

Aortic Valve Area and Strain Measurements by Cardiac MRI and Transthoracic Echocardiography in Severe Aortic Stenosis with Normal Left Ventricular Function

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What's Known

- Transthoracic echocardiography (TTE) is a technique for the initial evaluation of aortic stenosis (AS). Cardiac magnetic resonance (CMR) is superior in evaluating cardiac function and morphology. There is a good agreement between CMR planimetry and TTE.
- Substantial research is in progress on feature-tracking CMR as a novel technique.

What's New

- Myocardial strain is impaired in patients with severe AS and normal left ventricular (LV) systolic function, indicating subclinical myocardial dysfunction.
- LV global radial strain correlated with AS severity despite normal LV function.

Abstract

Background: Transthoracic echocardiography (TTE) is the recommended imaging technique for the evaluation of patients with aortic stenosis (AS). However, in cases with inconclusive findings, cardiac magnetic resonance (CMR) planimetry is used to grade AS severity. This study aimed to compare the results derived from TTE and CMR in patients with severe AS with normal left ventricular (LV) function.

Methods: In a prospective study, 20 patients with severe AS were recruited and data derived from TTE and CMR modalities were compared with the archived records of 28 age- and sex-matched healthy controls. The data included aortic valve area (AVA), MRI-derived biventricular global strains, and TTE-derived global longitudinal strain (GLS). SPSS software was used to analyze the data with independent samples *t* test, intraclass correlation coefficient (ICC), and Pearson correlation. $P < 0.05$ was considered statistically significant.

Results: An excellent agreement was found in AVA values derived from CMR and TTE with an average ICC of 0.932 (95% CI=0.829-0.973). There was a significant difference in LV-GLS, LV global radial strain (GRS), right ventricular (RV) GRS, and RV global circumferential strain between the groups. A good correlation was found between CMR- and TTE-derived GLS with an average ICC of 0.721 (95% C=0.255-0.896). The mean aortic valve pressure gradient in TTE had a significant inverse linear correlation with LV-GRS in CMR ($r = -0.537$). All *P* values were < 0.05 .

Conclusion: There was a good agreement between AVA and strain values derived from cardiac MRI and TTE. The myocardial strain was impaired in patients with severe AS and normal LV function and correlated with disease severity.

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Keywords • Aortic valve stenosis • Magnetic resonance imaging (MRI) • Echocardiography • Ventricular function

Introduction

Aortic valve diseases, particularly aortic stenosis (AS), are common in developed countries, and an increase in their

prevalence is associated with population aging.¹⁻³ Aortic valve surgery and interventions are often required in patients with severe symptomatic aortic valve diseases. However, these procedures are only applied after a comprehensive evaluation of the dysfunctional aortic valve and its effect on the rest of the heart, specifically the size and function of the left ventricle (LV). LV systolic function is used as a marker to predict the outcome of patients undergoing aortic valve replacement. Generally, the outcome is much worse in patients with severely reduced systolic function than those with preserved LV function.^{4, 5} LV function may remain normal in many patients with severe AS, even in symptomatic severe stenosis. Therefore, a more accurate marker should be used to evaluate subclinical myocardial abnormalities.

Global longitudinal strain (GLS) measured by speckle-tracking echocardiography is a powerful tool for assessing ventricular performance in patients with AS. Conditional upon early intervention to prevent severe and permanent LV dysfunction, GLS is a useful parameter to detect subclinical LV systolic dysfunction.⁶ Longitudinal strain, expressed as a percentage, is defined as the change in the length of a myocardial segment relative to its baseline length. Echocardiography is an ideal tool for the dynamic evaluation of cardiac mechanics.^{7, 8} In recent years, there has been a growing interest in the use of cardiac magnetic resonance (CMR) imaging as a safe and noninvasive method. Myocardial tissue deformity derived from CMR techniques may provide information to predict subtle changes in the myocardium and subclinical LV dysfunction, while LV ejection fraction (EF) is normal.⁹ Transthoracic echocardiography (TTE) is the initial modality of choice in the assessment of patients with AS.¹⁰⁻¹² However, in cases when findings are inconclusive, CMR planimetry is the best noninvasive method for AS grading.¹³

Given the aforementioned context, the present study aimed to compare aortic valve area (AVA) derived from TTE and CMR modalities. Additionally, we sought to compare measured strain, particularly GLS, between these modalities and explain the role of strain analysis in evaluating cardiac function in patients with severe AS and normal LV function.

Materials and Methods

A prospective study was conducted from October 2019 to February 2020 at Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran. The target population was patients scheduled for aortic

valve replacement. The inclusion criteria were patients with symptomatic severe AS based on echocardiographic guidelines¹¹ and normal LV function (LVEF>55%). The exclusion criteria were patients with LV dysfunction, moderate-to-severe aortic regurgitation, AS with other concomitant valvular diseases, previous aortic valve interventions, and cardiovascular risk factors (diabetes mellitus, hypertension, coronary artery disease). Accordingly, a total of 20 patients were recruited in the study and assigned to the AS group. All patients in the AS group underwent comprehensive functional assessment by TTE and CMR on the same day. They were all in stable condition and euvolemic on the examination day. In addition to the AS group, the TTE and CMR records of 28 age- and sex-matched healthy controls were retrieved from our archive of normal cardiac MRI studies. The controls had normal cardiovascular examinations without any reported risk factors such as diabetes mellitus, hypertension, and coronary artery disease.

The study was approved by the Ethics Committee of Iran University of Medical Sciences (code: IR.IUMS.FMD.REC.1397.019). Written informed consent was obtained from all patients.

Transthoracic Echocardiography

TTE was performed in all patients at rest in the left lateral position using a Philips EPIQ 7C ultrasound system with an X5-1 transducer (Philips Medical Systems, UK). TTE imaging modes included 2D grayscale, color Doppler, M-mode, pulsed wave Doppler, and continuous wave Doppler. Three consecutive beats were selected during image recording for offline synchronization with an electrocardiogram. Continuous wave Doppler mode was used to measure aortic transvalvular velocities. Peak and mean gradients were estimated using the simplified Bernoulli equation. The continuity equation was used to calculate AVA (figure 1). The end-diastolic and end-systolic volumes for the LV of the heart were calculated from the apical 2- and 4-chamber views, and LVEF was determined using the modified Simpson method. Severe AS was defined based on the presence of at least one of the following criteria: AVA<1 cm², mean aortic valve gradient >40 mmHg, and peak aortic jet velocity >4 m/s.^{11, 14, 15}

A two-dimensional speckle-tracking echocardiogram was used to measure LV-GLS in three standard apical views (2-, 3-, 4-chamber) at the rate of 40-70 frames per second. Offline analysis was performed using QLAB cardiac analysis software (Philips Medical Systems, UK) to measure two-dimensional strain values.

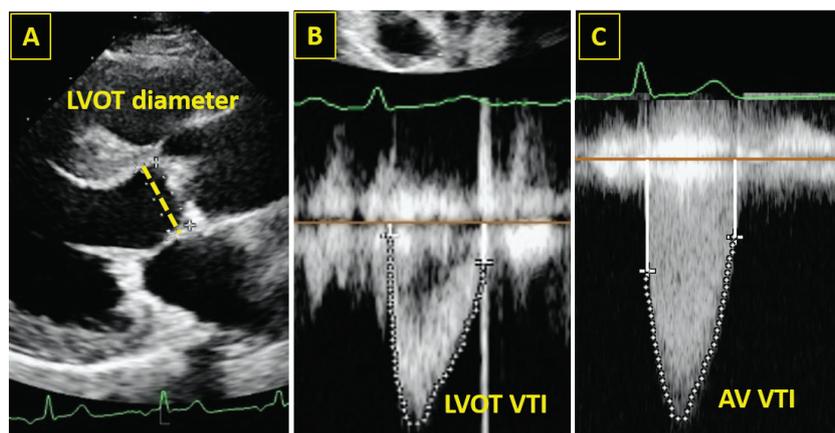


Figure 1: Transthoracic echocardiography for aortic valve (AV) area measurement using the continuity equation is shown. A: Left ventricular outflow tract (LVOT) diameter measurement in parasternal long-axis view. B and C: LVOT velocity-time interval (VTI) and AV VTI measurements by pulsed-wave Doppler and continuous-wave Doppler in apical five-chamber view, respectively.

Endocardial contours were traced manually throughout the complete cardiac cycle, and tracking quality was verified for each segment. GLS was calculated as the average peak systolic values of six segments in the four-chamber view. All examinations were performed by a single-blinded echocardiographer.

Cardiac Magnetic Resonance

The CMR data were obtained using an Avanto 1.5 T system with an eight-element phased-array receiver surface coil (Siemens, Erlangen, Germany). Electrocardiography-gated cine images in multiple long- and short-axis views during an end-expiratory breath-hold (slice thickness: 8 mm, field of view: 300 mm, imaging matrix: 156×192, repetition time/echo time: 31/1.2 ms) were acquired to assess cardiac function. Myocardial deformation was assessed using cvi42 software version 5.6.2

(Circle Cardiovascular Imaging Inc., Calgary, Alberta, Canada). Feature-tracking method was used for strain measurement by manually tracing endocardial and epicardial contours in the end-diastole frame in 2-, 3-, and 4-chamber views, as well as from all short-axis stacks. The contours were then propagated during the cardiac cycle to finally extract data on three-dimensional biventricular GLS, global circumferential strain (GCS), and global radial strain (GRS) (figure 2). Three-chamber and coronal LV outflow tract views were acquired for AVA planimetry. Five cine images were planned perpendicular to the aortic valve leaflets in both series (thickness: 4 mm) during ventricular systole. AVA was defined as the smallest area of the aortic valve during the maximal systolic excursion (figure 3). All CMR measurements were performed by a single-blinded cardiologist with expertise in cardiac imaging.

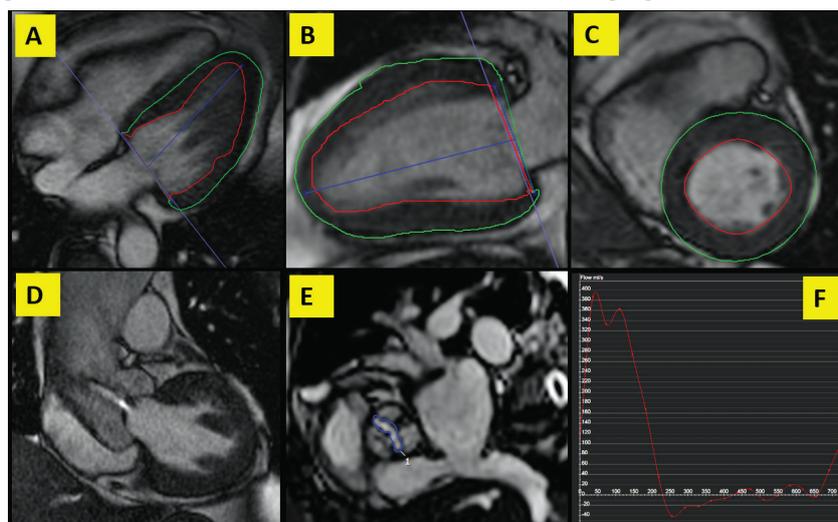


Figure 2: Cardiac magnetic resonance (CMR) for strain and aortic valve area (AVA) measurement is shown. A, B, and C: Endocardial and epicardial contours in 4- and 2-chamber as well as short-axis views for left ventricular (LV) strain measurements. D: LV outflow tract view shows a high-signal jet of the aortic valve in severe aortic stenosis. E: AVA in CMR planimetry measured as the smallest area of the aortic valve during the maximal systolic excursion. F: Aortic flow diagram in phase-contrast CMR.

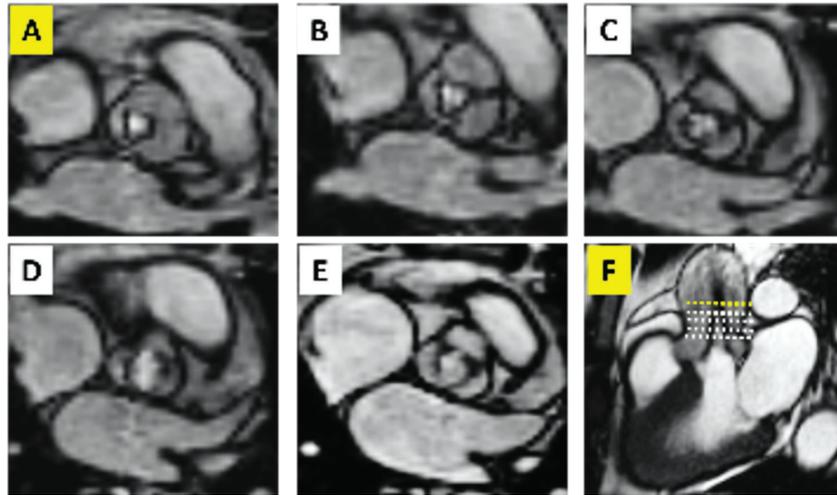


Figure 3: A series of cine function views for measuring the aortic valve area is shown. A: Cine short-axis at the level of the aortic tip. B, C, D, and E: Reveal increased aortic valve area with incorrect measurements not precisely at the tip level. F: Three-chamber view is used to correctly define the aortic valve tip (yellow dashed line).

Statistical Analysis

The data were analyzed using IBM SPSS statistics, version 22.00 (USA). Normally distributed continuous variables were expressed as mean±SD. Categorical variables were expressed as frequency and percentage. Cardiac functional parameters, including strain values, between the AS and control groups, were compared using the independent samples *t* test. The intraclass correlation coefficient (ICC) was used to determine the agreement between CMR and TTE in measuring AVA and strain. Pearson correlation was used to evaluate the relationship between AS severity parameters and strain values measured by feature-tracking CMR. P values less than 0.05 were considered statistically significant.

Results

The mean age of the participants in the AS and control groups was 59±19.8 years and 58±4.3 years, and the number of women was 8 (40%)

and 14 (50%), respectively. The mean LVEF (%) in the AS and control groups was 59.6±5.0 and 58.2±1.7, respectively. The mean AVA derived from TTE and CMR planimetry was 0.95±0.248 cm² and 0.96±0.253 cm², respectively. Table 1 presents the demographic and imaging data of the study population.

A high degree of agreement was found between AVA values derived from CMR planimetry and TTE. The average measure ICC was 0.932 (95% CI=0.829-0.973, F[14.774]=19, P<0.001). There was a significant difference in LV-GLS (P<0.001), LV-GRS (P=0.02), right ventricular (RV) GRS (P<0.001), and RV-GCS (P<0.001) between the AS and control groups.

The GLS values derived from CMR and TTE were compared, which showed a moderate to good correlation between the modalities with an average ICC of 0.721 (95% CI=0.255-0.896, F[3.588]=19, P=0.006) (table 2). The mean aortic valve pressure gradient in TTE exhibited a significant inverse linear correlation with LV-GRS in CMR (r=-0.537, P=0.01).

Table 1: Demographics and cardiac magnetic resonance parameters of the study population

Variables	AS patients (n=20)	Healthy Controls (n=28)	P value
Women (n, %)	8 (40%)	14 (50%)	0.5
Age (years)	59±19.8	58±4.3	0.24
LV-GLS (%)	13.8±2.6	18.1±1.3	<0.001
LV-GCS (%)	18.6±1.8	18.7±2.2	0.84
LV-GRS (%)	46.3±11.2	40±7.7	0.02
RV-GLS (%)	25.3±6.3	23.6±4.5	0.26
RV-GCS (%)	11.7±5.2	17.7±1.8	<0.001
RV-GRS (%)	19.2±10.6	31±7.7	<0.001
LVEFMR (%)	59.6±5	58.2±1.7	0.46
RVEF (%)	55.2±11.3	55.6±1.2	0.86

Data are expressed as mean±SD unless stated. Independent samples *t* test was used for statistical differences between groups. AS: Aortic stenosis; n: number; LV: Left ventricle; RV: Right ventricle; SD: Standard deviation; GLS: Global longitudinal strain; GCS: Global circumferential strain; GRS: Global radial strain; EF: Ejection fraction; MR: Magnetic resonance

Table 2: Comparison of aortic valve area and longitudinal left ventricular strain measurement between cardiac MRI and echocardiography

Variable	Average measure ICC	95% Confidence interval	P value
Aortic valve area	0.932	0.829-0.973	<0.001
LVGLS	0.721	0.255-0.896	0.006

LVGLS: Left ventricular global longitudinal strain; ICC: Intra-class correlation coefficient

Discussion

The results showed a good agreement between AVA derived from TTE and CMR planimetry. Besides, there was a good correlation in GLS measurement between speckle-tracking echocardiography and feature-tracking CMR in patients with severe AS and normal LV function. The measured strain values differed significantly between the AS and control groups. In addition, the mean aortic valve pressure gradient in TTE had a significant inverse linear correlation with GRS in CMR. There was an acceptable agreement between the AS severity derived from the continuity equation in TTE and direct planimetry in CMR.

In daily clinical practice, TTE is commonly used for the initial evaluation of AS and AVA.¹⁰⁻¹² According to the guidelines of the American College of Cardiology, American Heart Association,¹¹ and European Society of Cardiology,¹⁶ AVA less than 1 cm² and mean transvalvular pressure gradient greater than 40 mmHg are considered the main criteria for the diagnosis of severe AS. It is often necessary to measure valve orifice by direct planimetry, especially when disease severity determination is inconclusive due to poor image quality or a lack of Doppler angle alignment with the blood flow direction. In such circumstances, transesophageal echocardiography (TEE) is used as an alternative modality. More recently, CMR has been utilized as a useful technique with appropriate safety and accuracy.¹⁷ Our results showed a good agreement between estimates of AVA derived from CMR direct planimetry and the continuity equation in TTE. In line with our results, Malyar and colleagues reported a good correlation between TTE, TEE, and CMR-derived AVA values.¹⁸ Information obtained from CMR planimetry is independent of parameters such as blood flow velocity quantification, pressure gradients, or geometrical assumptions. Therefore, CMR can play an important role in obtaining information in patients with decreased cardiac output or other conditions that affect the above-mentioned parameters.^{11, 15, 17, 19, 20} Catheter-based invasive methods are the gold standard for grading the severity of AS. However, nowadays, they are rarely used for this purpose due to their invasiveness, cost, and significant

risk compared to noninvasive methods. Moreover, the Gorlin formula used to estimate AS severity involves some mathematical errors due to the effect of cardiac output, blood viscosity, and flow turbulence.¹⁰ Kupfahl and colleagues concluded that CMR planimetry is highly reliable and reproducible compared to cardiac catheterization using the Gorlin formula.¹³ They also stated that, in assessing AS severity, CMR planimetry has superior sensitivity and specificity compared to all other noninvasive methods (e.g., planimetry of AVA by TTE). CMR planimetry is particularly valuable in cases with inconclusive or discrepancies in the results. Our results reinforce the findings of previous studies in patients with severe AS. We, therefore, recommend CMR as a good noninvasive alternative to TTE/TEE for assessing AVA in AS.

Our results showed a good agreement between speckle-tracking echocardiography and feature-tracking CMR in patients with severe AS. In line with our results, previous studies have also shown an excellent agreement in GLS measurements between these modalities.^{21, 22} GLS has been evaluated in a variety of cardiac pathological conditions²³⁻²⁵ including AS.^{26, 27} The strain imaging method has an emerging role in evaluating ventricular performance in patients with aortic valve diseases. It is a valuable method in detecting subclinical LV dysfunction, as it allows early interventions and prevention of serious and long-term complications. GLS is an important parameter in AS management, as it identifies even subtle LV dysfunction in aortic valve disease including the effect on stenosis severity, prognosis, valve surgery timing, interventions, low-flow/low-gradient AS, and the presence of concomitant coronary artery disease. Several recent studies showed reduced GLS in patients with severe AS before any changes in LVEF.^{28, 29} We found a good agreement between TTE and CMR-measured strains. Given the role of strain in the early detection of cardiac dysfunction, we hypothesized that both TTE and CMR are helpful in the diagnostic evaluation of patients with severe AS.

In the present study, GLS in the AS and control groups was compared to estimate the extent of subclinical myocardial involvement. The measured GLS in the AS group was

significantly different compared to the control group, indicating subclinical myocardial damage. Therefore, in patients with AS who have normal LVEF and do not yet meet the criteria for intervention, strain can be used as a marker to initiate early interventions. In line with our results, based on speckle-tracking echocardiography, some studies reported impaired LV-GLS in a large number of patients with severe AS and normal LVEF.³⁰⁻³⁴ Vollema and colleagues investigated the prevalence of impaired LV-GLS in patients with asymptomatic severe AS and normal LVEF.³⁵ They found a significant LV-GLS impairment in patients compared to controls. They reported that LV-GLS further deteriorated over time and patients with impaired LV-GLS at baseline were at a greater risk of developing symptoms and requiring aortic intervention. In their study, subclinical myocardial dysfunction, indicative of impaired LV-GLS, was associated with the development of symptoms and the need for intervention.

The results showed a significant inverse linear relationship between the TTE-derived mean aortic valve pressure gradient and LV-GRS in the AS group, i.e., an increase in gradient alongside a significant reduction in strain. However, such a relationship was not found for GCS and GLS, which may be due to the low sample size. In a study by Miyazaki and colleagues, despite little difference in LVEF between patients, GLS gradually decreased as the severity of AS increased.³⁶ They recommended that GLS measured by two-dimensional speckle-tracking imaging might be useful to detect subtle changes in LV function in patients with AS.

The main limitation of the study was the low sample size. In addition, we did not perform a complete CMR including late gadolinium enhancement and parametric mapping methods. It is recommended to conduct a large-scale study to evaluate myocardial fibrosis and compare parameters in patients with varying degrees of AS severity.

Conclusion

There was a good agreement between AVA and strain derived from CMR and TTE. Myocardial strain, measured with feature-tracking CMR, was impaired in patients with severe AS and normal LV systolic function, indicating subclinical myocardial dysfunction. Furthermore, some CMR strain values, including LV GRS, correlated with the severity of AS. The inclusion of CMR in the diagnostic and therapeutic management protocol of AS is recommended.

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Authors' Contribution

N.R, L.H, N.S, M.A, A.R, Y.T, MM.HK, L.Sh, S.A: Study design, data collection, and manuscript preparation. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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