ORIGINAL RESEARCH PAPER

Cardiology

TISSUE DOPPLER VELOCITY IMAGING OF LEFT ATRIAL APPENDAGE FUNCTION IN PATIENTS WITH MITRAL STENOSIS

KEY WORDS: Eptb, Rntcp, Vitamin D Deficiency

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ABSTRACT

AIM OF THE STUDY

The most widely accepted method for assessing the left atrial appendage (LAA) function is the measurement of left atrial appendage late peak emptying velocity (LAAEV) by using pulse wave Doppler (PWD) on Transesophageal echocardiography (TEE) and reduced left atrial appendage late peak emptying velocity represents left atrial appendage dysfunction. The magnitude and pattern of left atrial appendage flow velocities are dependent on acute changes in loading conditions. Left atrial appendage flow velocities may also be affected by left atrial appendage size and morphology which are highly variable.

Myocardial velocities obtained by Tissue Doppler imaging (TDI) are less dependent on preload and left atrial appendage (LAA) tissue velocities may help in more accurate risk prediction. The aim of the study is to

(1) To asses Left Atrial appendage late peak Emptying Velocty (LAAEV) and Left Atrial appendage late peak Filling flow Velocty (LAAFV) by using Pulse Doppler imaging in Trans esophageal echocardiography (TEE)

(2) To asses Left Atrial appendage late peak Systolic tissue velocity (LSV) and Left Atrial appendage late peak Diastolic Velocty (LDV) by using Tissue Doppler imaging in Trans esophageal echocardiography (TEE)

(3) To correlate left atrial Spontaneous Echo Contrast (SEC) and thrombus with Left Atrial appendage late peak Systolic tissue velocity (LSV) and Left Atrial appendage late peak Emptying Velocty (LAAEV)

MATERIAL AND METHODS

This study was performed in the Department of Cardiology, Government General Hospital, Chennai, during the year 2006–2009. The study is a prospective case control study involving 48 patients.

STUDY GROUP SELECTION:

Ethical committee clearance was obtained to conduct the study in our hospital.

All subjects provided written informed consent to participate in the study before inclusion.

Inclusion Criteria:

1. Patients with isolated mitral stenosis
2. No significant other (more than mild) valve lesion.(except tricuspid regurgitation secondary to pulmonary hypertension)
3. NYHA Class I-III status

Exclusion Criteria:

1. Patients with NYHA Class IV status
2. Significant other (more than mild) valve lesion
3. Significant co-morbid conditions.
4. Previous cardiac surgery including closed mitral commissurotomy
5. Pregnancy and puerparium
6. Patients with hypertension, diabetesmellitus, evidence of coronary artery disease. The controls were with age and sex matched who underwent TEE due to suspicion of various cardiac diseases and had normal TEE examination

1. Patient characteristics:

The study population included 48 patients (35 male and 13 female) who attended the outpatient department Govt. General Hospital, Chennai-3, the patients were divided into two groups: Group 1 – Patients with sinus rhythm and LAAEV >25 cm/sec (n = 20) Group 2 – Patients with sinus rhythm and LAAEV <25 cm/sec (n = 16)

Group 3–Patients with atrial fibrillation (n=9)

A complete Transthoracic echocardiogram was obtained including M- mode, 2D, colour Doppler and pulse& continuous wave Doppler in every patient. PHILIPS ie33 echo machine is used for this study. A 2.5 MHZ probe is used for transthoracic echocardiography and a 5 MHZ multiplane probe is used for transesophageal echocardiography. Lesion severity in individual valve was characterised by various methods.

Specific attentions were paid in assessing mitral valve morphology, Wilkinson's scoring, and mitral valve area by planimetry & pressure half time method, peak and mean transmitral gradient.

Left ventricular ejection fraction (EF) was calculated by using modified Simpson's technique. M-mode echocardiograms at mitral & aortic valve level were obtained routinely for measurement.

Left atrial dimensions were measured in end systole in PLAX-antero posterior and two orthogonal diameters in four chamber view and left atrial volume calculated by using prolate ellipse method. Left atrial volume = (DI X D2 X D3) X 0.523

Left atrial appendage was visualised in PSAX view at aortic valve level and LAA thrombus is characterized by measuring its major and minor dimensions. A focused transoesophageal echocardiogram was obtained for all patients.

Transesophageal echocardiography is a very accurate technique to interrogate the left atrium for thrombi. Multiple views are used to visualise the entire left atrium for identifying evidence of thrombi. Specific attention was given to left atrial appendage from variety of planes, the appendage can be easily

visualised. It lies just below the left upper pulmonary vein and is separated from the vein by a ridge of tissue.

Care was taken to distinguish normal trabeculation from localised thrombus formation.Trabeculae tend to be more linear and are continuous with the atrial wall in more than one view.Thrombi typically protrude into the appendage, often with independent motion.

Once visualised thrombi is assessed for size, mobility and whether it extends to body of the left atrium.

Size of the thrombus is measured as major and minor dimensions.

LA appendage area in diastole & systole were measured and LAA ejection fraction calculated using formula;

LAA EF (%) = (LAA.max -LAA .min)/LAA. max X 100 LAA.max- Maximal LAA area (end atrial diastole), LAA.Min.- Minimum area (end atrial systole)- by planimetry.

Left atrial appendage function is assessed using pulsed Doppler imaging, with sample volume positioned at mouth of the appendage; the maximal velocity during atrial contraction is measured. This velocity corresponds to the force of atrial appendage contraction or emptying.

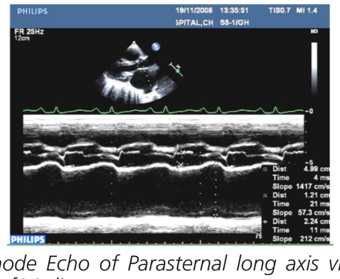
Pulmonary venous pulsed wave Doppler was obtained from left upper lobe pulmonary vein. Entire left atrium was searched for thrombus and specific note was made on mitral valve morphology and left atrial spontaneous echo contrast.

Transesophageal echocardiography. Multiplane TEE was performed in all subjects. The presence of SEC and thrombi were examined with appropriate gain setting to avoid noise artifacts. SEC was diagnosed by the presence of dynamic smoke like echoes in the left atria (LA) cavity and LA appendage with a characteristic swirling motion . The severity of SEC was graded from 0 to 4+.

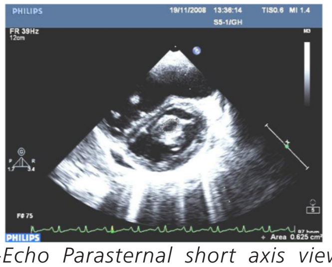
The LAA flow profiles were obtained by placing the sample volume of the PWD into the orifices of the appendage. LAAEV and filling (LAAFV) velocities were recorded. LAAEV and LAAFV were averaged for six consecutive cardiac cycles.

LAA tissue Doppler recordings were performed by the sample volume of PWD placed on LAA lateral wall .In cases with quadriphasic wave pattern, LAA late peak systolic wave (LSV,the positive wave observed after the P wave) and late peak diastolic wave (LDV , the negative wave following LSV) velocities were recorded .In patients with sinus rhythm and biphasic wave pattern or atrial fibrillation (AF) , positive and negative wave velocities were accepted as LSV and LDV, respectively. LSV and LDV were averaged for six consecutive cardiac cycles.

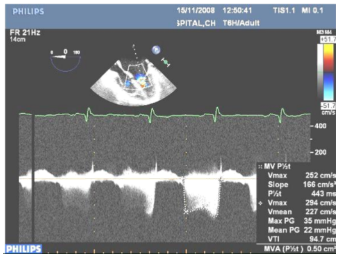
All patients received standard medical treatment with, Digoxin, Penicillin, KCL syrup, Verapamil, Dieuretics and other drugs as clinical condition warrants.



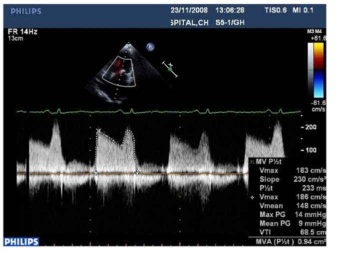
Picture-1 M-mode Echo of Parasternal long axis view showing measurement of LA diameter



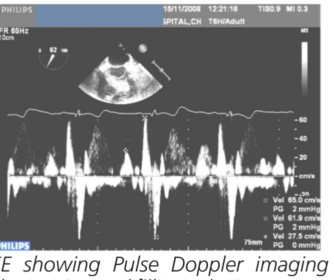
Picture-2 2D-Echo Parasternal short axis view showing measurement of Mitral valve annulus.



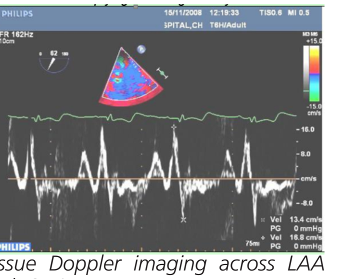
Picture-3 TEE 2D Echo continuous wave Doppler flow across mitral valve showing mitral valve gradient.



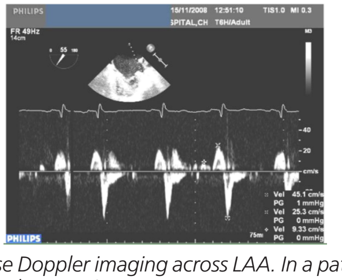
Picture-4 – TTE 2D echo continuous wave Doppler across mitral valve showing MV gradient.



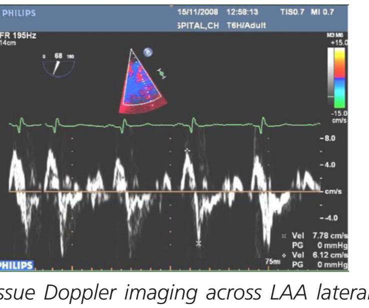
Picture 5 – TEE showing Pulse Doppler imaging across LAA showing normal emptying and filling velocity.



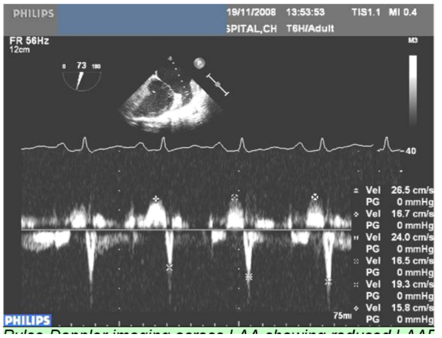
Picture 6 – Tissue Doppler imaging across LAA lateral wall, showing reduced LSV & LDV.



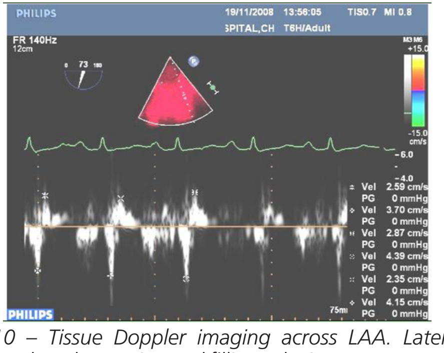
Picture-7 – Pulse Doppler imaging across LAA. In a patient with AF showing reduced LAAEV & LAAFV



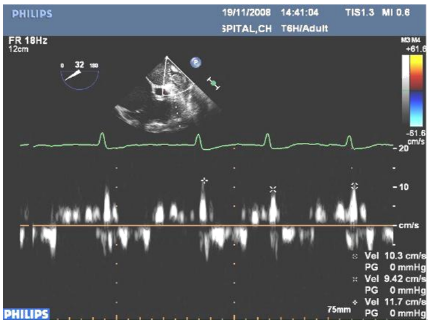
Picture-8 – Tissue Doppler imaging across LAA lateral wall in a patient with AF



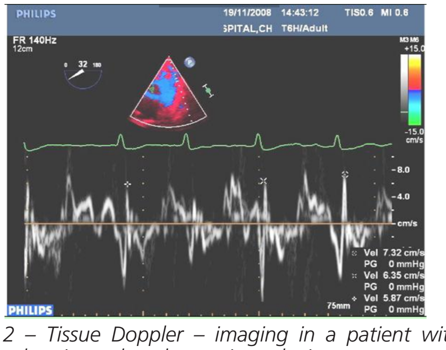
Picture-9 – Pulse Doppler imaging across LAA showing reduced LAAEV & LAAFV



Picture-10 – Tissue Doppler imaging across LAA. Lateral wall showing reduced emptying and filling velocity.



Picture-11 – Pulse Doppler imaging in a patient with LAA thrombus showing reduced systolic velocity



Picture-12 – Tissue Doppler – imaging in a patient with LAA thrombus showing reduced emptying velocity

STATISTICAL ANALYSIS

All calculations were performed with Statistical Package for the Social Sciences 10. Continuous variables were expressed as mean value +/- SD and compaired with the unpaired Student's t – test. Categorical variables were tested with the chi – square test. Person correlation analysis was used to establish the association between SEC density and LAAEV and LSV. A receiver operator characteristic (ROC) curve analysis was performed to identify the optimal cutoff point of LAAEV and LSV to discriminate between patients with and without thromboembolic events. The area under the curve value was calculated. Multivariate logistic regression analysis was used to identify the independent determinants of thromboembolic events. Age ,rhythm , EF , LA dimension , MVA , SEC , thrombus , LAAEV , LAAFV , LSV ,and LDV were selected in the multivariate model.

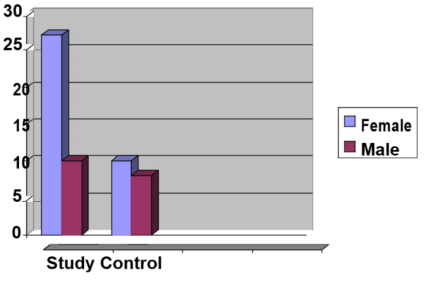
RESULTS

Clinical and Echocardiographic Characteristics of the Patients and the Controls.

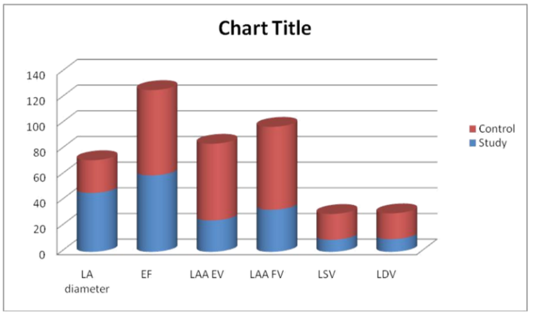
Table I shows the Clinical and Echocardiographic Characteristics of the Patients and the Controls

Table-i:clinical And Echocardiographic Characteristics Of The Patients And Controls

	Controls	*Patients*	*P*	
	n=(18)	*n=(48)*		
Age(years)	35.1	± 3.8	30.83 ± 3.8	
Gender(F/M)	10/8		27/13	
EF(%)	66.4	± 2.1	59.6 ± 2.8	<0.001
LA diameter(mm)	25.1	± 1.24	45.9 ± 3.0	<0.001
LAAEV(cm/sec)	59.7	± 5.0	24.5 ± 5.1	<0.001
LAAFV(cm/sec)	64.6	± 5.7	32.8 ± 5.0	<0.001
LSV (cm/sec)	20.1	± 1.7	9.4 ± 1.9	<0.001
LDV(cm/sec)	20.1 ± 3.3	9.9 ± 1.8	<0.001	
Thrombus	(0.0)	9(18.7)	<0.001	
SEC	(0.0)	26(56.5)	<0.001	



Echocardiographic Characteristics of the Patients and Controls



The mean MVA was 1.28 +/- 0.32 cm2 in patients. 12 patients had AF and 7 had thromboembolic events (stroke in6, one patient had TIA). Thromboembolic events had occured 5.0 +/- 4 months before TEE examination .The patients had larger LA size and lower LAAEV, LAAFV, LSV, and LDV than controls. However, age, gender, and EF were similar. Thrombus and SEC were detected in 9(18.7%) and 26 (56.5%) patients, respectively.

Table-2 Clinical and Echocardiographic Characteristics of the Patients and Groups

	Group I	*Group II*	*Group III*	*P 1*	*P 2*	*P 3*
	n=(20)	*n=(16)*	*n=(12)*			
Age(years)	30.4±3.4	31± 3.2	29±2.5			
Gender(F/M)	14/6	12/4	9/3			
Thromboemb olic	0(0)	3(18)	4(33)		<0.001	
events					<0.001	0.5
EF(%)						
	58.7±2.4	59.6±3.3	60.2±2.6	0.006	<0.001	0.02

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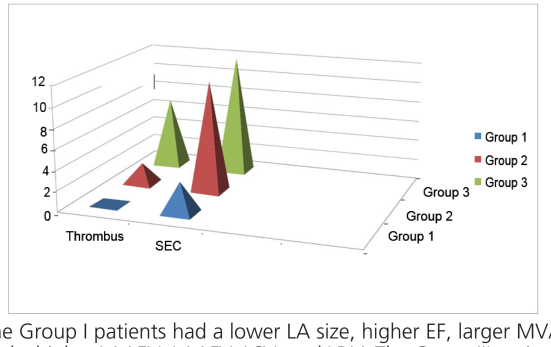
LA diameter(mm)	43.5±2.2	46.2±3.1	45.4±2.4	0.009	<0.001	0.9
MVA(sq.cm)	1.4±0.4	1.2±0.32	0.8±0.27	<0.001	<0.001	0.2
LAAEV(cm/sec)	34.3±5.2	19.6±4.4	14.2±3.1	<0.001	<0.001	0.1
LAAFV(cm/sec)	39.5±4.2	23±3.6	19.4±3.3	<0.001	<0.001	0.03
LSV (cm/sec)	12.4±	9.0±1.7	5.8±1.9	<0.001	<0.001	<0.05
LDV(cm/sec)						
Thrombus	12±1.6	9.1±1.4	7.2±1.0	0.002	<0.001	

SEC	0(0.0)	2(12)	7(58)	<0.001
	3(29.0)	11(68.7)	12(100)	<0.001

Echocardiographic Characteristics of the PatientGroups



The Group I patients had a lower LA size, higher EF, larger MVA, and a higher LAAEV, LAAFV, LSV, and LDV. The Group III patients had higher thromboembolic events, larger LA size, lower LSV and LDV, and higher frequency of thrombus and SEC than the other groups. MVA, EF, LAAEV, and LAAFV were similar in Group II and III.

SEC was observed in 29% of Group I patients, whereas it was not detected in 31.3% of Group II patients. Both LAAEV and LSV were decreasing, while the SEC frequency and density were increasing from Group I to Group III. SEC was strongly correlated with LSV (p<0.001), whereas weakly correlated with LAAEV (p=0.01)

Table-3 Comparison of Patients with and without Thromboe mbolic Events

	With out Embolic	**With Embolic**			
	Events. n=(41)	**Events. n=(7)**	**P**		
Age(years)	30.1 ± 3.3	29	±	3.2	
AF	7(17)	5(71)		<0.001	
EF (%)	60.5 ± 2.6	58.9 ± 2.4	0.02		
LA diameter(mm)	44.2 ± 3.3	48.9 ± 3.4	0.01		
MVA(sq.cm)	1.2 ± 0.34	0.9	±	0.26	0.001
LAAEV(cm/sec)	29.5 ± 5.8	14	± 5.3	<0.001	
LAAFV(cm/sec)	33.8 ± 5.2	22	± 4.5	<0.001	
LSV(cm/sec)	12.4 ± 1.8	8.4	±	1.4	<0.001
LDV(cm/sec)	11.7 ± 1.2	7.5	±	2.0	<0.001
Thrombus	5(12)	4(57)		<0.001	
SEC	19(46)	7(100)	<0.001		

Table-4. The independent determinants of thromboembolic events

Variables	***P***	***Odds ratio***	***95% CI***
Age	0.2	1.2	0.94-1.47
AF	0.3	1.9	0.74-13.03
EF	0.7	0.9	0.62-1.27
LA dimension	0.5	1.03	0.87-1.22
MVA	0.1	0.01	0.00-4.34
SEC	0.01	2.7	1.26-16.85
Thrombus	0.4	2.1	0.61-10.71
LAAEV	0.08	0.7	0.41-1.94
LAAFV	0.1	0.8	0.61-1.24
LSV	0.003	0.2	0.08-0.58
LDV	0.2	0.7	0.54-1.32

The patients with thromboembolic events were older and had a higher incidence of AF, lower EF, larger LA size, and smaller MVA.They also had significantly higher incidence of SEC and thrombus and a lower LAAEV, LAAFV, LSV and LDV .LAA function is more depressed among patients with embolic events. Multivariate logistic regression analysis showed that LSV and the presence of SEC were independently associated with thromboembolic events.

ROC curve analysis was performed to evaluate the clinical usefulness of LAAEV and LSV for discrimination between patients with and without thrombo embolic events .The area under the curve was higher for LSV than LAAEV. The cutoff value of LSV was 7.0 cm/s for the patients with thrombo embolic events with a sensitivity of 95.0% and a specificity of 91.2%.

DISCUSSION

Thromboembolic events are the most important complications in patients with MS .The incidence vary from 10% to 20%. The LAA is the commonest site of thrombus formation in MS .LAA is a highly dynamic structure and prevents stasis in healthy subjects, but when the LAA function impairs, stasis increases, which leads to formation of SEC and /or thrombus. However, LAA dysfunction is one of the most important risk factors for systemic embolization.

Today Doppler transesophageal echocardiography is mostly used to assess the LAA function. LAAEV by PWD reflects the LAA function and the value of LAAEV < 25 cm is generally accepted as a LAA dysfunction. However the measurement of LAAEV is an indirect sign of LAA contraction and influenced by different extrinsic factors, such as left atrial volume, pulmonary venous flow, the left ventricular diastolic filling properties, and LAA size and morphology. Hoit et al also reported that the magnitude and pattern of LAA flow velocities are dependent on acute changes in loading conditions.One of the most important findings of LAA dysfunction is the presence of SEC.

Previous studies showed that some patients have LAA dysfunction and an increased risk of SEC and thrombus formation independent of low velocities detected by standard Doppler. Daimee et al found that 23% of the patients with normal LAA function(LAAEV>25 cm/s) had SEC and 46% of patients with LAA dysfunction(LAAEV <25 cm/s) had no SEC.In our study,SEC was found in 29.0% of the patients with LAAEV > 25 cm/s,whereas it was not detected in 31.3% of the patients with LAAEV < 25 cm/s.Beside,on these findings,LAAEV may not accurately reflect the LAA function.So the additional parameters are needed for accurate assessment of LAA function.

Myocardial velocities obtained by TDI are less dependent on preload and recent studies showed that the LAA contractile functions can be evaluated by using TDI. LSV and LDV correspond with active LAA contraction and relaxation,respectively. Eryol et al reported that the decreased LSV was an independent predictor of an impaired LAA systolic function in patients with MS.They suggested that LSV provides a reproducible parameter for quantification of LAA systolic function.One of the most important findings of LAA systolic dysfunction is the presence of SEC .Ozer et al demonstrated that LSV was a better predictor of SEC than LAAEV in nonvalvular AF. In our study,LSV was significantly reduced in patients compared to the controls and strongly correlated with the density of SEC,whereas,LAAEV was weakly correlated with the density of SEC.

Accurate evaluation of Left Atrial Appendage function can provide better thromboembolic risk estimation and opportunity of treatment,such as anticoagulant therapy.Previous studies suggested that standard Doppler method had a potential limitation in predicting the risk of thromboembolism.But the relation between LAA tissue velocities and thromboembolic events has not been clearly shown.In our study,multivariate regression analysis showed that LSV was independently associated with thromboembolic events.The cutoff value of LSV obtained by ROC curve analysis was 7.0 cm/s for patients with thromboembolic events with a sensitivity of 95.0% and a specificity of 91.2%.

CONCLUSION

- Left Atrial Appendage function is depressed in patients with mitral stenosis as assessed by Left Atrial Appendage late peak

Emptying Velocity and Left Atrial Appendage late peak Systolic velocity.
- The deterioration of Left Atrial Appendage function is more prominent among patients with Atrial fibrillation and those with embolic events.
- Left Atrial Appendage late peak Systolic velocity as assessed by Tissue Doppler imaging seems to be more reliable than Left Atrial Appendage late peak Emptying Velocity assessed with Pulse Doppler imaging in assessing Left Atrial Appendage function.
- Left Atrial Appendage late peak Systolic velocity is a useful parameter in evaluating Left Atrial Appendage function in patients with mitral stenosis.

GLOSSARY AND ACRONYMS

TEE- Trans esophageal echocardiogram.
TTE- Trans thoracic echocardiogram. LAAEV- Left Atrial Appendage late peak Emptying Velocity LAAFV - Left Atrial Appendage late peak Filling Velocity LSV-Left Atrial Appendage late peak Systolic velocity LDV- Left Atrial Appendage late peak Diastolic velocity LAASEC-Left atrial appendage spontaneous echo contrast TDI - Tissue Doppler imaging .
TEE-Transesophageal echocardiography .
LA = Left atrial;
LVEDV = Left ventricular end-diastolic volume;
LVESV = Left ventricular end-systolic volume;

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