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Value of Global Left Ventricular Strain Using 2D Speckle Tracking for Prediction of Adverse Events in Severe Asymptomatic Aortic Valve Stenosis

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ABSTRACT

Background: Calcific aortic stenosis (AS) is the most common form of valvular heart disease in developed countries. Patients with severe aortic stenosis and a preserved LV ejection fraction have impaired global longitudinal strain (GLS).

Objective: This study aimed toassess the prognostic value of global left ventricular strain using 2-dimensional speckle tracking for patients with severe asymptomatic aortic stenosis and its correlation with appearance of symptoms and or major adverse cardiovascular events (MACE).

Patients and Methods:A total 160 patients were included in this observational study,80 patients with isolated senile degenerative severe aortic valve stenosis, all patients were asymptomatic at the beginning of the study and furthermore, we subdivided the patient group into 2 subgroups: patients who developed symptoms and those who remained asymptomatic.

80 normal healthy age and sex matched subjects. All subjects were evaluated by history taking, clinical examination, routine laboratory investigations and a 12-lead ECG. Conventional echo was performed on all patients to assess left ventricular function and aortic valve parameters. Peak systolic strain was measured from the mean strain profile for a total of 17 segments of the left ventricle for the longitudinal strain, then Global longitudinal strain was calculated separately as the average of the sum of the studied segments. All patients were followed up clinically and the development of any symptom of the cardinal symptoms of aortic stenosis was recorded.

Results: By comparing the global longitudinal strain in the two groups, the mean GLS in the patient group was -18.70 ± 2.08 % ranging from -23 to -15 % and in the control group the mean GLS was -22.50 ± 1.13 % ranging from -24 to -21 %, showing statistical significance between both groups. The mean GLS in the subgroup of patients who developed symptoms was -17.81 ± 1.10 % ranging from - 19.0 – -15.0 % and the mean GLS in the subgroup of patients who remained asymptomatic was -21.78 ± 1.66 % ranging from -23 to -18 %, there was a statistical significance between both subgroups.

Conclusion: Asymptomatic severe aortic stenosis is not always as benign as it seems to be and although severe aortic stenosis may remain silent for a long period, life expectancy is seriously reduced after development of symptoms. Global Longitudinal strain (GLS) can be used in assessment of severe AS due to its robust diagnostic and prognostic values over standard echocardiography.

Keywords: Global Left Ventricular Strain, 2D Speckle Tracking, Aortic Valve Stenosis.

INTRODUCTION

Aortic stenosis (AS) is the most common form of valvular heart disease ,in general about 25% of people aged over 65 have aortic valve thickening and 3% aged over 75 have severe stenosis**(1)**

Rheumatic heart disease is still the most common cause of aortic valve stenosis worldwide, although degenerative calcific aortic valve stenosis is the most common cause in Europe ,congenital bicuspid aortic stenosis is also an important etiology that affects ~2% of population**(2)**

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The early lesions of calcific degenerative disease resemble coronary artery atheroma and many of the risk factors for aortic stenosis are common to other atherosclerotic processes such as aging , smoking and dyslipidemia**(3).**

The main effect of aortic valve stenosis is on the left ventricle(LV) due to pressure overload whichcausesLVremodeling, then hypertrophy and ultimately cavity dilatation develops**(4).**

Left ventricular mass is only moderately related to the aortic gradient and also affected by gender and genetic factors**(5)**.

Severe AS remains asymptomatic for many years and the risk of death is then <1% per year. Once spontaneous symptoms develop, mortality rises sharply and the median survival is 4.5 years with exertional chest pain, 2.6 years with exertional dizziness, and 1 year with overt heart failure. Survival is particularly poor, 20% at 3 years, in the presence of New York Heart Association Class III or IV (NYHA III or IV) symptoms and an impaired LV systolic function**(6)**

Echocardiographic findings of severe aortic valve stenosis are aortic valve area (AVA) less than 1 $cm^{2,}$ peak velocity more than 4 m/secand mean gradient more than 40mmHg**(7).**

Previous studies have demonstrated that patients with severe aortic stenosis and a preserved LV ejection fraction have impaired global longitudinal strain (GLS) and that the impairment of GLS improves after aortic valve replacement**(8).**

AIM OF THE STUDY

This study aimed to assess the prognostic value of global left ventricular strain using 2-dimensional speckle tracking for patients with severe asymptomatic aortic stenosis and its correlation with appearance of symptoms and or major adverse cardiovascular events (MACE).

PATIENTS AND METHODS

This observational study was conducted at Cardiology Department in El Agouza Police hospital.A total 160 patients were included in this case control study, 80 patients with isolated senile degenerative severe aortic valve stenosis, all patients were asymptomatic at the beginning of the study and furthermore, we subdivided the patient group into 2 subgroups: patients who developed symptoms and those who remained asymptomatic.80 normal healthy age and sex matched subjects.

Inclusion criteria:

1. Age more than or equal 50 years.
2. Isolated severe aortic stenosis: aortic valve area (AVA) less than 1 cm2, peak velocity more than 4 m/sec and mean gradient more than 40mmHg**(31)**
3. Ejection fraction >50%.
4. Sinus Rhythm.

Exclusion criteria :

1. Significant valvular heart disease other than aortic valve.
2. Rheumatic heart disease.
3. Poor echocardiographic windows.
4. Presence of other co-morbidities (severe renal impairment, advanced liver disease or chronic obstructive pulmonary disease).
5. Hypertensive left ventricular hypertrophy.
6. Bicuspid aortic valve stenosis.
7. Diabetic
8. Hypertensive

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9. Other systemic disease
10. Smoker
11. Hyperlipidaemia.

Ethical considerations:

All the participants have been requested to sign a written informed consent regarding the procedures according to the study protocol and no harm to the patients would be allowed.

All included subjects were submitted to the following:

A. Clinical Data:

- Age, gender and family history of the patient.
- Full past history
- Special habits (tobacco use /alcohol intake) - (current, former or non-smoker).
- Full clinical assessment.
- 12 –lead electrocardiogram (ECG) data analysis.
- Routine laboratory data including hemoglobin and renal functions.

B. Echocardiography Details:

Conventional 2-dimensional echocardiography has been performed using commercially available equipment. LV ejection fraction were determined by biplane Simpson's method,**(9)** measurements of LV diastolic filling includeed E/A ratio**(10).**

In addition, tissue Doppler echocardiography were performed with the peak early diastolic velocity (E') measured at the basal septal segment in the apical 4-chmber view and the E/E' ratio has been calculated**(11)**.The maximum transaortic pressure gradient has been calculated using the Bernoulli equation, and mean transaortic pressure gradient was calculated by averaging the instantaneous gradients over the ejection period on the continuous wave Doppler recordings**(12)**

The aortic valve area was calculated with the continuity equation. **(13, 14)**

C. 2D Speckle tracking:

Two-dimensional speckle trackingstrain analysis was performed offline by using a commercially available program (QLAB 8). The Longitudinal strain was obtained from the apical 4-chamber, 2-chamber, and long-axis views in a 17-segment LV model**(15, 16)** . If 2 or more segments were inadequately tracked, we excluded the data because the images were not useable for speckle-tracking analysis**(17)** subsequently, peak longitudinal strain of the studied segments was averaged to obtain the GLS.

D. Follow up Data:

This included the follow up of the patients for six months regarding:

1. Development of symptoms (syncope, dyspnea, chest pain) in outpatient clinic.
2. Hospital admissions.
3. Causes of hospital admission.

Statistical Analysis

Data collected throughout history, clinical examination and laboratory investigations. The outcome measures coded, entered and analysed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X2). Differences between quantitative independent groups by t test, correlation by Pearson's correlation. P value was set at <0.05 for significant results &<0.001 for high significant results.

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RESULTS

In the patient group38 (47.5%) were females and 42(52.5%) were males while in the control group 34 (42.5%) subjects were females and 46 (57.5%) were male.In the patient group the mean age was 72.83± 4.33 years old ranged from 66to 84 years, while in control group it was 74.01 ± 4.01 ranged from 66 to 82 years. There was no significant difference between both groups regarding age and sex.

Table 1 showed that there was a statistical difference between different groups as regard all basic echo data except PWD and E/E'.

Table 2 showed that the mean GLS in the patient group was -18.70 ± 2.08 % ranging from -23 to -15 % and in the control group the mean GLS was -22.50 ± 1.13 % ranging from -24 to -21 %. There was a statistical significance between different groups as regard GLS.

Table 3 showed that among the patient group, out of 80 patients 62 (77.5%) patients developed symptoms and 18 (22.5%) patients remained asymptomatic.

Table 4and figure 1 showed Roc analysis which was performed for GLS in the prediction of adverse events in asymptomatic severe aortic stenosis it showed an excellent AUC 0.946 with a confidence interval ranging from 0.872 – 1.020 (P value < 0.001). The best cut off point was > - 19 at which sensitivity and specificity were 70.97, 88.89 respectively.

Table 5 showed that within the patient group, the mean GLS in the group of patients who developed symptoms was -17.81 ± 1.10 % ranging from - 19.0 – -15.0 % and the mean GLS in the group of patients who remained asymptomatic was -21.78 ± 1.66 % ranging from -23 to -18 %.There was a statistical significance between different groups as regard GLS.

Table 6 showed when performing both univariate and multivariate logistic regression analysis to estimate the effects of several parameters in the development of adverse events in patients group.In univariate analysis we found interventricular septum (IVS), E/A, V max, V max, global longitudinal strain (GLS) and rate of admission were significant with Pvalue (0.002, 0.049, 0.036, 0.028, 0.002 and 0.001 respectively). However, only global longitudinal strain (GLS) was significantly positively associated with increasing adverse events when performing multivariate analysis (P value: 0.009 and odd's ration (OR): 10.432 (1.792-60,743).

Table (1) Comparison between the two studied groups according to echo data

Echo data	**Group I (n = 80)**	**Group II (n = 80)**	**t**	**p**
LVIDd (mm)				
Min. – Max.	**47.0 – 55.0**	**48.0 – 58.0**		
Mean ± SD.	**50.95 ± 2.31**	**52.03 ± 2.39**	**2.898***	**0.004***
Median (IQR)	**52.0 (49.0 – 52.50)**	**52.0 (50.0 – 53.0)**		
LVIDs (mm)				
Min. – Max.	**28.0 – 39.0**	**28.0 – 40.0**		
Mean ± SD.	**32.30 ± 2.53**	**33.70 ± 3.21**	**3.066***	**0.003***
Median (IQR)	**32.0 (30.0 – 35.0)**	**34.50 (32.0 – 35.0)**		
FS (%)				
Min. – Max.	**30.0 – 44.0**	**30.0 – 40.0**		
Mean ± SD.	**35.90 ± 3.78**	**33.50 ± 2.09**	**4.968***	**<0.001***
Median (IQR)	**36.0 (32.50 – 38.0)**	**33.50 (32.0 – 35.0)**		
EF (%)				
Min. – Max.	**50.0 – 65.0**	**55.0 – 75.0**	**5.954***	**<0.001***

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Mean ± SD.	**58.53 ± 3.56**	**63.23 ± 6.09**		
Median (IQR)	**60.0 (55.0 – 60.0)**	**62.50 (57.50 – 67.0)**		
IVS (mm)				
Min. – Max.	**10.0 – 12.0**	**9.0 – 13.0**		
Mean ± SD.	**10.75 ± 0.60**	**11.08 ± 1.14**	**2.261***	**0.026***
Median (IQR)	**11.0 (10.0 – 11.0)**	**11.0 (10.0 – 12.0)**		
PWD (mm)				
Min. – Max.	**10.0 – 12.0**	**8.0 – 13.0**		
Mean ± SD.	**10.63 ± 0.59**	**10.44 ± 1.40**	**1.102**	**0.273**
Median (IQR)	**11.0 (10.0 – 11.0)**	**10.0 (9.0 – 12.0)**		
E/A				
Min. – Max.	**0.70 – 0.75**	**0.70 – 0.75**		
Mean ± SD.	**0.72 ± 0.02**	**0.71 ± 0.02**	**1.439**	**0.152**
Median (IQR)	**0.71 (0.70 – 0.75)**	**0.72 (0.70 – 0.72)**		
E/E' (8.13)				
Min. – Max.	**8.0 – 13.0**	**10.0 – 13.0**		
Mean ± SD.	**10.48 ± 1.19**	**11.48 ± 1.06**	**5.623***	**<0.001***
Median (IQR)	**10.0 (10.0 – 11.0)**	**11.50 (11.0 – 12.0)**		

IQR: Inter quartile range **SD: Standard deviation** **t: Student t-test**

Table (2) Comparison between the two studied groups according to GLS

GLS (%)	Group I (n = 80)	Group II (n = 80)	t	p
Min. – Max.	-23.0 – -15.0	-24.0 – -21.0		
Mean ± SD.	-18.70 ± 2.08	-22.50 ± 1.13	14.389*	<0.001*
Median (IQR)	-18.0 (-19.0 – -17.50)	-22.50 (-23.50 – -21.50)		

IQR: Inter quartile range **SD: Standard deviation** **t: Student t-test**

Table (3) Distribution of the studied cases according to adverse events in group I (n = 80)

Adverse events	No.	%
Adverse event	62	77.5
No adverse event	18	22.5

Table (4) Validity (AUC, sensitivity, specificity) GLS to prognoses adverse event patients (n = 62) from no adverse event (n = 18)

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
GLS (%)	0.946	<0.001*	0.872 –1.020	>-19	70.97	88.89	95.7	47.1

AUC: Area Under a Curve p value: Probability value

CI: Confidence Intervals

NPV: Negative predictive value PPV: Positive predictive value

*: Statistically significant at $p \leq 0.05$

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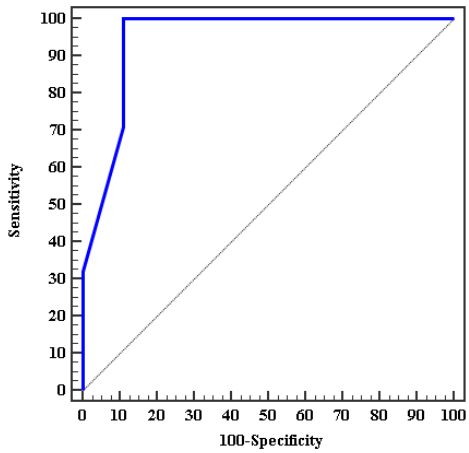

Figure (1): ROC curve for GLS to prognoses adverse event patients (n = 62) from no adverse event (n = 18)

Table (5) Relation between patients with adverse event from no adverse event according to GLS %

GLS %	Patient group		t	p
	Adverse event (n = 62)	No adverse event (n = 18)		
Min. – Max.	-19.0 – -15.0	-23.0 – -18.0		
Mean ± SD.	-17.81 ± 1.10	-21.78 ± 1.66	11.919*	<0.001*
Median	-18.0	-22.0		

Table (6) Univariate and multivariate Logistic regression analysis for the parameters affecting adverse event (n = 62 vs. 18) for different parameters

	Univariate		#Multivariate	
	p	OR (95%C.I)	p	OR (95%C.I)
Gender	0.438	0.659 (0.229 –1.893)		
Age (years)	0.359	1.064 (0.932 –1.214)		
Systolic	0.366	1.010 (0.988 –1.033)		
Diastolic	0.814	1.004 (0.970 –1.039)		
HR (bpm)	0.140	0.961 (0.912 –1.013)		
DCG	0.491	1.455 (0.501 –4.221)		
Abnormal Hb (g/dl)	0.295	1.925 (0.564 –6.566)		
Area	0.066	1.125 (0.992 –1.276)		
Ar	0.887	1.500 (0.006 –403.58)		
LVIDd (mm)	0.088	0.810 (0.635 –1.032)		
LVIDs (mm)	0.068	0.815 (0.655 –1.015)		
FS (%)	0.091	1.143 (0.979 –1.335)		
EF (%)	0.247	1.093 (0.940 –1.272)		
IVS (mm)	0.002*	0.165 (0.051 –0.529)	0.907	1.176 (0.077 –17.867)
PWD (mm)	0.095	0.461 (0.186 –1.145)		
E/A x100	0.049*	1.349 (1.001 –1.818)	0.398	1.530 (0.570 –4.104)
E/E' (8.13)	0.901	1.029 (0.660 –1.604)		
TR max (m/sec)	0.036*	0.113 (0.015 –0.871)	0.319	0.011 (0.0 –80.663)
MG (mmHG)	0.144	1.044 (0.985 –1.106)		
TRG (mmHg)	0.844	1.015 (0.875 –1.178)		
AVA (m^2)	0.028*	0.839 (0.718 –0.981)	0.349	0.600 (0.206 –1.748)
GLS (%)	0.002*	7.077 (2.037 –24.593)	0.009*	10.432(1.792 –60.743)
Admission	0.001*	8.556 (2.478 –29.539)	0.763	1.556 (0.088 –27.607)

OR: Odd`s ratio

C.I: Confidence interval LL: Lower limit UL: Upper Limit

#: All variables with p<0.05 was included in the multivariate

***: Statistically significant at p ≤ 0.05**

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DISCUSSION

Calcific aortic stenosis (AS) is the most common form of valvular heart disease in developed countries, and the number of affected individuals is rapidly growing as life expectancy increases.**(18)**

Although mortality is not increased when aortic stenosis is asymptomatic, the rate of death is more than 50% at 2 years for patients with symptomatic disease unless aortic valve replacement is performed promptly.

The severity of aortic stenosis is best characterized by integration of information concerning valve anatomy, hemodynamics, symptoms, and the left ventricular response to pressure overload, commonly used indexes of the severity of stenosis include the maximum transvalvular velocity and the mean transaortic pressure gradient.**(19)**

These measures remain relatively normal early in the disease course, and symptoms are unusual until the maximum transvalvular velocity is more than four times the normal velocity (i.e., increased to 4.0 m per second).**(20)**

Clinical factors associated with calcific valve disease mirror those associated with coronary atherosclerosis, and coronary artery disease is common among adults with aortic stenosis.(130)

The natural history of aortic stenosis involves a prolonged latent (asymptomatic) period, during which progressive worsening of left ventricular (LV) outflow obstruction leads to hypertrophic changes in the left ventricle.**(21, 22)**

No medical treatment has been proven to delay the progression of aortic valve disease or to improve survival and aortic valve replacement is the only effective treatment for hemodynamically significant aortic stenosis.**(23)**

Subendocardial fibrosis caused by increased mechanical stress imposed by AS itself is observed, even in normal LVEF.Moreover, LVEF is not a sensitive marker for detecting subclinical LV dysfunction.**(24)**

Therefore, a more sophisticated approach to evaluating LV mechanics is mandatory for selecting high-risk asymptomatic patients with severe AS and preserved patients who should undergo early surgical intervention. Among several proposed echocardiographic parameters for predicting adverse outcomes, global longitudinal strain (GLS) assessed by 2-dimensional (2D) speckle-tracking analysis can provide useful prognostic information.**(25, 26)**

In our study, we tried to identify high risk asymptomatic patients with severe AS using GLS measurements using 2d speckle tracking and determining its prognostic value.

We found no statistical significance as regard sex in our study, In the patients group38 (47.5%) were females and 42(52.5%) were males while in the control group 34 (42.5%) subjects were females and 46 (57.5%) were males.

Similar to Nagata et al **(27)** (a retrospective, multicenteric study, held in cardiology departments in Kitakyushu hospital, Japan, Chang Gung University, College of Medicine, Taipei, Taiwan and Tsukuba school of medicine, Tsukuba, Japan, conducted on 104 patients with severe asymptomatic AS, followed up for 5 to 15 months), 43 (41%) patients were males and 61 (59%) patients were females (p value 0.3717) showing no statistical significance.

The mean GLS in the patient group was -18.70 ± 2.08 % ranging from -23 to -15 % and in the control group the mean GLS was -22.50 ± 1.13 % ranging from -24 to -21 %, showing statistical significance between both groups. The mean GLS in the subgroup of patients who developed symptoms was -17.81 ± 1.10 % ranging from - 19.0 – -15.0 % and the mean GLS in the subgroup of patients who remained asymptomatic was -21.78 ± 1.66 % ranging from -23 to -18 %, there was a statistical significance between both subgroups.

Nagata et al **(28)**found that Global longitudinal strain was -15.8 ± 3.4% ranging from -6.6 to -25.1% and Global circumferential strain was_26.8 ± 6.0% ranging from -6.7 to -39.3%.

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Maréchaux et al**(29)**found that The mean GLS in the patient group was -15.2 ±3.2% ranging from -17.5 to -12.8% and the mean GLS in the group of patients who developed symptoms was -14.7 ±3.2 %.

Lancelotti et al**(30)**found that the mean Global longitudinal strain in the patient group was -16.0 ± 2.6 %.

In patients with severe asymptomatic AS, although having preserved systolic function, the reduced GLS is a strong prognostic factor for the development of symptoms or MACE.

In our study among the patient group, out of 80 patients with severe asymptomatic AS, 62 (77.5%) patients developed symptoms and 18(22.5%) patients remained asymptomatic

In Nagata et al**(28)**, The mean symptom free period was 12.5±6.0 months ranging from 5 to 15 months, 56(55%) patients developed dyspnea, 31(30%)patients developed chest pain on exertion,4(4%) cardiac deaths and 11 (10%) reported syncope.

In Maréchaux et al, **(29)**45(54.9%) patients reported significant breathlessness or dyspnea, 19 (23%) reported exertional chest pain and 5(6%) reported syncope. 16(19.5%) patients had a history of hospital admission.

Limitation of the study

The potential limitation of the present study is the relatively small sample size. There is no reference value for healthy subjects regarding GLS and of the LV. The same is true regarding the longitudinal strain of segmental regions of the LV. So, the data reported for global and regional longitudinal strain of the LV in normal subjects is not certain, yet and follow up was very difficult and we lost large number of patients due to lack of communications.

CONCLUSION

Incidence of severe asymptomatic aortic valve stenosis is high, a respectable number of cases of silent aortic stenosis was diagnosed for the first time during pre-operative assessment. Asymptomatic severe aortic stenosis is not always as benign as it seems to be and although severe aortic stenosis may remain silent for a long period, life expectancy is seriously reduced after development of symptoms. Global Longitudinal strain (GLS) can be used in assessment of severe AS due to its robust diagnostic and prognostic values over standard echocardiography.

REFERENCES

1. **García-Rodríguez, C., et al. (2018).** "Toll-like receptors, inflammation, and calcific aortic valve disease." Fron in physio 9: 201.
2. **Gulino, S., et al. (2018).** Aortic Stenosis: Epidemiology and Pathogenesis. Percutaneous Treatment of Left Side Cardiac Valves, Springer**:** 245-252.
3. **Rajamannan, N. M., et al. (2003).** "Calcific aortic stenosis: from bench to the bedside—emerging clinical and cellular concepts." Heart 89(7): 801-805.
4. **Nishimura, S., et al. (2016).** "Predictors of Rapid Progression and Clinical Outcome of Asymptomatic Severe Aortic Stenosis." Circ J 80(8): 1863-1869.
5. **Thoenes M, B. P., Zamorano P, et al.** Patient screening for early detection of aortic stenosis (AS)-review of current practice and future perspectives. J Thorac Dis. 2018;10(9):5584-5594. doi:10.21037/jtd.2018.09.02 (2018).
6. **Ito, S., et al. (2020).** "Prognostic Risk Stratification of Patients With Moderate Aortic Stenosis." J Am Soc Echocardiogr.
7. **Baumgartner, H., et al. (2017).** "Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography." J Am Soc Echocardiogr30(4): 372-392.

ISSN:0975-3583,0976-2833 VOL12,ISSUE06,2021

8. **Naeim, H. A., et al. (2020).** "Assessment of Left Ventricular Mechanics in Patients with Severe Aortic Stenosis after Transcatheter Aortic Valve Implantation: 2-D Speckle Tracking Imaging Study." 32(2): 248-255.
9. **Grebe SJ, Malzahn U, Donhauser J, Liu D, Wanner C, Krane V, et al.** Quantification of left ventricular mass by echocardiography compared to cardiac magnet resonance imaging in hemodialysis patients. Cardiovasc Ultrasound. 2020;18(1):39.
10. **Pineda AM, Kiefer TL.** Asymptomatic Severe Aortic Valve Stenosis—When to Intervene: a Review of the Literature, Current Trials, and Guidelines. Current Cardiology Reports. 2018;20(12):129.
11. **Silbiger JJ.** Pathophysiology and Echocardiographic Diagnosis of Left Ventricular Diastolic Dysfunction. J Am Soc Echocardiogr. 2019;32(2):216-32 e2.
12. **Gc VS, Alshurafa M, Sturgess DJ, Ting J, Gregory K, Oliveira Goncalves AS, et al.** Cost-minimisation analysis alongside a pilot study of early Tissue Doppler Evaluation of Diastolic Dysfunction in Emergency Department Non-ST Elevation Acute Coronary Syndromes (TEDDy-NSTEACS). BMJ Open. 2019;9(5): e023920.
13. **Maréchaux S, Ringle A, Rusinaru D, Debry N, Bohbot Y, TribouilloyCJJotAHA.** Prognostic value of aortic valve area by doppler echocardiography in patients with severe asymptomatic aortic stenosis. American Heart Association. 2016;5(5): e003146.
14. **del Villar CP, Yotti R, Espinosa MÁ, Gutiérrez-Ibañes E, Barrio A, Lorenzo MJ, et al.**The functional significance of paradoxical low-gradient aortic valve stenosis: hemodynamic findings during cardiopulmonary exercise testing. 2017;10(1):29-39.
15. **Perk G, Tunick PA, KronzonIJJotASoE.** Non-Doppler two-dimensional strain imaging by echocardiography–from technical considerations to clinical applications. the American Society of Echocardiography 2007;20(3):234-43.
16. **Stendahl JC, Parajuli N, Lu A, Boutagy NE, Guerrera N, Alkhalil I, et al.** Regional myocardial strain analysis via 2D speckle tracking echocardiography: validation with sonomicrometry and correlation with regional blood flow in the presence of graded coronary stenoses and dobutamine stress. Cardiovasc Ultrasound. 2020;18(1):2.
17. **LAURENZANO CS, NAVARTA DAC, JORGI MFC, MOSTO H, CASALE AD.** Prognostic Value of Longitudinal Strain by Velocity Vector Imaging in Asymptomatic Severe Aortic Stenosis with Preserved Ejection Fraction.
18. **Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Guyton RA, et al.** 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J of the Am Coll of Cardiol. 2014;63(22):2438-88.
19. **Makkar RR, Fontana GP, Jilaihawi H, Kapadia S, Pichard AD, Douglas PS, et al.** Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med. 2012;366(18):1696-704.
20. **Roberts WC, Ko JMJC.** Frequency by decades of unicuspid, bicuspid, and tricuspid aortic valves in adults having isolated aortic valve replacement for aortic stenosis, with or without associated aortic regurgitation. 2005;111(7):920-5.
21. **Deeb GM, Chetcuti SJ, Yakubov SJ, Patel HJ, Grossman PM, Kleiman NS, et al.** Impact of Annular Size on Outcomes After Surgical or Transcatheter Aortic Valve Replacement. Ann Thorac Surg. 2018;105(4):1129-36.
22. **Bonow RO, Carabello BA, Chatterjee K, De Leon AC, Faxon DP, Freed MD, et al.** ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular

ISSN:0975-3583,0976-2833 VOL12,ISSUE06,2021

Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. J of the Am Coll of Cardiol. 2006;48(3):e1-e148.

23. **Iung B, Cachier A, Baron G, Messika-Zeitoun D, Delahaye F, Tornos P, et al.** Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? Euro heart j. 2005;26(24):2714-20.
24. **Ng AC, Delgado V, Bertini M, Antoni ML, van Bommel RJ, van Rijnsoever EP, et al.** Alterations in multidirectional myocardial functions in patients with aortic stenosis and preserved ejection fraction: a two-dimensional speckle tracking analysis. Eur Heart J. 2011;32(12):1542-50.
25. **Lancellotti P, Donal E, Magne J, Moonen M, O'Connor K, Daubert JC, et al.** Risk stratification in asymptomatic moderate to severe aortic stenosis: the importance of the valvular, arterial and ventricular interplay. Heart. 2010;96(17):1364-71.
26. **Zito C, Salvia J, Cusma-Piccione M, Antonini-Canterin F, Lentini S, Oreto G, et al.** Prognostic significance of valvuloarterial impedance and left ventricular longitudinal function in asymptomatic severe aortic stenosis involving three-cuspid valves. Am J Cardiol. 2011;108(10):1463-9z.
27. **agata Y, Takeuchi M, Wu VC-C, Izumo M, Suzuki K, Sato K, et al.** Prognostic value of LV deformation parameters using 2D and 3D speckle-tracking echocardiography in asymptomatic patients with severe aortic stenosis and preserved LV ejection fraction. Cardiovascular Imaging. 2015;8(3):235-45.
28. **Nagata Y, Takeuchi M, Wu VC-C, Izumo M, Suzuki K, Sato K, et al.** Prognostic value of LV deformation parameters using 2D and 3D speckle-tracking echocardiography in asymptomatic patients with severe aortic stenosis and preserved LV ejection fraction. j cardio imag. 2015;8(3):235-45.
29. **Maréchaux S, Carpentier É, Six-Carpentier M, Asseman P, LeJemtel TH, Jude B, et al.**Impact of valvuloarterial impedance on left ventricular longitudinal deformation in patients with aortic valve stenosis and preserved ejection fraction. J Arch of cardiovasdise. 2010;103(4):227-35.
30. **Lancellotti P, Magne J, Donal E, Davin L, O'Connor K, Rosca M, et al.**Clinical outcome in asymptomatic severe aortic stenosis: insights from the new proposed aortic stenosis grading classification. J of the Am Coll of Card. 2012;59(3):235-43.
31. **Baumgartner H, Hung J, Bermejo J, Chambers JB, Edvardsen T, Goldstein S, et al.** Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. J Am Soc Echocardiogr. 2017;30(4):372-92.