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Clinical and hemodynamic profile of consecutive patients with aortic valve stenosis studied in the pre-transcatheter aortic valve implantation era at an academic institution. Comparative analysis of invasive evaluation with echocardiography

Perfil clínico e hemodinâmico de pacientes consecutivos com estenose aórtica valvar estudados na era pré-implante transcateter valvar aórtico em instituição acadêmica. Análise comparativa da avaliação invasiva com a ecocardiográfica

Larissa Rodrigues Garcia[1iD], Felipe Araújo Campos[2iD], José Antônio Marin-Neto[2iD], Renata Nabeiro Dias Angelo[1iD], Isabela Scatolini Capodifoglio[1iD], Henrique Turin Moreira[1iD], André Schmidt[3iD], Minna Moreira Dias Romano[3iD], André Vannuchi Badran[2iD], Moyses de Oliveira Lima-Filho[2iD], Igor Matos Lago[2iD], João Reynaldo Abbud Chierice[2iD]

[1] *Hospital das Clínicas, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.*

[2] *Laboratório de Hemodinâmica e Cardiologia Intervencionista, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.*

[3] *Division of Cardiologya, Internal Medicine Department, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.*

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Corresponding author:
Felipe Araújo Campos
Avenida dos Bandeirantes, 3.900 – Vila Monte Alegre
Zip code: 14040-906 – Ribeirão Preto, SP, Brazil
E-mail: felipe.araujo.campos@alumni.usp.br

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ABSTRACT - **Background**: In view of the better understanding of the pathophysiology of aortic valve stenosis, the complexity of assessing its severity has simultaneously grown, with relevant uncertainty persisting as to the applicability of invasive methods by cardiac catheterization and non-invasive methods based on echocardiography. The objective of this study was to analyze the hemodynamic patterns of evaluation with echocardiography compared to the estimation of severity of aortic stenosis with catheterization in consecutive patients referred for diagnostic evaluation by the laboratory of a tertiary academic hospital in the 2016 to 2018 triennium. **Methods:** An observational, descriptive and retrospective study of clinical characteristics and results of assessments of severity of aortic valve stenosis obtained in 96 consecutive patients, through catheterization and echocardiography. **Results:** A population sample of 49 men and 47 women, with a median age of 66.5 (56.5 to 72.8) years, degenerative aortic valve stenosis in 49%, and rheumatic aortic stenosis in 40%, in addition to several comorbidities, including coronary disease (37%). Using catheterization, based on the peak gradient of 48 (20 to 68), aortic valve stenosis was assessed as severe in 56%, with ventricular end-diastolic pressure of 20mmHg (16 to 30mmHg). Using echocardiography, the valve area was 0.9cm^2 (0.7 to 1.2cm^2), indexed valve area was 0.5cm^2/m^2 (0.43 to 0.5cm^2/m^2), with peak gradient of 62±26mmHg. Aortic valve stenosis was considered severe in 69.2%. There was disagreement between the methods regarding severity of aortic valve stenosis in 30% of exams, with a Spearman coefficient between the valve area on the echocardiogram and the peak gradient on catheterization of -0.7 ($p<0.001$). **Conclusion:** In a representative sample of various hemodynamic patterns, the assessment of severity of aortic valve stenosis, as routinely practiced in an academic laboratory, was limited to measuring the peak transvalvular gradient. The estimation of the valve area using the echocardiographic method was indirect and also subject to criticism, and contributed to the discrepancies found, rendering it justifiable to seek the improvement of both methods, in view of the clinical and hemodynamic complexity detected.

Keywords: Aortic valve stenosis; Cardiac catheterization; Hemodynamics; Echocardiography

RESUMO - **Introdução:** Face à melhor compreensão da fisiopatologia da estenose valvar aórtica, cresceu paralelamente a complexidade da avaliação de sua gravidade, persistindo relevante incerteza

quanto à aplicabilidade dos métodos invasivos pelo cateterismo cardíaco e os não invasivos, com base em ecocardiografia. O objetivo deste estudo foi analisar os padrões hemodinâmicos da avaliação com ecocardiografia comparativamente à estimativa da gravidade da estenose aórtica com o cateterismo em pacientes consecutivos referidos para avaliação diagnóstica por laboratório de hospital acadêmico terciário no triênio 2016-2018. **Métodos:** Estudo observacional, descritivo e retrospectivo das características clínicas e dos resultados das avaliações da gravidade da estenose valvar aórtica obtidas em 96 pacientes consecutivos, por meio de cateterismo e ecocardiografia. **Resultados:** Amostra populacional de 49 homens e 47 mulheres, com mediana de idade de 66,5 (56,5 a 72,8) anos, estenose valvar aórtica degenerativa em 49% e reumática em 40%, além de diversas comorbidades, inclusive doença coronária (37%). Pelo cateterismo, com base no gradiente pico de 48 (20 a 68), a estenose valvar aórtica foi avaliada como grave em 56%, sendo a pressão telediastólica ventricular de 20mmHg (16 a 30mmHg). Pela ecocardiografia, a área valvar foi 0,9cm^2 (0,7 a 1,2cm^2), sendo indexado 0,5cm^2/m^2 (0,43 a 0,5cm^2/m^2), com gradiente pico de 62±26mmHg. A estenose valvar aórtica foi considerada severa em 69,2%. Houve discordância entre os métodos sobre a severidade da estenose valvar aórtica em 30% dos exames, com coeficiente de Spearman entre área valvar pelo ecocardiograma e gradiente pico pelo cateterismo de -0,7 (p<0,001). **Conclusão:** Em amostra representativa dos vários padrões hemodinâmicos, a avaliação da gravidade da estenose valvar aórtica, como praticada rotineiramente em laboratório acadêmico, limitou-se à medida de pico de gradiente transvalvar. A estimativa da área valvar pelo método ecocardiográfico, sendo indireta e também passível de crítica, contribui para as discrepâncias encontradas, tornando-se justificável buscar o aperfeiçoamento de ambos os métodos, em vista da complexidade clínica e hemodinâmica detectada.

Descritores: Estenose da valva aórtica; Cateterismo cardíaco; Hemodinâmica; Ecocardiografia

INTRODUCTION

Aortic valve stenosis (AVS) is an acquired valve disease with a high prevalence today, especially in the currently fastest growing age group, due to the significant increase in life expectancy in many countries, including Brazil.[1-3] In addition, it is the valve disease with the most recent advances observed regarding its pathophysiology, and more specifically, the understanding of its diverse and complex hemodynamic expression, as assessed by some methods, such as transthoracic echocardiography.[4] Finally, with the advent of transcatheter aortic valve implantation (TAVI) procedures, the therapeutic perspective for this severe condition has greatly increased.[5]

As confirmed in autopsies,[6] AVS was clinically characterized by its protracted natural history and its symptomatic triad composed of progressive dyspnea, angina pectoris, and exertional syncope, even when its etiology was predominantly rheumatic.[7] Currently, from the epidemiological point of view, degenerative AVS predominates, and the physical examination, although usually very expressive for diagnosis, does not show a good correlation among workup alterations and severity and prognosis of the AVS.[8]

Severity of AVS was first estimated using an invasive cath lab method, applying the concepts underlying the formula by Gorlin et al., one of the most illustrative historical examples of scientific collaboration between a father (with an engineering background) and a son (with a biological/medical background).[9] This essential theoretical formulation was then partially transposed to a non-invasive assessment conducted by echocardiography, which became the preferred routine method of assessing AVS.[10] It is worth mentioning that with both methods, the "final" essential parameter of estimating the severity of the stenotic dysfunction of the aortic valve consists in quantifying the valve area, which is not measured directly, but deduced based on measurements of anatomical and functional parameters.[11]

The recent advances in the pathophysiological understanding of AVS, usually based on the assessment of its severity by echocardiography (ECHO), enabled recognizing different hemodynamic patterns that are associated with a severely stenotic valve area ≤1.0cm^2, i.e., a valve area normalized to the body surface ≤0.6cm^2/m^2: the classic pattern of high gradient and transvalvular flow and normal left ventricular ejection fraction (LVEF); the opposite of the above, also recognized for a long time, with low gradient and transvalvular flow, in conditions of reduced LVEF; the so-called "paradoxical pattern", with low gradient and transvalvular flow, but with preserved LVEF; the pattern with low gradient, but normal transvalvular flow, also with preserved LVEF. And there is yet another hemodynamic pattern, in which the AVS is only apparently severe, labeled as "pseudo-severe". In this pattern, the valve area is not reduced, but there is low gradient and transvalvular flow.

In the latter case, there are adverse hemodynamic conditions, linked to ventriculoarterial impedance, which cause the appearance of severe stenosis that can be unmasked by stress ECHO with dobutamine.[4,12-15] It is important to note that these various hemodynamic patterns can only be understood by individual analysis of the various parameters involved.

Although many patients with AVS are studied using cardiac catheterization (CAT), in most cases, for coronary angiographic exploration and eventual detection of associated coronary disease, the hemodynamic assessment of severity of the valve disease has been relegated to the background in many laboratories, and, routinely, only the peak transvalvular gradient is measured, by pulling-back a single catheter and without measuring the mean gradient or the concomitant systolic flow. Therefore, the inherent complexity of these hemodynamic patterns, observed with a non-invasive assessment of AVS severity, has not been properly contrasted with an assessment based on the CAT, according to the classic formulation by Gorlin. This may result in even greater difficulty in interpreting the results of CAT and ECHO tests in individual patients, which renders the selection of appropriate therapeutic approaches even more complicated.

The objective of the present study was to analyze the hemodynamic patterns of evaluation using echocardiography compared to estimation of severity of aortic stenosis using catheterization in consecutive patients referred for diagnostic evaluation by the laboratory of a tertiary academic hospital in the 2016-2018 period. Specifically, the hemodynamic patterns determined by the ECHO assessment were analyzed, and these results were compared with the AVS severity estimation as obtained during CAT in all patients with at least a 1-year follow-up after their procedure at the organization.

METHODS

A retrospective analysis was carried out from the medical records containing the clinical aspects and results of 96 consecutive patients, who underwent CAT in laboratories of the Cath Lab and Interventional Cardiology Unit of the *Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto*, University of São Paulo (USP), in the 2016-2018 triennium, with a prior diagnosis of AVS or a diagnosis of AVS detected during the CAT.

All patients signed a consent form containing aspects related to the CAT procedure, its objectives, characteristics, and risks involved, as clinically indicated by the respective physicians attending each patient. Besides this consent, the study was duly approved by the Research Ethics Committee of *Hospital das Clínicas* of the *Faculdade de Medicina de Ribeirão Preto* of USP, under protocol 5.992.871 and CAAE 68451823.0.0000.5440.

The ECHO assessment results were analyzed based on the examination closest to the moment of the CAT, with a 1-month interval between them (0.4 to 4.6 months), always preceding the final AVS treatment, for those undergoing a TAVI procedure or a classic surgery.

The follow-up of patients after CAT consisted of reviewing medical records, for a period of at least one year after CAT or until death.

Cardiac catheterization procedure

The vascular approach after local anesthesia was preferentially performed via radial access. Heparinization was carried out according to the laboratory routine, only during the procedure (usually unfractionated heparin, in a dose of 5,000IU, intra-arterial, immediately after the puncture). 5F introducers were used to allow passage of a multipurpose catheter for selective catheterization of both coronary arteries and also for crossing the stenotic aortic valve. Occasionally, operational circumstances required the use of preformed Judkins or Amplatz catheters, among others. The coronary arteries were selectively catheterized and opacified by manual injection of 3 to 7mL of radiological contrast for conventional angiographic filming in several views. In all cases, attempts were made to cross the aortic valve with the catheter, with successful maneuvers in 100% of patients. The exams were always performed by an experienced medical team, accompanied by training interventional cardiologists, as is typical in an academic environment. The crossing of the valve allowed the measurement of the LV telediastolic pressure ($LVDP_2$) and a ventriculography using a radiological contrast agent (15 to 25mL injected during 2 to 3 seconds) in a right oblique projection. Afterwards, the pullback of the catheter allowed the measurement of aortic pressure and transvalvular pressure gradient.

Resting transthoracic echocardiography procedure

The estimation of the aortic valve area by transthoracic echocardiogram at rest was performed using conventional methods, in two-dimensional mode and Doppler echocardiography.[16] From the positioning of the echocardiographic transducer close to the left sternal border, the so-called "parasternal longitudinal" projection was obtained, in which the LV outflow tract diameter was measured. In the modified apical four-chamber view for viewing the outflow tract, the measured time-velocity integral and the maximum velocity of the anterograde flow through the aortic valve were obtained, allowing an estimation of the aortic valve area that corresponds to the estimated maximum velocity.

Based on the definitions of the 2020 *Diretriz Brasileira de Valvopatias*, the AVS severity and hemodynamic patterns were classified, as well as the presence of other associated valvular heart diseases.[2]

Statistical analysis

Data distribution was assessed by histogram analysis and by the Shapiro-Wilk test. Non-normal variables were measured as median and interquartile range, whereas Gaussian variables were measured as mean ± standard deviation (SD). The agreement of results between methods was checked using a Bland-Altman diagram. Comparisons between different aortic stenosis (AS) patterns were performed using analysis of variance and chi-square test (or Fisher's exact test, if appropriate), for continuous and categorical variables, respectively.

RESULTS

The sample consisted of 96 patients, 49 men, with a non-Gaussian age distribution, and a median and interquartile age range of 66.5 (56.5 to 72.8) years. As shown in table 1, among the comorbidities, hypertension was found in 78.1%, dyslipidemia in 38.1%, diabetes mellitus in 34.4%, and coronary artery disease clinically diagnosed before CAT in 18.8%. As for the etiology of the AVS, in 49% the origin was degenerative, in 39.6% rheumatic, and in 8.4% congenital, due to a bicuspid aortic valve.

Table 1. Baseline demographic and clinical characteristics

Characteristic	
Age, years	66.5 (56.5±72.8)
Male	49 (52.0)
Hypertension	75 (78.1)
Diabetes mellitus	33 (34.4)
Dyslipidemia	38 (38.5)
Coronary artery disease	18 (19.1)
Asymptomatic	9 (9.6)
Dyspnea	81 (86.1)
NYHA functional class	
I	13 (13.8)
II	38 (39.6)
III	35 (36.5)
IV	8 (8.3)
Angina pectoris	53 (56.4)
Syncope	8 (8.3)
Etiology	
Degenerative	48 (51.1)
Rheumatic	38 (39.6)
Bicuspid	8 (8.4)

Results expressed as mean ± standard deviation or n (%).
NYHA: New York Heart Association.

As for the presence of symptoms of the classic AVS triad presented by patients at the time of the CAT, 81 (84.4%) reported dyspnea, with 13 (13.8%) in NYHA functional class (FC) I, 38 (39.6%) in FC II, 35 (36.5%) in FC III, and 8 (8.3%) in FC IV. *Angina pectoris* was described in 53 (55.21%) of them, and a previous episode of syncope in only 8 (8.3%). Syncope did not occur exclusively in any of them, but six (6.3%) patients described simultaneous onset of angina and syncope. Only nine (9.6%) of the total were asymptomatic.

Analysis of cardiac catheterization results

The indication criterion for CAT was to assess the coronary circulation with AVS already clinically diagnosed in 55 (57%) of patients. In another 23 (24%) patients, the primary diagnosis was CAD, and AVS was initially detected during CAT. In another 16 cases, there were previously diagnosed valvar lesions associated with AVS, and the test was requested for a complementary assessment of concomitant valvopathies and also to explore the coronary circulation.

There was concomitant significant CAD (stenoses with ≥50% reduction in luminal diameter) in 35 (37%) patients, 12 with a single-vessel pattern, 15 with a two-vessel pattern, and 8 with a three-vessel pattern. When evaluating the patients with indication for CAT due to CAD, totaling up 23 cases, the diagnosis was confirmed in only 16 (69.6%) of them, and AVS was, in fact, the main and only anatomical disorder.

During the examination, the group presented with a 48mmHg (20 to 68mmHg) median peak gradient by CAT, with 21 (22.3%) patients classified as having mild AVS, 20 (21.3%) as moderate, and 53 (56.4%) as severe. The median ventricular end-diastolic pressure (DP_2) of the group was 20mmHg (16 to 30mmHg). No complications directly related to the procedure were recorded.

Analysis of echocardiography results

An echocardiographic evaluation was not possible due to inadequate imaging in only four cases. In the remaining 92, 13 (14.1%) patients had mild AVS, 14 (15.2%) moderate, and 65 (70.6%) severe. The peak gradient by ECHO had values of 62±26mmHg, and the mean gradient by ECHO had values of 41.7±18.2mmHg. The median LVEF was 60% (52 to 65%). In the group, aortic valve area had a median of 0.9cm^2 (0.7 to 1.2cm^2) and indexed aortic valve area of 0.5cm^2/m^2 (0.43 to 0.5cm^2/m^2).

The hemodynamic patterns of severe AVS detected in 66 patients were, in 58 (84.8%) of them, high gradient and normal flow (classic form); in 4 (6.4%), low gradient and flow, besides reduced LVEF; in 2 (3.2%), low gradient and flow, but with preserved LVEF (paradoxical); and, in 4 (6.4%), low gradient, and normal flow, and also preserved LVEF. In six (9.5%) of these critically ill patients, the hemodynamic patterns remained undefined, due to inadequate assessment of the ventricular outflow tract.

Comparative assessment of severity of aortic valve stenosis

There was disagreement between both methods regarding severity of the AVS in 30% of exams (Figure 1), with a Spearman coefficient between valve area by ECHO and peak gradient by CAT of -0.7 ($p<0.001$). The difference between peak gradient by ECHO and peak gradient by CAT was, on average, 10 mmHg (95%CI 58-38mmHg), with a clear tendency to increase in a higher range of values and the presence of several outliers (Figure 2).

Follow-up

Median follow-up was 19 months (10 to 34 months), from enrollment by CAT date to last physician contact or death. Only one patient received TAVI, as the procedure had not yet been implemented at the time of the research in the routine of the institution. Surgical replacement of the aortic valve was performed in 47 patients, 9 with concomitant myocardial revascularization. Mortality in the immediate postoperative period (considering patients who did not leave the ICU after the procedure due to complications) was 17% (eight patients). In addition to the immediate postoperative deaths, another 5 (18.5%) who underwent surgery also died during the follow-up period, and another 14 (51.9%) died with no surgical treatment.

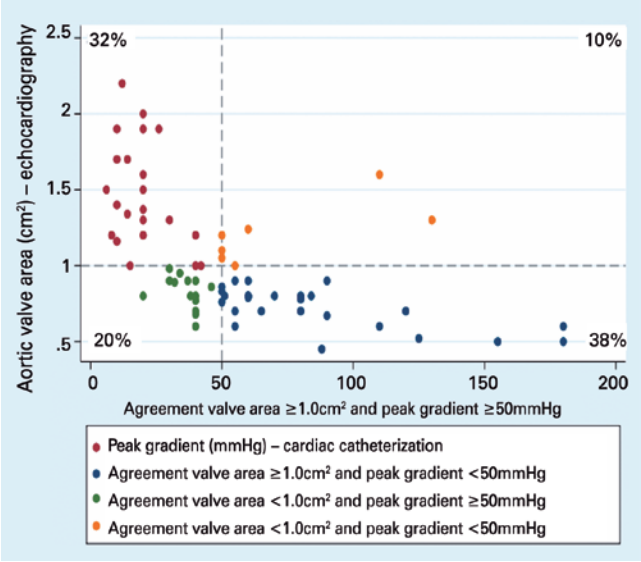
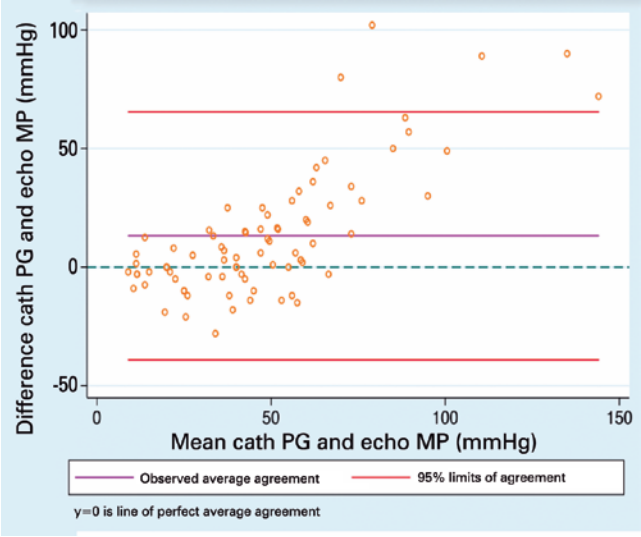


Figure 1. Agreement and disagreement of severity of aortic valve stenosis by estimating the valve area (echocardiography) and peak transvalvular gradient (cardiac catheterization).



PG: peak gradient; MP: medium peak.

Figure 2. Bland-Altman diagram correlating mean values between peak gradient (cardiac catheterization) and mean gradient (echocardiography) on the x-axis, and differences between these values on the y-axis of the graph.

DISCUSSION

An essential aspect of this article is to demonstrate that the AVS severity assessment, as performed in the routine of an eminently academic Cath Lab and Interventional Cardiology Service in a tertiary hospital, clearly deviates from the principles essentially formulated since the primordial standardizations based on the theorizations of Gorlin et al.[9] Actually, this hemodynamic assessment, performed using CAT, was limited to the measurement of a peak-to-peak gradient, using a transvalvular pull-back of a single catheter. Therefore, there was no record of simultaneous pressures in the LV and aorta, i.e., with two catheters, one in the LV and the other in the aorta. The mean transvalvular gradient was also not measured, not even by overlapping the pressure curves obtained at different times in the LV and the aorta. In addition, the systolic transvalvular flow rate was not computed, as recommended for the application of the original formula by Gorlin et al.[9]

From this methodological finding grounded on the data of the present study, it would perhaps be tempting and plausible to conclude that an AVS severity assessment based on CAT is no longer justified, i.e., it should be considered outdated and unnecessary, and CAT should be relegated to a mere secondary role of diagnostic complementation (for example, detection of associated coronary disease) given the wide availability of an echocardiographic evaluation for this same purpose.

Although the conclusion described above may even be based on current trends and with logistical implications, it may be premature to carry it out, based on at least three considerations. First, the echocardiographic method also does not directly measure the valve area, which is calculated based on analogous hemodynamic principles. Second, knowledge of the complex hemodynamic characteristics of many patients with AVS is currently still unclear in some respects, and there is still considerable uncertainty regarding the assessment of its severity based on ECHO. For example, the so-called paradoxical pattern is covered with controversy over its prognostic significance, with reports on its relative benignity in the clinical course of the patient[17] or reports on its association with a more ominous prognosis.[18] Third, although less susceptible to criticism than invasive cath lab procedures, the echocardiography evaluation is also debatable, as evidenced in the present study, since the method is essentially not applied in ideal conditions for the application of the principles of Gorlin et al.[9] In fact, by positioning the echocardiographic transducer next to the middle left sternal border, the so-called longitudinal parasternal projection is obtained, in which the following were measured: outflow tract diameter, maximum velocity of the aortic anterograde transvalvular flow, and time-velocity integral of the left ventricular outflow tract. The application of these parameters in the continuity equation, derived from the mass conservation law, allowed the calculation of the aortic valve area that corresponded to the estimated maximum velocity. The current guidelines do not limit the use of CAT to the context of just a subsidiary method, complementary to non-invasive ones, for exploring the coronary circulation, but recommend it as fundamental in the characterization of valve disease when there is uncertainty using non-invasive methods.

The analysis of the clinical characteristics of patients included in the study showed that the convenience sample, by spontaneous demand, revealed the coexistence of several comorbidities, namely, hypertension, dyslipidemia,

diabetes mellitus, and, also in a significant proportion, a concomitant coronary artery disease. These characteristics would be logically expected, in view of the relative longevity (median age of 66.5 years) of patients in whom AVS is epidemiologically most pronounced today, and also of the fact that, in a certain proportion (a quarter) of the cases, the lesion valve had not been diagnosed before a hemodynamic study whose clinical indication was precisely to clarify the suspected diagnosis of obstructive coronary artery disease. As for the basic etiology of AVS, although the past rheumatic history has manifested itself in a considerable fraction of cases, the clear predominance of degenerative mechanisms observed in the present sample follows the epidemiological tendency indicated in previous studies.[1,5] As indicated in old studies[7] as in a recent update of the natural history of AVS,[5] the earliest and most prevalent symptom is usually exertional dyspnea, which correlates well with a classic hemodynamic parameter - left ventricular diastolic hypertrophy and dysfunction -through increased LV end-diastolic pressure, which in this sample had a median value of 20 mmHg. The high mortality rate found in this sample of patients, both those treated surgically and those who did not undergo surgery for multiple reasons, should also be highlighted. This high mortality occurred despite relatively preserved left ventricular systolic function in this group of patients.

When comparing the AVS severity assessments by the two methods, it was observed that, proportionally, more individuals with severe AVS were detected by ECHO (69.2%), compared to those detected by CAT (56.4%). This discrepancy becomes even more pronounced when one considers that the severity criterion by CAT is based on a transvalvular peak gradient ≥ 50mmHg, whereas the severity criterion by ECHO is based on a valve area <1cm^2. With the recent increase in knowledge on the pathophysiology of AVS and the consequent unveiling of the complex hemodynamic patterns in force,[4,12,13,15] most of the cases in which there is severe AVS, i.e., reduced valve area, have paradoxically reduced transvalvular gradient values. However, a real disagreement in assessing AVS severity by the two methods is evidenced by the dispersion of the peak gradient values between CAT (despite measured with the limitations mentioned above) and those estimated by ECHO (also with the due reservations previously discussed), according to the Bland-Altman diagram in figure 2. Although the direct comparison of these values in the total group is inherently difficult (Gaussian distribution by only one of the methods), it is plausible to conclude that the results of this study highlight the need to improve the AVS assessment, both by one method as by the other, to guide the most complete diagnostic assessment and the best therapeutic referral of patients.

With the exception of the hemodynamic patterns of pseudo-severe AVS, all the other patterns described in the literature[4,2-15] were detected in the population sample included in this study, highlighting the most classically recognized patterns of preserved LVEF and high transvalvular gradient. Moreover, in a non-negligible percentage of these severe cases, the hemodynamic patterns could not be characterized due to technical difficulties in assessing the ventricular outflow tract (9.5%). It is possible that the non-identification of one of these patterns, or even the under-detection of others, results from the methodological limitations mentioned. However, the pathophysiological understanding of the inherent hemodynamic complexity of the AVS depends on subtle concepts that influence the measurements themselves, such as, for example, the pressure recovery phenomenon, studied in an *in vitro* model and also in humans.[12,19] Reported discrepancies between the echocardiographic evaluation and magnetic resonance imaging are also intelligible based on more sophisticated concepts, such as energy dissipation associated with apical aneurysm.[20]

Based on the conceptual and also analytical considerations of the results of the present study, it becomes plausible to propose a study, which is currently underway at our institution, aiming to methodologically improve the invasive and echocardiographic evaluations of patients with AVS, performed simultaneously, to resolve any discrepancies found. This investigation, approved by the Institutional Research Ethics Committee, even demands the measurement of the transvalvular ejection systolic flow, as well as the pressures in the pulmonary circuit, which can bring relevant subsidies to evaluate the effect of TAVI in the patients studied prospectively.[21] Very likely, it will be possible to find a link in surprising or even paradoxical results in some cases, through strict observance of the precepts and principles that should guide the invasive hemodynamic evaluation of the AVS, including the determination of the ventriculo-arterial impedance.[11,22] However, it is also timely to point out that, especially for less experienced interventionists, the crossing of the catheter through the stenotic valve is not devoid of risks, including calcium embolization. Recent studies conducted during TAVI indicate this high risk of calcium embolization, although the importance of these complications in causing stroke and dementia is controversial.[23] Therefore, safety standards that should prevail in environments such as the Cath Lab, to protect patients, have been adequately pointed out in a recent publication.[24] Finally, it is instructive to observe how, alongside the significant scientific and technological achievements of the past, such as the use of Swan-Ganz catheters to facilitate access to the pulmonary circulation,[25] other recent advances have also been made. The example is the recently proposed AVS assessment in a non-invasive way, consisting of computed tomography angiography in patients considered at low risk of coronary obstruction associated with the respective measurement of the calcium score.[4]

The main limitation that prevents a more adequate comparison of AVS severity assessments is the fact that both methods having been applied under non-ideal conditions. They were also not performed simultaneously, which

may have contributed to the dispersion of results, although there are reports in the literature that this factor does not represent, in itself, the cause of discrepancies between non-concomitant catheter and Eco-Doppler assessments.[26] Before perfecting the application of each method, perhaps it is necessary to recognize how difficult it is to establish the meaning of a correlation and an agreement between measurements of biological variables.[27]

CONCLUSION

The present study clearly showed that the aortic valve stenosis severity assessment, as routinely practiced in the cath lab of an academic institution, does not follow the fundamentally advocated principles for applying the formulation by Gorlin et al. As the severity estimation using the echocardiographic method is also subject to criticism, the discrepancies found cannot be explained in a simple way, and it is necessary to improve the evaluation of aortic valve stenosis, especially when considering the current clinical and hemodynamic complexity that many patients face.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest to disclose.

CONTRIBUTION OF AUTHORS

Conception and design of the study: JAMN, MOLF, HTM, AS and MMDR; data collection: LRG, RNDA, ISC, MOLF, AVB, IML JAMN, and JRAC; data interpretation: LRG, JAMN, HTM, AS, MMDR, FAC, MOLF and JRAC; text writing: LRG, JAMN, HTM, AS, MMDR and FAC; approval of the final version to be published: LRG, FAC and JAMN.

REFERENCES

1. Eveborn GW, Schirmer H, Heggelund G, Lunde P, Rasmussen K. The evolving epidemiology of valvular aortic stenosis. the Tromsø study. Heart. 2013;99(6):396-400. https://doi.org/10.1136/heartjnl-2012-302265.
2. Tarasoutchi F, Montera MW, Ramos AI, Sampaio RO, Rosa VE, Accorsi TA, et al. Atualização das Diretrizes Brasileiras de Valvopatias – 2020. Arq Bras Cardiol. 2020;115(4):720-75. https://doi.org/10.36660/abc.20201047
3. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al.; ESC/EACTS Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur J Cardiothorac Surg. 2021;60(4):727-800. https://doi.org/10.1093/ejcts/ezab389. Erratum in: Eur J Cardiothorac Surg. 2022;61(4):964. Erratum in: Eur J Cardiothorac Surg. 2022;62(1): PMID: 34453161.
4. Silva I, Salaun E, Côté N, Pibarot P. Confirmation of aortic stenosis severity in case of discordance between aortic valve area and gradient. JACC Case Rep. 2022;4(3):170-7. https://doi.org/10.1016/j.jaccas.2021.11.009
5. Généreux P, Stone GW, O'Gara PT, Marquis-Gravel G, Redfors B, Giustino G, et al. Natural history, diagnostic approaches, and therapeutic strategies for patients with asymptomatic severe aortic stenosis. J Am Coll Cardiol. 2016;67(19):2263-88. https://doi.org/10.1016/j.jacc.2016.02.057
6. Roberts WC. The structure of the aortic valve in clinically isolated aortic stenosis: an autopsy study of 162 patients over 15 years of age. Circulation. 1970;42(1):91-7. https://doi.org/10.1161/01.cir.42.1.91
7. Frank S, Johnson A, Ross J Jr. Natural history of valvular aortic stenosis. Br Heart J. 1973;35(1):41-6. https://doi.org/10.1136/hrt.35.1.41
8. Munt B, Legget ME, Kraft CD, Miyake-Hull CY, Fujioka M, Otto CM. Physical examination in valvular aortic stenosis: correlation with stenosis severity and prediction of clinical outcome. Am Heart J. 1999;137(2):298-306. https://doi.org/10.1053/hj.1999.v137.95496
9. Gorlin R, Gorlin SG. Hydraulic formula for calculation of the area of the stenotic mitral valve, other cardiac valves, and central circulatory shunts. I. Am Heart J. 1951;41(1):1-29. https://doi.org/10.1016/0002-8703(51)90002-6
10. Nishimura RA, Tajik AJ. Quantitative hemodynamics by Doppler echocardiography: a noninvasive alternative to cardiac catheterization. Prog Cardiovasc Dis. 1994;36(4):309-42. https://doi.org/10.1016/s0033-0620(05)80037-4
11. Nishimura RA, Carabello BA. Hemodynamics in the cardiac catheterization laboratory of the 21st century. Circulation. 2012;125(17):2138-50. https://doi.org/10.1161/CIRCULATIONAHA.111.060319
12. Pibarot P, Dumesnil JG. New concepts in valvular hemodynamics: implications for diagnosis and treatment of aortic stenosis. Can J Cardiol. 2007;23 Suppl B(Suppl B):40B-47B. https://doi.org/10.1016/s0828-282x(07)71009-7. Erratum in: Can J Cardiol. 2009;25(3):140.
13. Lauten J, Rost C, Breithardt OA, Seligmann C, Klinghammer L, Daniel WG, et al. Invasive hemodynamic characteristics of low gradient severe aortic stenosis despite preserved ejection fraction. J Am Coll Cardiol. 2013;61(17):1799-808. https://doi.org/10.1016/j.jacc.2013.02.009
14. Malkowski MJ, Comprehensive Assessment of Aortic Stenosis in the TAVR Era. Current Cardiovascular Imaging Reports. 2018:11:28. https://doi.org/10.1007/s12410-018-9469-x
15. Mohty D, Pellikka PA, Yeon SB, Clinical manifestations and diagnosis of low gradient severe aortic stenosis. In: Pellikka PA, editor. UpToDate; Mar 2021. [cited 2023 Mar 8]. Available from: https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-low-gradient-severe-aortic-stenosis
16. Baumgartner H, Hung J, Bermejo J, Chambers JB, Edvardsen T, Goldstein S, et al. Recommendations on the Echocardiographic Assessment of Aortic Valve Stenosis: A Focused Update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. J Am Soc Echocardiogr. 2017;30(4):372-92. https://doi.org/10.1016/j.echo.2017.02.009
17. Maes F, Boulif J, Piérard S, de Meester C, Melchior J, Gerber B, et al. Natural history of paradoxical low-gradient severe aortic stenosis. Circ Cardiovasc Imaging. 2014;7(4):714-22. https://doi.org/10.1161/CIRCIMAGING.113.001695
18. Hachicha Z, Dumesnil JG, Bogaty P, Pibarot P. Paradoxical low-flow, low-gradient severe aortic stenosis despite preserved ejection fraction is associated with higher afterload and reduced survival. Circulation. 2007;115(22):2856-64. https://doi.org/10.1161/CIRCULATIONAHA.106.668681

19. Garcia D, Dumesnil JG, Durand LG, Kadem L, Pibarot P. Discrepancies between catheter and Doppler estimates of valve effective orifice area can be predicted from the pressure recovery phenomenon: practical implications with regard to quantification of aortic stenosis severity. J Am Coll Cardiol. 2003;41(3):435-42. https://doi.org/10.1016/s0735-1097(02)02764-x
20. Garcia D, Dumesnil JG, Durand LG, Kadem L, Pibarot P. Discrepancies between catheter and Doppler estimates of valve effective orifice area can be predicted from the pressure recovery phenomenon: practical implications with regard to quantification of aortic stenosis severity. J Am Coll Cardiol. 2003;41(3):435-42. https://doi.org/10.1016/s0735-1097(02)02764-x
21. Goitia J, Phan DQ, Lee MS, Moore N, Mansukhani P, Aharonian V, et al. The prognostic utility of invasive right heart catheterization in patients prior to transcatheter aortic valve replacement. J Invasive Cardiol. 2022;34(1):E14-E23. PMID: 34866047.
22. Stanberry L, Ahmed A, Sorajja P, Cavalcante JL, Gossl M. Invasive versus non-invasive assessment of valvuloarterial impedance in severe aortic stenosis. Open Heart. 2020;7(1):e001240. https://doi.org/10.1136/openhrt-2020-001240
23. Fan J, Fang X, Liu C, Zhu G, Hou CR, Jiang J, et al. Brain injury after transcatheter replacement of bicuspid versus tricuspid aortic valves. J Am Coll Cardiol. 2020;76(22):2579-90. https://doi.org/10.1016/j.jacc.2020.09.605
24. Cardoso CO, Knebel AV, Lima CC, Staudt C, Duarte AF, Dei Ricardi AM, et al. Segurança do paciente em hemodinâmica: trajetória de um serviço em busca da excelência. J Transcat Intervent. 2022;30:eA20220013. https://doi.org/10.31160/JOTCI202230A20220013
25. Chatterjee K. The Swan-Ganz catheters: past, present, and future. A viewpoint. Circulation. 2009; 119(1):147-52. https://doi.org/10.1161/CIRCULATIONAHA.108.811141. Erratum in: Circulation. 2009;119(21):e548.
26. Aghassi P, Aurigemma GP, Folland ED, Tighe DA. Catheterization-Doppler discrepancies in nonsimultaneous evaluations of aortic stenosis. Echocardiography. 2005;22(5):367-73. https://doi.org/10.1111/j.1540-8175.2005.04006.x
27. Doğan NÖ. Bland-Altman analysis: A paradigm to understand correlation and agreement. Turk J Emerg Med. 2018;18(4):139-41. doi: 10.1016/j.tjem.2018.09.001