Chapter

Clinical Applications of Strain Imaging in Aortic Valve Disease

Ernesto E. Salcedo and Edward A. Gill

Abstract

The prevalence of aortic valve disease, particularly aortic stenosis, is increasing in parallel to the aging of the population, making it the most prevalent form of valvular heart disease. Surgery and percutaneous interventions of the aortic valve are conditional to a comprehensive evaluation of the aortic valve and the left ventricle (LV). Favorable results from aortic valve surgery or intervention are influenced by LV ejection fraction (EF), presence and severity of left ventricular hypertrophy (LVH), LV end-systolic volume (LVESV), degree of leaflet calcification, and trans-aortic valve gradients. Deformation imaging, particularly global longitudinal strain, is evolving as a powerful tool in the evaluation of ventricular function in patients with aortic stenosis. GLS is particularly suited to detect subclinical LV dysfunction, before a drop in LV ejection fraction, providing the opportunity to intervene earlier to prevent serious and permanent LV dysfunction. Similar added value has been demonstrated in the application of GLS in the detection of subclinical LV dysfunction in patients with aortic regurgitation. Very little information exists in the use of GLS in patients with mixed aortic valve disease, providing an opportunity for future research in this important group of patients with aortic valve disease.

Keywords: aortic stenosis, aortic regurgitation, aortic valve surgery, aortic valve intervention, global longitudinal strain

1. Introduction

As the population grows older, the prevalence of aortic valve disease, particularly aortic stenosis, is swelling, making it currently, the most prevalent form of valvular heart disease [1–3]. Surgery and percutaneous interventions of the aortic valve are frequently needed in patients with severe symptomatic aortic valve disease, the timing for these procedures' conditional on a comprehensive evaluation of the dysfunctional aortic valve and the resultant repercussions on the rest of the heart, particularly the left ventricle (LV). Parameters used to predict favorable/unfavorable results from aortic valve surgery or intervention include LV ejection fraction (EF), presence and severity of left ventricular hypertrophy

(LVH), LV end-systolic volume (LVESV), degree of leaflet calcification, and trans-aortic valve gradients. Because of the LV deformation indices potential to detect subclinical LV dysfunction, they are being used with increasing frequency in the management of patients with aortic valve disease [4] and advancing the timing for aortic valve surgery or intervention, before the LV is irreversibly damaged.

Our objective with this chapter is to describe the use of strain imaging, particularly global longitudinal strain in the assessment of cardiac function in patients with aortic valve disease. We review the current clinical applications of strain analysis in patients with aortic valve disease, highlighting strengths and weaknesses and emphasizing normal and abnormal findings in aortic stenosis (AS) aortic regurgitation (AR) and mixed aortic valve disease (ASAR); we summarize unresolved issues, potential future research priorities, and recommended indications for incorporating this technique into the clinical practice of patients with aortic valve disease.

2. Strain imaging: general principles

Strain is defined as the fractional change in length of a myocardial segment relative to its baseline length, it is expressed as a percentage. Strain rate is the temporal derivative of strain, providing information on the speed at which the deformation occurs. Echocardiography, because of its dynamic nature, is ideally suited for the evaluation of cardiac mechanics through the application of deformation indices [5, 6]. Two echocardiographic techniques have dominated the clinical and research arena of deformation echocardiography: (1) tissue Doppler imaging, and (2) speckle tracking imaging. Both techniques lend to the derivation of multiple parameters of myocardial function. Tissue Doppler Imaging (TDI) was the first method used to measure myocardial deformation by echocardiography. The method is well validated and has been shown to provide valuable data in a wide range of conditions. Tissue Doppler is currently used mainly for evaluation of diastolic LV function, its use in aortic valve disease will not be discussed in this chapter. Speckle tracking, mainly through the use of global longitudinal strain (GLS), is increasingly used to identify subclinical myocardial dysfunction in patients with valvular heart disease and to identify optimal timing for surgery or intervention and prognosticate outcomes after surgery/intervention, and is the main focus of this review.

3. Strain imaging in aortic stenosis

Aortic stenosis inflicts progressive pressure overload on the LV with compensatory concentric hypertrophy (**Figure 1**). Initially, the increased wall thickness and conservation of normal LV chamber dimensions offsets the increased LV pressure, maintaining a normal ejection fraction. If the aortic stenosis is not corrected it will inexorably lead to reduced myocardial perfusion, and eventual fibrosis with consequent drop in ejection fraction. It is well recognized that LV GLS is superior to LVEF in detecting perturbations in myocardial function. Compared with normal controls, severe aortic stenosis patients have impaired strain in all three layers of the LV myocardium. LV strain analysis in aortic stenosis has been evaluated in different settings as noted in the following sections.

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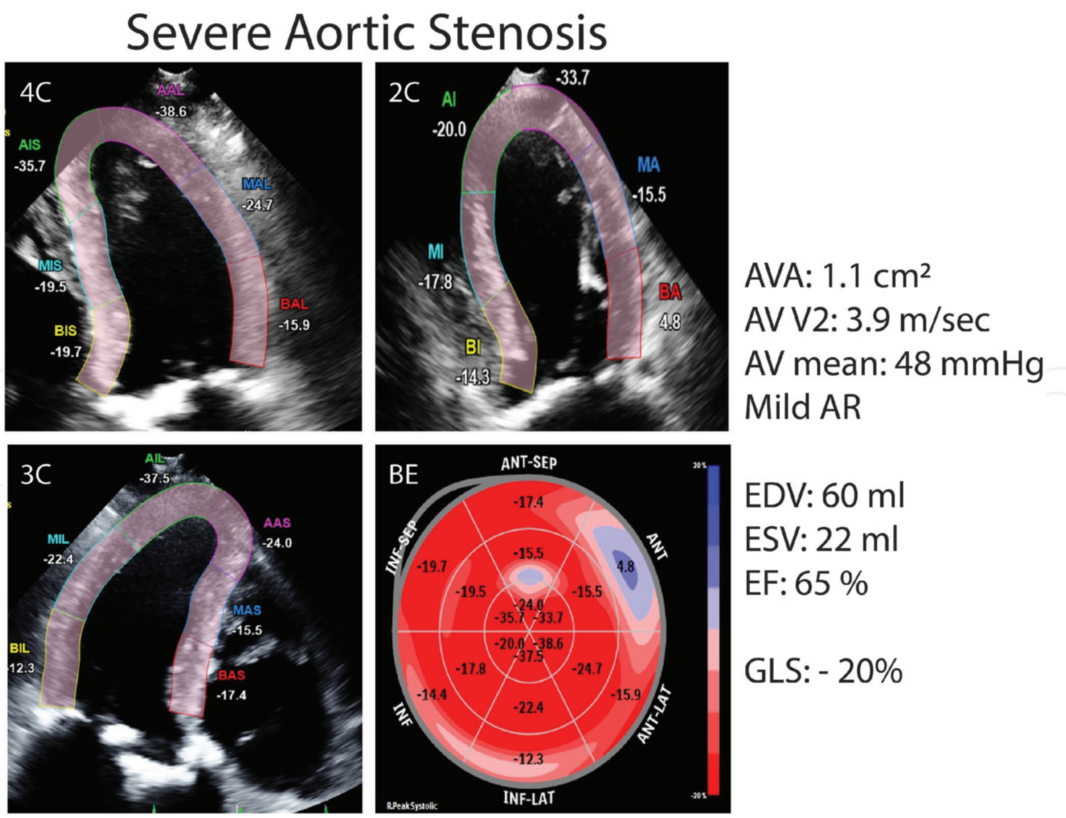

Figure 1.
Severe aortic stenosis: global longitudinal strain (GLS) in a patient with severe aortic stenosis with an aortic valve area (AVA) of 1.1 cm² maximal velocity (AV V2) of 3.9 m/s and a mean gradient of 48 mm Hg. Left ventricular end-diastolic and end-systolic volumes (EDV, ESV) are normal as well as the LV ejection fraction (EF). The GLS is normal at −20% indicating absence of any LV dysfunction.

4. Strain imaging and ejection fraction in aortic stenosis

Measuring LV ejection fraction is crucial in the management of patients with asymptomatic severe aortic stenosis (AS). According to the current American Heart Association/American College of Cardiology and European Society of Cardiology guidelines there is a Class I indication (Level of Evidence: B) to perform aortic valve intervention in asymptomatic patients with severe AS when the LVEF becomes <50% [7, 8]. Predictors of poor outcome in aortic stenosis include advanced age, significant leaflet calcification, rapid disease progression and decreased left ventricular (LV) ejection fraction (EF). Patients can develop impaired LVEF due to afterload mismatch or from true depression of myocardial contractility due to myocardial fibrosis. Myocardial fibrosis occurs early in the natural history of aortic stenosis, affecting diastolic and systolic function and offering a substrate for ventricular arrhythmias, playing a role in the progression to heart failure and sudden cardiac death. These observations indicate that current echocardiographic assessment of LV function by measuring only the LVEF is insufficient and that new parameters detecting subtle myocardial impairment are needed to improve risk stratification and predict outcomes in patients with AS.

Several studies have defined the added value of global longitudinal strain over LVEF to characterize and prognosticate the clinical evolution of patients with aortic stenosis:

- There is growing evidence suggesting the prognostic role of global longitudinal strain (GLS), in asymptomatic patients with AS. The American Society of

Echocardiography (ASE) on cardiac chamber quantification acknowledged the incremental value of LV GLS over traditional LVEF measurements, and recommended its clinical use in patients [9].

- Conventional measures of LVEF can be preserved until end-stage disease due to the compensatory development of concentric hypertrophy, and thus lacks accuracy in identifying subtle changes in myocardial contractility [2].

- Subclinical myocardial dysfunction with impaired LV GLS is frequently seen in patients with severe AS with preserved LVEF and no symptoms. Left ventricular global longitudinal strain deteriorates over time and impaired LV GLS at baseline is associated with an increased risk for progression to the symptomatic stage and the need for aortic valve surgery or intervention [10].

5. Strain imaging and aortic stenosis severity

A relationship between aortic stenosis severity and alterations in LV deformation indices has been demonstrated in the following studies:

- Strain and strain rate parameters relate to LV function and aortic stenosis severity. Further, they appear to be superior to tissue velocity and conventional echocardiography in detecting subtle changes in myocardial function after AVR before LV mass and LV function show improvement [11].

- Despite unchanged LVEF, GLS gradually decreased as severity of AS increases. GLS measured by 2D-speckle tracking imaging might be useful to assess subtle changes in LV function in AS patients [12].

6. Strain imaging—prognostic value in aortic stenosis

LV strain analysis has been demonstrated to provide prognostic information in patients with aortic stenosis:

- A recent met analysis, including 1067 asymptomatic patients, with AS and preserved LVEF, showed that LVGLS is strongly associated with mortality, with >2.5-fold increase in risk of death in patients with impaired LVGLS (−14.7% or less) [13].

- GLS detects subclinical dysfunction and has incremental prognostic value over traditional risk markers including hemodynamic severity, symptom class, and LVEF in patients with AS. Incorporation of GLS into risk models can improve the identification of the optimal timing for AV replacement [14].

- Kusunose et al. [15] demonstrated on 395 patients that Longitudinal strain (LS) is independently associated with death in patients with AS and preserved LVEF, in addition they made the point that the flow/gradient pattern should also be considered as an important parameter. In the management of AS patients the use apical 4 chamber LS should be considered a new parameter of evaluation of LV function and prognosis [16].

- LV GLS is independently associated with all-cause mortality in AS patients. It can further risk stratify severe AS patients and may influence the optimal timing of aortic valve replacement [2].

- GLS is an independent predictor of all-cause mortality in severe AS, irrespective of their type of treatment. GLS <9.7% indicates a significantly higher 1- and 5-year mortality in non-AVR patients. Therefore, GLS should be regularly assessed for enhanced risk stratification and clinical decision-making [17].

- In normal LVEF patients with significant aortic stenosis, brain natriuretic peptide (BNP) and LV-GLS provide incremental prognostic information over established predictors, suggesting that both play a synergistic role in defining outcomes [18].

- A drop in LVGLS in bicuspid aortic valve (BAV) with preserved LVEF is not infrequent and was independently associated with increased risk of events (mainly aortic valve replacement events), as found by Kong et al. [19] in 513 patients (68% men; mean age 44 ± 18 years) with BAV and preserved LVEF (>50%).

7. Strain imaging in combined aortic stenosis and coronary artery disease

Subclinical coronary artery disease is common in moderate and severe aortic stenosis, and should be suspected when regional longitudinal dysfunction is predominant in the apical and mid ventricular segments [20].

8. Strain imaging sublayers in aortic stenosis

Sublayer strain analysis may add additional information in the characterization of LV function in patients with aortic stenosis. The following studies address this issue:

- In severe AS, longitudinal strain impairment affects all three myocardial layers but is more noticeable in the endocardial layer. This becomes more manifest in the advanced phases of the disease when symptoms appear [21].

- Bilayer strain ratio (subendocardial and subepicardial) can reliably differentiate patients with varying degrees of AS severity and is a sensitive marker of LV function. These findings suggest that the evaluation of subendocardial and subepicardial radial strain might be a novel method for assessing LV mechanics in patients with AS [22].

- Medically treated patients with AS have worsening of GLS despite preserved LVEF, first appearing in the subendocardial layer. Global circumferential strain (GCS) becomes progressively impaired in moderate and severe AS. Improvement in LV strain after AVR is seen earlier with GLS than with GCS [23].

- There is differential impairment in LV systolic strain in all three cardiac axes in patients with AS. Left ventricular longitudinal strain impairment is proportional to AS severity. Subendocardial longitudinal strain correlates better with

AS severity than subepicardial longitudinal strain while correlations between circumferential and radial strain and AS severity are weak [24].

- Compared with normal controls, severe aortic stenosis patients have impaired strain in all three layers of the LV myocardium [25].

9. Strain imaging in low gradient severe aortic stenosis

Several studies have characterized the LV deformation indices in patients with low gradient aortic stenosis:

- GLS is depressed in patients with paradoxic low flow (PLF) AS. This implies that subclinical myocardial dysfunction may be more prominent in PLF AS compared with normal-flow AS and suggests the possible diagnostic and prognostic value of two-dimensional global strain in identifying PLF AS [26].

- In patients with low flow-low gradient aortic stenosis, 2-dimensional strain parameters are strong predictors of outcome. Peak longitudinal strain rate may add incremental prognostic value beyond what is obtained from N-terminal pro-B-type natriuretic peptide and peak stress left ventricular ejection fraction [27].

- Sato et al. [28] demonstrated in 204 patients that longitudinal LV function is severely impaired in patients with paradoxical low-flow, low-gradient (LFLPG) AS and they have a poor prognosis. GLS could stratify the high-risk group for future adverse outcomes.

- Patients with paradoxical low-flow severe aortic stenosis (PLF-AS) reportedly have higher left ventricular hydraulic load and more systolic strain dysfunction than patients with normal-flow aortic stenosis. Holmes et al. [29] investigated the relationship of systolic loading and strain to PLF-AS in 120 patients. Patients with PLF-AS were found to have more valvular load, lower energy loss coefficient, more arterial load and increased systemic vascular resistance and more total hydraulic load. They concluded that Increased hydraulic load, from more severe valvular stenosis and increased vascular resistance, and longitudinal strain impairment are associated with PLF-AS and their interplay is likely fundamental to its pathophysiology.

- Dahou et al. [30] examined the impact of left ventricular (LV) global longitudinal strain (GLS) measured at rest and at dobutamine stress echocardiography on the outcome of 202 patients with low LV ejection fraction and low-gradient aortic stenosis. GLS was found to be independently associated with mortality in patients with low LV ejection fraction, low-gradient aortic stenosis. Stress GLS measured during dobutamine stress echocardiography provided incremental prognostic value beyond GLS measured at rest in these patients. Hence, these authors concluded that measurement of GLS at rest and during dobutamine stress echocardiography may be helpful to enhance risk stratification in low LV ejection fraction, low-gradient aortic stenosis.

- In patients with LF-LG AS and low LVEF, reduced right ventricular longitudinal strain (RVLS) was found by Dahou et al. [31] to be independently associated with increased risk of mortality. Furthermore, stress RVLS provided incremental prognostic value beyond that obtained from rest RVLS. Thus, RVLS measurement at rest and with dobutamine stress may be helpful to enhance risk stratification in this high-risk population.

10. Strain imaging in aortic stenosis—effects of hypertension

The added effect of hypertension in deformation indices abnormalities has been defined in the following studies:

- Hypertension has significant negative effect on LV mechanics in patients with aortic stenosis. Blood pressure is associated with deterioration of LV global longitudinal and circumferential strains in aortic stenosis patients independently of clinical and demographic characteristics [32].

- In AS, both the AS severity and concomitant hypertension attenuate radial tissue Doppler imaging strain in the inferior LV wall. The subendocardial radial strain is mainly influenced by AS severity, while midmyocardial radial strain is attenuated by both hypertension and AS severity [33].

11. Strain imaging and aortic valve surgery/intervention

The contributions of LV strain analysis in the surgical or interventional management of patients with aortic stenosis has been extensively documented. The following statements summarize the conclusions of several studies addressing the use of strain imaging as it relates to valve replacement or intervention in patients with aortic stenosis.

- LV longitudinal systolic strain is depressed despite preserved LV ejection fraction and fractional shortening in AS. A significant association exists among natriuretic peptides, myocardial longitudinal contractility, and the degree of symptoms. Reverse LV remodeling after aortic valve replacement with regression of myocardial hypertrophy results in improvement of LV longitudinal myocardial strain and decrease of Nt-pro-BNP plasma levels. LV strain analysis has the potential to identify patients with asymptomatic AS who might benefit from earlier surgical intervention to preserve overall LV function [34].

- In patients with symptomatic severe aortic stenosis undergoing aortic valve replacement, reduced GLS (Particularly in the setting of normal LVEF) provides important prognostic information beyond standard risk factors [35].

- Shortly after balloon valvuloplasty for severe congenital AS, there is an improvement in systolic myocardial deformation. However, two-dimensional speckle-tracking echocardiographic parameters do not return to normal at 3-year follow-up. These abnormalities in systolic deformation cannot be fully attributed to residual stenosis or aortic regurgitation [36].

- Marcus et al. [36] showed in 37 children that shortly after balloon valvuloplasty for severe congenital AS, there is an improvement in systolic myocardial deformation. However, two-dimensional speckle tracking echocardiography parameters do not return to normal at 3-year follow-up. These abnormalities in systolic deformation cannot be fully attributed to residual stenosis or aortic regurgitation.

- Kafa et al. [37] evaluated 208 patients that underwent AVR for severe AS, measuring GLS pre and 12–24 months post AVR and found that in patients with severe aortic stenosis, approximately 20% of patients who survived more than 1 year after aortic valve replacement had an abnormal LV-GLS value on postoperative echocardiography, despite a preserved postoperative LVEF and demonstrable left ventricular mass regression. This finding was independently associated with adverse events, concluding that appropriately timed aortic valve replacement relieves left ventricular wall stress and prevents a decline in LVEF.

- In asymptomatic/minimally symptomatic patients with severe bioprosthetic AS undergoing redo aortic valve replacement (AVR), baseline LV-GLS provides incremental prognostic value over established predictors and could potentially aid in surgical timing and risk stratification [38].

- AVR reverses LA abnormalities and regains normal atrial function, a behavior which is directly related to the severity of preoperative LV outflow tract obstruction. Early identification of LA size enlargement and functional disturbances might contribute to better patient's recruitment for AVR [39].

- Speckle echocardiography analysis of left atrial (LA) myocardial deformation is considered a promising tool for the evaluation of LA subclinical dysfunction in patients undergoing AVR, giving a potentially better risk stratification for the occurrence of postoperative atrial fibrillation [40].

- Gelsomino et al. [41] explored the influence of global longitudinal strain measured with two-dimensional speckle-tracking echocardiography on left ventricular mass regression (LVMR) in 83 patients with pure aortic stenosis (AS) and normal left ventricular function undergoing aortic valve replacement (AVR) and found that global longitudinal strain accurately predicts LV mass regression in patients with pure AS undergoing AVR.

In summary LV GLS can detect subclinical myocardial dysfunction in patients with severe aortic stenosis, and progressively worsens with increasing aortic stenosis severity. Impaired LV GLS is independently associated with increased mortality in high-gradient aortic stenosis, in low-flow, low-gradient severe aortic stenosis with preserved LVEF, and in low-flow, low-gradient severe aortic stenosis with reduced LVEF. Strain analysis of specific myocardial sublayers may add value to the evaluation of strain in aortic stenosis. Coronary artery disease and hypertension produce additional variables in strain analysis that need to be considered. Finally, there is increasing support for the use of strain imaging to determine the need and timing for aortic valve surgery or intervention in patients with aortic stenosis.

12. Strain imaging in aortic regurgitation

In contrast to aortic stenosis, aortic regurgitation (AR) generates LV volume overload with progressive LV dilatation, initially with preservation of LVEF and wall thickness (eccentric LV hypertrophy), but eventually with the development of LV systolic dysfunction expressed by a drop in LVEF (**Figure 2**). Several studies have described the value of strain imaging in the management of patients with aortic regurgitation. The results and conclusion statement of these studies are summarized in the following paragraphs:

- In patient with AR, LV strain analysis can detect early subclinical myocardial dysfunction before the development of impaired LVEF. Using tissue Doppler imaging, Marciniak et al. [42] demonstrated that patients with severe AR had significant impairment of LV longitudinal strain, in contrast to patients with moderate AR where there was no difference with controls.

- Smedsrud et al. [43] evaluated 47 AR patients and 31 controls with Longitudinal peak systolic strain rate and found they were significantly decreased in the patient's population ($P < 0.001$). Global longitudinal peak systolic strain rate was also significantly decreased in aortic stenosis and regurgitation compared to the control group (-1 ± 0.5, -0.9 ± 0.3, and -1.6 ± 0.3, $P = 0.001$). As far as the comparison between patients with aortic stenosis and aortic regurgitation, neither global strain rate nor strain rate for each wall was found to be different. They concluded that there was reduced global longitudinal strain in patients with chronic AR with preserved LV ejection fractions. Global longitudinal strain might therefore disclose incipient myocardial dysfunction with a consequent potential for improved timing of aortic valve surgery.

- Di Salvo et al. [44] evaluated 26 young patients (3-16 years) with asymptomatic AR and found LV average longitudinal strain to be significantly reduced in patients with progressive AR compared to those with stable AR ($-17.8 \pm 3.9\%$ vs. $-22.7 \pm 2.7\%$, $p = 0.001$). On multivariate analysis, the only significant risk factor for progressive AR was average LV longitudinal strain ($p = 0.04$, cut-off value $> -19.5\%$, sensitivity 77.8%, specificity 94.1%, area under the curve 0.889). These authors concluded that two-dimensional strain imaging

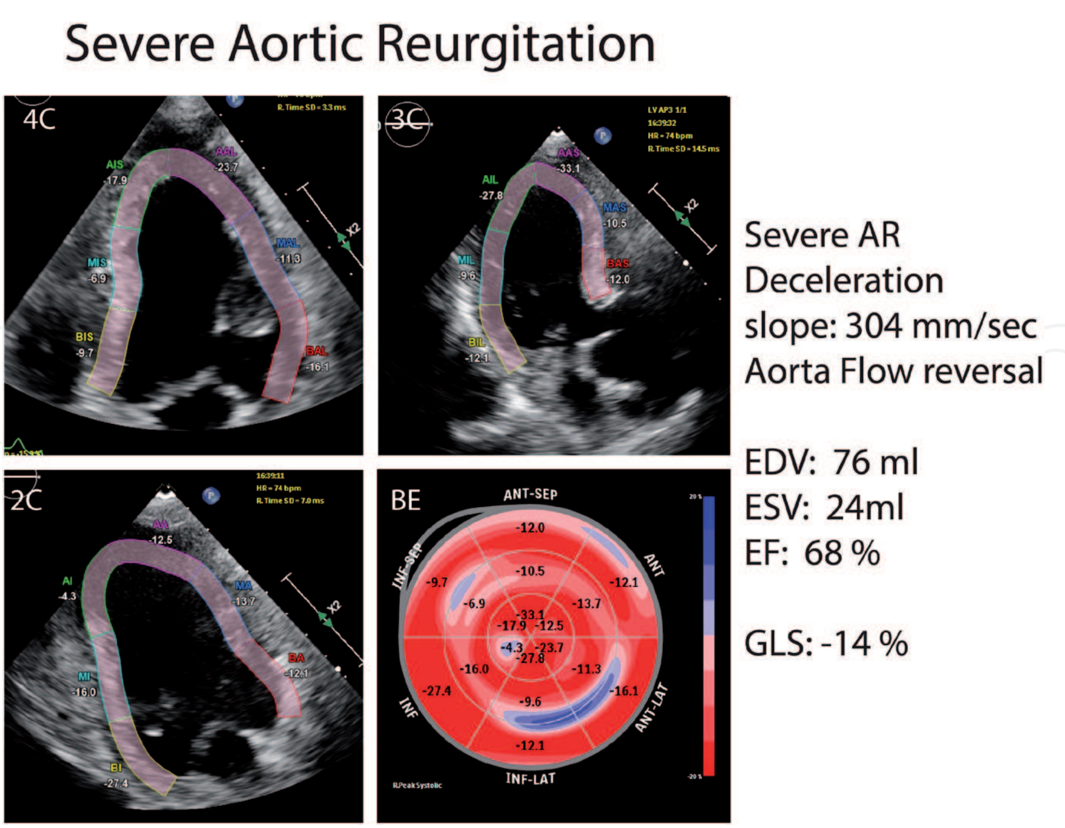

Figure 2.
Severe aortic regurgitation: this patient had severe aortic regurgitation with normal LV end-diastolic and end-systolic volumes (EDV, ESV) and preserved systolic function as estimated by a normal LV ejection fraction (EF) of 68%; however, there is already evidence of insipient LV dysfunction as demonstrated by a mild drop in global longitudinal strain at −14%.

can discriminate young asymptomatic patients with progressive AR. This could allow young patients with AR to have a better definition of surgical timing before the occurrence of irreversible myocardial damage.

- Kaneko et al. [45] evaluated 36 chronic AR patients undergoing surgical correction and found, with the use of speckle-tracking strain imaging, that LV subendocardial dysfunction was present in patients with chronic severe AR and preserved EF, this improved after surgical correction.

- Park et al. [46] evaluated 60 patients with chronic AR with LV global strain rate on apical four chamber image (GS-4CH). During 64 months follow-up duration, 16 patients (26.7%) were deceased and 38 patients (63.3%) underwent aortic valve replacement (AVR). Deceased group had lower longitudinal strain (−12.05 ± 3.72% vs. -15.66 ± 4.35%, p = 0.005). On multivariate analysis by cox proportional hazard model adjusting for age, sex, body surface area, history of atrial fibrillation, blood urea nitrogen, LV dilatation, LV ejection fraction and AVR, decreased GS-4CH proved to be an independent predictor of mortality in patients with chronic AR (hazard ratio 1.313, 95% confidence interval 1.010–1.706, p = 0.042). They concluded that GS-4CH may be a useful predictor of mortality in patient with chronic AR.

- Alashi et al. [47] evaluated 1063 patients with asymptomatic severe chronic AR and preserved LVEF to examine the prognostic utility of left ventricular (LV) global longitudinal strain (GLS). A significantly higher proportion (log-rank p = 0.01) of patients with LV-GLS worse than median (−19.5%) died versus those with an LV-GLS better than median [86 of 513 (17%) vs. 60 of 550 (11%)]. The risk of death at 5 years significantly increased with an LV-GLS of worse than −19%. They concluded that in asymptomatic patients with ≥III+ chronic AR and preserved LVEF, worsening LV-GLS was associated with longer term mortality, providing incremental prognostic value and improved reclassification.

- Alashi et al. [48] evaluated 865 patients with ≥3+ chronic AR and preserved LVEF undergoing AV surgery, a baseline LV-GLS value worse than −19% was associated with reduced survival. In a subgroup of patients who returned for 3- and 12-month postoperative follow-up examinations, persistently impaired LV-GLS was associated with increased mortality.

In summary, in patients with severe AR LV strain analysis detects early subclinical myocardial. Dysfunction before there is a drop in LVEF. This provides the potential for improving AVR/intervention timing. In addition GLS may be a useful predictor of mortality in AR patients by providing incremental prognostic value and improved reclassification. Finally, persistently impaired LVGLS in AR is associated with increased mortality.

13. Strain imaging in mixed aortic valve disease

Very little information has been published on the use of strain imaging in the management of patients with mixed aortic valve disease (**Figure 3**). The next paragraph summarizes the findings and conclusions in one study:

- Longitudinal LV function is reduced in both pressure and volume overload, and both of this overload patterns are equally harmful to the ventricle. Gorgulu et al. [49] evaluated a total of 27 subjects with mixed aortic valve disease

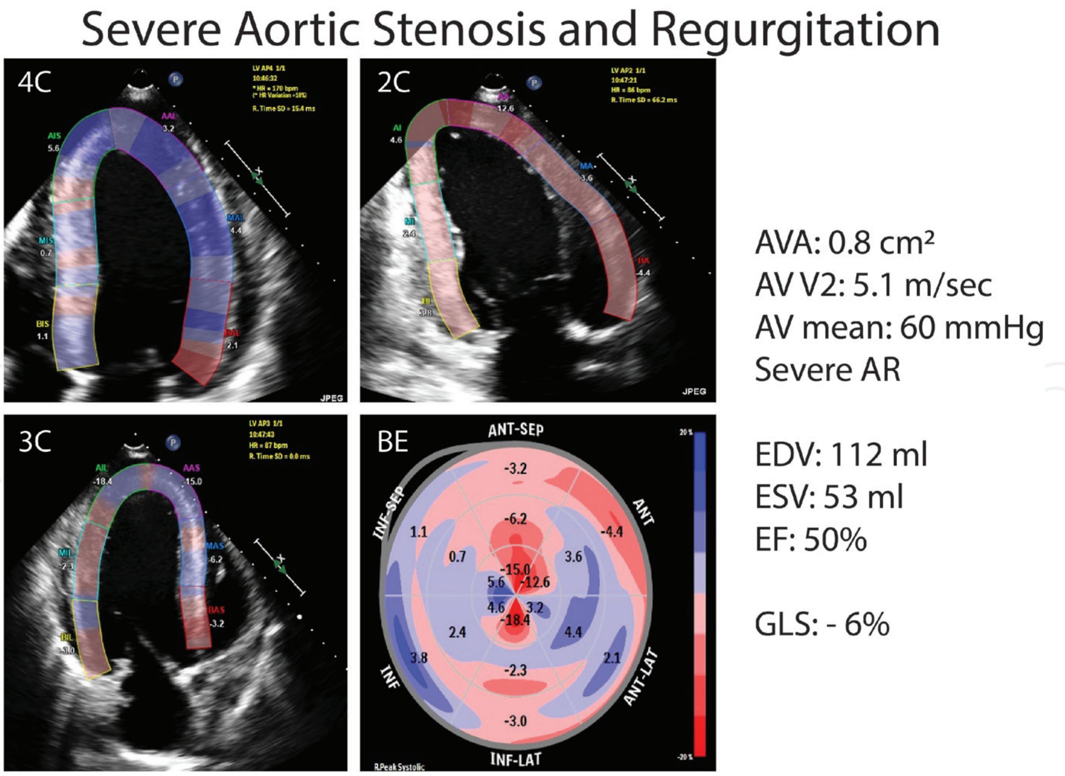

Figure 3.
Severe aortic stenosis and regurgitation: this example illustrates the presence of severe LV dysfunction as demonstrated by a marked drop of GLS to −6% despite a borderline drop of LV ejection fraction to 50%. The combination of severe aortic stenosis and regurgitation likely produces significant volume and pressure overload of the LV with significant LV dysfunction that is unmasked by strain analysis.

(53 ± 15 years). Fifteen healthy subjects (mean age 50 ± 6 years) were enrolled as the control group. Longitudinal peak systolic strain rate values of each segment derived from analysis of a total of 804 segments were significantly decreased in this patient population ($P < 0.001$). Global longitudinal peak systolic strain rate was also significantly decreased in aortic stenosis and regurgitation compared to the control group (−1 ± 0.5, −0.9 ± 0.3, and −1.6 ± 0.3, $P = 0.001$). As far as the comparison between patients with aortic stenosis and aortic regurgitation, neither global strain rate nor strain rate for each myocardial segment was found to be different.

14. Unresolved issues

Although strain analysis is been used with increasing frequency for the evaluation of cardiac function, there are still issues with reproducibility of deformation analysis data, particularly when different echocardiography machines or analysis software is used. Until this issue is resolved the current recommendation is to use the same machine and software when obtaining comparative studies.

The fidelity of the strain data sets is dependent on the quality of the echocardiographic data, unfortunately endocardial contrast enhancing agents cannot be used during strain analysis, therefore strain analysis sometimes has to be obtained with substandard images. The current recommendation is not to report strain values if the echocardiographic images are of poor quality. Hopefully work-around solutions will be found to permit strain analysis with endocardial enhancement agents use.

The current literature supports actionable interventions according to fairly well-defined values of decreased LV ejection fraction, this is not as developed on the characterization of LV dysfunction according to levels of decreased strain values.

Although the literature on strain is fairly robust in aortic stenosis, it is only moderately developed in aortic regurgitation and almost not existent in mixed aortic valve disease.

15. Incorporating strain analysis into clinical practice in aortic valve disease

Despite some of the shortcomings of strain analysis in aortic valve disease we have reviewed, we feel the added value this technique provides, justifies its use in the day to day imaging management of patients with diseases of the aortic valve. Our practice and recommendation is to characterize and sequentially follow global longitudinal strain in patients with moderate and severe aortic stenosis and/or moderate and severe aortic regurgitation. In asymptomatic patients with severe AS or AR and normal EF, the presence of an abnormal GLS should alert the clinician for the need of closer follow up or possibly aortic valve replacement/intervention.

16. Future directions

The following studies highlight areas of study with high potential for development in the area of strain analysis in patients with aortic valve disease.

16.1 Three-dimensional speckle tracking

- Broch et al. [50] studied, 31 patients with moderate to severe AR, 15 elite endurance athletes, and 17 healthy control subjects using three-dimensional speckle-tracking echocardiography. Global circumferential strain (GCS), global longitudinal strain (GLS), end-systolic circumferential wall stress (ESSc), end-systolic meridional wall stress (ESSm), and the wall stress ratio (ESSc/ESSm) were measured. LV end-diastolic volumes were similar in athletes and patients with AR and significantly larger than in healthy control subjects. Values of GLS in control subjects, athletes, and patients with AR were −18.8 ± 1.9%, −17.3 ± 2.0%, and −16.4± 2.0%, respectively (control subjects vs. athletes and patients, $P < .05$), whereas values of GCS were −16.9 ± 2.0%, −15.5 ± 1.9%, and −17.9 ± 2.6%, respectively (athletes vs. control subjects and patients, $P < .01$). The authors concluded that in compensated AR, relatively high GCS compensates for reduced GLS in a manner consistent with the preserved ejection fractions observed in these patients.

16.2 Stress GLS

- Uncovering post-exercise myocardial dysfunction in patients with asymptomatic AS with preserved left ventricular function can aid in risk assessment of these patients [51].

16.3 Multi-layer strain

- Left ventricular myocardial strain gradient using a novel multi-layer transthoracic echocardiography technique positively correlates with severity of aortic stenosis [23].

16.4 Diastolic strain

- Early diastolic strain rate in relation to systolic and diastolic function and prognosis in aortic stenosis [52].

16.5 Left atrial strain

- Preoperative left atrial strain predicts postoperative atrial fibrillation in patients undergoing aortic valve replacement for aortic stenosis [40].

17. Conclusions

Deformation imaging, particularly in the form of global longitudinal strain, has evolved as a powerful tool in the evaluation of ventricular function in patients with aortic valve disease. GLS is particularly suited to detect subclinical LV dysfunction, before a drop in LV ejection fraction, providing the opportunity to intervene earlier to prevent serious and permanent LV dysfunction. The role of GLS in the management of aortic stenosis is quite robust, illuminating nuances of LV dysfunction in aortic valve disease such as impact in severity of AS, prognosis, timing for surgery and interventions, low gradient aortic stenosis and presence of associated coronary artery disease, among others. Similar added value has been demonstrated in the application of GLS in the detection of subclinical LV dysfunction in patients with aortic regurgitation. Very little information exists in the use of GLS in patients with mixed aortic valve disease providing an opportunity for future research in this important group of patients with aortic valve disease.

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