Prognostic Echocardiographic Data in Asymptomatic Severe Aortic Stenosis

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Abstract

Aortic stenosis is the most common valve disease in developed countries and a valvular disease of growing importance in developing countries. In the natural history of the disease, the onset of symptoms correlates with significant worsening in prognosis and aortic valve replacement is the only procedure capable of changing the survival of these symptomatic patients. However, treatment of patients with asymptomatic severe aortic stenosis is still controversial as, classically speaking, the risks of surgery seemed to outweigh the benefit offered by valve replacement in these individuals. The importance of echocardiography in the early detection of aortic stenosis, in the classification of its severity and in its evolutional follow-up is already established. The objective of this study is to discuss how echocardiographic data help evaluate the risk in the asymptomatic severe aortic stenosis and thus facilitate its clinical management.

Introduction

Aortic stenosis (AS) is a chronic progressive disease with significant morbidity and mortality in our community. It is noteworthy for its clinical relevance and its growing socioeconomic impact. It is estimated that, by 2050, 10% of the Brazilian population will be older than 75 years and recent epidemiological data indicate that 3% to 4.5% of this age group will present degenerative AoS[1,2]. Although the symptoms represent the biggest prognostic milestone in this disease, echocardiographic findings allow a better stratification, which may mean surgical indication of exception in asymptomatic individuals at high risk or in those in which the characterization of symptoms is doubtful. Echocardiogram as the main diagnostic imaging method in AoS evaluates anatomical and functional data and can provide prognostic and evolutional data of this valve disease.

Keywords

Echocardiography; Aortic valve stenosis/mortality; Heart valve diseases/complications; Survivorship (Public Health); Prognosis.

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This manuscript aims to consistently review the main prognostic echocardiographic parameters in asymptomatic severe AoS and discuss how new echocardiographic technologies can help in a more effective risk stratification in this group.

Degree of valve calcification, aortic transvalvular peak velocity, gradients and aortic valve area

In a groundbreaking study published in 1997, Otto et al.[3] prospectively evaluated 123 asymptomatic adults with AoS greater than moderate. Symptom-free survival was 93% in the first year and 34% in the fifth year. The authors demonstrated that it is unlikely that individuals with aortic transvalvular peak velocity (PV) < 3 m/s develop symptoms in the first five years. However, in those with VP > 4 m/s there is a chance greater than 50% of death or onset of symptoms within two years[3].

A prospective study by Rosenhek et al.[4] with 128 patients with asymptomatic AoS and PV > 4 m/s, with aortic valve replacement (AVR) delayed until the onset of symptoms, outcomes-free survival (death or AVR due to onset of symptoms) was 67% in one year and 33% in five years, and the PV rate of progression was higher in patients who developed symptoms compared to those who remained asymptomatic (0.45 ± 0.38 versus 0.14 ± 0.18 m/s per year, p < 0.001). In this study, patients were classified according to the degree of aortic valve calcification, and the intensity of calcification was the only predictor of outcomes in multivariate analysis. Event-free evolution occurred in 92 ± 5% in one year and 75 ± 9% in four years in patients with absent or mild degree of calcification. Individuals with calcification greater than moderate had less chances of event-free survival: 60 ± 6% in one year and 20 ± 5% in four years[4].

In 2005, Pellikka et al.[5] published a retrospective study involving 622 patients with asymptomatic AoS and PV ≥ 4 m/s evaluated for five years. It was shown that survival free of cardiac events (cardiac death and AVR) was 80% in the first year and 25% in five years. In multivariate analysis, the Aortic Valve Area (AVA) and Left Ventricular Hypertrophy (LVH) were independent predictors of the development of symptoms, while chronic renal failure and PV were predictors of mortality[5].

In the same year, Lancellotti et al.[6] published a prospective study of 69 patients with asymptomatic severe AoS (AVA ≤ 1.0 cm^2), with preserved left ventricular ejection fraction (LVEF), accompanied for 15 ± 7 months. During follow-up, 61% of patients had cardiovascular events. The study showed that AVA < 0.75 cm^2 and increase in the average aortic valve gradient (TPG) ≥ 18 mmHg with effort were predictors of unfavorable outcomes[6].

In 2010, Rosenhek et al.[7] followed prospectively, for an average of 41 months, 113 asymptomatic patients with very severe AoS (PV ≥ 5 m/s, TPG > 60 mmHg and AVA < 0.6 cm²). The study showed that the higher the PV, the lower the event-free survival. This rate in individuals with PV ranging from 4 to 5 m/s was 39 ± 16% in four years, in individuals with PV ranging from 5 to 5.5 m/s, it was 17 ± 5% in four years, and in those with PV ≥ 5.5 m/s, it was only 4 ± 4% over four years (Figure 1). AVA, unlike PV, did not add any prognostic information in this population at very high risk[7].

Maréchaux et al.[8] prospectively studied 135 asymptomatic patients with AoS greater than moderate and demonstrated that exercise echocardiography provides additional prognostic information allowing a more accurate analysis of asymptomatic patients, helping to stratify their prognosis. Patients with baseline TPG greater than 35 mmHg and an increase of the gradient induced by physical exercise > 20 mmHg presented an 9.6-fold increase in the risk of events compared to a 2.5-fold increase in patients with a baseline gradient greater than 35 mmHg who had an increase in the gradient ≤ 20 mm Hg with exercise[8].

An Italian prospective study published by Cioffi et al.[9] evaluated 209 patients with severe asymptomatic AoS for a mean follow-up period of 22 months. The extensive calcification was present in 71% of patients who developed adverse events. Again, the strength of the calcification was shown to be independent predictor of unfavorable outcomes[9].

Analyzing this information together, we conclude that the PV, TPG at rest and during stress, AVA, the rate of progression of PV and AVA decrease over time are echocardiographic data relating to poor prognosis in AoS, even if asymptomatic. For this reason, the last American[10] and European[11] guidelines recommend that consideration be given to aortic valve replacement in asymptomatic patients at low surgical risk and PV ≥ 5 m/s, as well as those with marked elevation of TPG (> 20 mmHg) in exercise echocardiography, or those presenting rapid progression of the disease characterized by high PV > 0.3 m/s per year and reduction in AVA > 0.1 cm²/year.

Valvuloarterial impedance

Valvuloarterial impedance (Zva) corresponds to an index that estimates left ventricular (LV) afterload. It is a more robust descriptor of AoS hemodynamics and a better predictor of LV dysfunction compared to other traditional measures of stenosis severity[12,13].

Zva is calculated by dividing the estimated LV systolic pressure (systolic blood pressure measured in the upper limb + TPG) by the indexed systolic volume (iSV) (in mL/m²). Therefore, Zva represents the total pressure cost (in mmHg) for each milliliter of blood pumped by the LV during systole, indexed by body surface area[13].

$$ZVa = \frac{SBP + TPG}{iSV}$$

Based on a retrospective analysis of 544 patients with AoS greater than moderate, Hachicha et al. demonstrated that Zva was a strong predictor of mortality. In this study, the primary outcome was mortality regardless of valve replacement. Four-year survival was significantly lower in patients with Zva ≥ 4.5 mmHg/mL/m² (65 ± 5%) compared to patients with

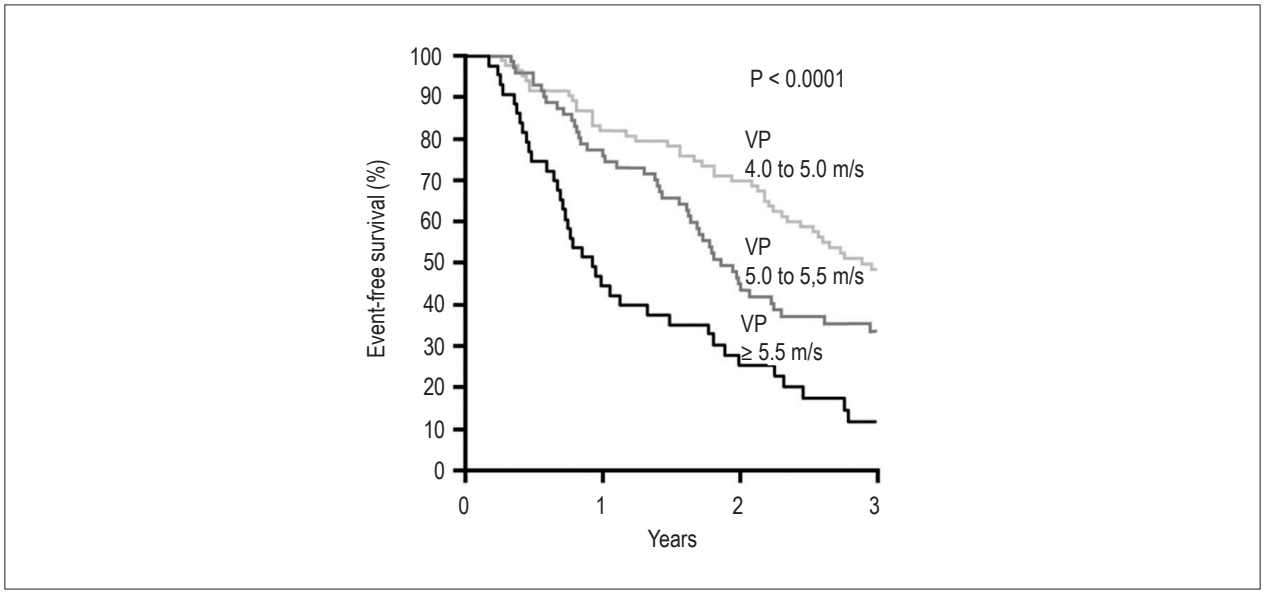

Figure 1 – *Kaplan-Meier curve showing the difference in event-free survival over the years, comparing the groups according to the PV value. PV: transvalvular aortic peak velocity. Adapted from Rosenhek et al.[7].*

Zva ranging from 3.5 to 4.5 mmHg/mL/m² (78 ± 4%) and those with Zva ≤ 3.5 mmHg/mL⁻¹/m² (88 ± 3%). Patients with low Zva had similar survival to the general population of the region (Quebec, Canada), while patients with medium and high Zva had lower survival than the control group (Figure 2). The presence of Zva ranging from 3.5 to 4.5 mmHg/mL/m² is associated with a 2.3-fold increase in overall mortality and 3.11-fold increase in cardiovascular mortality, while Zva ≥ 4.5 mmHg/mL/m² is associated with the rise by 2.76 and 3.71 times in overall and cardiovascular mortality, respectively. The multivariate analysis showed as independent risk factors older age, increased LV mass and the presence of high Zva, while surgical treatment was a protective factor[13].

Lancellotti et al.[14] confirmed these findings in a prospective study involving 163 asymptomatic patients with AoS greater than moderate. A Zva ≥ 4.9 mmHg/mL/m² was associated with worse prognosis, increased risk of major cardiovascular events, regardless of the PV value[14].

The results of the study by Hachicha et al.[13] were also supported by a substudy from the SEAS study (Sinvastatin and Ezetimibe in Aortic Stenosis), in which high Zva was an independent predictor of myocardial dysfunction in asymptomatic patients with AoS greater than moderate. The study included 1,418 patients aged 67 ± 10 in a prospective controlled randomized study with follow-up of 43 ± 14 months. The presence of a Zva > 5 mmHg/mL/m² was an independent factor of poor prognosis, increasing by 35% the risk of major cardiovascular events and 41% the risk of aortic valve event[15].

These studies stress the importance of blood pressure control in patients with AoS and demonstrate that degenerative AoS should not be seen as limited to the valve disease, but as part of a complex that also includes the reduction of systemic arterial compliance and changes to the LV function[13,16].

Tissue Doppler

New echocardiographic modalities such as Tissue Doppler (TD) and the Strain/Strain Rate have proven to be relevant among patients with a variety of valve disorders, such as AoS.

The LV filling pressure in patients with AoS can be estimated by the ratio between the mitral flow e-wave and TD e-wave. However, its usefulness in predicting clinical outcomes has not been consolidated[17]. The reduction in ventricular longitudinal contractility measured by TD has been reported in symptomatic and asymptomatic patients with AoS[18].

In a prospective study by Poh et al.[19] with 53 patients with AoS and preserved LVEF, patients with clinical outcomes defined by cardiovascular death and need for AVR presented, in addition to reduced AVA, low e', a' and S' velocities, higher values of transmitral protodiastolic flow wave velocity (e-wave) and E/e' ratio. Septal a' wave velocity smaller than 9.6 cm/s was associated with a significant reduction in event-free survival and predicted this outcome with

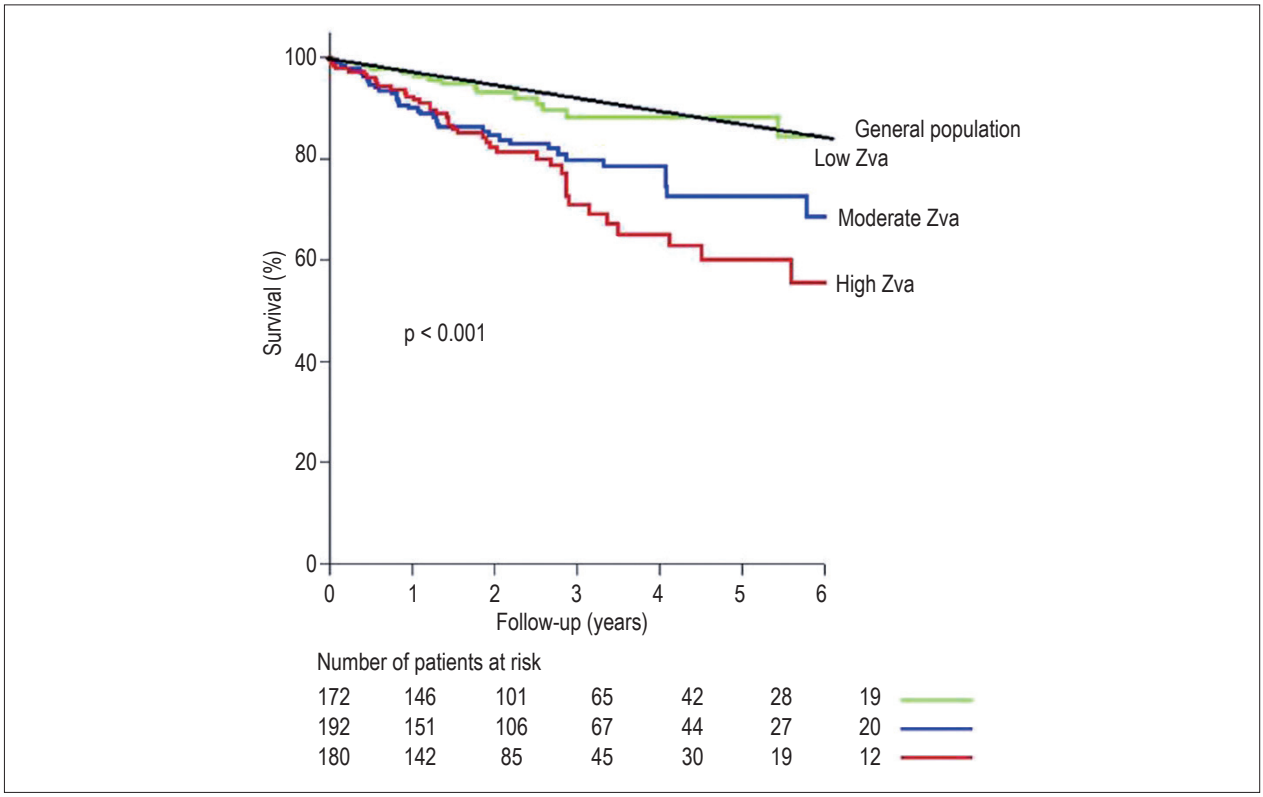

Figure 2 – *Overall survival as assessment of the Zva degree. Low Zva ≤ 3.5 (green line), moderate 3.5 ≤ Zva ≤ 4.5 (blue line) and high Zva ≥ 4.5 (red line). Survival was compared with the general population (control group, black line). Zva: valvuloarterial impedance. Adapted from Hachicha et al.[13].*

sensitivity, specificity and accuracy of 94%, 80% and 85%, respectively (Figure 3). Therefore, a lower a' velocity appears to be a predictor of cardiovascular death and need for AVR, suggesting an important and compensatory left atrial role in LV function. Moreover, the TD's ability to stratify diastolic function should have important clinical implications, since the extent of the dysfunction is an independent predictor of late mortality after AVR[19].

Lancellotti et al.[20] reported the additional prognostic value of TD in a prospective study with asymptomatic patients with AoS greater than moderate. In the multivariate analysis, the factors that associated independently with a predefined composite outcome were gender, indexed left atrial volume, e' wave velocity, E/e' ratio, a' wave velocity and BNP levels. In this study, the a' wave velocity ≤ 9 cm/s was associated with high risk of death, development of symptoms or need for AVR. A high E/e' ratio proved to be an important marker of adverse events in patients with preserved LVEF, considering that an E/e' ratio > 13.8 identified a group of patients at high risk of future events[20].

Strain and Strain rate

The TD is important in evaluating the LV function, checking the movement speed of myocardial tissues. However, it does not evaluate the strain of myocardial fibers, an important component of regional and global contractility. It can be measured by echocardiography, with the advent of new techniques: strain and strain rate[21,22].

Most studies evaluating the longitudinal myocardial strain in patients with AoS used TD, which calculates strain based on tissue velocity information. However, the use of Speckle Tracking (ST — which calculates the strain using two-dimensional echocardiography) as a tool for prognostic evaluation of patients with AoS is becoming more widespread[23-25].

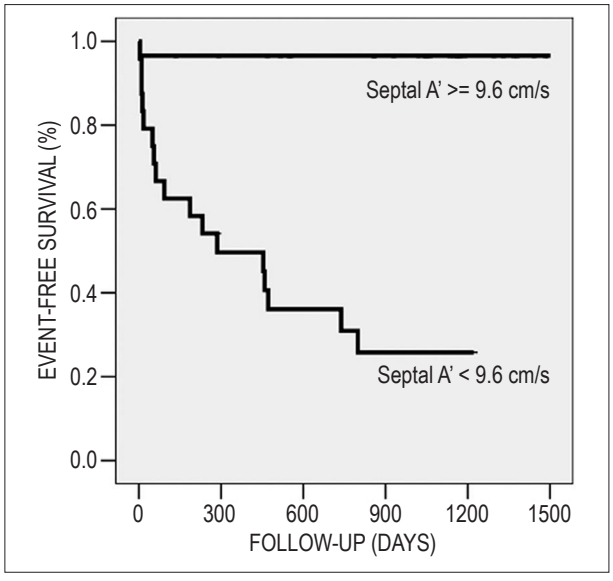

Figure 3 – *Kaplan-Meier curve showing survival free of cardiac death or aortic valve replacement in patients with aortic stenosis stratified according to the late diastolic septal annular velocity (A'). Adapted from Poh et al.[19].*

In asymptomatic AoS, myocardial analysis using strain has shown signs of incipient systolic dysfunction, that is, it is found in patients with preserved LVEF[26-28]. Circumferential strain, rotation and apical twist undergo changes to compensate for the overload of intracavity pressure and subendocardial ischemia. Apical rotation and LV twist are increased LV and the return to basal conditions (untwist) is delayed compared to normal individuals. Such mechanisms are lost with the deterioration of ventricular function.

Carasso et al.[29] in a study with 45 patients (mean age 65 years) investigated the changes in myocardial strain in patients with severe AoS. Some changes of longitudinal and circumferential strain were detected. In the analyzed images, compensated patients had increased apical rotation angles and high rates of circumferential strain while in decompensated patients the opposite was the case. Therefore, the analysis of these elements can serve as an important parameter to evaluate the degree of compensation of patients with asymptomatic severe AoS. With the evolution of the disease, the myocardium loses its compensatory mechanisms. Therefore, the strain and its variants tend to decrease, as well as the apical rotation and LV twist[29].

Ng et al.[25], in a study with 420 patients with AoS and preserved LVEF, showed that the progressive deterioration in the measurement of the longitudinal, radial and circumferential strain, is proportionally related to the severity of the progression of AoS[25]. A similar result was also reported by Delgado et al.[27], which showed a decrease of multidirectional strains, except for radial strain[27]. Furthermore, Maréchaux et al.[30] in a study with 82 patients, showed a proportionally inverse correlation between Zva and the Global Longitudinal Strain (GLS), which, interpreted jointly, proved to be worse prognosis predictors[30].

In a recent prospective study, asymptomatic patients with AoS greater than moderate were evaluated by GLS with two-year follow-up. In this study, a value smaller than -15% translated a thirty-fold increased risk of all-cause mortality. The association between GLS and all-cause mortality was independent of the coexistence of other variables such as age, sex, symptoms, aortic transvalvular gradients, AVA and LVEF. This suggests that GLS is a parameter that could help in the indication of an early invasive approach, as it indicates a group of high-risk patients (Figure 4)[23].

A study by Lancellotti et al.[14], prospective, with 163 patients, analyzed the risk stratification in asymptomatic patients with AoS greater than moderate, evaluating multiple outcomes: symptoms, cardiac death and the need for AVR. The authors concluded in a multivariate analysis that a GLS ≤ 15.9% (absolute value) was given a significant predictor for the development of symptoms, surgical intervention or death (Figure 5)[14].

The analysis of GLS through ST has the potential to provide more precise information about LV function and its contractile reserve during stress tests (dobutamine or exercise stress test)[31]. In another study, Lafitte et al.[24] studied 60 patients with severe asymptomatic AoS, with preserved LVEF, over twelve months, and found a smaller GLS, both at rest

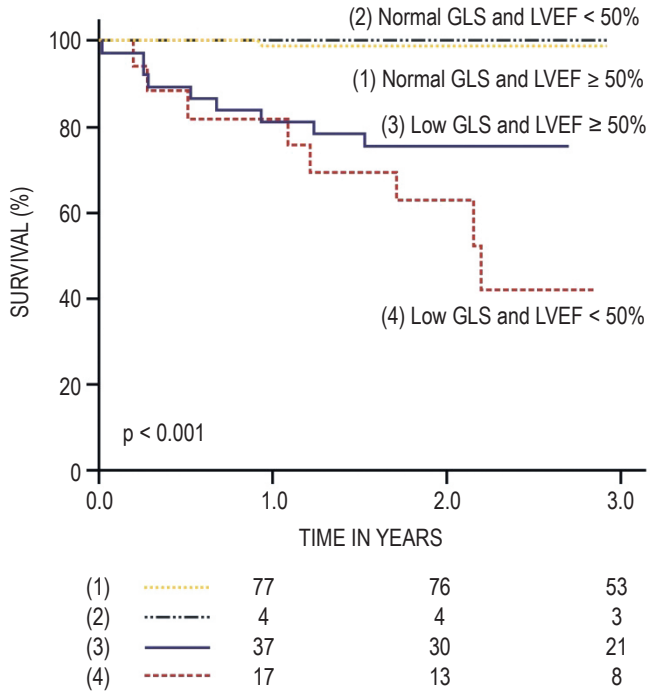

Figure 4 – *Kaplan-Meier curve showing the interaction between GLS and LVEF as prognostic factors related to mortality causes. Normal GLS > -15% (absolute value); low GLS ≤ 15% (absolute value). SGL: global longitudinal strain; LVEF: left ventricular ejection fraction. Adapted from Kearney et al.[23].*

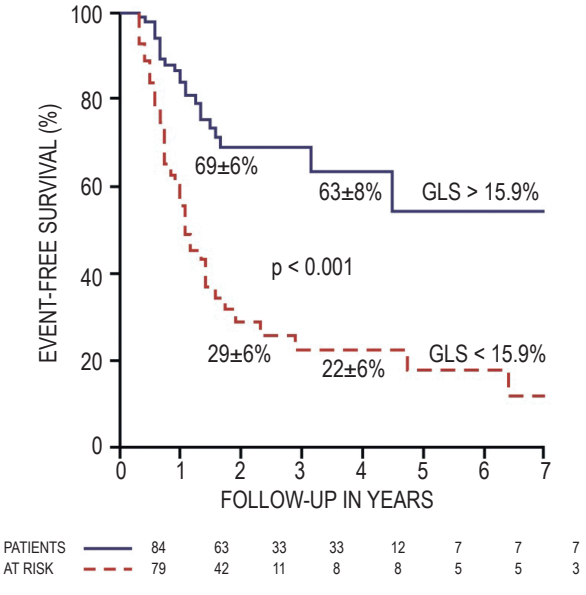

Figure 5 – *Event-free survival according to the categorical variables selected in the Cox proportional hazards regression analysis. GLS: global longitudinal strain. Adapted from Lancelotti et al.[14].*

and during exercise, in patients with AoS compared to the control group. They demonstrated an association between GLS and the need for cardiac hospitalization, cardiac events and cardiovascular death[24].

Abnormal GLS values, which reflect LV systolic dysfunction, are commonly found in patients with AoS greater than moderate, often precede the symptoms and on many occasions precede LVEF reduction (Figures 6 and 7). The measurement of GLS is quick, highly reproducible, and is a strong predictor of adverse cardiac events, including all-cause mortality. GLS can also be an important tool in the prognostic evaluation of patients with AoS with low low-flow gradient[32]. Thus, the incorporation of GlS in risk stratification can be useful in identifying the best moment for the therapeutic approach.

Evaluation of ventricular mass

In the study by Pellikka et al.[5] in 2005, as detailed above, half of the patients developed classic symptoms prior to AVR. The presence of LVH was an independent predictor for the development of symptoms in the multivariate analysis, with a risk ratio of 1.39 (CI 95% 1.02 - 1.89; p = 0.04). LVH was also associated with overall mortality with a risk ratio of 1.51 (CI 95% 1.02 - 2.22; p = 0.04)[5].

The Italian prospective study by Cioffi et al.[9], published in 2011, evaluated the occurrence of unfavorable outcomes (symptoms, hospitalization, AVR and death) in patients with severe asymptomatic AoS classified according to the left ventricular mass (LVM): appropriate versus inappropriately high. There were adverse events in 67% patients with inappropriate LVM and in 30% of patients with appropriate LVM (p < 0.001). The indexed LVM was better than the presence of classical LVH in predicting events. In the multivariate analysis, indexed LVM was the strongest independent predictor of adverse events[9].

Systolic dysfunction

A retrospective study by Pai et al.[33], published in 2006, evaluated 338 asymptomatic patients with severe AoS. The mean LVEF was 59 ± 17% and an average clinical follow-up of 3.5 years was conducted with a primary objective of analyzing the AVR effect in mortality from all causes. The AVR surgery in 99 patients (29%) was associated with lower mortality with a risk ratio of 0.17 and better LVEF (65 ± 14% versus 57 ± 18%); p < 0.0001). In the non-operated subgroup, a lower LVEF was independently associated with mortality and there was increased mortality of 1% for each 1% reduction in LVEF[33].

Patients with asymptomatic severe AoS and systolic dysfunction characterized by reduced LVEF (EF < 50%) constitute a high-risk group for major cardiovascular events. In these patients, the AVR indication in several international guidelines (Class I recommendation)[2,10,11] is consensual.

Diastolic dysfunction

Diastolic function by mitral inflow pulsed Doppler analysis[34] was one of the items evaluated in a prospective study by Lancellotti et al.[14], of 2010, cited above. The E-wave velocity and the E/A ratio correlated with event-free survival in the univariate analysis [E=2.6 m/s (1 - 6.2); p = 0.034 and E/A = 1.6 (1.1 - 2.4; p = 0.04)]. However, the E-wave and the E/A ratio were identified as independent predictors of clinical outcomes in the multivariate analysis[14].

Aortic regurgitation

In a retrospective cohort study conducted in Japan, published in 2012, Honda et al.[35] evaluated the prognostic impact of Aortic Regurgitation (AR) associated in patients with severe AoS (DLAo) initially not referred to AVR. The study included 306 patients, which were divided according to the presence or absence of moderate to severe AR associated. The outcome evaluated were hospitalization for heart failure and cardiac death during a mean follow up of 4.5 years. Thirty-three patients (45%) with DLAo and 111 patients with AoS (48%) were asymptomatic. Overall mortality was found to be 32%, with no difference between the two groups, but the event-free survival was worse in those with combined lesion. In the multivariate analysis, the presence of DLAo was independently correlated with the occurrence of events and hazard ratio of 2.1 (CI 95% 1.29 - 3.35; p = 0.03)[35].

Left atrial dimensions

Casaclang-Verzosa et al.[36], in a retrospective study published in 2010, evaluated asymptomatic patients with severe AoS in order to examine the Left Atrial (LA) diameter as a prognostic tool. The study included 513 patients by evaluating the development of symptoms and mortality from all causes[36] as outcomes.

LA diameter ≥ 45 mm correlated independently with mortality from all causes in five years. Survival in these patients was 92%, 83% and 51% in one, two and five, respectively, while in patients with LA diameter < 45 mm it was 97%, 90% and 66%, respectively, with a statistically significant difference[36].

In a prospective study by Lancellotti et al.[14], the LA indexed area was bigger in patients with unfavorable outcome. This difference was confirmed in a multivariate analysis and demonstrated the importance of this LV diastolic dysfunction indicator[14].

Evaluation of the LA diameter together with other variables that assess LV diastolic function was an independent and fundamental indicator in the follow-up of asymptomatic patients with severe AoS to identify those at greatest risk for progression to symptoms and death[36].

Subtypes of aortic stenosis with low gradients

Low gradient with reduced LVEF

Patients with severe AoS and LV dysfunction have a worse prognosis. However, in those with contractile reserve, the surgical treatment gives improved functional class and long-term prognosis, justifying the AVR indication in this subgroup[37]. The individuals in which dobutamine stress

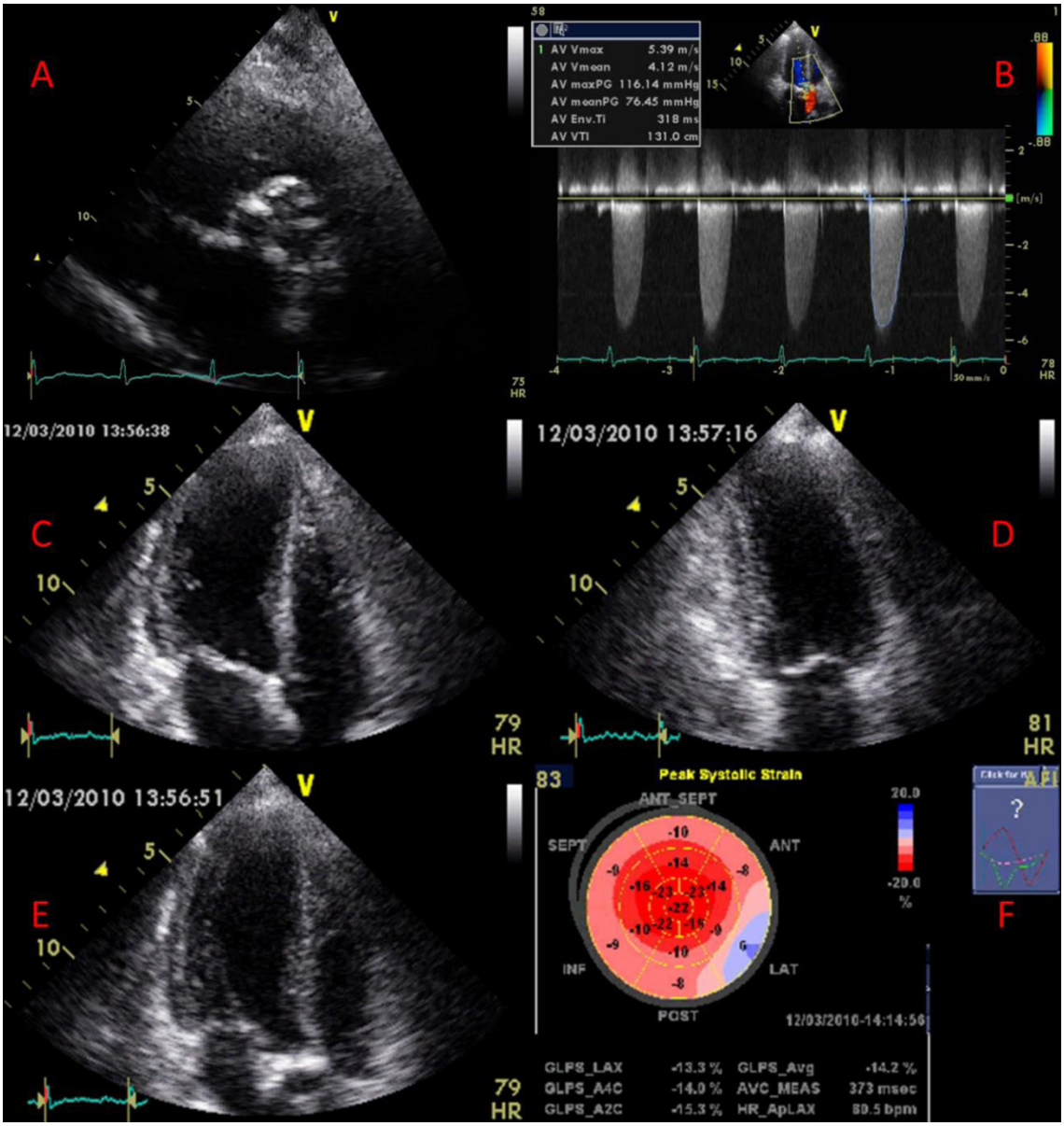

Figure 6 – *Example of asymptomatic patient with severe aortic stenosis. "A" shows an intensely calcified valve. "B" shows high aortic transvalvular gradients. "C", "D" and "E" are the apical views from which the total longitudinal strain was measured by speckle tracking. Note that the strain is reduced mainly in the middle and basal segments. The global value of -13.3% suggests a worse prognosis. Photo provided by Dr. David Le Bihan, IDPC.*

echocardiogram shows absence of contractile reserve have a very reserved prognosis, either with drug treatment or with surgery[2].

A number of studies showed that patients with symptomatic severe AoS, low transvalvular gradient and the presence of contractile reserve had perioperative mortality of 5% to 8%, while in those with absence of contractile reserve mortality was significantly higher (up to 33%)[37-40].

In 2006, Quere et al.[40] published a prospective study with 66 patients with low transvalvular gradient (TPG ≤ 40 mmHg), severe symptomatic AoS (AVA ≤ 1 cm^2) and LVEF ≤ 40% who survived the AVR surgery, with follow-up of 26 ± 20 months. This study showed that in patients with contractile reserve, there was improvement in LVEF ≥ 10% in 83% of cases, with improvement in functional class in 96%. On the other hand, in patients without contractile reserve, there was increased LVEF

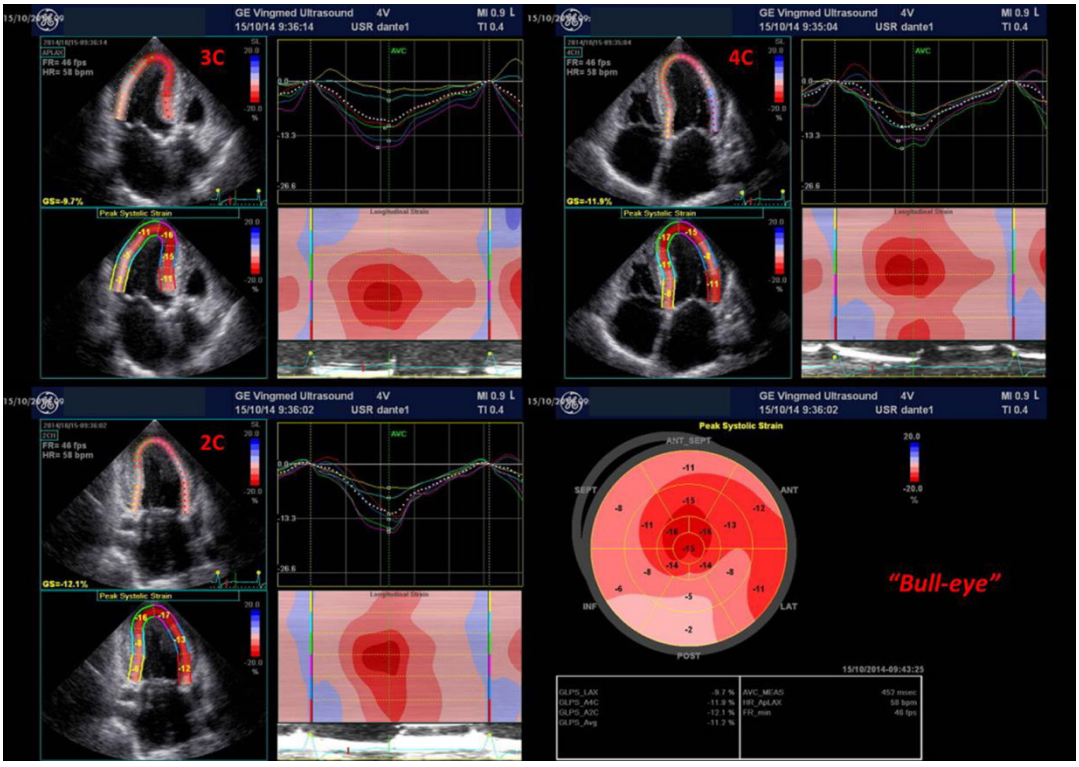

Figure 7 – *Example of a patient with severe aortic stenosis, normal left ventricular ejection fraction (68%) and reduced longitudinal strain. Parametric images and strain curves are observed by segment in apical three-chamber (3C), four chamber (4C) and two chamber (2C) views. In the right lower corner, we can see the bull-eye of the left ventricle, showing colors compatible with diffuse reduction of longitudinal strain. Photo given by Dr. David Le Bihan, IDPC.*

≥ 10% in 65% of cases, and improvement in functional class in 90%. The authors concluded that the absence of contractile reserve in the preoperative echocardiography is not always related to LV dysfunction persistence postoperatively and, despite representing a worse prognosis, it should not be seen as an impedance to valve replacement[40].

Therefore, stress echocardiography with dobutamine is a way to evaluate the LV contractility and the AVA in individuals with symptomatic severe AoS, reduced LVEF and low transvalvular gradient in order to identify those most likely to benefit from AVR. However, due to the lack of literature data that best characterize the profile of these individuals, the decision should be individualized, considering not only the presence of contractile reserve, but also other risk factors[2,37,40].

Low gradient with preserved ejection fraction (low paradoxical flow)

Patients with low paradoxical flow are individuals with severe AoS that, even with preserved LVEF, do not have high transvalvular gradients, due to low secondary preload at varying degrees of diastolic dysfunction resulting from reduced ventricular complacency. These patients typically present little complacent LV, with reduced dimensions and increased myocardial thickness. This group is defined by the following echocardiographic parameters: Indexed AVR < 0.6 cm^2/m^2, LVEF > 50%, TPG < 40 mmHg and volume ejected by the left ventricular outflow tract per indexed beat (Systolic Volume) < 35 mL/m^2[41].

The SEAS[42] study, published in 2011, was conducted with 1,525 asymptomatic patients with PV ≥ 2.5 and ≤ 4 m/s LVEF ≥ 55%. After a 46-month follow-up, the results showed that the outcome (defined by valvular heart disease-related events, major cardiovascular events and death from cardiac causes) and the rate of progression of disease in patients with low gradients and severe AoS (AVA < 1.0 cm^2 and TPG < 40 mmHg) are similar to those with moderate AoS. The prognosis was similar even when the group with severe AoS and low gradients was subdivided into patients with low Systolic Volume (SV) (< 35 mL/m^2) and normal systolic volume. Surgical indication can be safely restricted to those patients in whom symptoms are clearly assigned to AoS[42]. Although the prognosis was similar in terms of clinical outcomes, it has not so benign as to progression to symptoms, since 40% of patients became gradually symptomatic, requiring AVR in five years[42,43].

Conclusion

Aortic stenosis has become a matter of public health. Population aging has become the largest cause of AVR in Europe and in North America[2,44]. The indication of intervention is well established in symptomatic patients due to exponential increase in mortality from the appearance of any of the components of the classic triad (angina, dyspnea and syncope), and also in those with systolic ventricular dysfunction[45]. Aortic valve replacement is the only option capable of altering the natural history of this disease. With technical evolution and the emergence of TAVI (Transcatheter Aortic Valve Implantation), a large number of patients before ineligible for surgery due to high operative risk can benefit from this therapeutic modality[2,46].

Echocardiography is the test of choice for diagnosing and guiding the treatment of patients with AoS. In asymptomatic patients, the rational analysis of echocardiographic parameters enables individualized management of therapy. Therefore, we believe that knowledge of the information provided by echocardiography may help the clinician to indicate intervention even in asymptomatic patients when this is considered of high risk and the interpretation of the "absence of symptoms" is doubtful. This can prevent an irreversible myocardial lesion and reduce morbidity and mortality in an increasing number of patients.

The decision to intervene in patients with severe asymptomatic AoS remains in debate and new echocardiographic parameters (tissue Doppler and Strain/Strain rate) help therapeutic decisions considering the prognosis of patients. There is a progressive risk of irreversible myocardial lesion that can affect survival. Early detection of its onset is a big challenge[47].

Authors' contributions

Research creation and design: Gomes MCC, Teixeira FRC, Etto JP, Verri PH, Meneguz-Moreno RA; Data collection: Gomes MCC, Teixeira FRC, Etto JP, Verri PH, Meneguz-Moreno RA Data analysis and interpretation: Gomes MCC, Teixeira FRC, Etto JP, Verri PH, Meneguz-Moreno RA; Manuscript drafting: Gomes MCC, Teixeira FRC, Etto JP, Verri PH, Meneguz-Moreno RA; Critical revision of the manuscript as for important intellectual content: Gomes MCC, Teixeira FRC, Etto JP, Verri PH, Meneguz-Moreno RA.

Potential Conflicts of Interest

No relevant potential conflicts of interest.

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