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Choosing between velocity-time-integral ratio and peak velocity ratio for calculation of the dimensionless index (or aortic valve area) in serial follow-up of aortic stenosis

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ABSTRACT

Background: It remains unclear which echocardiographic measure is most suitable for serial measurement in real-world aortic stenosis (AS) follow-up. We determine whether the dimensionless index (DI) between aortic valve and left ventricular outflow tract velocities is measured more consistently using velocity-time-integral (VTI) or peak velocities (V_{peak}) in real life.

Methods: Serial echocardiograms acquired within 6 months in subjects with AS were analysed with blinding, to compare the variability over time of DI calculated using V_{peak}, with that of DI calculated using VTI.

Results: Paired echocardiograms, acquired on average 72 days apart, were analysed from 70 patients with a range of severities of AS (59% severe). DI, calculated using either V_{peak} or VTI, did not significantly change over this short time. Coefficient of variation was significantly better when DI was calculated using V_{peak} than VTI (12.6 versus 25.4%, $p<0.0001$). The variabilities of mean and peak trans-aortic valve $4v^2$ and left ventricular outflow tract VTI were no better: 26.9%, 19.1% and 22.1% respectively.

Conclusions: Serially-followed variables require minimal noise to maximise detection of genuine change. For AS surveillance, calculating DI – or effective orifice area – from the ratio of V_{peak} rather than VTIs would reduce 95% confidence intervals from ±51% to a still-disappointing ±25%. Guidelines recommend noisy surveillance measures, causing conscientious echocardiographers to 'peek' at previous values, and impairing clinicians' faith in echocardiographically-observed changes when making clinical decisions. For us in echocardiography to improve our ability to contribute to AS follow-up requires us to first acknowledge and discuss this honestly.

1. Introduction

Since the pivotal Ross and Braunwald report [1] that across multiple post-mortem studies of aortic stenosis, mortality was 100% and almost all had symptoms in the final years of life, clinicians have relied on symptoms as the primary guide to appropriate timing of valve replacement. Despite modern technological advances in equipment and measurement, echocardiography is still subordinate in status to clinical judgement during follow-up decision making.

For echocardiography to contribute meaningfully to follow-up requires exquisite test–retest reproducibility: narrow error bars within individuals. Wide error bars cause three harms. First, patients may falsely appear to have deteriorated. Second, true deteriorations may not be reflected in measurements and hence remain undetected. Third, clinicians may reject even substantial detected deteriorations due to a lack of confidence in the measures (defeating the purpose of the scan), or schedule excessively frequent visits in an effort to reduce the influence of measurement variability (draining resources).

As echocardiographers, to enhance our relevance to aortic stenosis follow-up, we should start by actively selecting the index we report for serially assessing disease severity based on the narrowness of its within-individual error-bars. In real life clinical practice, patients may have scans by different operators who may not only acquire images slightly differently, but also make measurements (including tracing Doppler envelopes) slightly differently. In the UK, the majority of echocardiography is performed in centres which use more than one type of scanner and conduct scans under relentless time pressure. In contrast, most of the published studies of reproducibility in aortic stenosis were conducted within a research environment with a single operator acquiring images who had unlimited time to concentrate on maximising the measurement reproducibility.

Guidelines recommend measuring AS severity using several haemodynamic features. AS jet peak velocity (V_{peak}), peak instantaneous pressure drop $4V_{peak}^2$ and mean $4V^2$ form one family of variables [2]. To counter confounding from changes in stroke volume, a second family of variables uses the ratio of velocities between the left ventricular outflow tract and the aortic valve: the 'dimensionless

Abbreviations: AS, aortic stenosis; V_{peak}, AS jet peak velocity; DI, dimensionless index; LVOT, left ventricular outflow tract; VTI, velocity-time-integral.

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index' (DI). This DI is often made into an Effective Orifice Area by multiplying it by the cross sectional area of the left ventricular outflow tract (LVOT): the continuity equation [3,4].

How should we measure DI during aortic stenosis follow-up to deliver narrow within-patient error-bars? The two options are the ratio of velocity-time-integral (VTI), or ratio of peak velocities (V_{peak}), between LVOT and aortic valve. This study evaluates the test–retest reproducibility of measuring DI using VTI or V_{peak} in aortic stenosis, using data from real-world clinical practice.

2. Methods

2.1. Subjects

Clinical echocardiographic data from consecutive patients with aortic stenosis who underwent serial echocardiography with 2 scans acquired within 6 months of each other between November 2007 and July 2011 in our hospital were retrospectively reviewed.

In total, 548 patients with aortic stenosis were identified who had undergone echocardiography in this time period, of whom 70 patients had had repeat echocardiograms within a 6 month timeframe. The severity of the aortic stenosis was defined in the subjects at their first echocardiogram: 5 (7%) had mild stenosis (DI <2), 24 (34%) had moderate stenosis (DI 2–4) and 41 (59%) had severe stenosis (DI >4). The average age at first visit was 79 years (range 53–92 years). Sixty-three percent were female. The time between repeat echocardiograms averaged 72 (standard deviation 59) days.

2.2. Difference in echocardiographic Doppler measurements of aortic stenosis between two scans

Echocardiography was conducted according to standard clinical guidelines [4] in the manner conventional in our hospital and most other hospitals. The separate visits were often conducted by different operators, and using machines made by different manufacturers. Images had been acquired and stored in digital format. For this study they were analysed offline by a single observer (JF), with measurements of each study blinded to the results of the paired study.

Standard Doppler measurements of flow in the left ventricular outflow tract (LVOT) and aortic valve were recorded from multiple windows to calculate the peak velocity across the valve and the velocity time integral (VTI) as recommended by guidelines [5,6]. We then calculated the DI using the ratio of measurements for aortic and LVOT, using both peak velocities (V_{peak}) and VTI flow data (Fig. 1). The mean trans-aortic pressure drop was calculated automatically by the echocardiography machines, by averaging the instantaneous gradient over the period of flow. The peak instantaneous trans-aortic pressure drop was calculated as:

$$\text{Peak instantaneous trans-aortic pressure drop} = 4\left(V_{\text{peak, aortic valve}}\right)^2.$$

2.3. Statistics

The original intention had been to subtract the change in mean between the two visits, so as to expose the variability distinct from what we expected might be a group trend towards deterioration. In practice because there was no significant change in mean in this short period of time, this subtraction step was not required.

Changes in the average values of the DI and the mean and peak trans-aortic valve pressure drops between visit 1 and visit 2 were assessed using the paired Student t test. The relative proportions showing progression versus regression of these variables between visits were tested for difference from chance alone using Fisher's exact test.

Variability was calculated using the coefficient of variation (standard deviation of differences divided by the mean). The spread of variability between visit 1 and visit 2 was compared for the paired echocardiograms using the F test. The results were also assessed using the Bland–Altman method [7].

A p value of <0.05 was considered significant. Statistical analysis was performed using Prism software (version 5.0).

All authors confirm that the study was designed to make measurements without bias, to be held responsible for procedural deficiency, and to retract the paper if any are suspected. Patient data were selected only by the method described. Measurements were made blinded and uniformly. No data were deleted, nor re-measured to favour one result over another [8].

3. Results

3.1. Progression of aortic stenosis during the inter-test interval

Across the group of patients as a whole there was no statistically significant evidence of progression of aortic stenosis during the ~72-day period between echocardiograms when the DI was calculated using either VTI or V_{peak} measurements (Table 1).

Analysis of serial changes in the DI using VTI showed that 48.6% of patients had a lower DI on their second visit, and 51.4% had a higher DI ($p = 1.0$ by Fisher's exact test). Analysis of serial changes in the DI

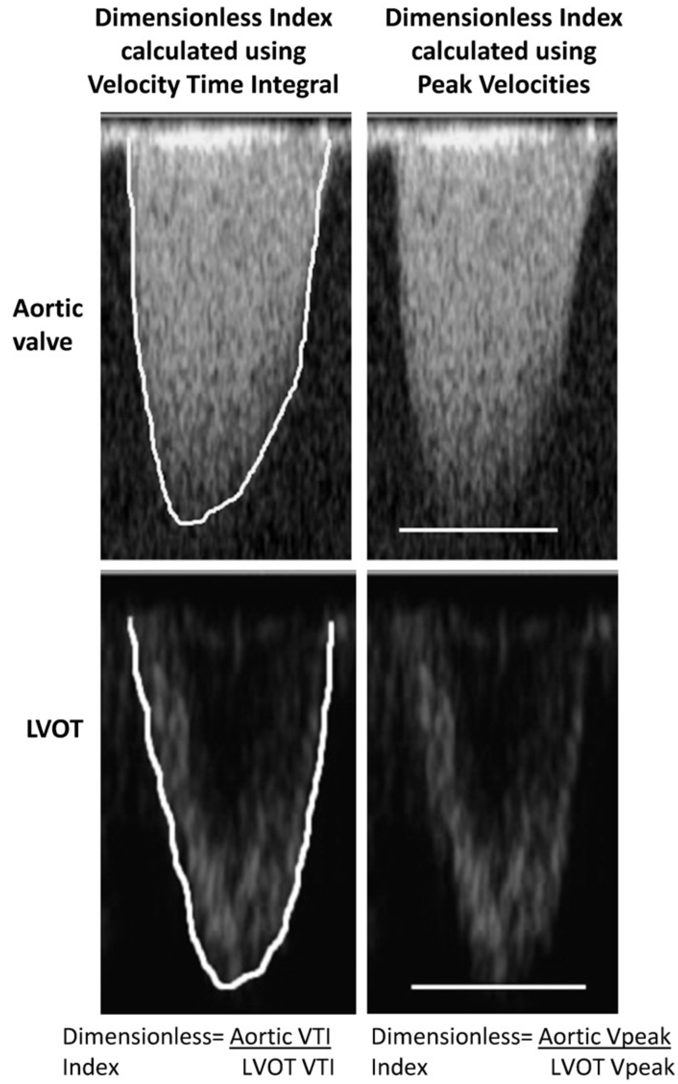

Fig. 1. Calculation of the dimensionless index.Calculation of the dimensionless index using either (left panel) the ratio of the left ventricular outflow tract and aortic valve velocity time integrals or (right panel) the ratio of the peak velocities.

Table 1
Differences in the dimensionless indices, mean and peak trans-aortic pressure drop and left ventricular outflow tract VTI on the serial echocardiograms.

	Average visit 1	Average visit 2	Difference between visit 2 and visit 1	p Value	Coefficient of variation (%)
Dimensionless index by VTI	4.12 ± 1.23	4.20 ± 1.32	+0.08	0.54	25.4
Dimensionless index by V_{peak}	4.32 ± 1.22	4.33 ± 1.32	+0.01	0.88	12.6
Mean trans-aortic pressure drop (mm Hg)	33.9 ± 15.5	34.6 ± 17.7	+0.66	0.61	26.9
Peak instantaneous trans-aortic pressure drop (mm Hg)	57.6 ± 25.6	58.6 ± 27.3	+0.97	0.47	19.1
LVOT VTI (cm)	21.1 ± 5.85	21.4 ± 6.84	+0.29	0.60	22.1