

Role of Exercise Testing and Speckle Tracking Echocardiography in Paradoxical Severe Aortic Stenosis

Belén Marí-López

Hospital Universitario de Canarias

María Manuela Izquierdo-Gómez

Hospital Universitario de Canarias

Ignacio Laynez-Cerdeña

Hospital Universitario de Canarias

Amelia Duque-González

Hospital Universitario de Canarias

Leopoldo Pérez de Isla

Hospital Clínico San Carlos

Flor Baeza-Garzón

Hospital Universitario de Canarias

Javier García-Niebla

Servicios Sanitarios del Area de Salud del Hierro

Juan Lacalzada-Almeida (✉ jlacalzada@gmail.com)

Hospital Universitario de Canarias

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Abstract

Background The clinical behavior and prognosis of patients with asymptomatic paradoxical low-gradient aortic stenosis (PLGAS) still remain controversial. Some authors consider PLGAS as an echocardiographically poorly quantified moderate AS (MAS). We aimed to investigate the clinical behavior of PLGAS by comparing it with that of asymptomatic high-gradient aortic stenosis (HG-AS) and MAS using transthoracic echocardiography (TTE) with speckle tracking imaging (STI) and cardiopulmonary exercise testing (CPET).

Methods A cohort of 113 patients was included and categorized into three groups according to AS type: MAS (n=63), HG-AS (n=29), and PLGAS (n=21). Patients' clinical data were obtained. Patients underwent 2D TTE with STI and CPET.

Results There were no significant differences in the clinical variables between the three AS groups. In the multivariate multinomial logistic regression analysis, with PLGAS being the reference category, the most powerful variable for establishing a difference with HG-AS was the left ventricular mass (LVM) indexed by body-surface area (odds ratio [OR]=1.04, confidence interval [CI]=1.01-1.06, $p<0.05$). The MAS group showed a lower valvuloarterial impedance (OR=0.262, CI=0.12-0.59, $p=0.001$), fewer abnormal CPET (OR=0.198, CI=0.06-0.69, $p<0.05$), and higher left ventricle global longitudinal strain rate (GLSR) (OR=0.003, CI=0.00-0.35, $p<0.05$) than the PLGAS group.

Conclusions TTE with STI and CPET established the clear differences between patients with asymptomatic PLGAS and those with asymptomatic MAS, as well as the similarities between patients with PLGAS and those with HG-AS. Our data identifies PLGAS as a completely different entity from MAS.

Background

Valvular aortic stenosis (AS), moderate AS (MAS), or severe AS affects approximately 2.8% of the population aged >75 years [1]. The clinical behavior and prognosis of severe paradoxical low-gradient AS (PLGAS) and preserved left ventricular ejection fraction (LVEF) still remain controversial. Some authors did not find any prognostic differences between patients with PLGAS and those with MAS [2, 3]. Contrarily, other authors observed the lower survival in patients with PLGAS than in those with high-gradient severe AS (HG-AS) [4-6].

The functional evaluation of the asymptomatic AS by cardiopulmonary exercise testing (CPET) can provide prognostic information to guide the proper clinical management of patients [7, 8]. Numerous studies have reported a decrease in strain in severe AS patients compared to mild AS patients, which was related to a worse prognosis [9-12]. In addition, patients with symptomatic severe AS present a decrease in multidirectional strain compared to asymptomatic patients, even when having a preserved LVEF [13].

Methods

Patient population and established groups

For this single-center, prospective, observational study, a total of 281 consecutive patients with AS who presented at the Cardiology Department of University Hospital of Canary Islands from 2015 to 2018 were screened for inclusion. A cohort of 113 patients was included in the final analysis (Figure 1). The patients were categorized into the following AS three groups: MAS, HG-AS, and PLGAS [7].

The inclusion criteria were as follows: patients aged >18 years; both sexes; asymptomatic; and diagnosed with MAS, HG-AS, and PLGAS with LVEF $\geq 60\%$. The exclusion criteria were presence of a non-sinus rhythm, other significant valvulopathy, subvalvular or supra-valvular AS, active endocarditis, known coronary disease, chronic obstructive pulmonary disease, malignant neoplasm under treatment, anemia, poor echocardiographic window, or physical inability to undergo CPET (Figure 1). On the same day, TTE with STI and CPET were performed.

Transthoracic echocardiography

Conventional two-dimensional images with STI were acquired using a commercial ultrasound system applied to echocardiography (iE33 xMATRIX Koninklijke Philips NV, Eindhoven, The Netherlands) with a 2–4-MHz multifrequency probe. The analysis was performed offline by an expert observer using the Xcelera R2 echocardiographic analysis system, Philips Medical Systems, following the recommendations of the American Society of Echocardiography [14].

Speckle Tracking Imaging

Second-harmonic images were obtained in B mode from the apical view (4, 2, and 3 chambers) and from the midventricular short axis. The images were acquired in grayscale with two-dimensional echocardiography with a sector narrowing of 30°–60° and an acquisition frequency of 60–90 images per second [15]. Subsequently and semi-automatically, the STI analysis was performed with appropriate software “QLAB *Advance Tissue Motion Quantification* v. 8.1 (Phillips)”. All measurements were performed offline by the same operator, who was blinded to the study protocol.

The global longitudinal strain (GLS) was calculated as the mean of the values of the systolic peak of the longitudinal strain observed in each of the 16 segments of the left ventricle (LV). The global basal longitudinal strain of the LV was calculated as the mean of the values of the systolic peak of longitudinal strain of the ventricular basal segments. The mid-ventricular circumferential strain and the mid-ventricular radial strain systolic peak was determined as the mean of the values of the six midventricular segments of the short axis [15].

Cardiopulmonary exercise testing

The CPET was performed with a Marquette Case 8000 system (GE Medical) equipment according to the established guidelines [16,17], using the Bruce Rampa protocol [18]. All of the main classical variables of CPET were obtained. An abnormal CPET was defined if it ended prematurely due to dyspnea, chest pain,

presyncope, or syncope. Other abnormality criteria were as follows: ST segment depression of ≥ 2 mm measured at 80 ms from point J, ≥ 3 consecutive premature ventricular beats, and decreased or increased systolic blood pressure (SBP) by ≤ 20 mm Hg from baseline. The parameters related to the gas analysis were not the criteria for discontinuing the CPET.

Statistical analyses

Continuous normally distributed data are presented as mean with standard deviation (SD), which were compared between groups using Student's t distribution. Variables that did not follow a normal distribution were expressed as the medians and interquartile range, which were compared between two groups using the Mann-Whitney U test. The categorical variables were expressed as absolute values with their corresponding percentages and were compared using the χ^2 test or Fisher's exact test. The Spearman's rank test was used to assess the correlations between continuous variables. Continuous variables of the three AS groups were compared with the two-tailed analysis of variance (ANOVA) test and non-parametric variables were compared with the Kruskal-Wallis test. Univariate and multivariate multinomial logistic regression models were used with the backward step method; the three AS types were used as the dependent variables. The corresponding odds ratio (OR) and 95% confidence intervals (CI) for the different covariates were calculated. The receiver operating characteristic (ROC) curves and the area under the curve of the variables that differentiated the PLGAS from MAS and the PLGAS from HG-AS were obtained. Sensitivity, specificity, and predictive values were calculated to determine the optimal cut-off point, which was obtained using the Youden index. The intra and interobserver variabilities for strain measurements were analyzed using the Bland-Altman test.

Statistical analysis was performed with SPSS version 21 software (SPSS Inc., Chicago, IL, USA). The two-tailed p value of <0.05 was considered significant.

Results

Study Population

Patients' mean age was 74 SD 8 years, and the study cohort was predominantly male (54%). There were no significant differences in the clinical and demographic variables among the three AS types, except for SBP ($p = 0.001$) and pulse pressure ($p = 0.001$), which showed higher values in the HG-AS group than in other two groups (Table 1 and Additional file 1 supplemental material Table 1).

The most frequent cause of initial exclusion was the inability to perform CPET (36.3 %), followed by a poor echocardiographic window (9.9%). The other reasons are found in Figure 1. From the 113 patients analyzed, 63 presented MAS (55.8%), 29 presented HG-AS (25.7%), and 21 presented PLGAS (18.6%).

Results of the cardiopulmonary exercise testing according to the aortic stenosis classification

In total, 44.2% of the patients had abnormal CPET. According to the AS types, 66.7%, 55.2%, and 31.7% of the PLGAS, HG-AS and MAS groups, respectively, had abnormal CPET, with the differences being

significant ($p < 0.05$) (Table 1).

Significant differences were found in baseline SBP during CPET ($p = 0.001$), maximum SBP during CPET ($p < 0.05$), and decrease in ST segment ≥ 2 mm ($p < 0.005$) (Table 1 and Additional file 2). All of the 19 patients with a decrease in ST segment underwent a coronary angiography, and only one had coronary artery disease. Post-hoc analysis revealed that patients with MAS had a lower proportion of abnormal CPET than patients with HG-AS and PLGAS ($p < 0.05$). Patients with HG-AS had CPET basal SBP, and CPET SBP during maximum effort greater in than in those with MAS and PLGAS ($p < 0.05$ and 0.001 , respectively). There were no significant differences in the CPET variables (Additional file 1 supplemental Table 1).

Result of echocardiographic variables according to the aortic stenosis classification

In the post-hoc analysis, we observed that the HG-AS group had greater left ventricular mass (LVM) indexed by body-surface area (BSA) than the MAS and PLGAS groups ($p < 0.001$ and $p < 0.05$, respectively) (Table 1, Additional file 1 supplemental material Table 2, and Additional file 3: Figure A).

The relative wall thickness (RWT) was > 0.42 in all groups, but it was more prominent in the HG-AS group than in the MAS and PLGAS groups. This finding was consistent with the increase in the left atrium, with the HG-AS group showing higher increased compared to the other groups (Additional file 3: Figure B).

The MAS patients had a lower valvuloarterial impedance (Z_{VA}) than the HG-AS ($p < 0.001$) and PLGAS ($p < 0.001$) patients (Table 1 and Additional file 3: Figure C).

Results of echocardiographic variables of myocardial deformation according to the aortic stenosis classification

The HG-AS group had worst LV global longitudinal strain rate (GLSR) than the MAS group [-0.62 (-0.72 to -0.55) vs. -0.77 (-0.86 to -0.65), respectively ($p < 0.05$)]. The PLGAS group also had a worst GLSR than the MAS group [-0.60 (-0.68 to -0.54) vs. -0.77 (-0.86 to -0.65), respectively ($p = 0.001$)] (Table 1).

The HG-AS and PLGAS groups had worst global basal longitudinal strain than the MAS group (both $p < 0.05$). The GLS of the LV worst in the PLGAS group than in the MAS group (-12.65 SD 1.8 vs. -14.37 SD 2.65 respectively, $p < 0.05$).

We did not observe a difference in the distribution of the circumferential and radial deformities of the LV among the three groups (Additional file 1 supplemental material Table 2).

Bland-Altman analysis showed good intra- and inter-observer agreement with a non-significant bias. The intraobserver and interobserver variabilities for GLS were 1.18% (95% CI, 1.09% - 1.31%) and 1.31% (95% CI, 1.15% - 1.82%) respectively.

Univariate multinomial logistic regression analysis

Among the differences observed between PLGAS and MAS, the following data were prominent in PLGAS: higher number of abnormal CPET ($p < 0.05$), higher Z_{VA} ($p < 0.001$), worst GLS ($p < 0.05$), worst GLSR ($p < 0.05$), and worst global basal longitudinal strain ($p < 0.05$) (Table 2 and Additional file 1 supplemental material Table 3).

When comparing the PLGAS and HG-AS groups, the PLGAS group had lower SBP ($p = 0.001$), lower pulse pressure ($p = 0.001$), lower basal SBP during CPET ($p = 0.001$), lower maximum SBP during CPET ($p < 0.05$), lower LVM indexed by BSA ($p < 0.05$), and lower left atrial diameter ($p = < 0.05$).

Multivariate multinomial logistic regression analysis

When comparing MAS with the reference category (PLGAS), MAS showed lower Z_{VA} (OR = 0.262 CI = 0.12-0.59, $p = 0.001$), lesser abnormal CPET (OR = 0.198 CI = 0.06-0.69, $p < 0.05$), and better GLSR of LV (OR = 0.003 CI = 0.00-0.35, $p < 0.05$); these variables characterized the difference between the two groups (Table 2).

With PLGAS used as the reference category, the most powerful variable in establishing a difference with respect to HG-AS was the LVM indexed by BSA (OR = 1.04 CI = 1.01-1.06, $p < 0.05$), with HG-AS showing a greater indexed LVM than PLGAS.

Study of the overall diagnostic accuracy with ROC curves

The ROC curve analysis of the LVM indexed by BSA to differentiate between HG-AS and PLGAS is shown in Figure 2A, with an area under the ROC curve of 0.71 (95% CI: 0.56-0.83, $p < 0.012$). The best cut-off point was 108.4 g/m², with a diagnostic sensitivity of 72.4% (95% CI: 63-80%) and a specificity of 52.4% (95% CI: 42-62%). The area under the ROC curve for Z_{VA} and GLSR to differentiate between MAS and PLGAS was 0.77 (95% CI: 0.65-0.88, $p < 0.001$) (Figure 2B) and 0.75 (95% CI: 0.63-0.86 $p = 0.001$) (Figure 2C), respectively.

Discussion

To the best of our knowledge, this study is the first to comparatively analyze the functional behavior of asymptomatic patients with MAS, PLGAS, and HG-AS using TTE with STI and CPET. Our findings demonstrated that PLGAS is a completely different form of AS from MAS and that, on the other hand, PLGAS has a similar behavior to HG-AS.

Jander et al. [2] and Tribouilloy et al. [3] found that the prognosis of PLGAS is similar to that of MAS, although other authors indicated that PLGAS has a lower survival than HG-AS [4-6]. Although there is no consensus about the prognosis of patients with PLGAS, a meta-analysis published in 2016 concluded that these patients presented a prognosis similar to those with HG-AS [19].

There are no comparative data on the behavior in CPET between PLGAS and MAS or HG-AS, to characterize them as authentic severe AS or not. In our study, we observed a clear difference in abnormal

CPET among the AS groups. However, no difference was found in the CPET gas analysis, which could be probably due to the careful patient selection, wherein symptomatic patients or with doubtful clinical data were excluded. Regarding Z_{VA} in PLGAS and MAS, a study established that a $Z_{VA} \geq 4.5$ mmHg/ml /m² would indicate lower survival [20]. Patients with PLGAS usually have higher Z_{VA} related to the greater myocardial dysfunction, possibly indicating a more advanced stage of AS [4, 21]. In our series, we observed greater Z_{VA} in the PLGAS group than in the MAS group. This finding could not be attributed to the greater SBP because there were no differences in the SBP between the two groups, being directly related to the aortic valve area.

Our study resembles that of Maréchaux et al. [22] who observed how patients with MAS, with a lower value of Z_{VA} , had a higher value of GLS and GLSR compared with patients with HG-AS and PLGAS, whose Z_{VA} value was higher. However, despite these differences, no significant differences were observed in LVEF. Despite what was published about its prognosis [2, 3], we considered that Z_{VA} , GLS, and GLSR of the LV are essential parameters to differentiate PLGAS and MAS.

Regarding the deformation of the LV, the GLS and GLSR were significantly decreased in the PLGAS group compared with the MAS group. Even in the multivariate analysis, this difference in the GLSR was maintained. Recently, it has been reported that a deterioration of GLS in PLGAS would be a predictor of poor prognosis, suggesting a benefit in asymptomatic patients with early aortic valve replacement [23]. We have demonstrated this significant decrease in the longitudinal deformity despite the absence of difference in LVEF between the two groups. Thus, the systolic deformity of the LV is a more robust marker of myocardial dysfunction than LVEF, which allowed the differentiation between PLGAS and MAS. In addition to the ease of determining LV systolic deformity compared to a high percentage of patients in our sample where CPET could not be performed.

When we analyzed the behavior of PLGAS against HG-AS, PLGAS has a behavior similar to the HG-AS. In our series, the variable that best differentiated PLGAS from HGAS was the LVM indexed by BSA, being significantly increased in the latter. Conversely, Hachicha et al. [4], observed greater concentric remodeling in PLGAS than in HG-AS. This, in our series, would be justified by the significant difference found between PLGAS and HG-AS in SBP, with higher values presented in HG-AS, which would indicate concentric remodeling of the LV by AS and hypertension.

Both groups, PLGAS and HG-AS, presented decreased GLS compared with the normal published values (-19.7% to -22.4%) [15, 24, 25]. Donal et al. [26] described similar results of GLS in patients with asymptomatic severe AS, which was greatly reduced compared to those of healthy controls. Other authors observed that PLGAS with decreased GLS had a prognosis similar to HG-AS, but, if the GLS was normal, the prognosis resembled that of the Normal flow-Low-gradient severe AS group, whose behavior is compared with the MAS group [27], concluding that the GLS marked the prognosis of the PLGAS group.

The CPET did not show significant differences between PLGAS and HG-AS groups. Our results support the theory that PLGAS is an entity similar to HG-AS, since both present similar results in CPET and have a

decreased SGL, but without significant differences.

Strengths and limitations

First, the exclusion criteria of our study, especially due to functional limitations of the patients when performing CPET, mean that the data obtained are not fully extrapolated to the entire population with AS. However they portray the real life associated with patients with AS an advanced age.

Second, the sample size of patients with PLGAS may have been insufficiently large to detect other relevant significant differences, but it was enough to show that PLGAS is a different entity from MAS.

Third, the presence of asymptomatic coronary artery disease could alter the results of the CPET and the strain values; however, all patients with a history of coronary heart disease were carefully excluded.

Fourth, our results of myocardial deformation by STI should be interpreted with caution when compared with those from other authors who have used different software programs. In addition, the absence of healthy controls to compare these results may be a limitation.

Conclusion

In our study, PLGAS is a different entity from MAS, presenting worse results in CPET, greater deterioration of the GLSR, and greater Z_{VA} . However, the PLGAS resembled the HG-AS, showing similar results in the CPET and GLS. Therefore, we considered that the first comparison characterizes two differentiated entities; therefore, their clinical management should also be as such. As for the second comparison, there would be two similar entities that could benefit from a similar management.

The combined use of CPET and TTE with STI allows, for a better characterization of the functional behavior of the asymptomatic patient with PLGAS and its differentiation from the patients with MAS.

Abbreviations

AS: aortic stenosis; MAS: moderate aortic stenosis; PLGAS: paradoxical low-gradient aortic stenosis; HG-AS: high-gradient aortic stenosis; TTE: transthoracic echocardiography; STI: speckle tracking imaging; CPET: cardiopulmonary exercise testing; LVM: left ventricular mass; GLSR: global longitudinal strain rate; LVEF: left ventricular ejection fraction; GLS: global longitudinal strain; LS: LV: left ventricle. SBP: systolic blood pressure; ZVA: valvuloarterial impedance; BSA: body-surface area.

Declarations

Ethics approval and consent to participate before inclusion, written informed consent was obtained from all participants. The study was designed and conducted in compliance with the ethical guidelines of the 1975 Declaration of Helsinki and received approval by the clinical research ethics committee of the University Hospital of the Canary Islands.

Consent for publication Not required.

Availability of data and materials The dataset analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests The authors declare that they have no competing interests.

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Authors' contributions All authors have been have made substantial contributions to the conception or design of the work, or the acquisition, analysis or interpretation of data and preparation of the manuscript. All authors contributed to manuscript preparation, manuscript revision, quality control and conduct of the study. BML, MMIG, ILC, ADG, LPI, FBG, JGN and JLA contributed to the study design/ planning. BML, MMIG and JLA contributed to data acquisition, analysis and interpretation. BML and JLA contributed to statistical analysis. BML and JLA are guarantors for the study.

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Authors' details

1Department of Cardiology, Hospital Universitario de Canarias, Tenerife, Spain.

2Department of Cardiology, Hospital Clínico San Carlos, Madrid, Spain.

3Servicios Sanitarios del Área de Salud de El Hierro, Valle del Golfo Health Center, El Hierro, Spain.

ORCID iDs

Juan Lacalzada-Almeida <https://orcid.org/0000-0002-9863-3222>

María Manuela Izquierdo-Gómez <https://orcid.org/0000-0002-6379-9820>

Ignacio Laynez Cerdeña <https://orcid.org/0000-0003-4934-8502>

Javier García-Niebla <https://orcid.org/0000-0003-2851-5885>

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Tables

Table 1. Clinical and echocardiographic variables of patients according to the classification of aortic stenosis.

Variables	MAS (a) (n: 63)	HG-AS (b) (n: 29)	PLGAS (c) (n: 21)	p ANOVA	p Post-Hoc
Age (years)	74 (70 to 80)	76 (72 to 81)	74 (67 to 78)	0.475	
Gender (male)	50.8%	62.1%	52.4%	0.594	
SBP (mm Hg)	130 (120 to 140)	140 (130 to 140)	130 (120 to 130)	0.001	a vs. b = 0.001 b vs. c = 0.001
DBP (mm Hg)	70 (70 to 80)	80 (70 to 80)	70 (70 to 80)	0.126	
Pulse pressure	60 (50 to 60)	60 (50 to 70)	50 (50 to 60)	0.001	a vs. b < 0.05 b vs. c = 0.001
Abnormal CPET	20 (31.7%)	16 (55.2%)	14 (66.7%)	<0.05	a vs. b < 0.05 a vs. c < 0.05
Dyspnea in CPET	14 (22.2%)	8 (27.6%)	9 (42.9%)	0.186	
ST Decline \geq 2 mm	5 (7.9%)	10 (34.5%)	4 (19%)	<0.05	a vs. b = 0.001
CEPET basal SBP (mm Hg)	120 (110 to 130)	140 (130 to 145)	125 (110 to 130)	0.001	a vs. b < 0.05 b vs. c = 0.001
CPET max. SBP (mm Hg)	150 (140 to 150)	155 (150 to 160)	130 (120 to 140)	<0.05	a vs. b = 0.001 b vs. c < 0.05
PG (mm Hg)	39.65 (32.8 to 44.35)	101.5 (83.2 to 104.4)	43.05 (42.8 to 43.3)	<0.001	a vs. b < 0,001 a vs. c = 0,05 b vs. c < 0,001
LVEF (%)	72.5 (67 to 76.1)	75.4 (70 to 79.3)	68.05 (64 to 72.1)	0.102	
Indexed AVA	0.69 SD 0.8	0.41 SD 0.08	0.45 SD 0.08	<0.001	a vs. b <

(cm ² /m ²)					0.001
					a vs. c < 0.001
					b vs. c < 0.001
Indexed LVM (g/m ²)	99.28 SD 22.69	132.32 SD 35.16	106.01 SD 25.92	<0.001	a vs. b < 0.001
					b vs. c < 0.05
	3.4 SD 0.70	4.12 SD 0.72	4.26 SD 1.07	<0.001	a vs. b < 0.001
					a vs. c < 0.001
LV GLS (%)	-14.37 SD 2.65	-13.72 SD 1.94	-12.65 SD 1.80	< 0.05	a vs. c < 0.05
LV GLSR (1/s)	-0.77 (-0.86 to -0.65)	-0.62 (-0.72 to -0.55)	-0.60 (-0.68 to -0.54)	< 0.05	a vs. b < 0.05
					a vs. c = 0.001
Global Basal LS (%)	-15.37 SD 3.10	-13.48 SD 3.42	-13.44 SD 3.49	< 0.05	a vs. b < 0.05
					a vs. c < 0.05
Basal GLSR (1/s)	-0.95 (-1.13 to -0.80)	-0.86 (-0.95 to -0.70)	-0.92 (-0.99 to -0.73)	< 0.05	a vs. b < 0.05

SD: standard deviation; AS: aortic stenosis; MAS: moderate aortic stenosis; HG-AS: high-gradient severe aortic stenosis; PLGAS: paradoxical low-gradient aortic stenosis; SBP: systolic blood pressure; DBP: diastolic blood pressure; CPET: cardiopulmonary exercise testing. IEV: indexed ejection volume; PG: peak gradient; LVEF: left ventricular ejection fraction; AVA: aortic valve area; LVM: left ventricular mass; Z_{VA}: valvuloarterial impedance; GLS: global longitudinal strain; GLSR: global longitudinal strain rate; LS: longitudinal strain.

Table 2. Univariate and multivariate multinomial analysis results.

Univariate analysis						
Variables	MAS			HG-AS		
	OR	95% CI	p	OR	95% CI	p
Abnormal CPET	0.23	0.08-0.67	< 0.05	0.62	0.19-1.97	0.410
Indexed LVM (g/m ²)	0.99	0.97-1.01	0.260	1.04	1.01-1.06	< 0.05
Z _{VA} , (mmHg/ml/m ²)	0.23	0.11-0.49	< 0.001	0.85	0.46-1.58	0.600
LV GLS (%)	0.71	0.55-0.91	< 0.05	0.8	0.61-1.04	0.096
LV GLSR (1/s)	0.001	0.00-0.10	< 0.05	0.03	0.00-2.78	0.127
Multivariate analysis						
AS Grade	Variables	p	OR	CI		
HG-AS	Indexed LVM	< 0.05	1.04	1.01-1.06		
	Z _{VA}	0.96	1.02	0.50-1.06		
	Abnormal CPET	0.46	0.61	1.17-2.25		
	LV GLSR	0.13	0.02	0.00-2.99		
MAS	Indexed LVM	0.57	0.99	0.97-1.02		
	Z _{VA}	0.001	0.262	0.12-0.59		
	Abnormal ST	< 0.05	0.198	0.06-0.69		
	LV GLSR	< 0.05	0.003	0.00-0.35		
Reference category: PLGAS: paradoxical low-gradient aortic stenosis. MAS: moderate aortic stenosis; HG-AS: high-gradient severe aortic stenosis; OR: odds ratio; CI: confidence interval; CPET: cardiopulmonary exercise testing; LVM: left ventricular mass; Z _{VA} : valvuloarterial impedance; GLS: global longitudinal strain; GLSR: global longitudinal strain rate.						

Figures

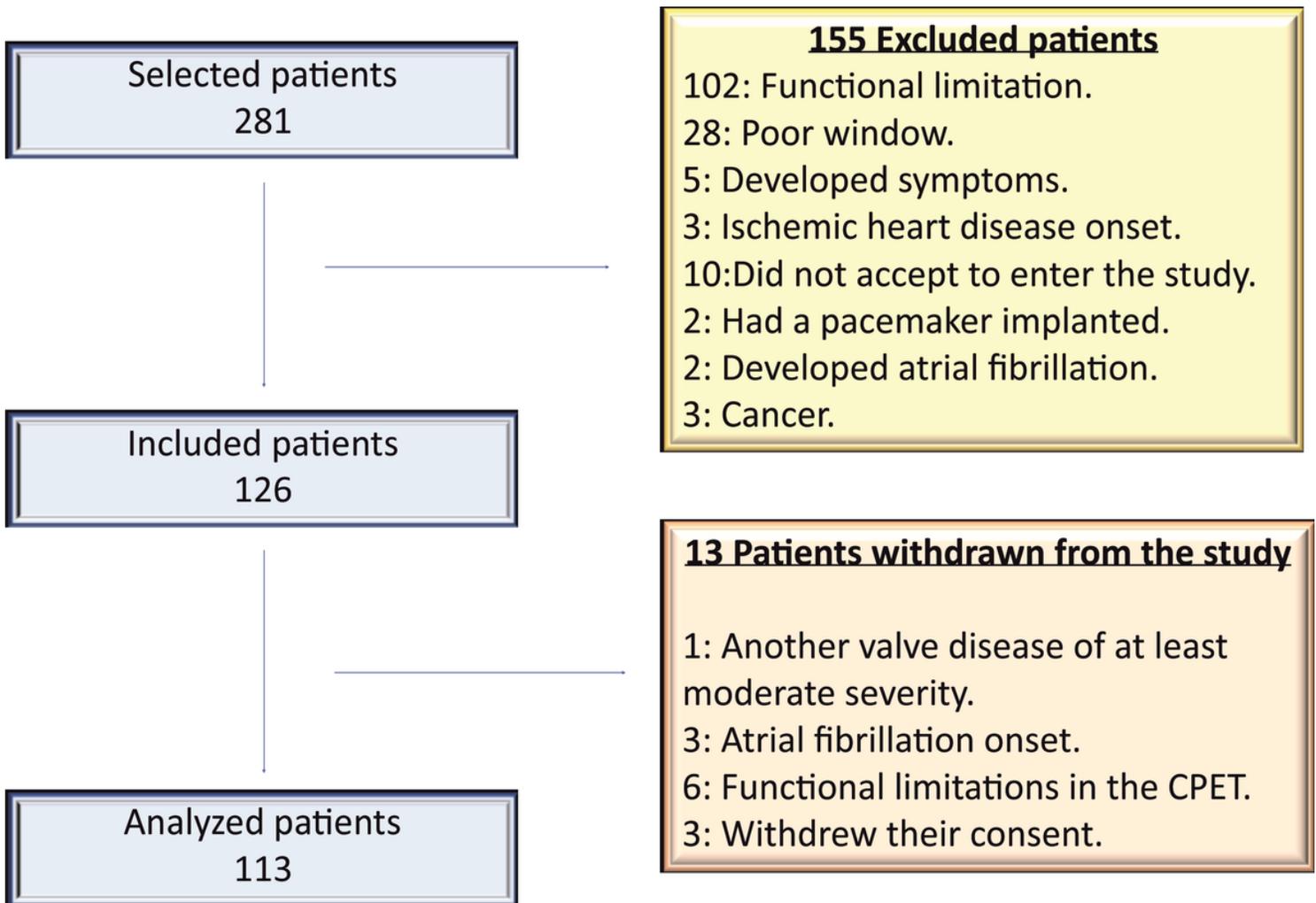


Figure 1

Flow diagram of the present study. CPET indicates cardiopulmonary exercise testing.

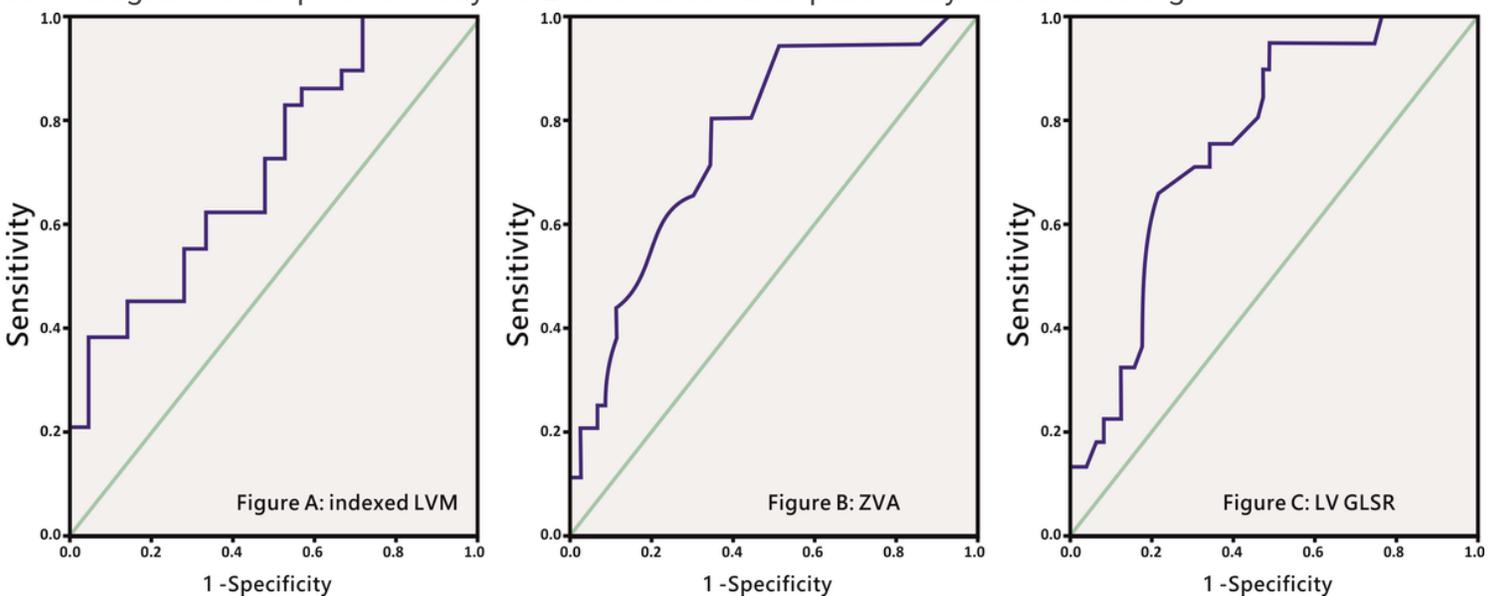


Figure 2

Receiver operating curves. Indexed LVM by BSA to differentiate between HG-AS and PLGAS (A). ZVA to differentiate between MAS and PLGAS (B). GLSR to differentiate between MAS and PLGAS (C). LVM indicates left ventricular mass, BSA indicates body-surface area, HG-AS indicates high gradient-aortic stenosis, PLGAS indicates paradoxical low gradient aortic stenosis, ZVA valvuloarterial impedance, MAS moderate aortic stenosis, and GLSR left ventricular global longitudinal strain rate.

Supplementary Files

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