CLINICAL RESEARCH

Correlates of the ratio of acceleration time to ejection time in patients with aortic stenosis: An echocardiographic and computed tomography study

Corrélations entre le rapport du temps d'accélération et le temps d'éjection chez les patients porteurs de sténose aortique: une étude échocardiographique et scannographique

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Abbreviations: AS, Aortic Stenosis; AT/ET, Acceleration Time/Ejection Time Ratio; AU, Agaston Units; CT, Computed Tomography; CT-AVC, Computed Tomography Aortic Valve Calcium; LV, Left Ventricular; LVEF, Left Ventricular Ejection Fraction; ROC, Receiver Operating Characteristic.

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KEYWORDS
Aortic valve stenosis;
Ejection dynamics
parameters;
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tomography;
Aortic valve calcium

Summary

Background. — An increased acceleration time to ejection time (AT/ET) ratio is associated with increased mortality in patients with aortic stenosis (AS).

Aim. — To identify the factors associated with an increased AT/ET ratio.

Methods. — The relationships between the AT/ET ratio and clinical and Doppler echocardiographic variables of interest in the setting of AS were analysed retrospectively in 1107 patients with AS and preserved left ventricular (LV) ejection fraction (LVEF). The computed tomography aortic valve calcium (CT-AVC) score was studied in a subgroup of 342 patients.

Results. — In the univariate analysis, the AT/ET ratio was found to correlate with peak aortic jet velocity ($r = 0.57$; $P < 0.0001$), mean pressure gradient ($r = 0.60$; $P < 0.0001$), aortic valve area ($r = -0.50$; $P < 0.0001$) and CT−AVC score ($r = 0.24$; $P < 0.0001$). The AT/ET ratio had good accuracy in predicting a peak aortic jet velocity ≥ 4 m/s, a mean pressure gradient ≥ 40 mmHg and an aortic valve area $\leq 1.0\,cm^2$, with an optimal cut-off value of 0.34. Multivariable linear regression analysis showed that presence of AS-related symptoms, decreased LV stroke volume index, LVEF, absence of diabetes mellitus, systolic blood pressure, increased LV mass index, relative wall thickness and peak aortic jet velocity were independently associated with an increased AT/ET ratio (all $P < 0.05$). In the subgroup of patients who underwent CT-AVC scoring, the CT-AVC score was independently associated with an increased AT/ET ratio ($P < 0.05$).

Conclusions. — The AT/ET ratio is related to echocardiographic and CT-AVC indices of AS severity. However, multiple intricate factors beyond the haemodynamic and anatomical severity of AS influence the AT/ET ratio, including LV geometry, function and systolic blood pressure. These findings should be considered when assessing the AT/ET ratio in patients with AS and preserved LVEF.

MOTS CLÉS
Rétrécissement
aortique ;
Paramètres
d'éjection
dynamique ;
Échocardiographie ;
Scanner cardiaque ;
Score calcique
aortique

Résumé

Contexte. — L'allongement du ratio « temps d'accélération » sur « temps d'éjection » aortique (AT/ET) est associé à une augmentation de la mortalité chez les patients présentant un rétrécissement aortique (RA).

Objectif. — Identifier les facteurs associés à un allongement du ratio AT/ET.

Méthodes. — Les relations entre le ratio AT/ET, les variables cliniques et échocardiographiques d'intêret dans l'évaluation du RA ont été analysées de manière rétrospective chez 1107 patients présentant un RA à fraction d'éjection (FE) ventriculaire gauche (VG) préservée. Le score calcique aortique évalué par scanner cardiaque était étudié chez un sous-groupe de 342 patients.

Résultats. — En analyse univariée, il était retrouvé une corrélation entre le ratio AT/ET et le pic de vélocité transaortique ($r = 0,57$; $p < 0,0001$), le gradient moyen transaortique ($r = 0,60$; $p < 0,0001$), la surface fonctionnelle aortique ($r = -0,50$; $p < 0,0001$) et le score calcique aortique ($r = 0,24$; $p < 0,0001$). Le ratio AT/ET avait une bonne capacité pour prédire un pic de vélocité transaortique ≥ 4 m/s, un gradient moyen transaortique ≥ 40 mmHg ou une surface fonctionnelle aortique $\leq 1,0\,cm^2$, avec une valeur seuil de 0,34. L'analyse par régression linéaire multivariée, a montré que la présence de symptômes associés au RA, la diminution du volume d'éjection systolique indexé, de la FEVG, l'absence de diabète, et l'augmentation de la pression artérielle systolique, de la masse VG indexée, de l'épaisseur pariétale relative et du pic de vélocité transaortique étaient indépendamment associés à un allongement du ratio AT/ET ($p < 0,05$). Dans le sous-groupe des patients où le score calcique aortique par scanner cardiaque avait été réalisé, le score calcique aortique était indépendamment associé à un allongement du rapport AT/ET ($p < 0,05$).

Conclusions. — Le ratio AT/ET est relié aux indices échocardiographiques et scannographiques de sévérité du RA. Cependant, de multiples facteurs au-delà de la sévérité anatomique et hémodynamique du RA influencent le ratio AT/ET incluant la géométrie et la fonction VG, ainsi que la pression artérielle systolique. Ces données devraient être prises en considération lors de l'interprétation de l'AT/ET chez les patients présentant un RA à FEVG préservée.

Background

The ratio of acceleration time to ejection time (AT/ET) may be used to assess native aortic valve stenosis (AS). Indeed, the AT/ET ratio increases with growing AS haemodynamic severity [1]. In a recent study, an AT/ET ratio ≥ 0.35 had a relatively poor sensitivity of 59%, but a fair specificity of 86% for the diagnosis of severe AS defined by an aortic valve area $\leq 1.0\,cm^2$ by Doppler echocardiography [2]. In addition, we recently reported that an AT/ET ratio ≥ 0.36 predicted a 2.5-fold mortality risk during follow-up in patients with AS [3]. This relationship between AT/ET ratio and mortality persisted after adjustment for classical predictors of outcome in AS, including left ventricular (LV) stroke volume index, symptoms and aortic mean pressure gradient. However, the factors associated with an increased AT/ET ratio, beyond echocardiographic indices of haemodynamic severity in AS, are not yet fully understood.

In the present study, derived from a multicentre registry of patients with AS and preserved LV ejection fraction (LVEF), we aimed to evaluate: (1) the diagnostic value of AT/ET in identifying severe AS, using classical echocardiographic indices of AS severity, and computed tomography (CT) aortic valve calcium (CT-AVC) scoring in a subgroup of patients; and (2) the factors associated with an increased AT/ET ratio, beyond classical echocardiographic indices of severity in AS.

Methods

Patient population

The present population was built with patients diagnosed with at least a mild form of AS (aortic valve area $\leq 2\,cm^2$) and preserved LVEF ($\geq 50\%$) in the echocardiographic laboratory of three centres (Groupement des Hôpitaux de l'Institut Catholique de Lille, Amiens and Saint-Denis). A subgroup of patients underwent clinically indicated CT-AVC scoring for AS assessment or before transcatheter aortic valve implantation. The CT-AVC score data were used if the maximal delay between the two examinations was < 2 months. Data were obtained prospectively in each centre, but were pooled retrospectively. We excluded patients with > mild aortic and/or mitral regurgitation, and those with prosthetic valves, supravalvular or subvalvular AS or dynamic subaortic obstruction.

A co-morbidity index summating the patient's individual co-morbidities was calculated [4]. Coronary artery disease was defined by the presence of a documented history of acute coronary syndrome, coronary artery disease previously confirmed by coronary angiography (reduction of the normal diameter by $\geq 50\%$ in the left main coronary artery and by $\geq 70\%$ in the right coronary, left anterior descending and circumflex arteries) or history of coronary revascularization.

We obtained institutional review board authorizations before conducting the study. The study was carried out in accordance with institutional policies, national legal requirements and the revised Declaration of Helsinki.

Echocardiography

A comprehensive Doppler echocardiographic study was performed by experienced echocardiographers using commercially available ultrasound systems. Peak aortic jet velocity was recorded using continuous-wave Doppler systematically in several acoustic windows (apical five-chamber, right parasternal, suprasternal and subcostal views) [5]. The highest aortic velocity was used to calculate the aortic time-velocity integral and the mean pressure gradient. Pulsed Doppler LV outflow tract velocity was recorded in the apical five-chamber view, with the sample volume at 5 mm proximal from the plane of the aortic valve. The alignment of both pulsed- and continuous-wave Doppler was optimized to be parallel with the flow. Pressure gradients were calculated using the simplified Bernoulli equation [6]. Aortic valve area was calculated using the continuity equation [7]. Stroke volume was calculated by multiplying the area of the LV outflow tract by the outflow tract time-velocity integral, and was indexed to the body surface area. LV dimensions were assessed from parasternal long-axis views by two-dimensional guided M-mode, using the leading-edge methodology at end-diastole and end-systole [8]. LVEF was calculated using Simpson's biplane method. The maximal velocity of the tricuspid regurgitation was estimated using continuous-wave Doppler. LV mass was calculated using the corrected formula of the American Society of Echocardiography, and was indexed for body surface area. Relative wall thickness was calculated for assessment of LV geometry using the formula: (septal + posterior diastolic wall thickness)/LV diastolic diameter [9]. The AT was defined as the time from the start to the peak of flow through the valve by continuous-wave Doppler. The ET was defined from aortic valve opening to aortic valve closure (Fig. 1). Continuous-wave Doppler recordings were performed at a sweep speed of 100 mm/s. The AT/ET ratio was then calculated. All measurements were averaged over three consecutive cardiac cycles in patients in sinus rhythm, and five consecutive cycles or more in patients in atrial fibrillation/flutter. Echocardiograms were stored in Digital Imaging and Communications in Medicine (DICOM) format to allow subsequent offline analysis. Severe AS was considered if the aortic valve area was $\leq 1\,cm^2$ and/or the peak aortic jet velocity was ≥ 4 m/s and/or the mean pressure gradient was $\geq 40\,mmHg$, as recommended by European Society of Cardiology guidelines on valvular heart diseases [10]. In addition, severe AS was considered if the dimensionless index was ≤ 0.25.

CT-AVC scoring

All centres performed non-contrast CT scans using the following parameters: prospective electrocardiogram triggering adapted to heart rate (75% of R-R cycle if heart rate < 75 bpm; 45% of R-R cycle if heart rate > 75 bpm); a body mass index-adapted scanning protocol for tube current; and a tube voltage of 120 kVp. Imaging was performed on a range of different scanners (SOMATOM Definition Edge [Siemens, Munich, Germany] in Lille; CT 750 HD or CT 660 [GE Healthcare, Milwaukee, WI, USA] in Amiens; and Revolution CT [GE Healthcare] in Saint-Denis). Beta-blockade
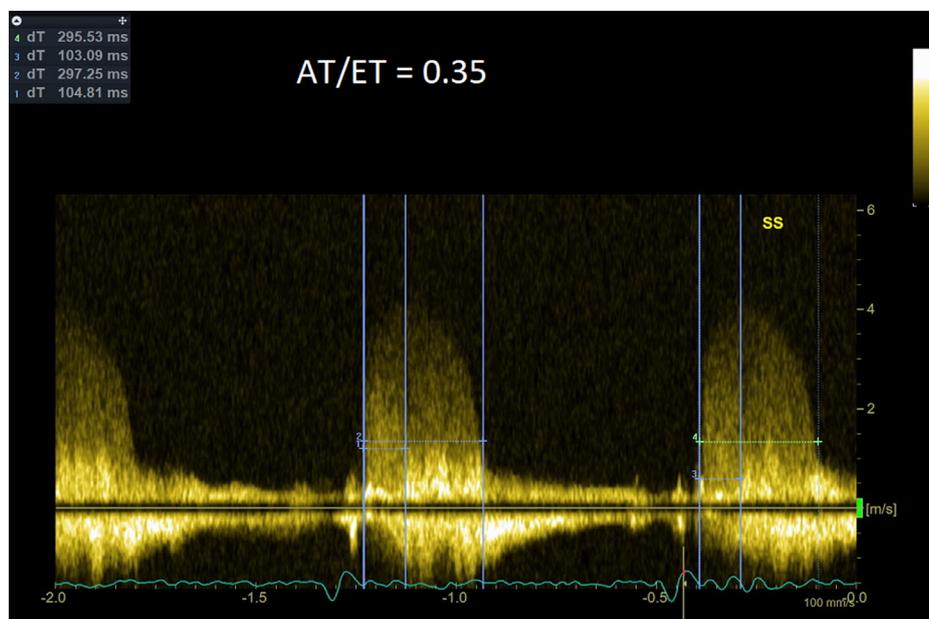
Figure 1. Systolic time interval measurement on a continuous-wave Doppler recording of transaortic flow. AT/ET: acceleration time/ejection time ratio.

was administered in Amiens to achieve a resting heart rate of < 65 bpm, but not in Lille and Saint-Denis. Image analysis was performed locally using a range of different software packages (CT calcium scoring syngo.via [Siemens] in Lille; and Smart Score 4.0 [GE Healthcare] in Amiens and Saint Denis). CT-AVC scores were quantified on contiguous 3 mm axial slices in Lille, and on 2.5 mm axial slices in Amiens and Saint-Denis, with the axial slices commencing at the base of the valve, and care taken to exclude calcium originating from extravalvular structures, such as the mitral valve annulus, the ascending aorta and the coronary arteries. The total AVC in Agaston units (AU) was calculated. Severe AS was considered likely if the CT-AVC score was $\geq$ 1200 in women and $\geq$ 2000 in men, and very likely if the CT-AVC score was $\geq$ 1600 in women and $\geq$ 3000 in men, as recommended by current European Society of Cardiology guidelines on valvular heart diseases [10].

Statistical analysis

Continuous variables are expressed as means $\pm$ standard deviations, medians (interquartile ranges) and ranges. Categorical variables are summarized as percentages. CT-AVC data underwent square root transformation to achieve normality ($\sqrt{AU}$) [11]. The relationships between AT/ET values and other indices of AS severity were analysed using Pearson r correlation coefficients. Receiver operating characteristic (ROC) curves were then used to evaluate the diagnostic value of the AT/ET ratio in predicting severe AS, defined as a peak aortic jet velocity $\geq$ 4 m/s, a mean pressure gradient $\geq$ 40 mmHg, an aortic valve area $\leq$ 1.0 cm^2 or a dimensionless index $\leq$ 0.25. In addition, in the subgroup of patients who underwent CT-AVC scoring, ROC curves were built to predict a CT-AVC score of $\geq$ 1600 AU for women and $\geq$ 3000 AU for men (severe AS very likely), and of $\geq$ 1200 AU in women and $\geq$ 2000 AU in men (severe AS

likely). The AT/ET ratio cut-offs were defined as the values providing the best balance between sensitivity and specificity. The areas under the ROC curves were calculated. Univariate linear regression analysis was performed to identify the clinical, echocardiographic and CT scan variables associated with the AT/ET ratio. To identify independent correlates of the AT/ET ratio, all variables associated with the AT/ET ratio in the univariate analysis ($P < 0.10$) were included in the multiple regression analysis, using an enter method instead of stepwise multiple-regression analysis. Collinearity was assessed by the variance inflation factor. To avoid collinearity, either peak aortic jet velocity, mean pressure gradient, dimensionless index or aortic valve area was entered into multivariable models. A P value < 0.05 was considered statistically significant. All P values were the results of two-tailed tests. Statistical analyses were performed using R, version 3.4.4 (R 319 Foundation for Statistical Computing, Vienna, Austria), SPSS software, version 20.0 (IBM, Armonk, NY, USA) and GraphPad Prism, version 8.0 (GraphPad Software Inc., San Diego, CA, USA).

Results

Baseline characteristics of patients with AS

The study population consisted of 1107 patients with a median age of 81 (74—86) years; 570 (52%) patients were female. A total of 342 patients underwent both Doppler echocardiography and CT-AVC scoring. Clinical, echocardiographic and CT scan data from the study population are detailed in Table 1. Median peak aortic jet velocity, mean pressure gradient and dimensionless index were 3.90 (3.10—4.40) m/s, 37 (23—49) mmHg and 0.24 (0.19—0.30), respectively. The median aortic valve area was

Table 1 Characteristics of the study population (*n* = 1107).

Age (years)	81 (74—86)
Female sex	570 (52)
Hypertension	863 (78)
Diabetes	347 (31)
Dyslipidaemia	583 (53)
Chronic renal failure	252 (23)
Current smokers	119 (11)
Renin-angiotensin system blockers	615 (56)
Beta-blockers	519 (47)
Statins	634 (57)
Loop diuretics	583 (53)
Antiplatelet therapy	511 (46)
Charlson Comorbidity Index: 0 or 1	383 (35)
Charlson Comorbidity Index: $\geq$ 2	722 (65)
Coronary artery disease	439 (40)
AS-related symptoms	469 (42)
Systolic blood pressure (mmHg)	140 (123—150)
Heart rate (bpm)	72 (64—83)
LVEF (%)	62 (57—66)
LV end-diastolic diameter (mm)	46 (42—52)
LV mass index (g/m^2)	115 (93—143)
Relative wall thickness	0.52 (0.44—0.62)
LV stroke volume index (mL/m^2)	41 (34—48)
LA volume index (mL/m^2)	43 (33—55)
Aortic valve area (cm^2)	0.87 (0.69—1.10)
Mean pressure gradient (mmHg)	37 (23—49)
Peak aortic jet velocity (m/s)	3.90 (3.10—4.40)
Dimensionless index	0.24 (0.19—0.30)
Systolic PAP (mmHg)	35 (30—44)
AT/ET ratio	0.34 (0.29—0.38)

Data are expressed as median (interquartile range) or number (%). AS: aortic stenosis; AT/ET: acceleration time/ejection time; LA: left atrial; LV: left ventricular; LVEF: left ventricular ejection fraction; PAP: pulmonary artery pressure.

0.87 (0.69—1.10) cm^2. The median CT-AVC score was 2614 (1673—4988) AU.

The AT/ET ratio and other indices of AS severity

Fig. 2 illustrates the relationships between the AT/ET ratio and other indices of AS severity. Fair correlations were found for AT/ET ratio and peak aortic jet velocity (*r* = 0.57; *P* < 0.0001; Fig. 2A), mean pressure gradient (*r* = 0.60; *P* < 0.0001; Fig. 2B), aortic valve area (*r* = −0.50; *P* < 0.0001; Fig. 2C) and dimensionless index (*r* = −0.53, *P* < 0.0001, Fig. 2D). ROC analysis (Fig. 3) showed that the AT/ET ratio could discriminate severe AS according to the echocardiographic definition (peak aortic jet velocity $\geq$ 4 m/s, mean pressure gradient $\geq$ 40 mmHg, aortic valve area $\leq$ 1.0 cm^2, dimensionless index $\leq$ 0.25) with good accuracy. The area under the curve (95% confidence interval) ranged from 0.767 (0.740—0.795) for peak aortic jet velocity $\geq$ 4 m/s to 0.792 (0.764—0.819) for dimensionless index $\leq$ 0.25. The cut-off values that provided the best balance between sensitivity and specificity were determined for each variable (Table 2).

The best cut-off value for the AT/ET ratio to predict severe AS was uniform (0.34) among echocardiographic indices of AS severity. In the subgroup of patients who underwent CT-AVC scoring, a modest correlation was found between the AT/ET ratio and the CT-AVC score (*r* = 0.24; *P* < 0.0001; Fig. 2E). Using the two thresholds of AS severity recommended by current guidelines (severe AS likely and very likely), the accuracy of the AT/ET ratio in predicting severe AS was modest (area under the curve 0.616, 95% confidence interval 0.542—0.689, and area under the curve 0.624, 95% confidence interval 0.565—0.682, respectively; Fig. 3 and Table 2). The cut-off value for the AT/ET ratio to predict a high likelihood of severe AS according to the CT-AVC score was 0.34 (Table 2). The cut-off value for the AT/ET ratio to predict very high likelihood of severe AS according to the CT-AVC score was higher, at 0.37 (Table 2).

Correlates of the AT/ET ratio

The correlates of the AT/ET ratio are detailed in Table 3. Univariate linear regression analysis showed, beyond indices of AS severity, that the AT/ET ratio correlated inversely with systolic blood pressure, LVEF and stroke volume index, but correlated positively with the presence of coronary artery disease and AS-related symptoms, absence of diabetes mellitus, use of diuretics, increased LV end-diastolic diameter, left atrial volume index, relative wall thickness and LV mass index (all *P* < 0.05). After multivariable linear regression analysis, increased peak aortic jet velocity, LV mass index, relative wall thickness, presence of AS-related symptoms, absence of diabetes mellitus and decreased systolic blood pressure, LVEF and stroke volume index were independently associated with an increased AT/ET ratio (all *P* < 0.05; R^2 of the multivariable model 0.3868). Results were unchanged when replacing peak aortic jet velocity with aortic mean pressure gradient (β = 0.561; *P* < 0.001), aortic valve area (β = −0.450; *P* < 0.001) or dimensionless index (β = −0.477; *P* < 0.001).

In the subgroup of patients who underwent a CT scan, after multivariable linear regression analysis, decreased systolic blood pressure (β = −0.178; *P* < 0.001), absence of diabetes mellitus (β = −0.098; *P* = 0.048), increased peak aortic jet velocity (β = 0.259; *P* < 0.001), LV mass index (β = 0.164; *P* = 0.001), relative wall thickness (β = 0.115; *P* = 0.026) and CT-AVC score (β = 0.115; *P* = 0.030) were independently associated with an increased AT/ET ratio (all *P* < 0.05; R^2 of the multivariable model 0.2199).

Discussion

The AT/ET ratio, reflecting ejection dynamics through the valve, is a convenient, angle-independent and reproducible variable. Landmark AS studies demonstrated that moderate AS has a fast up-stroke and a slow down-stroke; in contrast, severe calcified, AS has a slower up-stroke, resulting in an aortic flow with rounded contour. Rapid early systolic opening of a normal aortic valve on Doppler spectrograms is replaced by a slow end-systolic opening of the stenotic aortic valve [12]. The AT/ET ratio had a good diagnostic value in predicting severe AS according to classical echocardiographic indices of AS severity in the present report. The
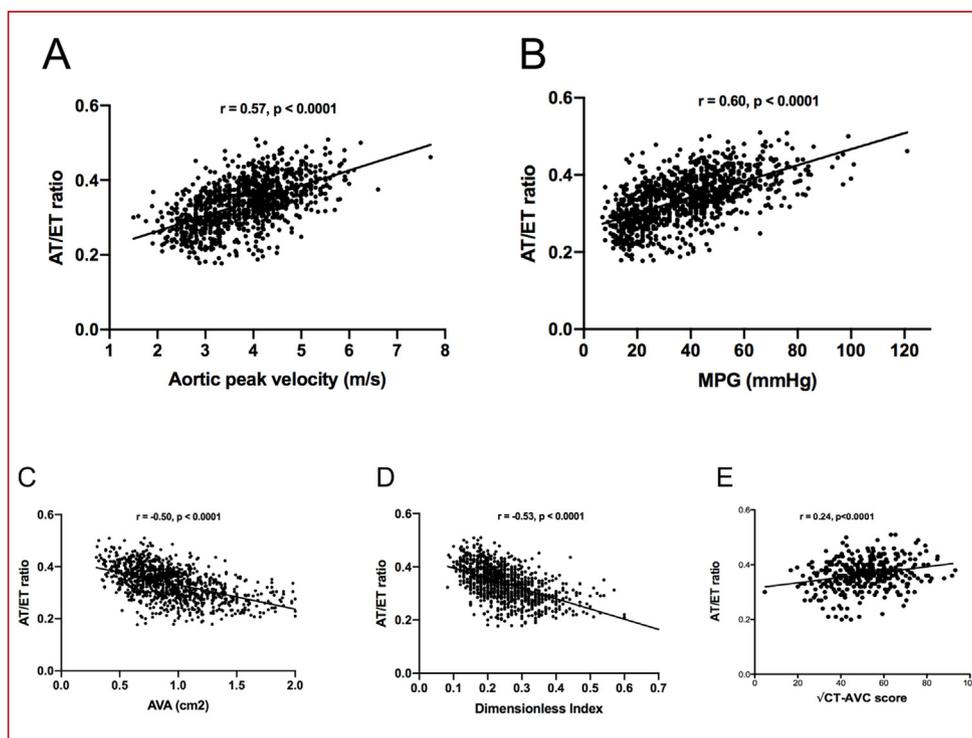
Figure 2. A–E. Relationships between acceleration time/ejection time (AT/ET) ratio and (A) peak aortic jet velocity, (B) mean pressure gradient (MPG), (C) aortic valve area (AVA), (D) dimensionless index and (E) computed tomography aortic valve calcium (CT-AVC) score[a]. [a] Data available in 342 patients.
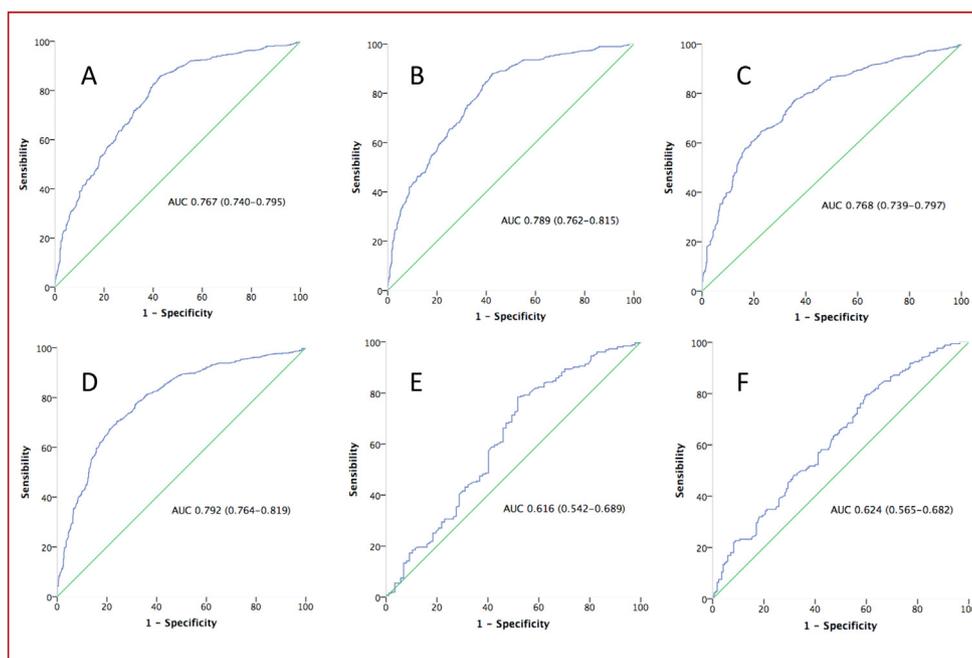

Figure 3. A–F. Receiver operating characteristic curves evaluating the diagnostic value of the acceleration time/ejection time ratio in predicting severe AS, defined as: (A) a peak aortic jet velocity ≥ 4 m/s; (B) a mean pressure gradient ≥ 40 mmHg; (C) an aortic valve area ≤ 1.0 cm^2; (D) a dimensionless index ≤ 0.25; (E[a]) a computed tomography aortic valve calcium (CT-AVC) score of ≥ 1200 Agaston units (AU) for women and ≥ 2000 AU for men; or (F[a]) a CT-AVC score of ≥ 1600 AU for women and ≥ 3000 AU for men. AUC: area under curve. [a] Data available in 342 patients.

Table 2 Diagnostic value of acceleration time/ejection time ratio to predict severe aortic stenosis by echocardiography or computed tomography.

	Peak aortic jet velocity ≥4 m/s	Mean pressure gradient ≥ 40 mmHg	Aortic valve area ≤ 1 cm²	Dimensionless index ≤ 0.25	CT-AVC score ≥ 1200/2000 AU[a]	CT-AVC score ≥ 1600/3000 AU[a]
Number of patients identified as having severe AS (%)	519/1107 (47%)	497/1103 (45%)	726/1107 (66%)	655/1100 (59%)	255/342 (68%)	172/342 (50%)
Area Under Curve (95% CI)	0.767 (0.740—0.795)	0.789 (0.762—0.815)	0.768 (0.739—0.797)	0.792 (0.764—0.819)	0.616 (0.542—0.689)	0.624 (0.565—0.682)
Threshold	0.34	0.34	0.34	0.34	0.34	0.37
Sensitivity (%)	71	75	65	70	78	58
Specificity (%)	68	68	77	76	48	58
Positive predictive value (%)	66	66	84	81	82	58
Negative predictive value (%)	73	76	53	63	43	58

AS: aortic stenosis; AU: Agaston units; CI: confidence interval; CT-AVC: computed tomography aortic valve calcium.
[a] Data available in 342 patients; women/men.

Table 3 Correlates of acceleration time/ejection time ratio by univariate and multivariable regression analysis.

	Univariate analysis		Multivariable analysis		
	Standardized β	P	Standardized β	P	VIF
Age (years)	0.054	0.072			
Female sex	0.009	0.773			
Systolic artery pressure (mmHg)	−0.144	< 0.001	−0.110	< 0.001	1.02
Diabetes mellitus	−0.074	0.013	−0.057	0.032	1.04
Coronary artery disease	0.108	< 0.001			
Dyslipidaemia	−0.030	0.307			
Current smoker	0.037	0.213			
Use of diuretics	0.091	0.002			
Antiplatelet therapy	0.028	0.337			
Charlson Comorbidity Index	0.041	0.164			
AS-related symptoms	0.210	< 0.001	0.069	0.013	1.17
Heart rate (bpm)	0.044	0.137			
LVEF (%)	−0.100	< 0.001	−0.090	< 0.001	1.04
LV end-diastolic diameter (mm)	0.078	0.009			
LV mass index (g/m²)	0.252	< 0.001	0.090	0.001	1.19
Relative wall thickness	0.130	< 0.001	0.069	0.011	1.09
LV stroke volume index (mL/m²)	−0.072	0.016	−0.085	0.002	1.15
LA volume index (mL/m²)	0.075	0.014			
Systolic PAP (mmHg)	0.007	0.832			
Peak aortic jet velocity (m/s)	0.569	< 0.001	0.533	< 0.001	1.14

AS: aortic stenosis; LA: left atrial; LV: left ventricular; LVEF: left ventricular ejection fraction; PAP: pulmonary artery pressure; VIF: variance inflation factor.

optimal cut-off value was uniform for all these indices, at 0.34. We recently reported, in a large cohort of patients with AS, that the AT/ET ratio is a strong predictor of poor survival [3]. Patients with an AT/ET ratio > 0.36 had a considerably increased risk of both overall and cardiovascular mortality, even after adjustment for known predictors of outcome in AS, including LVEF, mean pressure gradient, stroke volume index and AS-related symptoms. The AT/ET ratio was

a better predictor than the AT value. Together these results suggest that an AT/ET ratio of 0.34 may be considered as a ''diagnostic'' cut-off for severe AS, while a cut-off at 0.36 identifies a patient with a very poor outcome (i.e. a patient with very severe AS). Consistently, the 0.34 cut-off identifies, at best, patients with likely severe AS according to CT-AVC calcium scoring, while the identification of patients with very likely severe AS with this imaging modality was, at best, achieved using a cut-off value of 0.37—a value that is closer to our 0.36 prognostic threshold.

As expected, we observed here a link between CT-AVC score and the AT/ET ratio. Interestingly, both haemodynamic indices of AS severity by echo Doppler and anatomical calcium load by CT were related to the AT/ET ratio in the multivariable analysis. This may provide an explanation for the strong prognostic value of the AT/ET ratio reported previously in patients with AS, as it may integrate the classical severity of AS by echocardiography, but also CT-AVC data. CT-AVC scoring is actually recommended in patients with paradoxical low-gradient severe AS with preserved LVEF or in patients with discordant grading [11,13]. Hence, the prognostic value of the AT/ET ratio should be tested in this specific challenging population. The present data also indicate that the AT/ET ratio increases with the haemodynamic severity of AS, and with increasing anatomical aortic valve calcium load, but also with increasing LV mass and relative wall thickness, and with decreasing LV flow and LVEF. In addition, increased systolic blood pressure reduces the AT/ET ratio. Hence, the AT/ET ratio should be considered not only as an index of AS severity, but also as an integrator of the properties of the underlying ventricle and arterial vasculature.

Increased LV mass and relative wall thickness were independently associated with increased AT/ET ratio in the present study. It has been shown repeatedly that among patients with AS, those with LV concentric hypertrophy and remodelling have a worse outcome compared with those with normal LV geometry [14]. Hence, the AT/ET ratio also integrates LV remodelling, hence providing another explanation for the detrimental prognostic value of an increased AT/ET ratio.

Lastly, we found that increased systemic systolic blood pressure reduced the AT/ET ratio. From a physiopathological viewpoint, in the presence of arterial stiffness, reflected waves have greater magnitude and propagate more rapidly, arriving at the LV outflow tract earlier than those with compliant aorta [15]. This might result in early systolic flow deceleration of aortic flow, and therefore induce shortening of the AT [16]. In addition, an increase in loading during systole induces compensatory lengthening of systolic duration, potentially resulting in a reduced AT/ET ratio, and leading to morphological change in aortic flow to a somewhat triangular shape in patients with raised central systolic blood pressure and reduced aortic compliance [17,18]. Therefore, systolic blood pressure should be assessed and taken into account when evaluating ejection dynamic parameters in patients with AS.

Study limitations

Outcome data were not available for the present study. Only a subgroup of patients from the study population

underwent CT-AVC scoring. LV deformation was not available in the present study. Reduced global longitudinal strain might influence the AT/ET ratio beyond LVEF and LV flow. It is worth noting that the correlation between the AT/ET ratio and CT-AVC scoring was lower than with classical echocardiographic indices of AS severity. This may be explained by the fact that patients who underwent clinically indicated CT-AVC scoring had a reduced range of severity of AS, with a high proportion of severe AS, resulting in lower correlations than when patients with mild or moderate AS are also analysed.

Conclusions

The AT/ET ratio is related to echocardiographic and CT-AVC indices of AS severity. However, multiple intricate factors beyond the haemodynamic and anatomical severity of AS influence the AT/ET ratio, including LV geometry, function and systolic blood pressure. These findings should be considered when assessing the AT/ET ratio in patients with AS and preserved LVEF.

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