Energy Loss Index in Aortic Stenosis
From Fluid Mechanics Concept to Clinical Application

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In the American Heart Association–American College of Cardiology and European Society of Cardiology–European Association for Cardio-Thoracic Surgery guidelines,[1,2] aortic valve replacement (AVR) is considered a class I indication in patients with aortic stenosis (AS) if the stenosis is severe and the patient has symptoms or left ventricular ejection fraction <50%. Hence, accurate assessment of the hemodynamic severity of the valvular stenosis is crucial for clinical decision making. The stenosis severity is generally determined by measuring the transvalvular pressure gradient or the aortic valve effective orifice area (AVA); however, these conventional parameters do not account for the extent of pressure recovery that may occur downstream of the stenosis. In an article published in 2000 in *Circulation*,[3] we proposed a new Doppler echocardiographic parameter based on the energy loss concept to adjust the AVA for pressure recovery, and we postulated that this energy loss index (ELI) would improve assessment of stenosis severity and risk stratification in AS. Thirteen years later, Bahlmann and colleagues[4] publish in this issue of *Circulation* the first prospective study to demonstrate that ELI provides independent and incremental prognostic information to that derived from conventional measures of AS severity. In this elegant substudy of the SEAS (Simvastatin Ezetimibe in Aortic Stenosis) trial, the authors report that a 1 cm²/m² reduction in baseline ELI predicts a 2-fold increase in the risk of aortic valve events and of the composite of mortality and heart failure hospitalization after adjustment for peak aortic jet velocity or mean gradient.

The Fluid Mechanics Concept Behind the ELI

The current guidelines[1,2] make no distinction between catheterization and Doppler echocardiographic measurements, as though values for gradient and AVA measured by either technique were interchangeable (Figure 1). Yet Doppler estimates the maximum pressure drop through the valve from the maximum flow velocity recorded at the level of the vena contracta, whereas catheterization provides a measure of the net gradient between the left ventricle and the ascending aorta (Figure 1). However, as blood flow decelerates between the valve and the ascending aorta, part of the kinetic energy is converted back to static energy because of a phenomenon called pressure recovery, and hence, the maximum pressure gradient measured by Doppler overestimates the net gradient, that is, the "irreversible" gradient, recorded at catheterization (Figure 1).[3,5,6] Likewise, the AVA obtained at catheterization by use of the Gorlin formula is derived from recovered pressures, such that its value is higher than the Doppler AVA derived by the continuity equation. The latter measures the actual area occupied by flow at the valvular level (ie, the vena contracta), whereas the AVA calculated by the Gorlin formula is an estimate of the energy loss related to the stenosis rather than a true effective orifice area.

The extent of pressure recovery is determined by the ratio between the valve effective orifice area and the cross-sectional area of the ascending aorta, a situation that becomes particularly relevant in patients with moderate to severe AS and small aortas, in whom measurement of AVA by Doppler echocardiography may lead to overestimation of severity (Figures 1 and 2).[3,5,6,7] Conversely, patients with a dilation of the ascending aorta will have less or no pressure recovery and therefore a more important energy loss for a given valve effective orifice area.

Fortunately, pressure recovery can be accounted for by calculating the ELI as follows: $ELI = [(AVA \times A_A)/(A_A - AVA)]/BSA$, where A_A is the cross-sectional area of the aorta measured at the sinotubular junction and BSA is the body surface area.[3] Hence, the ELI consists of an adjustment of the Doppler AVA for the size of the ascending aorta (Figure 2) and is thus more or less equivalent to the "recovered" AVA obtained by catheterization.[3,6,8] From a physiological standpoint, the ELI is superior to the Doppler AVA or gradient in the sense that it better represents the actual energy loss caused by the stenosis and thus the increased burden imposed on the ventricle.

From the Fluid Mechanics Concept to Clinical Validation

In a retrospective analysis of 138 patients with moderate to severe AS, we reported that ELI is superior to the indexed AVA (AVAI) in predicting the composite of death or AVR during an 8-month follow-up.[3] In the large multicenter prospective study published in this issue of *Circulation*,[4] Bahlmann and colleagues show that a decrease of 1 cm²/m² in ELI predicts a 6.06-fold increase in AVR, a 5.25-fold increase in aortic valve events, a 1.93-fold increase in total mortality, and a 2.28 increase in combined mortality and hospitalization for heart failure. The hazard ratios for AVR and aortic valve events were
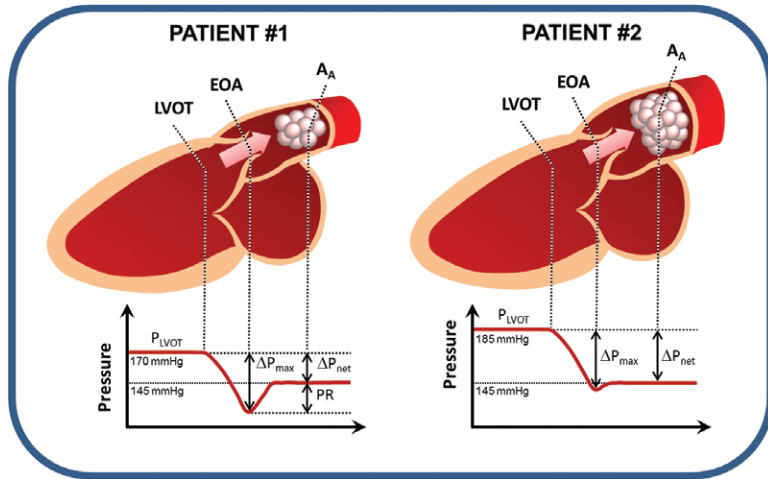
Figure 1. The phenomenon of pressure recovery in aortic stenosis. Schematic representation of flow and blood pressure across the left ventricular outflow tract (P_{LVOT}), aortic valve, and ascending aorta (A_A) during systole in 2 theoretical patients having the same stroke volume (80 mL) and valve effective orifice area (EOA; 0.9 cm^2) but different sizes of ascending aorta (2.0 cm diameter in patient 1 vs 4.0 cm in patient 2). The maximum pressure gradient recorded at vena contracta (ΔP_{max}; ie, the mean gradient measured by Doppler) is the same in the 2 patients, but patient 1 with the small aorta has a large amount of pressure recovery (PR) downstream of the valve, whereas patient 2 has minimal pressure recovery. Consequently, the net "irreversible" gradient (ΔP_{net}; ie, measured by catheter) and thus the left ventricular systolic pressure are significantly higher in patient 2 than in patient 1. LVOT indicates left ventricular outflow tract.

attenuated (≈2.0) but remained significant after adjustment for peak jet velocity or mean gradient, whereas those for mortality and hospitalization were unchanged. Hence, this study provides compelling evidence that ELI yields incremental prognostic value over that obtained from peak aortic jet velocity or mean gradient, and this represents an important contribution given that the latter are the most frequently used and the most relied-on Doppler echocardiographic parameters for the assessment of stenosis severity and therapeutic decision making. On the other hand, it remains unclear from the data presented in this article whether and in which patients the ELI provides incremental prognostic information beyond that obtained from the AVAI. In a previous substudy of the SEAS trial,[7] the authors reported that the use of the ELI in place of the AVAI led to reclassification of stenosis from severe to moderate in ≈20% of patients. The cut point values selected in the previous study to define severe AS were 0.6 cm^2/m^2 for both parameters. The present study, however, suggests that the best

cutoff value to predict outcomes is larger for ELI (0.76) than for AVAI (0.60; Figure 2). This difference may be explained by the fact that a high proportion of patients in the present series had a small ascending aorta, and such patients can probably tolerate a more important reduction in the Doppler AVA (ie, the valve effective orifice area) because they have a larger pressure recovery and thus a larger ELI (or catheter AVA) and a lower left ventricular pressure overload (Figures 1 and 2).

The primary goal of therapeutic management in AS is to improve longevity and quality of life, and therefore, mortality is the most robust and clinically relevant end point; however, previous studies have generally used the composite of AVR or death as the primary and often the sole end point, and when such is the case, this composite end point has, in very large part, been driven by AVR. In this context, AVR accounted for 86% of the aortic valve events in the present study. The main limitation of this end point is that as opposed to death, the occurrence of AVR is essentially determined by the clinician's perception of disease severity, which is in turn highly influenced by the magnitude of the gradient (or peak aortic jet velocity) and the presence of symptoms. Hence, it is not surprising that these Doppler parameters were found to be the most powerful predictors of aortic valve events in the present study (ie, they are the main reasons why the cardiologist refers the patient to AVR). On the other hand, the association between mean gradient (or peak jet velocity) and the composite of mortality and hospitalization was much weaker on univariate analysis and no longer significant on multivariate analysis. As opposed to the mean gradient or peak velocity, the ELI was a strong independent predictor of both aortic valve events and the composite of mortality and hospitalization. Consistent with the fluid mechanics concept of pressure recovery (Figure 1), the incremental prognostic value provided by ELI was more important in the subset of patients with a small aorta.
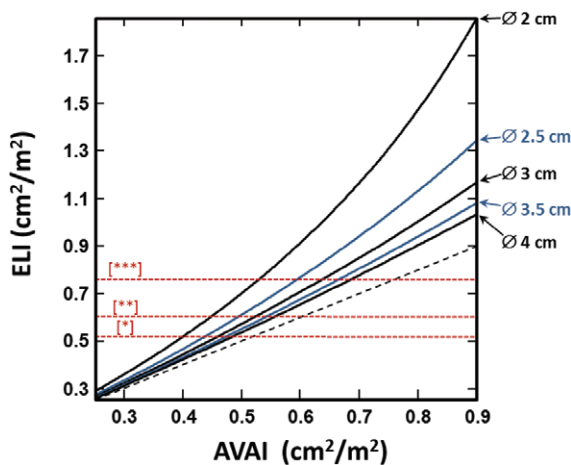
The Dilemma of Inconsistent Grading of AS Severity

The guidelines are inconsistent from 2 standpoints. First, as discussed above, they make no distinction between Doppler echocardiography and catheterization data, although because of pressure recovery, gradients will always tend to be higher

Figure 2. Relationship between energy loss index (ELI) and indexed aortic valve area (AVAI) for different aorta sizes. The calculation of ELI becomes more relevant in patients with an ascending aorta diameter (∅) <3.0 cm and/or with an AVAI >0.5 cm^2/m^2. *Best cut point of ELI to predict outcomes over an 8-month follow-up in the study by Garcia et al.[3] **Cut point of ELI used for reclassification of stenosis severity in the previous study by Bahlmann et al.[7] ***Best cut point of ELI to predict outcomes over a 4-year follow-up in the present study.[4] The **black dashed line** is the identity line.

and AVA lower by echocardiography than by catheterization. Second, the severity criteria are inherently inconsistent with one another; indeed, in a patient with normal transvalvular flow rate, the mean gradient that theoretically corresponds to an AVA value of 1.0 cm² is closer to 30 to 35 mm Hg rather than to the 40-mm Hg cutoff value proposed in the guidelines.[1,2] In light of these findings, some investigators have proposed maintaining the same cut point for the gradient but lowering the cutoff value of AVA for severe AS from 1.0 to 0.8 cm².[9] However, the results of the present study would support the opposite proposal, that is, lower the gradient cut point and keep the current criteria for AVA. Indeed, the optimal cut-point values of AVA (1.03 cm²) and AVAI (0.60 cm²/m²) identified in the present study to predict outcomes are very similar to those proposed in the guidelines,[1,2] whereas those for mean gradient (24 mm Hg) and peak jet velocity (3.2 m/s) are much lower than the guidelines criteria (40 mm Hg and 4 m/s, respectively).

It should be emphasized, however, that by study design, patients with severe AS (peak jet velocity >4 m/s), coronary artery disease, or diabetes were excluded from the SEAS trial, thereby introducing an important selection bias. Furthermore, the sensitivity-specificity (receiver operating characteristic) analyses were based on the values of the Doppler echocardiographic parameters measured at baseline, which do not necessarily reflect the values of these parameters during the 4-year follow-up of the study. Also, these analyses did not account for the timing of the adverse event (ie, early [eg, 6 months] versus late [eg, 4 years]). Hence, the cut-point values of the stenosis parameters reported in the present study may not be directly transposable to the "real-life" AS population for the prediction of events in the short-term (1–2 years), which is most relevant from a clinical standpoint.

Besides the inherent inconsistency in the guidelines criteria discussed above, the other causes of AVA (<1 cm²)–gradient (<40 mm Hg) discordance are (1) measurement errors, (2) the effect of small body size, and (3) the presence of a low-flow state. In the present study, the investigators used stroke volume measured by the Teichholz method instead of that measured by Doppler to calculate AVA, AVAI, and ELI because the readers of the SEAS echocardiography core laboratory considered that the Doppler stroke volume was often underestimated. Furthermore, in the present study, the AVA was indexed for body surface area to account for the effect of small body size, and the ELI was calculated to account for pressure recovery. The calculation of ELI may yield a reclassification of stenosis from severe (on the basis of AVA and AVAI) to nonsevere (Figure 2), and this may thus help to reconcile the issue of inconsistent grading in some patients.

In a previous substudy of the SEAS trial,[9] patients with discordant grading (ie, small AVA and low gradient) had similar outcomes as those with moderate AS (large AVA and low gradient), although they likely had much smaller ELIs. These results may appear to be in disagreement with the results of the present study[4] and with those of the previous study by Cramariuc et al,[10] which report that smaller ELI is associated with worse left ventricular function and clinical outcomes, independent of the gradient. However, as opposed to these 2 studies,[4,10] the study by Jander et al[9] used Doppler stroke

volume and did not take into account the effects of small body size and pressure recovery.[11]

Another frequent cause of AVA (small)–gradient (low) discordance is the presence of a low-flow state, and this may occur with both reduced (classical low flow) or preserved (paradoxical low flow) left ventricular ejection fraction.[12] In the present study, all patients had a normal ejection fraction at baseline. The 2012 European Society of Cardiology–European Association for Cardio-Thoracic Surgery guidelines[2] recommended that AVR should be considered in symptomatic patients with paradoxical low-flow, low-gradient AS with normal ejection fraction only if comprehensive evaluation suggests significant obstruction. This comprehensive evaluation should include recognition of the pathognomonic features of paradoxical low flow,[12] assessment of valve morphology, and, in particular, quantification of valve calcification by echocardiography or preferably by computed tomography, as well as corroboration of hemodynamic severity of the stenosis by stress echocardiography. In light of the results of the present study, calculation of the ELI should also be part of this evaluation given that a large proportion of patients with paradoxical low flow–low gradient have a small aorta.

Thirteen years after the introduction of the ELI, this elegant study from the SEAS investigators demonstrates that this new stenotic index provides independent and incremental prognostic information in asymptomatic AS patients without known atherosclerotic disease or diabetes. Calculation of the ELI appears most useful in patients with a small aorta and in those with inconsistent grading of stenosis severity on the basis of AVA and gradient. Additional studies are needed to further establish the prognostic value of the ELI compared with AVA and AVAI, as well as its optimal cut-point values to predict outcomes in higher-risk AS populations.

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