Research Article

Reducing the Inconsistency between Doppler and Invasive Measurements of the Severity of Aortic Stenosis Using Aortic Valve Coefficient: A Retrospective Study on Humans

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Background. It is not uncommon to observe inconsistencies in the diagnostic parameters derived from Doppler and catheterization measurements for assessing the severity of aortic stenosis (AS) which can result in suboptimal clinical decisions. In this pilot study, we investigate the possibility of improving the concordance between Doppler and catheter assessment of AS severity using the functional diagnostic parameter called aortic valve coefficient (AVC), defined as the ratio of the transvalvular pressure drop to the proximal dynamic pressure.

Method and Results. AVC was calculated using diagnostic parameters obtained from retrospective chart reviews. AVC values were calculated independently from cardiac catheterization (AVC catheter) and Doppler measurements (AVC Doppler). An improved significant correlation was observed between Doppler and catheter derived AVC (𝑟 = 0.92, 𝑃 < 0.05) when compared to the correlation between Doppler and catheter measurements of mean pressure gradient (𝑟 = 0.72, 𝑃 < 0.05) and aortic valve area (𝑟 = 0.64, 𝑃 < 0.05). The correlation between Doppler and catheter derived AVC exhibited a marginal improvement over the correlation between Doppler and catheter derived aortic valve resistance (𝑟 = 0.89, 𝑃 < 0.05).

Conclusion. AVC is a refined clinical parameter that can improve the concordance between the noninvasive and invasive measures of the severity of aortic stenosis.

1. Introduction

Aortic stenosis (AS) is a type of valvular heart disease that results from abnormal narrowing of the aortic valve opening. A stenotic aortic valve creates an increased pressure gradient between the left ventricle and the aorta. The resulting increased ventricular workload and associated increased ventricular wall stress may contribute to left ventricular dysfunction and heart failure over time. AS is typically caused by progressive degeneration and calcification of the aortic valve; hence, the prevalence of calcific aortic valve disease increases with age [1, 2]. Calcific aortic valve disease ranges from mild valve thickening with minimal flow obstruction termed aortic sclerosis to severe calcification and flow obstruction termed AS. Generally, aortic valve replacement is indicated for symptomatic severe AS, since the outcome without valve replacement is poor with survival rates as low as 50% at two years [3–5]. Accurate assessment of the severity of stenosis is critical for clinical decision making in patients with AS. Severity of AS is currently assessed by one or more diagnostic indices obtained by Doppler echocardiography and/or cardiac catheterization [6, 7].

Severity of AS is currently assessed by Doppler echocardiography using a combination of transvalvular pressure gradients, aortic jet velocity, stenotic aortic valve area, and aortic valve resistance [6, 7]. The hydrodynamic principle of flow through stenotic orifices indicates progressive acceleration and convergence of flow field through the stenosis. The point of maximum convergence is termed vena contracta and usually lies just distal to the orifice area. Doppler measures the jet velocity at the vena contracta of the valve and velocity in the left ventricular outflow tract (̅𝑉 LVOT). The cross-sectional
area at the left ventricular outflow tract is also approximately calculated using 2D echo. The obtained velocities and the left ventricular outflow tract area are then used to calculate the mean transvalvular pressure gradient ($\Delta \tilde{p}$), aortic valve area ($A_{V}\text{A}_\text{doppler}$), and aortic valve resistance (AVR) [7, 8]. The corresponding anatomical locations of the vena contracta and the left ventricular outflow tract are shown in Figure 1.

Invasive cardiac catheterization is the other common method used for determining the diagnostic end-points to assess AS severity. The mean transvalvular pressure gradient ($\Delta \tilde{p}$) is directly measured during catheterization. The $\Delta \tilde{p}$ is the pressure difference between the left ventricle and the ascending aorta after pressure-recovery [3] as shown in Figure 1. The cardiac output (CO) is measured using Fick’s principle and/or the thermodilution method. The aortic valve area ($A_{V}\text{A}_\text{catheter}$) is then determined from the measured pressure gradient and CO using the Gorlin equation [10].

One of the most common causes for misclassification is due to the pressure-recovery phenomenon in the ascending aorta [3, 11–14]. The extent of pressure-recovery depends on the ratio of the vena contracta area to the cross-sectional area of the ascending aorta (Figure 1). A relatively larger pressure-recovery in relation to the overall pressure gradient is seen in subjects with mild to moderate stenosis and in subjects with small aorta [13, 15, 16]. Doppler measurements are taken at the vena contracta just distal to the aortic valve orifice and do not account for the pressure-recovery in the aorta, whereas catheterization measures the pressure difference between the left ventricle and a point in the aorta well beyond the aortic valve where the pressure is, in general, completely recovered. Thus, there are significant differences between the pressure gradient obtained by Doppler and catheterization. While $\Delta \tilde{p}_\text{doppler}$ will often overestimate the AS severity, $\Delta \tilde{p}_\text{catheter}$ is typically recorded after pressure-recovery and therefore it usually represents the net pressure drop due to AS. The $A_{V}\text{A}_\text{catheter}$ does not represent the anatomical valve area but is one that reflects the hemodynamic consequence of the stenosis [13]. Moreover, $\Delta \tilde{p}_\text{doppler}$ and $A_{V}\text{A}_\text{doppler}$ are quantities derived from velocity and measured area using simplified forms of the Bernoulli’s equation which ignore the pressure loss due to frictional (viscous) effects and momentum change due to area reduction. Previous studies have shown that the Doppler and catheter measurements of the aortic valve area can vary up to 50% depending on the size of the aorta and the severity of AS [3, 15, 17].

We hypothesize that the proposed hemodynamic diagnostic parameter, based on fundamental fluid dynamics principles, will improve the concordance between Doppler and catheter assessment of AS severity. The proposed functional diagnostic index, aortic valve coefficient (AVC), is defined as the ratio of the mean net transvalvular pressure gradient to the mean proximal dynamic pressure ($0.5 \times$ blood density $\times$ $V^2$). The mean net transvalvular pressure gradient is the $\Delta \tilde{p}_\text{doppler}$ corrected for pressure-recovery or the $\Delta \tilde{p}_\text{catheter}$ and is represented by $P_1 - P_3$ in Figure 1. AVC, in general, is a nondimensional parameter that accounts for the resistance to the flow due to the area reduction caused by the stenosed valve and also the frictional loss. In this study, the correlation between Doppler and catheter derived mean transvalvular pressure gradient, aortic valve area, AVR, and AVC is examined to determine the potential of the proposed diagnostic index to reduce the variability in the assessment of the severity of AS between the two diagnostic methods.

2. Methods

2.1. Study Patients. The study population consisted of 36 patients that were selected by a retrospective review of patient records. The study protocol was approved by the Institutional Review Board at University of Cincinnati. The selected patients were aged 42–92 years with suspected AS who underwent precatheterization 2D transthoracic Doppler echocardiograms and left heart catheterizations from 2010 to 2012. Data from thirteen patients with inconsistent pressure-flow measurements (e.g., 1 patient with procedural error as catheterization transducer was not properly zeroed, 1 patient with $\Delta \tilde{p}_\text{catheter} = 4 \times \Delta \tilde{p}_\text{doppler}$, and 1 patient with Doppler measurement taken after cardiac arrest) and incomplete data (e.g., 10 patients with poor quality or incomplete Doppler measurements) were excluded. Three patients with bioprosthetic aortic valves were also excluded.

2.2. Data Analysis. The values of jet velocity ($V_\text{jet}$), $V_{\text{LVOT}}$, aortic root area ($\text{CSA}_{\text{aorta}}$), $A_{V}\text{A}_\text{doppler}$, and $\Delta \tilde{p}_\text{doppler}$ (superscript “~” indicates mean values) were obtained from the standard Doppler echocardiography reports. Similarly, $\Delta \tilde{p}_\text{catheter
and \( \overline{AVA}_{catheter} \) were obtained from standard catheterization reports. AVR, defined as the ratio of the mean pressure gradient to the mean flow rate expressed in units of N \( \cdot \) s \( \cdot \) m\(^{-5} \) [7, 8], was calculated independently from Doppler (AVR\(_{doppler} \)) and catheterization measurements (AVR\(_{catheter} \)). The proposed hemodynamic diagnostic parameter, AVC, was calculated independently from Doppler (AVC\(_{doppler} \)) and catheterization (AVC\(_{catheter} \)) measurements, where \( \Delta P_{doppler-r} \) is the pressure-recovery corrected Doppler transvalvular pressure gradient and \( \rho \) is the density of blood (1050 kg/m\(^3\)). \( \Delta P_{doppler-r} \) was calculated from the Doppler measured \( \Delta P_{doppler} \) based on fluid mechanics theory [7, 11, 12, 14]. Consider

\[
AVC_{doppler} = \frac{\Delta P_{doppler-r}}{0.5 \times \rho \times V_{LVOT}^2}
\]

\[
\Delta P_{doppler-r} = \Delta P_{doppler} \left(1 - \left(\frac{\overline{AVA}_{doppler}}{CSA_{aorta}} \left(1 - \frac{\overline{AVA}_{doppler}}{CSA_{aorta}}\right)\right)\right)
\]

\[
AVC_{catheter} = \frac{\Delta P_{catheter}}{0.5 \times \rho \times V_{LVOT}^2}.
\]

(1)

The velocity is not measured during standard of care catheterization and hence Doppler measured \( V_{LVOT} \) was used to calculate AVR\(_{catheter} \), and AVC\(_{catheter} \) in this retrospective study.

2.3. Statistical Analysis. A linear regression analysis was performed on data from the 20 patients to assess significant linear correlations between the Doppler and catheterization derived parameters. Data from 1 patient was found to be a significant outlier and excluded from the data analysis. Thus, 19 patients (7 females) were included in this retrospective study. A probability value of \( P < 0.05 \) was considered statistically significant. Statistical data analysis was performed using SAS version 9.3 (SAS Institute, NC). All diagnostic parameters are represented as mean \( \pm \) SE unless otherwise specified.

3. Results and Discussion

Table 1 summarizes the Doppler and catheter data obtained by retrospective review of the records of 19 patients included in this study. For the patient group analyzed, there was no significant difference between the mean \( \Delta P_{doppler} \) (4506 \( \pm \) 373 Pa) and the mean \( \Delta P_{catheter} \) (4680 \( \pm \) 307 Pa), with \( P = 0.72 \). Following AHA guidelines [6] for classifying AS severity by \( \Delta P_{doppler} \), 4 patients had mild AS (less than 3333 Pa), 9 patients had moderate AS (3333 to 5333 Pa), and 6 patients had severe (greater than 5333 Pa) AS. Categorizing the patient group based on \( \Delta P_{catheter} \), 5 patients had mild AS, 10 patients had moderate AS, and 4 patients had severe AS.

The results of the linear regression analysis between Doppler and catheter derived diagnostic parameters are presented in Figures 2, 3, 4, and 5(a). The \( \Delta P_{doppler} \) correlated moderately with the \( \Delta P_{catheter} \) \((r = 0.72, P < 0.05; \text{Figure 2})\). Similarly, \( \overline{AVA}_{doppler} \) also correlated moderately with \( \overline{AVA}_{catheter} \) \((r = 0.64, P < 0.05; \text{Figure 3})\). However, AVR\(_{doppler} \) exhibits a superior correlation with AVR\(_{catheter} \) \((r = 0.89, P < 0.05; \text{Figure 4})\). Similarly, AVC\(_{doppler} \) also exhibits a statistically improved significant correlation with AVC\(_{catheter} \) \((r = 0.92, P < 0.05; \text{Figure 5(a)})\). Thus, the correlation between Doppler and catheter derived AVC shows significant improvement when compared to Doppler and catheter derived AVC. Additionally, the agreement between the Doppler and catheter derived AVC was assessed using the Bland-Altman test (Figure 5(b)). The mean of the differences between the AVC\(_{doppler} \) and AVC\(_{catheter} \) is \(-2.7 \pm 6.6 \) (mean \( \pm \) SD) and the limits of agreement are \(-15.7 \) to \(10.3 \). The Bland-Altman analysis reveals neither bias nor trend between the differences and magnitude of the measurements of AVC.

It is well known that, in flow through constrictions like arterial lesions and valvular stenosis, the mean pressure gradient \( \Delta P \) is related to the mean velocity \( \overline{V} \) as \( \Delta P = A \times \overline{V} + B \times \overline{V}^2 \), where \( A \) is the linear coefficient of viscous (frictional) loss and \( B \) is the nonlinear coefficient of pressure loss due to momentum change caused by area reduction [18]. At the higher Reynolds numbers (~5000)
that are typically observed in the human ascending aorta [19], the flow is transitional to turbulent and the nonlinear pressure loss due to the momentum change caused by aortic stenosis is generally more than the linear pressure loss due to viscous effects. Therefore, it should be noted that AVC (1) is a nondimensional diagnostic parameter that better accounts for the predominantly nonlinear pressure loss in stenosed aortic valves. In contrast, AVR is a dimensional flow dependent diagnostic parameter with limited prognostic value [7, 8] and it primarily represents the linear pressure loss due to frictional effects that is commonly observed in diffused arterial lesions.

The results of this retrospective study show a significant improvement in the correlation between Doppler and catheter derived AVR when compared to that between Δ̃𝑝 and ÁVA (Figures 2, 3, and 4). In addition, with the application of pressure-recovery correction, further improvement in the correlation between Doppler and catheter derived AVC is observed (Figure 5(a)), although there is only a marginal difference in Doppler-catheter correlations of AVC and AVR (Figures 4 and 5(a)). The mean difference of −2.7 between Doppler and catheter derived AVC observed in the Bland-Altman analysis (Figure 5(b)) can be attributed to the small sample size of this study. Moreover, AVCcatheter was calculated using ̃𝑉̂LVOT obtained retrospectively from Doppler echocardiography. Nevertheless, the results of this retrospective study support our hypothesis that AVC would further reduce the inconsistency between Doppler and catheter measurements. Further prospective studies are needed to confirm these results.

A diagnostic parameter pressure loss coefficient (ratio of the peak transvalvular pressure gradient to the peak outflow tract dynamic pressure), which is similar to AVC, has been previously evaluated for in vivo assessment of the degree of stenosis in both pulmonary and aortic valves [20]. Pressure loss coefficient was found to be independent of the blood velocity and its value of 15 was proposed as the cut-off value for decision on surgical procedure. Similarly, the hemodynamic parameter pressure drop coefficient (CDP), which is also similar to AVC, has been previously evaluated for assessing the severity of epicardial coronary artery stenosis by our group and shown to be independent of the hemodynamic influence of heart rate fluctuations [21–23]. Hence, AVC is expected to be largely independent of the variations in cardiac output, preload, and afterload and can better delineate the different grades of AS severity.

Recent studies have evaluated the parameter energy loss coefficient (ELCo) to reconcile Doppler and catheterization measurements [24]. The theoretical energy loss (EL) between the left ventricular outflow tract (LVOT) and the ascending aorta is defined as (𝑃1 − 𝑃3) + 0.5𝜌(𝑉2 − 𝑉3), where subscripts 1, 2, and 3 represent the LVOT, vena contracta, and ascending aorta after pressure recovery, respectively, as shown in Figure 1 [15]. Ignoring the net change in kinetic energy [0.5𝜌(𝑉12 − 𝑉32)], which is typically negligible compared to (𝑃1 − 𝑃3) for patients with AS, theoretically, the EL, Δ̃𝑝doppler-𝑟 (𝑟: indicating pressure after recovery), and Δ̃𝑝catheter represent the net pressure gradient, that is, (𝑃1 − 𝑃3). However, the ELCo, developed from the modified Bernoulli’s equation, is a dimensional parameter with an atypical unit of cm² and is very similar to the valve area derived from catheterization data using the Gorlin equation [15, 24]. On the contrary, the AVC proposed in this study (1) is a nondimensional parameter where the normalization of the net pressure gradient is based on the differential mass and momentum equations [22]. Moreover, the EL is calculated from Doppler measurements [15] under the assumption of the limiting high Reynolds number condition where only loss due to momentum change caused by aortic stenosis is significant (Supplement A, [22]). This assumption may not be accurate for low flow or low Reynolds number conditions (for example, in patients with left ventricular dysfunction due to myocardial disease or hypertrophy). However, the Δ̃𝑝 in AVC includes both the frictional (viscous) loss and pressure loss due to momentum change irrespective of the flow status. Further, the normalization of the net pressure gradient with the native LVOT velocity in AVC is fundamentally more accurate from a fluid dynamic perspective and can provide...
3.1. Study Limitations. The primary limitation of this retrospective study was the nonavailability of left ventricular outflow tract velocity from standard of care cardiac catheterization. Hence, $\text{AVR}_\text{catheter}$ and $\text{AVC}_\text{catheter}$ were calculated using the Doppler measured $\tilde{V}_{\text{LVOT}}$. True $\text{AVR}_\text{catheter}$ and $\text{AVC}_\text{catheter}$ should be evaluated in a prospective study where the pressure gradient and proximal velocity are measured simultaneously during catheterization.

4. Conclusion

This preliminary retrospective study has confirmed that AVC with the pressure-recovery correction has the potential to minimize the inconsistency between Doppler and catheter assessment of AS severity. As traditional surgical methods have improved and since the introduction of less invasive techniques for treatment like transcatheter aortic valve implantation (TAVI) technology, it is essential that more accurate diagnostic end-points be pursued. Presently, the inconsistencies in the diagnostic parameters derived from Doppler and catheterization measurements for assessing the severity of AS can result in suboptimal clinical decisions. Using a wide range of values, it is expected that AVC will be able to provide consistent and reproducible assessment of AS severity independent of the diagnostic method. In the future, it is of interest to conduct a prospective study to evaluate the specificity and sensitivity of AVC in delineating the severity of AS.

Conflict of Interests

The authors report no financial relationships or conflicts of interest regarding the content herein.

Authors’ Contribution

Rupak K. Banerjee and Jason J. Paquin contributed equally to this work.

References


