The value of left ventricular longitudinal strain in the therapeutic approach to aortic stenosis: a systematic review of the literature

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1 INTRODUCTION

Aortic stenosis (AoS) is currently one of the most common valve diseases, a reality that is related to the progressive increase in average life expectancy (COFFEY et al, 2021). Among individuals with AoS, about 40-50% have no symptoms (PELLIKKA et al, 2005). This absence of symptoms is related to compensatory mechanisms that initially allow sufficient ventricular function. The long-term outcome involves ventricular remodeling, with hypertrophy and fibrosis of the myocardium (MAGNE et al, 2019).

AoS does not have a single form of presentation. The phenotype can be diverse, impacting the timing at which symptoms appear, and this can occur before ventricular dysfunction or the threshold definition of severe AoS (CASACLANG-VERZOSA et al, 2019).

Currently, aortic valve replacement is recommended in severe AoS, regardless of the presence or absence of symptoms, with a left ventricular ejection fraction (LVEF) below 50% (BAUMGARTNER et al, 2017). In any case, the absence of symptoms and decreased LVEF are rarely concomitant. Most commonly, symptoms arise even with preserved LVEF (DAHL et al, 2015).

Although the LVEF is an important parameter in the context of cardiac performance evaluation, it is dependent on pre- and afterload, and may not faithfully portray the quality of systole. Left ventricular hypertrophy (LVH), a consequence of AoS, can confound the value of LVEF, which can show normal values throughout the natural history of the disease, even when fibrosis and longitudinal dysfunction are already present (PONIKOWSKI et al, 2016; HERRMANN et al, 2011).

Currently, there is awareness that normal LVEF does not exclude the existence of a problem requiring early therapy, avoiding adverse events or irreversible damage to the myocardium. The study of myocardial deformation, particularly Left Ventricular Longitudinal Strain (LLS), has been shown to be an important ally in the diagnosis of early changes in ventricular function, especially when compared with conventional echocardiographic parameters (KALAM et al, 2014; WANG et al, 2022).

The portrayal of myocardial strain allows the assessment of muscle fiber contractile function even before the deterioration of LVEF, which only takes into account the difference in ventricular chamber size at end-diastole and end-systole (NESBITT et al, 2009).

Because of the impact this knowledge has on therapeutic decision making, the interest in this topic is unavoidable, accompanied by a growing number of related investigations.

2 OBJECTIVE

The aim of this systematic literature review is to evaluate the incremental value of GLS, compared to conventional echocardiographic parameters, in assessing early, subclinical systolic dysfunction in patients with AoS, anticipating diagnosis and treatment.

3 METHODOLOGY

This document reflects an RSL, which followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The search for information was based on the analysis of scientific articles indexed in MEDLINE (via PubMed). For this, the following keywords were used: "strain and aortic stenosis". For each set of keywords, clinical studies and clinical trials were included, and review articles, letters to the editor, and clinical cases were excluded. Filters were also set for articles in English, Portuguese, or Spanish that had been published 10 years or less ago and that reflected results in the human species.

In a first phase, the articles were selected based on the title. After this first selection phase, the abstract of the articles resulting from the first phase was analyzed. Here we excluded all articles whose abstract demonstrated an inadequate objective or methodology for the theme. The full text was then read, and those whose information was not pertinent to the present RSL were eliminated. Here the major inclusion criterion was: studies that estimated to demonstrate the importance of GLS in the prognosis of patients with AoS. In order to decrease bias, articles that focused on specific groups of individuals with other associated known comorbidities, namely coronary artery disease, were excluded.

Of the 1373 articles that resulted from the initial search, using the aforementioned keywords, 1278 were excluded by the exclusion criteria. Then, 81 articles were eliminated by reading the title, leaving 14 articles with potential interest. After reading the abstract, the number of articles was reduced to 7, which became 5 by reading the full text, as described in Diagram 1.

PRISMA

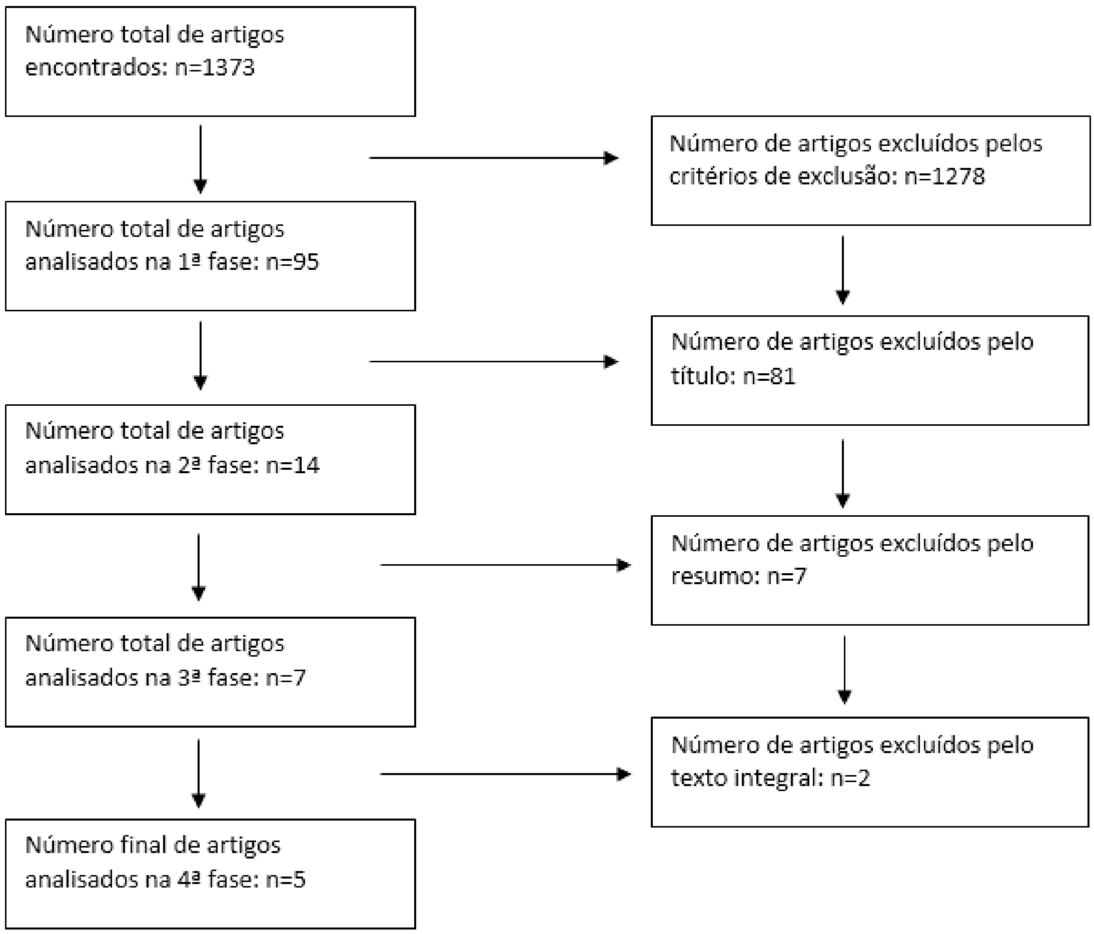

Diagrama 1 – *Workflow*

4 RESULTS

The corpus of the present SLR includes 5 final articles that were included because they met all the predefined inclusion criteria. Table 1 shows information regarding the year of publication, authors, type of study, and objective(s) for each article. All articles are written and published in English and reflect results from different populations and age groups.

In common they had the main objective - to study patients with moderate or severe AoS with preserved ejection fraction, and to assess what role and impact GLS plays in distinguishing between different levels of disease severity and/or on possible outcomes in patients over a given period of time.

Table 2 summarizes the methodology, results and conclusions of each of the selected articles. It should be noted that the methodology differed between each of the 5 articles, although in all of them, patients were evaluated using the same diagnostic method - echocardiography (2D and/or 3D).

Sato et al. (2014), who aimed to evaluate whether LV GLS was able to help discriminate between different outcomes in patients with paradoxical severe AoS with low flow and low gradient, concluded that GLS, achieved using speckle tracking, has predictive value in patients with severe AoS with low flow and low gradient, patients considered to be at high risk.

Nagata et al. (2015), in turn, wanted to determine which measurement of LV GLS, by 2D or 3D echocardiography, is more reliable in predicting major adverse cardiac events in patients with AoS. In asymptomatic patients with AoS and preserved LVEF, the results allowed for the conclusion that GLS, obtained by 3D echocardiography, is the independent predictor with the most impact on the development of future major adverse cardiac complications. However, the GLS resulting from 2D echocardiography showed important predictive ability relative to conventional echocardiography.

Salaun et al. (2018) estimated to evaluate the value of LV GLS, in apical 4-chamber (4C), in the prognosis of patients with AoS. The results showed that the longitudinal strain value, obtained in the apical 4C window, is related to the percentage of deaths in patients with AoS and preserved LVEF. The evaluation and grading of AoS should, however, take into account the flow and gradient through the aortic valve orifice, since in this study, the strain cutoff value is only valid for severe AoS patients with normal flow and high gradient. In patients with AoS and preserved LVEF, the longitudinal strain value in apical 4C should therefore be used for reliable assessment of left ventricular function and prognosis of the pathology, in addition to the flow-gradient classification, a parameter that is also mandatory in these cases.

Bi et al. (2020) aimed to assess the impact of severe AoS and its consequent increase in left ventricular afterload, myocardial strain and rotation mechanisms by 2D and 3D echocardiographic speckle tracking. They concluded that in patients with severe AoS, GLS and radial strain are decreased. Circumferential strain, basal rotation and torsional motion are, in turn, increased with likely effect on normalization of cardiac output and LVEF. These facts are confirmed on 2D and 3D ultrasound by speckle tracking. The deformation of myocardial fibers, with a consequent decrease in GLS is apparently related to the increase in LV preload and afterload. They were thus able to confirm the importance of studying myocardial deformation in patients with severe AoS and preserved LVEF.

Anwer et at. (2021) had as their main objective to investigate the existing changes in routine echocardiography and strain in patients with moderate to severe AoS during a 6-month follow-up period. The left atrium was shown to be the first cavity to undergo changes, dilating, in patients with low-flow and gradient AoS, even when LV systolic-diastolic structure and function remain intact. GLS has been shown to be determinant in the assessment of LV systolic function and degree of LV diastolic dysfunction.

Table 1 - Year and author, title and objective of the investigations included in this RSL

	Year and author	Title	Study Type	Goal
1	**2014** Kimi Sato, Yoshihiro Seo, Tomoko Ishizu, Masaaki Takeuchi, Masaki Izumo, Kengo Suzuki, Eiji Yamashita, Shigeru Oshima, Yoshihiro J. Akashi, Yutaka Otsuji, Kazutaka Aonuma.	Prognostic Value of Global Longitudinal Strain in Paradoxical Low-Flow, Low-Gradient Severe Aortic Stenosis with Preserved Ejection Fraction	Retrospective, multi-center	To evaluate whether Left Ventricular GLS can discriminate high-risk patients with different outcomes in severe AoS with paradoxical low-flow, low-gradient.
2	**2015** Yasufumi Nagata, Masaaki Takeuchi, Victor Chien-Chia Wu, Masaki Izumo, Kengo Suzuki, Kimi Sato, Yoshihiro Seo, Yoshihiro J. Akashi, Kazutaka Aonuma, Yutaka Otsuji.	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	Retrospective, multi-center	To determine which LV GLS, by 2D or 3D echocardiography, has more importance in determining major adverse cardiac events in patients with AoS.
3	**2018** Erwan Salaun, Anne-Claire Casalta, Erwan Donal, Yohann Bohbot, Elena Galli, Christophe Tribouilloy, Sandrine Hubert, Julien Magne, Julien Mancini, Sebastien Renard, Jean-Francois Avierinos, Laurie-Anne Maysou, Ce'cile Lavoute, Catherine Szymanski, Julie Haentjens, Gilbert Habib.	Apical four-chamber longitudinal left ventricular strain in patients with aortic stenosis and preserved left ventricular ejection fraction: analysis related with flow/gradient pattern and association with outcome	Retrospective, multi-center	To evaluate the value of LV apical 4-chamber GLS in the prognosis of patients with AoS.
4	**2020** Xiaojun Bi, Darwin F. Yeung, Husam M. Salah, Maria C. Arciniegas Calle, Jeremy J. Thaden, Lara F. Nhola, Hartzell V. Schaff, Sorin V. Pislaru, Patricia A. Pellikka, Alberto Pochettino, Kevin L. Greason, Vuyisile T. Nkomo, Hector R. Villarraga.	Dissecting myocardial mechanics in patients with severe aortic stenosis: 2-dimensional vs 3-dimensional-speckle tracking echocardiography	Prospective, unicenter	To evaluate the impact of severe AoS and its consequent increase in left ventricular afterload on myocardial deformation and turnover mechanisms through speckle tracking by 2D and 3D echocardiography
5	**2020** Shehab Anwer, Didem Oguz, Laura Galian-Gay, Irena Peovska Mitevska, Lilit Baghdassarian, Raluca Dulgheru, Tomas Lapinskas, Ciro Santoro, Savvas Loizos, Matteo Cameli, Elizabeta Srbinovska, Julia Grapsa, Julien Magne, Erwan Donal.	Echocardiographic findings on aortic stenosis: an observational, prospective, and multi-center registry	Prospective, unicenter	To investigate existing changes on routine echocardiography and strain in patients with moderate to severe AoS during a 6-month follow-up period.

Table 2 - Methodology, results and main findings of the investigations included in this RSL

	Methodology	Results/Conclusion
1	- They studied 509 patients with severe AoS, valve area <0.6cm /m^{22} and preserved ejection fraction; - They performed echocardiograms on all patients following the ASE guidelines obtaining M-mode, 2D and Doppler images and the other parameters present in a routine echocardiogram; - They found the peak jet velocity at Vao through several acoustic windows; - They estimated the left ventricular afterload; - Area Vao obtained by the continuity equation; - Patients are classified as to flow through the aVo: NF (normal flow) or LF (low flow) and as to gradient through the aVo: LPG (low gradient) or HPG (significant gradient); - Global Longitudinal Strain of the left ventricle obtained automatically; - The occurrence of major adverse cardiovascular complications was predicted using the previous parameters.	- Prevalence of symptoms and complications was higher in the LFHPG group and lower in the NFLPG group; - The LFLPG group had a higher prevalence of Coronary Artery Disease; - It has been shown that in the LFLPG group the LA is smaller in size as well as the LV mass; - The aortic valve area is smaller in the LFHPG group followed by the NFHPG group, LFLPG being larger in the NFLPG group; - LV diastolic function similar in all groups; - As for LV afterload, patients in the LF group had higher impedance and lower systemic arterial compliance; - LV GLS was lower in patients in the HPG groups than in patients with low gradient; - GLS of the LV plays a major role in detecting high-risk patients with severe AoS with LFLPG.
2	- They studied 104 patients with severe AoS and indexed area <0.6cm /m^{22} and preserved EF (<50%); - They performed 2D and 3D echo to analyze different parameters: pulsed Doppler, tissue, maximum velocity and mean and maximum gradient of aortic transvalvular flow, area of VAo (continuity eq.), EF, LA and LV volume and strain (longitudinal, circumferential and radial (using speckle tracking); - Follow-up of 373 days (on average) in each patient to study the appearance of major adverse cardiac complications; - Major adverse cardiac complications included death, sustained VT, VAo replacement due to increased symptoms, and hospitalization for heart failure at less than 2 years of follow-up.	- 33 patients developed major adverse cardiac complications: 4 deaths, 1 sustained VT, 11 heart insufflations requiring hospitalization, 17 VAo replacements, decreased EF in 2 patients, and hemodynamic changes in 2 patients; - 72 patients without developing complications after 1 year of follow-up and 58 after 2 years; - Patients who developed complications presented significantly higher values for: peak aortic flow velocity, mean gradient and LA area, and lower values for VAo; - 2DGLS, 3DGLS and 3DGRS significantly depressed for patients who develop complications; - 3DGLS cutoff value for development of complications: -14.5%; - 3DGRS cutoff value for developing complications: 39.0%; - 2DGLS cutoff value for development of complications: -17.0%; - 3DGLS was the parameter that changed most significantly between patients with and without developing complications.
3	- They studied 582 patients with moderate or severe AoS and preserved EF >/= 50%; - All had 2D echocardiography with Doppler study to obtain the different relevant echocardiographic parameters; - Patients are classified as to flow: low flow (LF) or normal flow (NF) and as to gradient: normal gradient (NG) or high gradient (HG); - GLS evaluated in apical 2, 3 and 4 chambers or only 2 and 4 chambers; - Patients were followed up during a 2-year follow-up period.	- 38 patients had moderate and 544 had severe AoS (451 NF and 93 LF; 442 HG and 102 LG); - Moderate EAo in younger, female patients with AF, with fewer symptoms and less need for surgery or TAVI at follow-up; - Severe EAo LF with higher incidence of AF than NF; - Severe LG EAo with less surgical recurrence/TAVI than HG; - A4CLS more impaired in patients with severe AoS LF than NF, LFHG than NFHG and NFLG than moderate AoS; - Presence of symptoms not associated with impairment of longitudinal strain; 2-year follow-up: 58 deaths (10.5% moderate AoS and 9.9% severe AoS); - LFLG associated with more deaths (17.6%); - A4CLS with a cutoff value of -13.5% associated with mortality in patients with NFHG EAo; are related to risk of death; - Strain 2D and classification regarding flow and gradient of significant importance in patients with AoS.
4	- They studied 168 patients with severe AoS;	- Patients with severe AoS and preserved LVEF have lower GLS and GRS;

	- All performed real-time 2D and 3D echocardiography with vital signs measurement immediately before; - 2D echocardiogram performed according to ASE guidelines; - The GLS, GCS, GRS, apical and basal left ventricular systolic peak and systolic peak twist were obtained; - 3D echocardiography allowed automatic imaging of different structures and speckle tracking; - They estimated LV preload by studying LV size at end-diastole and LV volume; - To estimate LV afterload, they measured total arterial stiffness, total arterial compliance, effective arterial elasticity, vascular systemic resistance, and arterial impedance.	- Patients with severe AoS and preserved LVEF have more apical rotation and twisting motion at the systolic peak; - There was no significant difference in baseline rotation by 2D and/or 3D echo in patients with severe AoS compared to healthy patients; - The agreement between 2D and 3D images was poor for GCS; - GLS is related to artery impedance as opposed to apical rotation and torsional motion; - LV mass is not related to GLS; - Patients with severe AoS have lower than normal GLS and GRS; - Patients with severe AoS have increased GCS, basal rotation and twisting motion to maintain cardiac output and compensate for LVEF.
5	- A total of 197 patients with a valve area <1.5cm were studied ;[2] - All had 2 echocardiograms, 1 baseline and one after 6 months of follow-up, according to ESC/EACTS guidelines for valve disease; - Patients subdivided into: patients with AoS and preserved LVEF (subdivided into severe or moderate AoS) and low-flow, low-gradient AoS (LFLG).	- GLS decreased after 6 months of follow-up; - LA volume increased relative to baseline echocardiogram; - LV diameter and mass increased on follow-up echocardiogram; - LV systolic pressure was statistically significantly higher after 6 months; - Patients in the LFLG group had statistically lower GLS; - There was no significant difference in LV diastolic function in the two groups; - RV systolic pressure was higher in the LFLG group; - There was no significant difference in GLS between patients with moderate or severe AoS; - LA dilatation is the first change to occur in patients with LFLG EAo even with preserved LV systolic and diastolic dimensions and function; - GLS is an important marker of LV systolic and diastolic function; - RV function is an important parameter in the evaluation of AoS.

5 DISCUSSION

This systematic review of the literature, which gathered 5 investigations that included a total of 1560 individuals, suggests that the GLS when compared with the classical LVEF quantification, informs in advance about subclinical changes in myocardial mechanics. The GLS has, therefore, great prognostic utility in asymptomatic populations with AoS, allowing to anticipate therapeutic decision making, providing information that would hardly be available otherwise.

The most recent European and American recommendations limit surgery in severe AoS, regardless of symptomatology, to an LVEF of less than 50% (BAUMGARTNER et al, 2017; NISHIMURA et al, 2017)

Although LVEF has in itself important prognostic information, it is load-dependent and not a faithful index of myocardial contractility. The alteration in ventricular geometry, with the presence of hypertrophy, contributes to the fact that the parameter may remain within the normal range until the final stage of the disease, even if myocardial fibrosis and longitudinal dysfunction are already present. LVEF does not follow the progressive severity of AoS, whereas, in turn, GLS progressively degrades as the disease progresses (PONIKOWSKI et al, 2016; HERRMANN et al, 2011).

Also the concept of paradoxical AoS, with low flow/low gradient, has to be taken into consideration in this context. It is estimated to represent about 5 to 10% of cases of AoS (BARTKO et al, 2013). In these cases, the functional area of the aortic valve is reduced, but paradoxically the mean transvalvular gradient and systolic ejection volume are low, yet they have preserved LVEF. Inconsistency in the application of the continuity equation, a method used in echocardiography to calculate the aortic valve area, may lead to errors since it is an indirect measurement, which in turn may be at the origin of this paradox. Failure to index valve area to body surface area can also influence diagnosis (CAVACA et al, 2017). The non-existence of a significant transvalvular gradient can shift the focus to LVEF, and this parameter too can misrepresent the severity of the problem. GLS can help make a more assertive diagnostic approach in these cases.

Studies using cardiac magnetic resonance imaging describe changes in the myocardium in individuals with various stages of AoS, despite preserved LVEF (CHIN et al, 2017; BARONE-ROCHETTE et al, 2014). Many studies have found that myocardial contractility of longitudinal fibers appears earlier, which eludes LVEF quantification (DONAL et al, 2009; NG et al, 2011; LANCELLOTTI et al, 2010).

The study of histological processes, allow us to realize that the extent of hypertrophy and myocardial fibrosis is strongly related to the decrease in myocardial mechanics, assessed by GLS (MÁTYÁS et al, 2018). The pressure overload, imposed by AoS, has as its main structural consequence the development of LVH, as an adaptive response to this same pressure increase. Simultaneously, ventricular chamber volumes are smaller, resulting this context in normal LVEF, which may mask a decreased longitudinal strain (STOKKE et al, 2017).

Changes in LV longitudinal function are a consequence of AoS. The study of longitudinal function allows monitoring of disease progression, since its degradation accompanies changes in LV geometry and proliferation of myocardial fibrosis (WEIDEMANN et al, 2009; NG et al, 2011).

For this reason, current scientific evidence highlights the fact that LVEF is an insufficient parameter that can distort the perception of the quality of systolic ventricular function, and this has an influence on the timing of the implementation of appropriate therapy (BARONE-ROCHETTE et al, 2014; MENG et al, 2021). A recent study found that 13.1% of deaths occurred in individuals without significant LVEF compromise, who did not meet the current criteria in the recommendations and were not subjected to adequate therapy (NG et al, 2018).

Myocardial fibrosis develops early in a pressure overload scenario, as is the case with AoS. The establishment of fibrosis is progressive and may reach a point of no return, i.e., irreversible. This awareness alerts to the fact of the importance of assertive diagnosis and the implementation of adjusted therapy, relieving the pressure overload and allowing the regression of the fibrotic process (RUPPERT et al, 2019).

Speckle tracking is a modality of echocardiography that allows the assessment of the quality of myocardial deformation (MOR-AVI et al, 2011). It is now well established that the quantification of GLS is of tremendous interest in the context of valvular heart disease. GLS has numerous advantages, yet it remains dependent on afterload and geometry, which highlights the need to analyze some cases with extra care. The GLS, by integrating functional (contractility), hemodynamic (afterload) and also morphological (hypertrophy and fibrosis) factors, is profiled as an effective method with a huge potential to be part of the echocardiographic study in individuals with AoS (MAGNE et al, 2019).

In AoS, the GLS is compromised and can be seen as a predictor of adverse cardiac events, predicting the progression to heart failure, even in asymptomatic individuals. Fibrosis can be seen as the main factor influencing the decrease in GLS, which not being taken into account when evaluating LVEF makes it perceived that symptom-free individuals are highly benefited by its use (MAGNE et al, 2019).

Also, increased LV mechanical dispersion, which reflects intraventricular macanic dyssynchrony and can be assessed with Speckle Tracking, is associated with adverse outcomes in individuals with AoS, regardless of LVEF (KLAEBOE et al, 2017).

Regarding the clinical repercussion of the implementation of the use of GLS in individuals with AoS, the evidence seems to point to a tendency for an earlier diagnosis of subclinical alterations, with impact on the therapeutic decision making. Two review articles concluded that with GLS values lower than 14.7%, a defined cut-off value, a marked increase in mortality or decreased quality of life seems to occur, even when LVEF is normal (WANG et al, 2022; MAGNE et al, 2019).

Although the GLS obtained using 3D echocardiography has demonstrated advantages, we are still not close to a scenario where even 2D Speckle Tracking is used in the routine of most hospitals. Even so, the predictable impact of the use of GLS for an assertive diagnosis, which prevents the progression of the disease to an irreversible stage, accompanied by a decrease in mortality and associated morbidity, cannot but draw attention to the need to consider the possibility of including Speckle Tracking evaluation of individuals with AoS in the next recommendations, regardless of the stage of the disease. The economic impact can also be taken into consideration, since successive hospitalizations can be avoided among individuals with AoS, with apparently normal function, but already with reduced GLS.

6 LIMITATIONS

Two staff members were involved in the screening, data extraction and analysis of the articles, and the protocol for this purpose was established according to PRISMA recommendations. However, the protocol was not published, which can be seen as a limitation of this RSL. The search was performed in only one bibliographic database, PubMed/MEDLINE. The quality assessment of the studies was not performed by anyone outside the team.

7 CONCLUSIONS

GLS provides additional information of extraordinary relevance in the study of individuals with AoS, regardless of the presence or absence of symptoms, LVEF value or stenosis severity. Cases of AoS with low flow/low gradient also benefit from the use of GLS. Given its potential in risk stratification in this type of patients, its introduction in the algorithms that guide their assessment is recommended.

REFERENCES

ANWER, S. et al. Echocardiographic findings on aortic stenosis: an observational, prospective, and multi-center registry. **Perfusion**, v. 36, n. 3, p. 269-276, 2021.

BARONE-ROCHETTE, G. et al. Prognostic significance of LGE by CMR in aortic stenosis patients undergoing valve replacement. **Journal of the American College of Cardiology**, v. 64, n. 2, p. 144-154, 2014.

BARTKO, P. E. et al. Two-dimensional strain for the assessment of left ventricular function in low flow-low gradient aortic stenosis, relationship to hemodynamics, and outcome: A substudy of the multicenter TOPAS study. **Circulation**. **Cardiovascular imaging**, v. 6, n. 2, p. 268-276, 2013.

BAUMGARTNER, H. et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. **European heart journal**, v. 38, n. 36, p. 2739-2791, 2017.

BI, X. et al. Dissecting myocardial mechanics in patients with severe aortic stenosis: 2-dimensional vs 3-dimensional-speckle tracking echocardiography. **BMC cardiovascular disorders**, v. 20, n. 1, 2020.

CASACLANG-VERZOSA, G. et al. Network tomography for understanding phenotypic presentations in aortic stenosis. JACC. **Cardiovascular imaging**, v. 12, n. 2, p. 236-248, 2019.

CAVACA, R. et al. Paradoxical aortic stenosis - systematic review. **Revista portuguesa de cardiologia [Portuguese journal of cardiology]**, v. 36, n. 4, p. 287-305, 2017.

CHIN, C. W. L. et al. Myocardial fibrosis and cardiac decompensation in aortic stenosis. JACC. **Cardiovascular imaging**, v. 10, n. 11, p. 1320-1333, 2017.

COFFEY, S. et al. Global epidemiology of valvular heart disease. Nature reviews. **Cardiology**, v. 18, n. 12, p. 853-864, 2021.

DAHL, J. S. et al. Effect of left ventricular ejection fraction on postoperative outcome in patients with severe aortic stenosis undergoing aortic valve replacement. **Circulation. Cardiovascular imaging**, v. 8, n. 4, 2015.

DONAL, E. et al. Influence of afterload on left ventricular radial and longitudinal systolic functions: a two-dimensional strain imaging study. **European journal of echocardiography: the journal of the Working Group on Echocardiography of the European Society of Cardiology**, v. 10, n. 8, p. 914-921, 2009.

HERRMANN, S. et al. Low-gradient aortic valve stenosis. **Journal of the American College of Cardiology**, v. 58, n. 4, p. 402-412, 2011.

KALAM, K.; OTAHAL, P.; MARWICK, T. H. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. **Heart (British Cardiac Society)**, v. 100, n. 21, p. 1673-1680, 2014.

KLAEBOE, L. G. et al. Prognostic value of left ventricular deformation parameters in patients with severe aortic stenosis: A pilot study of the usefulness of strain echocardiography. **Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography**, v. 30, n. 8, p. 727- 735.e1, 2017.

LANCELLOTTI, P. et al. Impact of global left ventricular afterload on left ventricular function in asymptomatic severe aortic stenosis: a two-dimensional speckle-tracking study. **European journal of echocardiography: the journal of the Working Group on Echocardiography of the European Society of Cardiology**, v. 11, n. 6, p. 537-543, 2010.

MAGNE, J. et al. Distribution and prognostic significance of left ventricular global longitudinal strain in asymptomatic significant aortic stenosis: An individual participant data meta-analysis. **JACC. Cardiovascular imaging**, v. 12, n. 1, p. 84-92, 2019.

MÁTYÁS, C. et al. Comparison of speckle-tracking echocardiography with invasive hemodynamics for the detection of characteristic cardiac dysfunction in type-1 and type-2 diabetic rat models. **Cardiovascular diabetology**, v. 17, n. 1, p. 13, 2018.

MENG, Y. et al. Prognostic value of right ventricular 3D speckle-tracking strain and ejection fraction in patients with HFpEF. **Frontiers in cardiovascular medicine**, v. 8, p. 694365, 2021.

MOR-AVI, V. et al. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. **European journal of echocardiography: the journal of the Working Group on Echocardiography of the European Society of Cardiology**, v. 12, n. 3, p. 167-205, 2011.

NAGATA, Y. 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. JACC. **Cardiovascular imaging**, v. 8, n. 3, p. 235-245, 2015.

NESBITT, G. C.; MANKAD, S.; OH, J. K. Strain imaging in echocardiography: methods and clinical applications. **The international journal of cardiovascular imaging**, v. 25 Suppl 1, n. S1, p. 9-22, 2009.

NG, A. C. T. et al. Alterations in multidirectional myocardial functions in patients with aortic stenosis and preserved ejection fraction: a two-dimensional speckle tracking analysis. **European heart journal**, v. 32, n. 12, p. 1542-1550, 2011.

NG, A. C. T. et al. Left ventricular global longitudinal strain is predictive of all-cause mortality independent of aortic stenosis severity and ejection fraction. **European heart journal cardiovascular Imaging**, v. 19, n. 8, p. 859-867, 2018.

NISHIMURA, R. A. et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American college of cardiology/American heart association task force on clinical practice guidelines. **Circulation**, v. 135, n. 25, 2017.

PELLIKKA, P. A. et al. Outcome of 622 adults with asymptomatic, hemodynamically significant aortic stenosis during prolonged follow-up. **Circulation**, v. 111, n. 24, p. 3290-3295, 2005.

PONIKOWSKI, P. et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. **European journal of heart failure**, v. 18, n. 8, p. 891-975, 2016.

RUPPERT, M. et al. Incomplete structural reverse remodeling from late-stage left ventricular hypertrophy impedes the recovery of diastolic but not systolic dysfunction in rats. **Journal of hypertension**, v. 37, n. 6, p. 1200-1212, 2019.

SALAUN, E. et al. Apical four-chamber longitudinal left ventricular strain in patients with aortic stenosis and preserved left ventricular ejection fraction: analysis related with flow/gradient pattern and association with outcome. **European heart journal cardiovascular Imaging**, v. 19, n. 8, p. 868-878, 2018.

SATO, K. et al. Prognostic value of global longitudinal strain in paradoxical low-flow, low-gradient severe aortic stenosis with preserved ejection fraction. **Circulation journal: official journal of the Japanese Circulation Society**, v. 78, n. 11, p. 2750-2759, 2014.

STOKKE, T. M. et al. Geometry as a confounder when assessing ventricular systolic function: Comparison between ejection fraction and strain. **Journal of the American College of Cardiology**, v. 70, n. 8, p. 942-954, 2017.

WANG, Y. et al. Prognostic value of global longitudinal strain in asymptomatic aortic stenosis: A systematic review and meta-analysis. **Frontiers in cardiovascular medicine**, v. 9, 2022.

WEIDEMANN, F. et al. Impact of myocardial fibrosis in patients with symptomatic severe aortic stenosis. **Circulation**, v. 120, n. 7, p. 577-584, 2009.