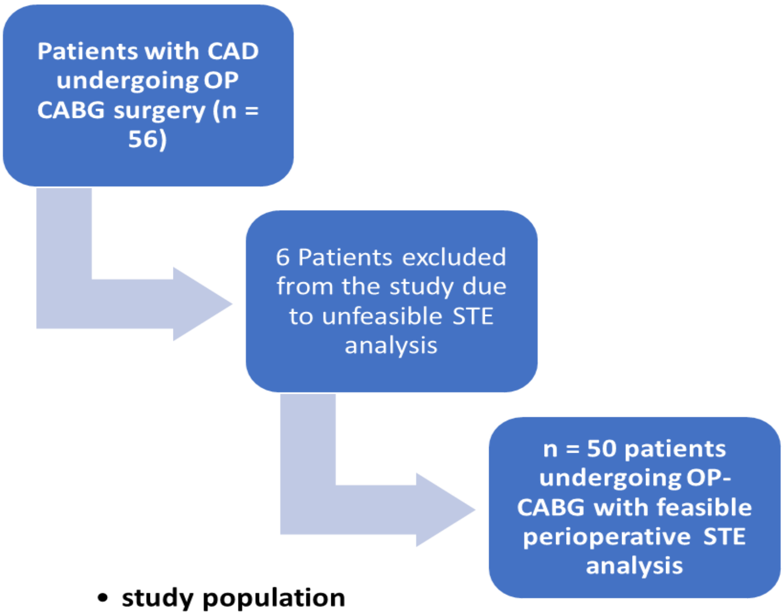

Figure 1 Study Population

In the pre-anesthetic examination, a comprehensive clinical evaluation with all the significant history, cardiovascular risk factors, comorbidities, and medications were documented. Lab Tests including Blood reports (total leucocyte count, differential counts, hemoglobin level, platelet count, electrolytes, glycosylated hemoglobin, blood urea, serum creatinine, TSH level, C-Reactive Protein) 12- lead ECG, chest X-ray, detail coronary angiography for type and extension of coronary artery disease, etc. were recorded. Informed consent was taken for a comprehensive transesophageal echocardiographic (TEE) evaluation.
Monitors as per the American Society of Anesthesiology protocol for CABG surgery were attached and baseline vitals were recorded. All patients were induced and endotracheal intubation was done as per institutional-based protocol. The transesophageal probe is inserted after endotracheal intubation under direct vision with the aid of a direct laryngoscope in a sterile condition. During surgery type of conduits used for grafting (arterial vs venous), the

ISSN:0975 -3583,0976-2833 VOL 16, ISSUE 03, 2025

number of vessels that are grafted, and the duration of cardiac surgery was recorded. After completion of operation patients were followed up for the next 3 days in the Intensive Care Unit (ICU), where continuous ECG was recorded. Any new arrhythmia particularly atrial fibrillation (AF), which was defined as an irregularly irregular rhythm with a fluctuating baseline and no discernible P waves (irregular RR interval). POAF episodes lasting >30 seconds during the postoperative hospital stay that required either pharmacologic or electrical intervention were considered significant and were recorded. Serial ABGs were done for assessment of acid-base status and electrolyte assessment. Inotropic support, invasive blood pressure, and intravascular volume status by CVP monitoring were also recorded.

Trans-oesophageal echocardiography (TEE)

Transesophageal echocardiography (TEE) was performed after endotracheal intubation, during the intraoperative period, according to the American Society of Echocardiography/ European Society of Cardiovascular Imaging recommendations, by an experienced anesthesiologist, using EPIQ Elite 7G PHILIPS (Bothell W A) with X7-2T probe. Speckle tracking analysis was done on deep trans-gastric 5 chamber view, and deep trans-gastric 2 chamber view with ECG gating. 3 to 5 consecutive beats with proper delineation of the LA border with a frame rate of 40-60 frames/sec in 2-Dimensional echocardiography were recorded. STE analysis was performed with the same software that was installed for left ventricle strain analysis. The LA endocardial border was manually adjusted, so that reliable delineation of the region of interest of 6 segments in each view was achieved. Then on running the software using QRS as a starting point, we get peak atrial longitudinal strain (PALS) and peak atrial contraction strain (PACS). PALS is calculated at the end of the reservoir phase, while PACS corresponds to the second peak which is at the beginning of the contraction phase.

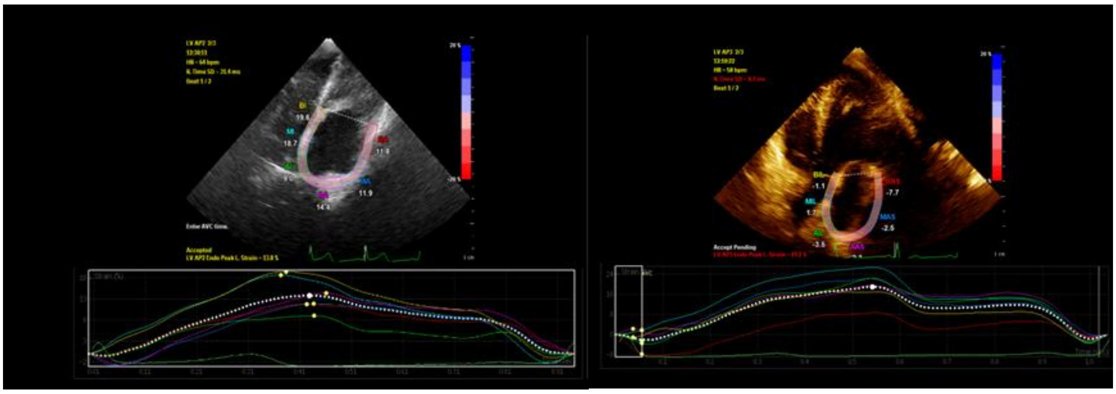

Figure 2 shows strain analysis in deep trans-gastric five-chamber view in TEE

Statistical analysis;

Statistical analyses were performed using the SPSS 20.0 statistical package for Windows (Chicago, IL, USA). The results were presented as mean / SD for continuous variables and frequency (percentage) for categorical variables. We compared demographic variables, medical-related variables, and echocardiographic data between POAF and sinus rhythm groups using the Student t-test for continuous variables and the Fisher’s exact test for categorical variables. $P < 0.05$ was considered statistically significant. The odds ratio is used to evaluate the strength of association between the reduced PALS and POAF.

Results;

56 patients with the same demographic criteria and baseline characteristics were selected for the study but due to difficult Deep Trans gastric 5-Chamber transesophageal echocardiographic image and so, unreliable speckle track imaging (STE), 6 patients were excluded from our study.
50 patients with CAD undergoing CABG surgery were finally included in this study, out of which 16 patients (32%) developed POAF. Demographic characteristics are summarised in Table 1, the mean age of the sample population is 63 ±8, And the prevalence of male gender of 85%
The conventional echocardiographic parameter and STE parameter are summarised in Table 2 on average there is a mild reduction in left ventricular ejection fraction of 55.2% and also reduced global PALS (36 ± 5%) all patients underwent isolated off-pump coronary artery bypass graft surgery. 16 Patients develop atrial fibrillation, at a mean of 1.7 ± 1 days postoperatively. They were treated with anti-arrhythmic agents (amiodarone infusion). As compared with the sample patients who developed POAF were older and also had poor left ventricular ejection fraction. In comparison to STE analysis patients with POAF had reduced global PALS and PACS concerning patients who did not develop POAF. The optimal cutoff value of PALS for the prediction of POAF was < 28% based on a previous study, out of 50 patients, 13 patients had PALS < 28% and 11 among them developed POAF, so the incidence of POAF among Patients with PALS< 28% is 84%. 5 patients with PALS >28% also develops POAF. The odds ratio of POAF with PALS < 28%, is 35.2, p-value of this odd ratio is <0.001 which shows a strong correlation between the two.
Patients with impaired global PALS were older, low ejection fraction, increased left atrium volume, increased e/e' ratio, increased grade of diastolic dysfunction, and increased left ventricular mass. Patients with a decreased value of PALS <28% have a higher incidence of POAF, reduction in PALS reflects impaired atrial function either due to fibrosis or remodelling, which are known contributors of POAF.

ISSN:0975 -3583,0976-2833 VOL 16, ISSUE 03, 2025

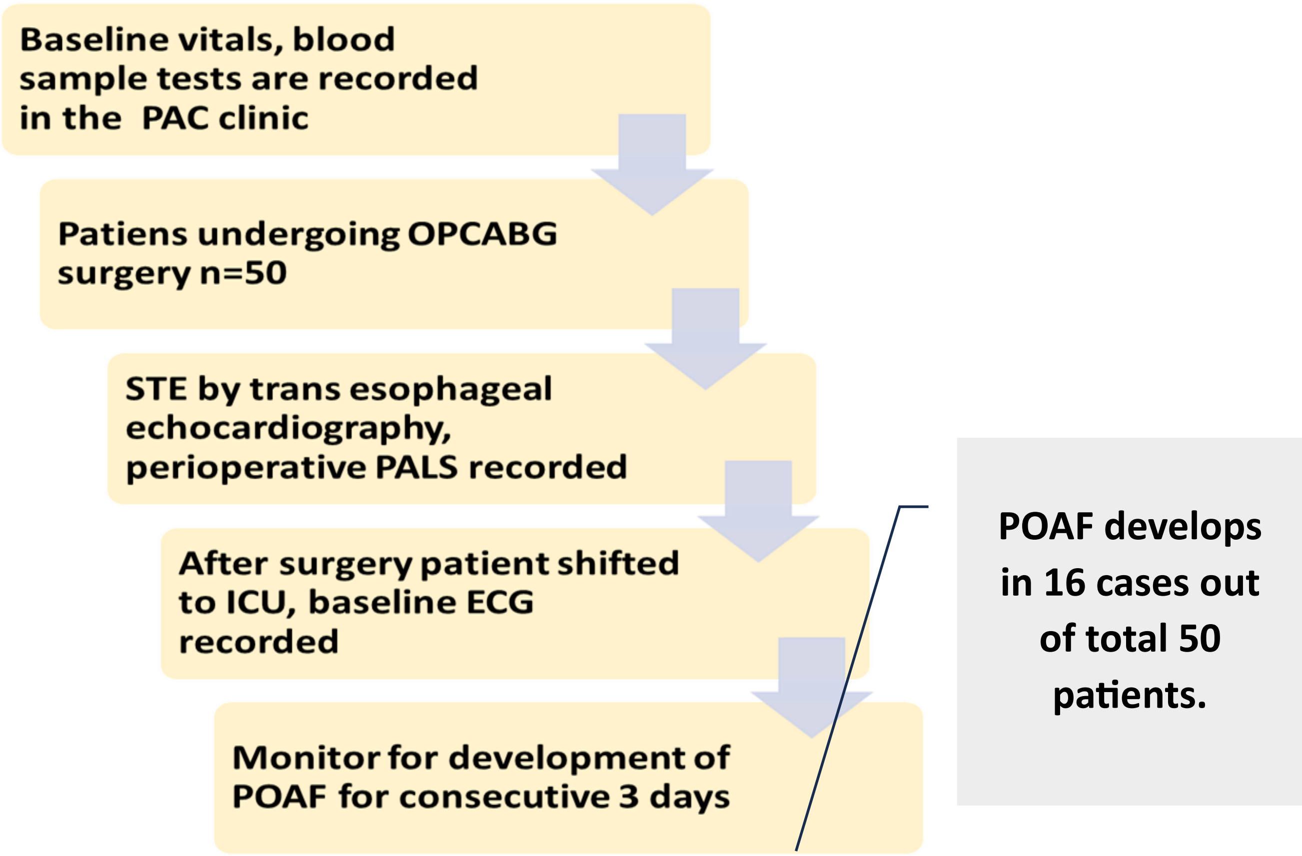

Figure 3

Table 1 Demographic and Clinical characteristics of the study population

	Total case (n=50)	POAF (n=16)	No POAF (n=34)	P value
Age (years)	63	68	61	<0.005
Sex (male)	42	13	39	NA
Sex (female)	8	3	5	NA
Weight (kg)	63.6 ± 7.6	66± 6.2	62± 8.4	NA
Height (cm)	161.8 ± 8.7	166 ± 4.5	158 ± 9.2	NA
Heart rate (per minute)	68 ± 8	76 ± 6	62 ± 4	NA
Systolic blood pressure (mm Hg)	155 ± 10	162 ± 8	153 ± 10	
Diastolic BP (mm Hg)	86 ± 6	90 ± 4	84 ± 6	
H/O hypertension	40	16	34	NA
H/O DM	34	12	22	NA
H/O Dyslipidaemia	50	16	34	NA
H/O Smoking	28	13	15	NA
B Blocker	50	16	34	NA
CCB	10	3	7	NA
Ace Inhibitors	40	12	28	NA
Statins	50	16	34	NA

ISSN:0975 -3583,0976-2833 VOL 16, ISSUE 03, 2025

OHA	34	12	22	NA

Table 2 Echocardiographic parameter of the study population

Echocardiography assessment			
	Total case (n=50)	POAF (n=16)	No POAF (n=34)
Ejection fraction	55.2	52	60
Diastolic dysfunction grade 2 or more	8	8	0
Average E/E' > 15	10	10	0
Global PALS	36 ± 5%	18 ± 4%	38 ± 6%
Regional wall motion abnormality	10	8	2
No of vessels grafted			
TVD/DVD	45/5	16/0	29/5
Lima	50	16	34
Saphenous vein	50	16	34

Discussion;

POAF being one of the most frequent arrhythmias seen after coronary artery bypass graft surgery, with an incidence of 15-40%[11-12], has a multifactorial origin including advanced age, female sex, history of hypertension, atrial myocardial ischemia as a result of atherosclerosis in a left circumflex coronary artery, left ventricular dysfunction, electrolyte imbalance, and increased postoperative sympathetic activity. All these factors influence structural and functional changes in the left atrium leading to increased LA volume and left atrial interstitial fibrosis predisposing the patients to increased risk of POAF[13-14].
POAF is associated with hemodynamic instability, needs high inotropic support, longer ICU stays, and thromboembolic complications[3], which increases morbidity and mortality[4-5]. Villarreal et al. reported an increased incidence of thromboembolic complications and cardiac death in patients developing post-operative AF[11]. Mariscalco et al also found a similar association in their study[15].
So early prediction of patients with a higher risk of POAF is important to start prophylactic management at the earliest to prevent its occurrence. However precise functional assessment of LA is difficult, due to various limitations. Invasive functional assessment of LA is not feasible in many patients. With the advent of advanced echocardiography, like Pulse Doppler, Tissue Doppler, and strain analysis it is feasible to assess LA function. LA function evaluation is a more reliable predictor of POAF after cardiac surgery than LA size and volume i.e. dimension evaluation[16-17].

Various methods to assess LA function, invasive methods like atrial biopsy for assessment of fibrosis, Non-invasive methods like Cardiac MRI, echocardiography for assessment of deformation by STE, annular motion by TDI, etc.[16]

Transmitral A velocity and its velocity time integral, LA ejection force (peak A velocity) is a measure of LA contractile function assessment. Tissue Doppler derived A' velocity is a less load dependent surrogate of LA function. The above methods mandate the presence of sinus rhythm. To overcome this LA function index (LAFI), volumetric measurements like LA ejection fraction and LA expansion index are used to assess LA function in the absence of sinus rhythm[18].

Tissue Doppler imaging is also a reliable method to assess mitral annular systolic motion, hence the LA function[19]. Mitral annular tissue Doppler velocity with a value < 9 cm/sec strongly predicts POAF. However, it has inherent limitations like angle dependency, noise interference, and myocardial tethering.

2D STE by Transesophageal Echocardiography

Strain and strain rate analysis is an emerging concept to evaluate LA function. Various methods to calculate LA strain are tissue Doppler imaging (TDI), velocity vector imaging, and two-dimensional speckle tracking echocardiography (2D-STE). 2-D STE has an added advantage over TDI by its angle independence, decreased noise interference, and tethering effects. Even STE has its limitations like high inter-operator variability, high dependence on the echocardiographic acoustic window, and requirement of high image resolution.[20-21]

Our study, used 2D STE to calculate LA strain, by the same software that was initially developed for LV strain analysis, with the adjustment of change in region of interest. 2D STE tracks speckle patterns (acoustic markers) within serial 2D -B mode sector scan thereby calculating strain and strain rate.

LA has three functions, reservoir function in systole when blood fills the left atrium, as a conduit in early diastole which corresponds to passive filling of left ventricle, and as an active contraction which corresponds to filling of LV in late diastole.

In the reservoir phase, as the left atrium starts filling and volume starts increasing and positive atrial strain also increases which reaches its peak in systole before the opening of the mitral valve, maximum strain at this time (after the reservoir Phase) is peak atrial longitudinal strain (PALS) or **Reservoir strain (Figure 4).** It encompasses the time of left ventricular isovolumic contraction, ejection, and isovolumic relaxation and is calculated as the difference between the strain value at the strain curve peak and end-diastole.

In the conduit phase, the mitral valve opens and the volume of the left atrium decreases, which corresponds to early rapid filling of the left ventricle reaching a plateau just before LA contraction. **Conduit strain is** calculated as the difference between the strain value at the onset of atrial contraction and the peak value of the curve **(Figure 4)**.

The next deflection in the strain curve is at the time of active atrial contraction, which pushes blood from LA to LV actively. Peak atrial contraction strain (PACS) is measured following the P wave of ECG, corresponding to active atrial contraction. **Contraction strain** starts from the onset of LA contraction until the end diastole in patients with sinus rhythm and is therefore calculated as the difference between the strain value at the end diastole (by definition zero) and the value at the onset of atrial contraction **(Figure 4)**.

ISSN:0975 -3583,0976-2833 VOL 16, ISSUE 03, 2025

LA strain curve has two patterns based on the time in the cardiac cycle at which software processing starts. Atrial cycle or diastolic gating, strain processing starts at the P wave. Ventricular cycle or systolic gating when software processing starts at QRS wave. Reference zero is based on the gating.

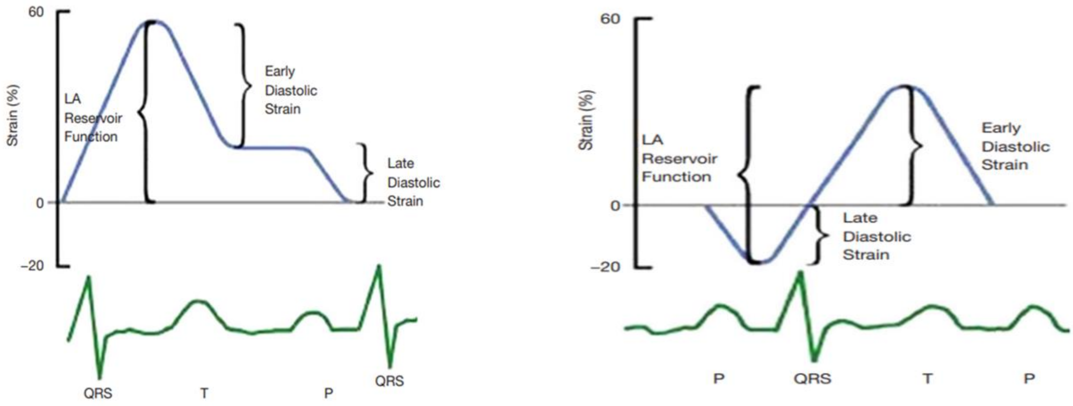

Figure 4 shows reservoir strain, conduit strain, and contraction strain based on Systolic gating and diastolic gating respectively.

In a multicentre study involving 329 healthy subjects, Morris et al. reported LA systolic strain (i.e., PALS) to be 45.5%±11.4% and LA strain rate during late diastole (i.e., PACS) to be −2.11±0.61 s-1. The lowest expected values (using mean −2 SD) were 23.1 % for LA systolic strain and −0.91 s-1 for A sr in late diastole [22-23].

Patients having a preoperative reduction in PALS show an increased incidence of POAF. Kislitsina Olga N et al showed a positive correlation between preoperative PALS and POAF[28]**Error! Bookmark not defined.**. While Pastore M C et al in their multicentric study postulated a pre-surgical global PALS < 28% to be associated with POAF. Our study showed an acceptable, reliable, and reproducible association between new onset POAF and a PALS value of < 28%[24-25] in patients with CAD undergoing off-pump CABG surgery. We also observed a strong correlation between decreased global longitudinal strain by 2D STE and POAF after OP-CABG surgery. Reduced strain is either due to atrial interstitial fibrosis or remodelling due to chronic pressure or volume overload. Which is a known contributor to POAF [26-29].

Limitations:

Limitations of this study include small sample size, Single institutional study, Follow-up for less duration (3 days), Type (Arterial vs Venous) and patency of graft after surgery, Ischemia during the perioperative period, Anti-arrhythmic therapy during the intraoperative period, multiple operating surgeons and their approach, and requirement of Sophisticated software and non-availability of software for LA Strain analysis.

ISSN:0975 -3583,0976-2833 VOL 16, ISSUE 03, 2025

Conclusion;

LA dysfunction is assessed by global longitudinal strain, PALS, and strain rate through STE to provide accessible, feasible, and reproducible results[30]. Our study shows Global PALS <28% is a strong predictor of POAF in patients of CAD undergoing OPCABG surgery. So, more attention should be paid to preventive strategies in patients who have increased clinical risk factors and positive echocardiographic predictors of POAF.

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