Left Ventricle Outflow Area Measured by Computer Tomography Scan Planimetry Reclassifies Echocardiographic Grading of Aortic Stenosis

Luca Moderato1,2,*, Davide Lazzeroni2, Simone Maurizio Binno3, Matteo Pessina3, Giovanni Quinto Villani3 and Nicola Gaibazzi4

1Department of Medical Science, University of Parma, Italy
2IRCSS Fondazione Don Gnocchi, Milano, Italy
3Guglielmo da Saliceto Hospital, Piacenza, Italy
4University Hospital of Parma, Italy

*Corresponding Author: Luca Moderato, Department of Medical Science, University of Parma, Guglielmo da Saliceto Hospital, Piacenza, Italy.

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Abstract

Background: Measurement of left ventricular outflow tract (LVOT) diameter and area for estimation of aortic valve area (AVA) using transthoracic echocardiography (TTE) and the continuity equation assumes circular LVOT. The use of direct planimetric measurement of LVOT area by gated-CT can theoretically improve accuracy of AVA calculation.

Methods: We retrospectively studied 93 patients, 43 of whom with severe AS. LVOT Area was measured with 2D TTE by 2 expert echocardiographers and gated-CT by an expert radiologist; inter-reader agreement and inter-method (Echo vs gated CT) agreement and correlation were measured. Finally, we used the measurement of CT scan in the continuity equation instead of TTE measurement to assess potential reclassification of AS severity.

Purpose: We aim to assess reproducibility of LVOT Echo measurement and its correlation and agreement with Gated CT measurements. In the subgroup with aortic stenosis (AS) we secondarily assessed the potential change in AS severity using LVOT area by CT instead of TTE in the continuity equation.

Conclusion: LVOT anatomy is usually elliptical and TTE tends to underestimate LVOT area and AVA due to the measurement of the shorter diameter of this ellipse.

CT scan can provide more geometrically accurate measurement and requires different cut-offs compared with traditional TTE AVA measurement.

By the way, in the current study the LVOT area by CT was on average 38% larger of the LVOT area measured by TTE; such correcting factor (increase TTE LVOT area by 38%) should apparently be used to assess anatomical true planimetric area to be compared with gated-CT LVOT.

Keywords: Aortic Stenosis; Echocardiography; CT Scan; LVOT; Low Flow Low Gradient

Abbreviations

AVA: Aortic Valve Area; AVACT: Aortic Valve Area Computed Tomography; AS: Aortic Stenosis; CT: Computed Tomography; CCTA: Coronary Computed Tomography Angiography; CMR: Cardiovascular Magnetic Resonance; EOA: Effective Orifice Area; LFLG: Low Flow Low Gradient; LVOT: Left Ventricular Outflow Tract; LV: Left Ventricle; MDCT: Multiple Detector Computed Tomography; TAVI: Transcatheter Aortic Valve Implantation; TTE: Trans Thoracic Echocardiography; TEE: Transesophageal Echocardiography; VTI: Velocity Time Integral

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Background
The accurate assessment of valve stenosis severity is crucial for optimal management of patients with aortic stenosis (AS).

The valve effective orifice area (EOA) is one of the most frequently used index to quantify stenosis severity and current ACC/AHA/ESC guidelines propose an EOA < 1.0 cm$^2$ or < 0.6 cm$^2$/m$^2$ BSA as the criteria to be utilized to identify severe AS.

Given its non-invasive, radiation-free, low-cost, and versatility nature, Transthoracic Doppler-echocardiography (TTE) is currently the method of choice to measure the valve EOA and grade AS severity.

However, TTE has several limitations including: i) inability to obtain reliable measurements of EOA due to inadequate acoustic window and poor image quality in some patients; ii) potential for underestimation of flow velocity due to misalignment of Doppler beam with flow direction; iii) risk of underestimation of LV outflow (LVOT) diameter due to inadequate quality and/or positioning of image plane; iv) measurement variability related to manual tracing of flow velocity contours, etc.

These limitations may significantly alter the performance of TTE to accurately quantify AS severity. Furthermore, the cardiologist often confronted to discordant results among the different stenotic indices (i.e. EOA, transvalvular gradient, peak velocity, dimensionless velocity index) measured by Doppler-echocardiography or between the Doppler-echocardiographic evaluation of stenosis severity and the patient’s clinical status [1].

These discordances may raise some uncertainty about the actual severity of the stenosis and thus about the indication for aortic valve replacement if the patient is asymptomatic. When Doppler-echocardiographic evaluation is inconclusive and/or discordant with other clinical findings, catheterization may be used to confirm valve EOA and gradients.

In fact, AVA measured by Doppler echocardiography has long been regarded as a long-standing validated method and as part of routine clinical practice but recently has been criticized as underestimating AVA, when it is calculated with the more anatomically sound LVOT Area measured by MDCT [2].

The possibility that a faulty AVA by TTE may be responsible for "discordant" AS cases, with low gradient despite tight AVA, resonates with other challenges to the authenticity of this syndrome [3].

The contrast between AVA by TTE being revered as fully validated and considered as the major independent predictor of outcome in AS but typically underestimated if compared with AVA measured by computed tomography (AVA CT) has not been resolved and is crucial to the management of patients with AS.

The role of CT scan in the literature has been variant during the last years; at the beginning, the aim of the CT was to assess the planimetric area of aortic valve in aortic stenosis, and compare with the AVA by TTE, but results have been inconclusive [4].

CT was used to measure the LVOT diameter and area, highlighting that LVOT is elliptical and consequently associated with underestimation of AVA measurements using TTE which assesses the lower diameter of such an ellipse. TTE-based AVA, corrected with MDCT planimetered LVOT area, can be theoretically useful in severe AS [5].

The aim of our study is to assess reproducibility of LVOT echo measurement and its correlation and agreement with Gated CT measurements; in the subgroup with aortic stenosis (AS) we secondarily assessed the potential change in AS severity grading using LVOT area by CT in place of TTE in the continuity equation.

Methods
Study population
We retrospectively studied 93 patients, 43 of whom with TTE diagnosis of severe AS, who underwent comprehensive Doppler-echocardiography and contrast-enhanced MDCT within a period of 60 days. Clinical indications for CT included aortic valve replacement, aortic aneurysm repair, evaluation of coronary artery disease and evaluation of aortic annulus for indication to TAVI.
The mean age was 78 years, with a standard deviation of 11, the youngest subject being aged 23 years and the oldest aged 98 years; subjects were 63 males and 30 women.

CT scan protocol and CT image analysis

CCTA was performed using a 256-slice scanner (Brilliance iCTPhilips Medical Systems, Cleveland, OH) with retrospective electrocardiographic gating, because of the better quality of the images and the possibility of image reconstruction in systole, diastole, or anywhere in between. Oral and/or intravenous b-blockers were used to lower the heart rate to <70 beats/min when possible. Contrast enhance scans were performed using a bolus of 70 to 100 mL contrast medium (Iomeprol, Iomeron 400, Bracco, Milan, Italy), at a rate of 6 ml/s.

Scanning was performed with 2 x 64 x 0.6 mm collimation, gantry rotation time of 0.280 sec, and pitch of 0.16 - 0.35, at a tube voltage of 120 kV and an effective tube current of 320 - 360 mas, on the basis of patient size.

The prospect modulation of amperage for the tube has been used with an High dose winds 65% - 80% of R-R interval, and a Mindose protocol (Siemens, Germany) in the other phases of heart cycle. LVOT diameter was evaluated in parasternal long axis view, during midsystole, 5 mm below the insertion of aortic cusps (Figure 1).

Planimetric measurement of aortic valve area in patient with severe aortic stenosis patients was not performed due to his intrinsic low correlation with aortic valve gradient ed aortic valve area calculated by continuity equation [3].

Echocardiography

Two-dimensional echocardiography (ie33 system, Philips Healthcare) was performed by two experienced echocardiographers. Echocardiographic studies were stored on a PACS (Estensa, EBIT Healthcare).

LVOT diameter was measured during midsystole, 5mm below the aortic annulus, in the parasternal long-axis view [6,7]. Doppler measurements of LVOT velocity were recorded in the apical view with pulsed-wave Doppler recording. Doppler measurements of aortic valve velocity were obtained from multiple windows with continuous wave Doppler recordings to identify the highest velocity through the aortic valve, angle correction was not used for these velocity recordings.
VTI measurements were obtained for both the LVOT and the aortic valve Doppler tracings.

The two echocardiographers, unaware of the CCTA results, measured the LVOT diameter and recorded VTI values for each case. Aortic valve area was estimated by the continuity equation according to current echocardiography guidelines. Inter-reader agreement and inter-method (Echo vs. gated CT) agreement and correlation were measured. Then we used the measurement of LVOT Area by CT scan in the continuity equation instead of TTE measurement to assess potential reclassification of AS severity.

**Statistical Analysis**

Results are expressed as mean SD or percentage. Inter-observer and inter-method agreements were measured by Pearson Correlation Coefficient. Correlation and agreement between LVOT and AVA measures were determined with the use of the Pearson correlation and Bland-Altman methods, respectively.

**Results**

**Baseline Characteristics**

The population enrolled initially was of 100 patients, but 7 were excluded because of unacceptable low-quality echo images. The remaining 93 patients were 60 males and 33 females; mean age was 78 with a standard deviation of ± 11.

**Echocardiography And Computed Tomography Scan Measurement**

The LVOT diameter measured by TTE varied from 17 to 29 mm (mean 21,25 mm ± SD 2,16 mm) for the first observer and from 17 mm to 25,3 mm for the second observer (mean 21,49 mm ± SD 1,80 mm). The inter-observer variability was good (Spearman's rank rho = 0,78) for the LVOT diameter, and implicitly the same for the LVOT area (calculated by πr²). The LVOT area was consequently 2,26 cm² to 6,6 cm² (mean 3,58 cm² ± 0,74) and from 2,27 cm² to 5,02 cm² (mean 3,60 cm² ± 0,61), respectively.

LVOT diameters in 3-chamber view, measured by CT scan were significantly greater, 17 mm to 29 mm (mean 22,10 mm ± 2,49 mm). LVOT Area measured by CT was elliptical (r = 0,93 with an elliptical area calculated using both minor and major diameters compared with planimetry). The LVOT area resulted then, due to his elliptical shape, greater then by TTE, with an average of 1,4 cm² greater area using CT. The correlation between 2 echocardiophers for LVOT measurements was good (rho = 0,77) although not perfect, instead there was a low correlation between CT scan for LVOT area and 3- chamber diameters (respectively rho = 0,32 - 0,43 and rho = 0,42 - 0,51, respectively for the 2 (Figure 2).

![Figure 2: LVOT area by CT scan and Echocardiography.](image_url)
In our population there were 23 classical aortic stenosis, and 20 low-gradient aortic stenosis. The mean gradients for the patients with aortic stenosis was $42 \text{ mmHg} \pm 16$; the mean AVA with the continuity equation was respectively $0.88 \text{ cm}^2$ and $0.82 \text{ cm}^2$ for the two echo observers (Figure 3,4 and Table 1).

**Figure 3:** Mean Gradient in patient with aortic stenosis.

**Figure 4:** Partition of Low Gradient Aortic Stenosis and Classical Aortic Stenosis.
Left Ventricle Outflow Area Measured by Computer Tomography Scan Planimetry Reclassifies Echocardiographic Grading of Aortic Stenosis

<table>
<thead>
<tr>
<th>Age</th>
<th>All</th>
<th>78 ± 11</th>
<th>Aortic Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>60 (93)</td>
<td>26 (43)</td>
<td></td>
</tr>
<tr>
<td>LVOT minor diameter (3-ch) by CT scan</td>
<td>22.10 mm ± 2.49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVOT diameter (3-ch) by First TTE observer</td>
<td>21.25 mm ± 2.16</td>
<td>20.00 mm ± 2.00</td>
<td></td>
</tr>
<tr>
<td>LVOT diameter (3-ch) by Second TTE observer</td>
<td>21.49 mm ± 1.80</td>
<td>21.01 mm ± 1.75</td>
<td></td>
</tr>
<tr>
<td>LVOT Area by CT scan</td>
<td>4.98 cm² ± 0.98</td>
<td>4.75 cm² ± 0.86</td>
<td></td>
</tr>
<tr>
<td>LVOT Area by First TTE observer m²</td>
<td>3.58 cm² ± 0.74</td>
<td>3.26 cm² ± 0.96</td>
<td></td>
</tr>
<tr>
<td>LVOT Area by Second TTE observer m²</td>
<td>3.60 cm² ± 0.61</td>
<td>3.39 cm² ± 0.57</td>
<td></td>
</tr>
<tr>
<td>Mean gradient</td>
<td>-</td>
<td>42 mmHg ± 16</td>
<td></td>
</tr>
<tr>
<td>Classical Severe Aortic Stenosis</td>
<td>-</td>
<td>23 (43)</td>
<td></td>
</tr>
<tr>
<td>Low-Flow Low Gradient Aortic Stenosis</td>
<td>-</td>
<td>20 (43)</td>
<td></td>
</tr>
<tr>
<td>Mean AVAeq by First TTE observer</td>
<td>-</td>
<td>0.88 cm² ± 0.52</td>
<td></td>
</tr>
<tr>
<td>Mean AVAeq by Second TTE observer</td>
<td>-</td>
<td>0.82 cm² ± 0.43</td>
<td></td>
</tr>
<tr>
<td>Mean AVAeq by CT scan</td>
<td>-</td>
<td>1.21 cm² ± 0.62</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Echocardiography and CT scan results.

The Mean AVA calculated with the CT scan LVOT Area in the continuity equation was 1.2 cm².

Using the CT measurement of LVOT Area in the AVA (continuity equation), 19 patients with severe aortic stenosis diagnosed with echo (AVA < 1 cm²) were reclassified to moderate aortic stenosis, of this 12 with low gradient Aortic Stenosis and 7 with classical Aortic Stenosis (Figure 5 and 6).

Figure 5: Reclassification of Aortic Stenosis with LVOT measurement by CT scan.

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Discussion and Conclusion

Our study shows that 2D TTE measurement of LVOT area is highly reproducible, also in patients with aortic stenosis and also with diffuse calcifications.
The present study also confirms that LVOT area, measured by CT Scan has an oval shape, which leads to significant underestimation by TTE of the real anatomic LVOT area; actually, TTE estimates LVOT area by measurement of a single anterior-posterior LVOT diameter, with a geometric assumption that LVOT cross sectional area is circular, which turns out not to be the case. In our population we found an average difference of 1.4 cm$^2$ or 38% that, to our knowledge, is the greatest difference between TTE and CT scan measurement of LVOT area in literature.

The aortic valve area by continuity equation using Doppler echocardiography has long been regarded as validated and as part of routine clinical practice but recently has been criticized because of the mentioned intrinsic conceptual underestimation of LVOT area by 2D Ultrasound [6].

Incorporation of the true cross-sectional area of the LVOT in the calculation of the AVA may reduce the prevalence of inconsistently graded severe AS by reclassifying patients into moderate AS [8].

The current literature analysed LVOT measurements in multiple studies, using different methods as CMR, TTE, 3D-Echo and MDCT, but the most accurate data result from MDCT.

The 3D Transthoracic echocardiographic technology has proved to be probably inadequate to accurately measure LVOT area, primarily because of insufficient image quality and spatial resolution [6], even though in patient with severe septal hypertrophy it has been demonstrated to better predict the outcome of AS [9].

Cardiac magnetic resonance reported a very good correlation with estimated orifice area, determined with the use of continuity equation obtained by TTE [10], however it still implies high costs and it is not ready for prime time.

Few studies have shown that CT leads to a more accurate estimation of AVA compared with TTE [10,11], but interestingly, other smaller studies reported no significant difference between AVA by TTE and by CCTA [12,13].

Gaspar, et al. [6] have shown for the first time that applying a correction factor of 1.17 (derived from LVOT area measurements on CCTA) to AVA measurements on 2D TTE, it resulted in an identical value to AVA by CCTA directly measured by planimetry, thus allowing a more accurate absolute assessment of AVA using the continuity equation and an adjusted value that takes into account the oval shape of the LVOT.

Otani., et al. [14] assessed the aortic root using 2D and 3D transesophageal echocardiography (TEE) and CCTA; in their study, LVOT area was underestimated by both 2D and 3D TEE compared with CCTA, but the difference was larger using 2D TEE (due to the assumption of a circular LVOT).

Halpern., et al. [15] found that TTE underestimated AVA by 0.6 cm$^2$ on average compared with CCTA, and that substituting CCTA LVOT area in the continuity equation decreased the difference in AVA to 0.17 cm$^2$ and improved the correlation between the two methods.

O’Brien., et al. [11] reported an observational study of 51 elderly patients with severe AS. AVA by TTE was significantly smaller compared to planimetry with CCTA but using LVOT area by CCTA it was not different than CCTA AVA.

This different AVA calculation obtained by different methods increases the confusion regarding the best threshold of AVA which should identify severe AS.

The last study by Clavel published on JACC 2015 on the comparison of CT and Doppler echocardiography refutes the hypothesis of MDCT superiority for AVA calculation; in this study the AVA with CT measurement of LVOT was actually 0.16 cm$^2$ larger than AVA by TTE, so consequently much less then in our population; this can be explained by the differences in the measurement of LVOT diameter (at the annulus versus 5 mm proximal to the cusps). The clinical outcome impact of combining the two methods was not significantly improved.
because the use of MDCT resulted in a simple translation of mortality spline curves; so Clavel conclusions are that LVOT measurement by MDCT should not replace Doppler echocardiography for hemodynamic assessment of AS severity, simply suggesting to use a larger cut-point values to define severe AS if AVA is to be measured by CT scan (< 1.2 cm²).

This study also showed that CT scan planimetric measurement of aortic valve area had the worse correlation with AVA gradient, and consequently was not recomended.

Kamperidis instead, in a recent article on the European Heart Journal [7], taking into account the Low-flow low-gradient aortic stenosis, states that “incorporation of the true cross-sectional area of the LVOT (meaning LVOT area by CT scan) in the calculation of the AVAi, may reduce the prevalence of inconsistently graded severe AS by reclassifying patients into moderate AS”. He therefore proposes this novel method to reclassify patients with low gradient severe AS, with normal or low flow, and preserved LVEF.

Our conclusions are that probably, as already mentioned in literature, there is a bias at the basis of hemodynamic data versus AVA calculation: the AVA cut-point value of 1.0 cm², as proposed in the guideline to define severe AS, does not correspond for example to a mean gradient of 40 mmHg, but rather to a gradient of 30 - 35 mmHg; this lead to a difficult graduation of aortic stenosis when the gradient is low or near the cut-off value of 40 mmHg/AVA 1.0 cm². These patients often are candidate at high surgical risk, candidate to TAVI, with many co-morbidities and so clinically more complex to evaluate.

In this subgroup of patients, MDCT planimetry measure of LVOT area can improve accuracy of graded AS severity, reclassifying to moderate stenosis a possibly overestimated severe stenosis by 2D Echo; in this regard, MDCT can also be used to quantify the calcium score to assess the LFLG AS, as suggested by ESC recommendations, giving useful extra data to globally assess the patient and his valvular disease. Adding these informations in a selected population can potentially be cost-effective as it would truly reclassify non-severe aortic stenosis patients, preventing unnecessary and risky valve replacement.

Limitations of the Study
In the current analysis, the AVA was not indexed to body surface area, because of the lack of body surface area data. The relative small number of aortic stenosis obviously is another clear limitation of this study.

Finally, the prognostic implications of using MDCT to re-evaluate Classical Aortic Stenosis and Low gradient AS has not been analyzed, and so need to be demonstrated in larger prospective studies to assess the prognostic impact of the combined methods.

Bibliography


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