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Editorial

Is the Leaning Tower of PISA Starting its Fall?

MITRAL REGURGITATION (MR) is assessed using an integrative multiparametric approach including qualitative, semiquantitative, and quantitative measures. These include jet appearance and size, vena contracta, effective regurgitant orifice area, regurgitant volume, regurgitant fraction, pulmonary venous Doppler, as well as secondary effects (eg, left atrial size, left ventricular size and function, and the evidence of pulmonary hypertension). The assessment and quantification of mitral valve regurgitation rarely are determined by a singular measurement. Current guidelines proposed by the American Society of Echocardiography, through the initial use of transthoracic echocardiography (TTE), differentiate mild and severe by specific nonvolumetric criteria and suggest quantitative methods that include volumetric calculations for the differentiation of mild-moderate and moderate-severe MR.[1,2] In the setting of difficult assessment and indeterminate MR, cardiac magnetic resonance (CMR) may be used.

According to the current guidelines, calculation of regurgitant volume is an important step in the quantification and grading of MR, especially in cases of moderate severity. However, the quantification of regurgitant volume can be calculated using the following 2 distinct methods: proximal flow convergence techniques (eg, proximal isovelocity surface area [PISA]) and volumetric techniques using the continuity equation (subtracting left ventricular outflow volume from left ventricular total stroke volume). Although PISA-based techniques are employed through echocardiography, volumetric methods may be calculated by either echocardiography or CMR. Current guidelines do not specify the method to be used and use one reference range for regurgitant volume (eg, severe MR regurgitant volume ≥60 mL). However, studies have highlighted a discrepancy between the 2 methods.[3]

In a recent publication in the *Journal of the American Society of Echocardiography*, Altes et al. sought to evaluate the discrepancy and any potential relationship to differing ventricular volumes.[4] The study compared 188 patients with at least moderate-to-severe primary MR due to prolapse across 2 heart valve centers. The regurgitant volume was calculated via 3 methods: the PISA-based flow convergence method, a volumetric method using TTE, and a volumetric method using CMR. The authors found that PISA- based methods poorly correlated with both volumetric methods, thereby concluding that the regurgitant volume values are not directly comparable. Attempts at angle correction with the PISA method did not improve the correlation. Well-known limitations with the PISA technique include geometric assumptions, eccentric or multiple jets, and reproducibility, yet concerns also exist with TTE volumetric methods that also are based on geometric assumptions and tend to underestimate ventricular volumes as compared with CMR.[5] However, Altes et al. found the differences between the PISA techniques and both volumetric methods were similar. Although it is previously understood that the PISA technique overestimated the regurgitant volume compared to CMR, this study found that in one-third of patients with severe MR, there was a trend toward underestimation. This discrepancy could lead to a potential misclassification and management of patients with primary MR. Altes et al. noted that applying the cutoff of 60 mL of regurgitant volume for severe MR to volumetric methods may lead to a reclassification to moderate MR in one-third of patients.

Further analysis was performed to establish a correlation between ventricular volumes and the magnitude of the difference between the 2 regurgitant volume techniques. The authors observed that the CMR left ventricular end-diastolic volumes (LVEDV) independently correlated with the difference in which, with a smaller LVEDV, there was an overestimation by the PISA techniques; whereas with a larger LVEDV, there was an underestimation by the PISA technique in comparison to both volumetric methods. The authors explained this via the technical details involved in each technique. The PISA-based techniques require a simultaneous measurement corresponding to the PISA radius and peak MR velocity measurement, both captured during mid-systole. This may not be ideal in primary MR patients with predominant mid-late systolic regurgitation, whereas the volumetric methods estimate regurgitant volume over the entire systolic portion of the cardiac cycle.

Lastly, the authors evaluated the relationship between the techniques of regurgitant volume determination and LVEDV, demonstrating that both volumetric techniques correlated well, whereas PISA-based techniques demonstrated no correlation to ventricular volumes. Altes et al. explained that this finding demonstrated that volumetric techniques of regurgitant volume

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determination may be a better reflection of the impact of MR severity on the left ventricle, thereby representing a more preferred technique for calculating mitral regurgitant volume.

The overall impact of the work by Altes et al. on perioperative echocardiographers is several-fold. Current guidelines suggest a singular cutoff of severe primary MR regurgitant volume to be >60 mL without specification of PISA versus volumetric techniques.[1] As noted above, there is a discrepancy identified that may lead to an inaccurate assessment or reclassification based upon the singular cut-off value. Attention to multiple variables of assessment will be essential to determine appropriate classification.

An understanding of the benefits and pitfalls of each technique is key to their successful implementation. Flow-convergence techniques are more applicable in primary MR with isolated leaflet prolapse, which yield a more circular regurgitant orifice, thereby more closely approximating the geometric assumptions of the PISA technique. However, these assumptions begin to invalidate the assessment in the setting of multiple jets, eccentric jets with nonhemispheric flow convergence, more elliptical regurgitant orifices, and jets without holosystolic flow.[6] This difficulty extends to other types of MR, such as functional or ischemic MR, which may have less-predictable regurgitation orifice shapes or potential regurgitation along the entire coaptation line. Volumetric methods by echocardiography also possess pitfalls, primarily through the 2 individual measurements—total left ventricular stroke volume and the forward ejected volume through the left ventricular outflow tract (LVOT). Most commonly, left ventricular stroke volume is obtained through a two-dimensional (2D)−based Simpson's method of discs estimation. This technique notably underestimates ventricular volumes as compared to CMR, particularly with difficulty in apical assessment.[5] Measurement of the left ventricular outflow tract flow is also susceptible to measurement error, as the LVOT area is often obtained through diameter assessment in a long-axis view, whereas the LVOT is rarely circular in shape and more often trapezoidal or elliptical.[7,8]

Technical challenges of the PISA and volumetric methods aside, the 2 techniques are measuring slightly different aspects of the regurgitant jet. As pointed out by Altes et al. and Levy et al., in patients with myxomatous mitral valve prolapse, there is an amount of blood that is contained within the prolapsed leaflets that is neither ejected through the LVOT nor regurgitated back into the left atrium.[4,9] With volumetric techniques, this amount will be included in the mitral regurgitant volume, whereas PISA techniques only account for regurgitant flow across the valve plane. This also contributes to discrepancies in the regurgitant volume measurement. Ultimately, the determination of regurgitant volume is a singular tool in the overall multiparametric integrative approach to assessing severity. That is, the regurgitant volume identified should be interpreted in conjunction with other measures of MR severity.

There are several technologic advancements that potentially may refine and improve the assessment of mitral regurgitant volume. As noted above, 2D assessments often fail to accurately represent measurements of three-dimensional (3D) structures. The use of 3D echocardiography (3DE) allows for the measurements of structures with orthogonal planes that are not available with conventional 2D echocardiography (2DE). Examples of superior 3DE based measurements include the noncircular LVOT as described above, as well as the well-known assessment of the aortic valve annulus in the setting of transcatheter aortic valve replacement.[8,10] The often noncircular shape of the aortic valve annulus precludes accurate measurement with 2DE alone; multiplanar reformatting of 3DE datasets helps overcome this limitation. The use of 3DE also may aid in the assessment of primary mitral regurgitation. To improve the volumetric method, 3DE assessment of LV volumes, which has been shown to improve correlation to CMR volume assessment over 2DE methods, potentially can be used to improve the assessment of regurgitant volume.[5] Levy et al. used the volumetric technique of mitral regurgitant volume with 3D TTE automated LV volume determination for the total LV stroke volume variable.[11] They concluded that, in patients with primary MR, 3D TTE-based regurgitant volume correlated well with CMR. Of course, as identified by Altes et al., the volumetric methods require further research to standardize appropriate cut-off values for regurgitant volume in primary MR.

The application of color-flow Doppler (CFD) to a 3D data set allows a unique assessment not afforded by 2DE—the vena contracta area.[1] Using multiplanar reformatting, a cross-sectional area of the regurgitant orifice can be determined via planimetry. This technique has the theoretical advantage of identifying multiple jets or regurgitation orifices that are noncircular, contributing to underestimation using PISA-based techniques. However, this technique has a similar disadvantage to the PISA method in regurgitant jets that are not holosystolic, as the technique is estimating the severity based upon the vena contracta area from only 1 frame in the cardiac cycle. An additional concern includes the limited temporal and spatial resolution with 3D data sets with CFD. Current ASE guidelines suggest an area >0.4 cm^2 represents severe MR; however, further studies are needed to evaluate this technique.[1]

Technologic advances combining 3DE with PISA techniques to overcome many of the assumptions and pitfalls of 2D PISA are on the horizon. Automated algorithms evaluating a 3D surface area of the flow convergence zone have been developed and used clinically to overcome some of the geometric assumptions.[12,13] Using a different approach with 3D velocity vector fields, a semiautomated software can simulate the flow convergence that is proximal to the regurgitant orifice to assess the regurgitant volume potentially better without reliance on geometric assumptions.[14] The software models the flow convergence based on a simplified fluid dynamics model using multiple velocity vectors in the flow convergence zone. Combined with a 3D surface-rendered model of the valve, the software integrates the velocities over both the surfaces of the valve and over time during systolic ejection to obtain instantaneous volume flow for each frame. By removing geometric assumptions, the software can account for regurgitation through multiple regurgitation orifices and noncircular orifices. Militaru et al. recently evaluated the feasibility of the novel

MR flow quantification software from 3D transesophageal echocardiography CFD data sets in patients with MR in comparison to 2D PISA, by both TTE and transesophageal echocardiography as well as CMR.[14] The authors concluded that the new software correlated with CMR regurgitant volume better than either 2D PISA technique, with high accuracy for diagnosing severe MR. The study included patients with prolapse, restriction, functional MR, and eccentric or multiple jets, and the software analysis was feasible in all patient types.

Overall, as technologic advancement occurs with improvement in assessment, further research will be necessary to ensure that appropriate cutoffs are determined and, ultimately, guidelines are updated to reflect the most current data. An accurate perioperative assessment of severity is imperative for guiding decisions toward mitral valve interventions. As these advancements develop, the reliance on 2D PISA, with its shortcomings, likely will fall away. Despite these innovations, the perioperative assessment of MR likely will remain, for the time being, a multiparametric integrative approach without sole reliance on one technique.

Conflict of Interest

None.

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