Original Article

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Evaluating ejection dynamic parameters for assessing severe aortic stenosis

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Abstract

Background: Accurate diagnosis of aortic stenosis (AS) severity is crucial for effective treatment. This study aimed to define cutoff values for aortic ejection dynamic parameters, including ejection time (ET), acceleration time (AT), and the AT/ET ratio in patients with severe AS.

Methods: In both severe AS and control groups, the aortic valve area (AVA) was estimated using the continuity equation, and the trans-aortic mean pressure gradient (MPG) was measured using continuous-wave Doppler echocardiography. Blood flow time-velocity integral in the left ventricular outflow tract (LVOT TVI) was measured with pulsed-wave Doppler ultrasound, placing the sample volume 1 cm below the aortic valve. Severe AS was defined as AVA ≤1 cm^2 and MPG ≥ 40 mmHg. Clinical data were recorded, and 2D and Doppler echocardiography, including ejection dynamic parameters were analyzed.

Results: AT with a cutoff of 73 ms demonstrated perfect accuracy in diagnosing severe AS, with both sensitivity and specificity of 100%. ET with a cutoff of 278 ms showed 90% sensitivity and 100% specificity for identifying severe AS. Additionally, the AT/ET ratio exhibited a positive relationship with MPG (r = 0.55, P = 0.001) and a negative relationship with AVA (r = -0.52, P = 0.003). The AT/ET ratio, using a cutoff value of 0.278, yielded a sensitivity of 96% and a specificity of 100% for diagnosing severe AS.

Conclusion: Aortic Doppler ejection dynamic parameters can serve as complementary assessment indices, diagnosing severe AS with acceptable accuracy.

Keywords: Cardiovascular disease, Doppler effect, Echocardiography, Acceleration, Aortic valve stenosis.

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Aortic stenosis (AS) is a prevalent heart valve disease that often leads adults to require surgical intervention. It ranks as the third most common cardiovascular disease, following hypertension and coronary artery disease. AS is characterized by the fibrosis, thickening, and calcification of the aortic valve. This condition becomes more common as people age, affecting between 2% and 7% of individuals over 65 and 70 years, although the distribution of AS severity has remained stable (1-4). Symptoms of AS are syncope, angina, shortness of breath, or other symptoms of heart failure (5, 6), and significant symptoms typically emerge in those with severe AS (7). Traditionally, the severity of AS is assessed using 2D and Doppler echocardiography with key measurements including the aortic valve area (AVA), the mean pressure gradient (MPG), and the peak velocity of blood flow (8). AS is classified as severe if the mean MPG is 40 mmHg or higher, the peak velocity of the aortic jet is 4 meters per second or higher, and if the AVA is 1 square centimeter or less. Notably, discrepancies of 24-38% can occur between AVA and MPG, even in patients with preserved left ventricular ejection fraction (LVEF) (6, 8-11).

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The continuity equation indicates that the AVA depends on LVOT cross sectional area (CSA), LVOT TVI and the TVI of aortic valve. LVOT CSA is calculated as LVOT diameter^2×0.875; this means that any small error in measurement of LVOT diameter in 2D echo leads to a significant change in LVOT CSA and eventually in calculated AVA. Additionally, LVOT CSA is often assumed to be circular, but it can be elliptical in many patients with significant AS (12, 13). Moreover, the gradient depends on LVOT stroke volume and chronotropy; for a given AVA and stroke volume, a slower heart rate (i.e., longer LV ejection time) results in a smaller gradient (14). Measurements of MPG and peak velocity can also be influenced by blood flow rates, potentially leading to overestimation of AS severity when blood flow is elevated. Furthermore, the continuity equation has limitations when severe left ventricular dysfunction is present (15). Indeed, each modality or parameter used for grading AS severity has its inherent limitation. Grading AS severity based on a single parameter or modality will not be accurate and may lead to inappropriate treatment. (6, 8-11, 16). Currently, there is no ideal echocardiographic method to quantify the severity of AS. It cannot be accurately achieved with a single measurement, and it is likely to lead to incorrect evaluation of the AS severity (17). There are studies that assessed stenosis severities in native and prosthetic aortic valves with attention to echocardiographic ejection dynamics (18-23). Accordingly, we aimed to evaluate the relationship between the ejection dynamic parameters, such as acceleration time (AT), ejection time (ET), and the ratio of the AT/ET with MPG and AVA, and to define cutoff values for these parameters in diagnosing severe AS.

Methods

Study population: This prospective study included patients with severe AS and a matched control group without a history of AS, heart failure, valvular disease, or prior cardiac surgery. All participants were referred to the echocardiography lab at Heshmat Cardiovascular Research Center in Rasht, Iran, for evaluation. A detailed history and physical examination regarding symptoms, heart rate, and blood pressure were recorded. All patients with AS and the control group had 50≤ HR ≤100. To accurately classify the severity of AS and include severe and symptomatic AS in the study, clinical manifestations of AS symptoms (syncope, angina, and shortness of breath), heart failure symptoms, LV geometry, function and tissue architecture, ECG changes, most common cause of AS (degenerative calcification, bicuspid aortic valve, and rheumatic disease) were also evaluated as much as possible. Exclusion criteria included LVEF< 45%, discrepancies between MPG and AVA in diagnosing severe AS, mild to severe aortic regurgitation, prosthetic heart valve, significant valvular heart disease other than AS, supravalvular or subvalvular AS, and an ascending thoracic aorta diameter < 28 mm. Written informed consent was obtained from all participants, who underwent physical and echocardiographic examinations. We ensured data confidentiality and participant privacy throughout the study. Results were reported as averages rather than individual data. The participants had the right to end their participation in the research for any reason and at any time. Our study protocol was approved by the research council of Healthy Heart Research Center, research council of Guilan University of Medical Sciences and the local ethical committee (Ethics code number: GUMS1930309903), respectively.

Echocardiography: Echocardiographic assessments were performed using an ACUSON SC2000 ultrasound system with a 1.25-4.5 MHz transducer. The LVEF was determined using the biplane Simpson method. The AVA was estimated through the continuity equation, and the MPG across the aortic valve was measured using continuous-wave Doppler echocardiography from the apical 5-chamber and right parasternal views. To assess AS severity, we measured the aortic valve annulus size from the zoomed parasternal long-axis view. Severe AS was defined as MPG ≥ 40 mmHg and AVA ≤ 1 cm², in accordance with ESC/EACTS guidelines for valvular heart disease (4). Blood flow time-velocity integral in the left ventricular outflow tract (LVOT TVI) was measured with pulsed-wave Doppler ultrasound, sample volume placing 1 cm below the aortic valve in apical 5-chamber view. The Doppler recordings were conducted at 150 mm/s to capture detailed flow information. The ejection time (ET) was measured from the onset to the end of systolic flow, while the acceleration time (AT) was measured from the onset to peak systolic velocity. The ratio of AT to ET was then calculated (figure 1). All measurements were averaged over three heartbeats during normal heart rhythm.

Statistical analysis: We utilized the Kolmogorov- Smirnov test to check the data for normal distribution and homogeneity. When dealing with continuous variables, they were represented by their average value and the standard deviation (SD) to indicate variability. For categorical data, the information was presented in terms of exact counts or percentages to convey proportions. To determine the differences between the two groups, we used statistical methods: the independent samples t-test for continuous and the chi-squared test for categorical variables. Differences among variables were considered significant at p values less than 0.05. The Pearson correlation coefficient was used to analyze the relationships between continuous variables. To identify the most effective cutoff values for the all ejection dynamic parameters, a receiver operator characteristic (ROC) curve was plotted. These cutoffs were determined as the values providing the maximal summation of sensitivity (true positive rate) plus specificity (true negative rate). The area under the ROC curve (AUC) provides a single measure of overall accuracy that summarizes the performance of the diagnostic test. Cross-validation of discriminant analysis was done for all aortic ejection dynamic parameters (AT, ET, and AT/ET) to assess the performance of predictive models. In this analysis, each case is classified with the functions derived from all cases other than that case. Also, by using logistic regression, the ability of classification of dynamic parameters (significance and impact of each predictor variable) was evaluated in the belonging of cases to the studied groups. Statistical evaluations were conducted using SPSS software (SPSS Ver. 21 Inc., Chicago, IL).

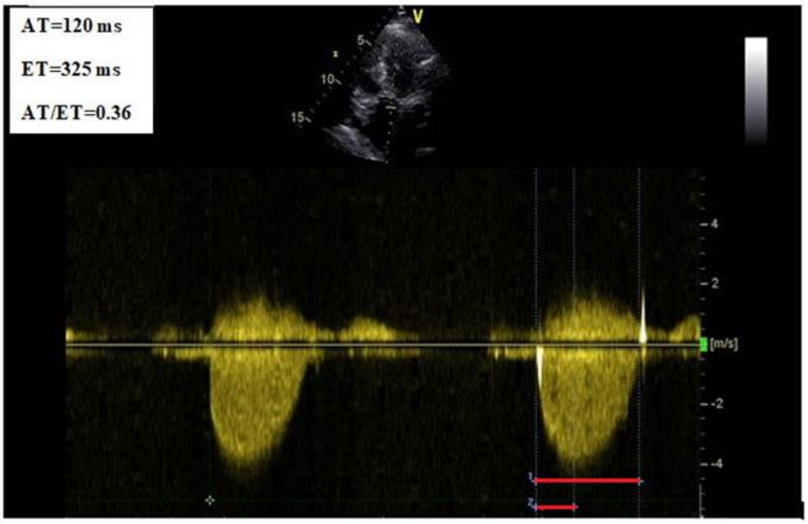

Figure 1. Ejection time intervals for AT/ET calculation

Results

Sixty patients with native aortic valve were enrolled: 30 (43% females) patients with severe AS and 30(40% females, 97% (sex-matched) subjects without AS as a control group. The mean age of individuals diagnosed with AS was 64.2 ± 13.2 years, while those without the condition had an mean age of 59.8 ± 9.4 years (83% age matched), showing no notable age disparity between the groups (P = 0.14). Additionally, there were no meaningful differences in gender distribution, blood pressure measurements (both systolic and diastolic) and clinical baseline characteristics between the study groups (all p-values > 0.05). Table 1 provides an overview of demographic and echocardiographic findings of the study participants. Ejection dynamic parameters are shown in table 2.

The ROC analysis revealed that the AT and ET effectively distinguish patients with severe AS from those who do not have the condition (AUC = 1, 95% CI: 1 to 1, p < 0.001 and AUC = 0.943, 95% CI: 0.87 to 1, p <0.001; respectively). Using a cutoff of 73 ms, AT had both perfect sensitivity and specificity of 100% for diagnosing severe AS (figure 2). An ET cutoff value of 278 ms demonstrated high sensitivity of 90% and perfect specificity of 100% in identifying severe AS (figure 3).

Table1. Demographic, hemodynamic and echocardiographic characteristics of the participants

Variables	Without AS (n=30)	With severe AS (n= 30)	P-value
Age (year)	59.8±9.4	64.2±13.2	0.142
Women (n, %)	12 (40%)	13 (43%)	0.979
BMI (Kg/m^2)	23.4±2.6	22.7±3.1	0.347
DM (n, %)	5 (17%)	6 (20%)	0.973

Variables	Without AS (n=30)	With severe AS (n= 30)	P-value
Dyslipidemia (n, %)	11 (37%)	12 (40%)	0.979
Smoking (n, %)	3 (10%)	4 (13%)	0.968
Systolic BP (mmHg)	127.3±8.8	129.9±8.9	0.259
Diastolic BP (mmHg)	83.0±4.3	83.7±4.5	0.540
LVEF (%)	55.3±3.8	54.3±4.9	0.381
AVA (cm^2)	3.1±0.32	0.76±0.23	<0.001

Aortic valve area (AVA), Aortic stenosis (AS), Blood pressure (BP), Diabetes mellitus (DM), Mean pressure gradient (MPG), Left ventricular ejection fraction (LVEF).

Table 2. Comparison of ejection dynamic parameters between the patients with and without aortic stenosis

	Without AS	With severe AS	P-value
AT, ms	67.8±1.3	115.9±22.3	<0.001
ET, ms	260.5±10.0	310.8±29.8	<0.001
AT/ET	0.26±0.01	0.37±0.05	<0.001

Aortic stenosis (AS), Acceleration time (AT), Ejection time (ET)

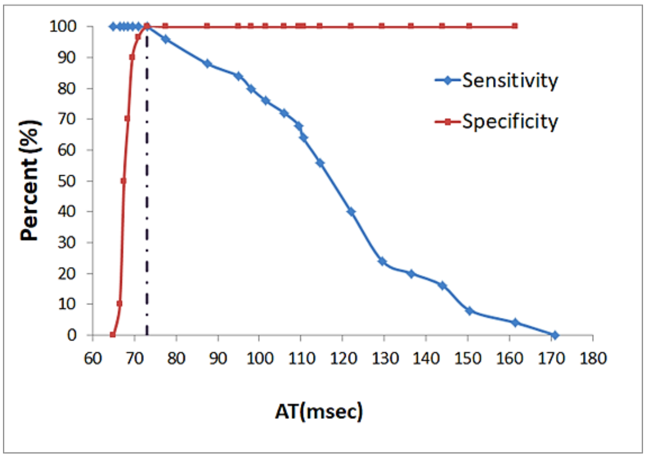

Figure 2. Optimal cutoff point of acceleration time (AT) with the highest combined score of sensitivity and specificity for discriminating patients with severe aortic stenosis

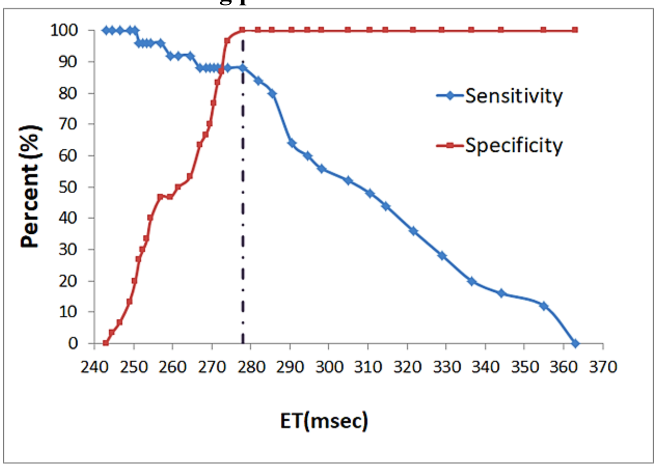

Figure 3. Optimal cutoff point of ejection time (ET) for discriminating patients with severe aortic stenosis

The AT/ET ratio positively correlated with MPG (r = 0.55; P = 0.001) and a negatively correlated with AVA (r = -0.52, P = 0.003). The ROC analysis confirmed that the AT/ET ratio is a reliable indicator for distinguishing patients with severe AS from those without the condition (AUC, 0.967; 95% CI, 0.9 to 1; p < 0.001). With a cutoff value of 0.278, the AT/ET ratio showed 96% sensitivity and 100% specificity for diagnosing severe AS (figure 4). The cross-validation results of discriminant analysis for all aortic ejection dynamic parameters under investigation (AT, ET, and AT/ET ratio) confirmed high accuracy (sensitivity for AT, ET, and AT/ET ratio were 87%, 83% and 83%, respectively) for assessing predictive model-performance. Logistic regression results also indicated that these parameters accurately classify the examined groups (sensitivity for AT, ET, and AT/ET ratio were 93%, 92% and 92%, respectively).

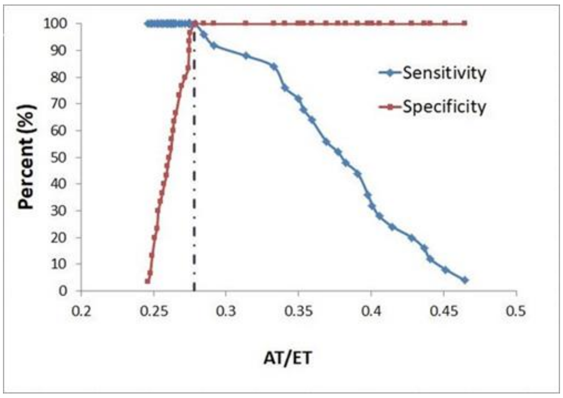

Figure 4. Optimal cutoff point of AT/ET for discriminating patients with severe aortic stenosis

Discussion

In this study, aortic AT and ET were effective for diagnosing severe AS. AT showed perfect sensitivity and specificity at a cutoff of 73 ms, while ET demonstrated high sensitivity and perfect specificity at a cutoff of 278 ms. Additionally, the AT/ET ratio emerged as a reliable indicator for severe AS, positively correlating with MPG and negatively with AVA, highlighting its clinical utility.

A hybrid approach using multi-detector computed tomography, cardiovascular magnetic resonance imaging, or three-dimensional echocardiography for measuring LVOT area, combined with Doppler echocardiography for assessing LVOT and aortic velocities, has a number of limitations including overestimation of the area (11, 24-26). To address these issues, alternative measurements beyond conventional valve hemodynamics are needed. Our study demonstrates that aortic ejection dynamics serve as complementary indices, enhancing the diagnosis of severe AS. These parameters have been utilized for over 40 years (27-30), in patients with pure severe AS palpation of the carotid pulse reveals a delayed and gradual rise (pulsus tardus et parvus). On auscultation, the systolic murmur of AS is also late peaking. Bonner et al.,identified the ET index, maximal carotid pulse rate increase, and time to peak systolic murmur as key indicators of AS assessed via phonocardiography and external carotid pulse recordings (27). Although authors reported a good correlation between echocardiographic ejection dynamic parameters with hemodynamic data of cardiac catheterization determining, the cutoff has received less attention (31). Researchers have also explored whether the dynamics of aortic ejection be used to differentiate between prosthetic AV (PAV) stenosis, normal controls, and prosthetic valve mismatch. Ben Zekry et al. found that AT and the ratio of AT/ET ratio are reliable, angle-independent measures that can effectively assess valve performance and identify PAV stenosis (32).

Gamaza et al. enrolled 262 patients with varying degrees of AS, including severe cases, and utilized a comprehensive echocardiographic evaluation to establish correlations between aortic ejection dynamics and AS severity. Specific cutoffs had moderate sensitivity (cutoff of 94ms for AT: sensitivity of 71% and specificity of 81% for severe AS) and specificity (cutoff of 0.35ms for AT/ET ratio: sensitivity of 59% and specificity of 86% for severe AS) (16). Burns et al. emphasized the utility of aortic AT and the AT/ET ratio as intraoperative indicators of AS severity, demonstrating that intraoperative measurements significantly differentiate between severe and non-severe AS, with specific cutoffs yielding moderate sensitivity and specificity (74% and 72%, respectively) (21). Both studies investigated the assessment of AS through echocardiographic measurements. Conversely, we comprised a smaller cohort of subjects, focusing on severe AS without the presence a discrepancy between MPG and AVA and a matched control group without AS, aiming to identify practical cutoff values for aortic ejection dynamics in diagnosing severe AS. This may explain the lower cutoff values and higher sensitivity and specificity found in our study. Altes et al. emphasized that an AT/ET ratio exceeding 0.35 is a significant predictor of mortality in patients with high-gradient severe AS (23). In contrast, our study concentrated on the diagnostic utility of ejection dynamics parameters, while they highlighted the prognostic significance of the AT/ET ratio. Collectively, the findings of our study in conjunction with the referenced studies, highlight the critical role that echocardiographic assessments play in the management of AS severity, improving both diagnostic and prognostic evaluations in clinical practice. Compared to traditional echocardiographic methods, ejection dynamic parameters offer a quick, straightforward, and quantitative tool that improves diagnostic precision, facilitating a more personalized management strategy for each patient. Understanding the severity of AS can assist in deciding the timing for surgical intervention, such as valve replacement. Additionally, the flow independence of the AT/ET ratio can be especially beneficial in situations where flow rates are abnormal. Overall, incorporating these parameters into clinical practice may enhance decision-making and contribute to improved patient outcomes in the management of AS. Further studies could explore standardized protocols for its implementation in echocardiography labs to maximize its clinical utility.

This study presents several potential sources of error that could limit its findings. Measurement errors may arise from the echocardiographic assessments, such as inaccuracies in calculating AVA, MPG and the subjective interpretation of Doppler parameters due to operator dependency. Selection bias may also be a concern, as the study population was limited to patients referred to our echocardiography lab (study's single-center design) and limited number of participants. To achieve a comprehensive understanding of the effectiveness of the cutoff values in more realistic clinical conditions, additional research involving patients with different stages of AS and external validity testing is required. Such biases may limit the generalizability of the findings in clinical settings. Considering the exploratory nature of this study's findings, we conclude that aortic ejection dynamic parameters such as, AT, ET and the ratio of AT/ET can serve as complementary indices or alternatives to traditional echocardiographic assessments in patients with AS, offering a reliable diagnosis of severe AS with acceptable accuracy.

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