Editorial Comment

Left Atrial Filling Revisited: A Noninvasive Index in Quantifying the Severity of Mitral Regurgitation*

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The optimal timing for surgery in mitral regurgitation remains controversial. Even in asymptomatic patients with significant mitral regurgitation (MR) and normal left ventricular ejection fraction, the long-term outlook may be compromised, especially with regard to the development of congestive heart failure (1). Following surgical correction of mitral regurgitation, left ventricular dysfunction is frequently encountered, resulting in heart failure and occasionally death (1,2). In patients with flail mitral leaflets and severe MR despite initially having minimal symptoms, the mortality rate is 6.3% per year and is associated with high morbidity (3). With the advent of valve repair and preservation of the mitral valve apparatus, extremely low mortality rates of about 1% in patients younger than 75 years of age have been reported (4). Therefore, precise and accurate noninvasive techniques are necessary in assessing patients with mitral regurgitation even in the absence of symptoms.

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Two-dimensional echocardiography and Doppler techniques hold great promise in assessing the anatomy of the mitral valve apparatus (for evaluating the etiological causes for mitral regurgitation) as well as semiquantifying the severity of MR (5,6). In those patients with suboptimal images or where precise anatomical information concerning the mitral valve apparatus cannot be obtained with 2-D echocardiography, transesophageal echocardiography would be required. In the majority of reported studies, great emphasis has been placed on evaluating left ventricular function, with the best survival rates reported on those patients whose preoperative ejection fraction was greater than 60% (4). Little emphasis has been placed on the evaluation of left atrial size and function in the assessment of postoperative outcome. Recent studies suggest that with progressive left atrial enlargement and with the advent of atrial fibrillation, increased mortality has been reported (3,7,8).

Quantification of Mitral Regurgitation by Echocardiographic Doppler Techniques

Color-flow Doppler is extremely useful for detecting the presence of mitral regurgitation. The size of the maximum jet area in the left atrium or the ratio of the size of the jet in the left atrium to the left atrial area are the more widely used techniques used to assess the severity of MR (9,10). However, there are problems with both methods. In patients with central mitral regurgitation, the jet can expand freely in an enlarged left atrium, resulting in overestimation of the severity of MR (11). In contrast, measuring maximal eccentric-directed MR jets, which is often constrained by the atrial wall, will often underestimate the severity of MR (12). In addition, various technical and hemodynamic factors will also affect jet size that may cause under- or overestimation of the severity of MR.

In MR, the mitral stroke volume in diastole is larger than the aortic stroke volume, and the difference between the two represents the regurgitant volume. In the absence of aortic regurgitation, pulsed-wave Doppler techniques are based on the principle that the stroke volume flowing across an open valve orifice is equal to the area of the orifice multiplied by the integral of blood velocities (VTI, or velocity time integral) (13). Measuring mitral stroke volume may be more difficult than measuring aortic stroke volume because the annulus changes its shape during the cardiac cycle, especially with enlargement of the left ventricle. The pulsed-wave Doppler technique has been well validated for isolated pure mitral regurgitation but falls down in patients with concomitant aortic valve disease, especially if aortic regurgitation is present.

Quantitative 2-D echocardiography by tracing left ventricular (LV) contours during end-systole and end-diastole and using the biplane Simpson’s method can determine stroke volume (14,15). Aortic stroke volume or forward stroke volume can be calculated by using standard Doppler techniques. The difference between total stroke volume and aortic stroke volume represents the mitral regurgitant volume. Problems with imaging are encountered, which include defining muscle trabeculations and endocardial borders. However, techniques that include automatic border detection, harmonic imaging and the newer contrast agents coupled with new developments in computation of LV volumes by 3-D echocardiography may overcome some of these limitations.

Measuring effective regurgitant orifice (ERO) area directly has been shown to correlate accurately with the severity of MR. The vena contracta method directly measures the diameter of the vena contracta—that is, the size of the jet that immediately exits at the regurgitant orifice (16,17). The vena
contracta method is relatively simple but may require the addition of a zoom lens to assess with accuracy the size of the regurgitant jet. Any error obtained by the measurement will result in gross over- or underestimation of the severity of MR because of the small diameter of the jet as it exits the regurgitant orifice. The proximal isovelocity surface area method (PISA) is based on analysis of the flow convergence proximal to the regurgitant orifice (18–20). Regurgitant flow and effective regurgitant orifice can be calculated by manipulating the Nyquist limit of the color flow and measuring the radius of the flow convergence zone. The ERO can be calculated by dividing regurgitant flow by regurgitant velocity, the latter measured by Continuous Wave (CW) Doppler techniques. The principle of flow convergence depends on the hemispheric assumption used in the calculation, and oval or oblong proximal acceleration shapes would cause errors in the calculation (21). In addition, paying careful attention to the aliasing velocity or Nyquist limit particularly using low-velocity color flow rates is important. Moreover, the PISA method may be inaccurate in patients with flail mitral valve leaflets and/or mitral valve prolapse with eccentric jets because of the presence of suboptimal flow convergence areas (22).

The Role of the Left Atrium in Mitral Regurgitation

A severely enlarged left atrium in a patient with chronic MR who has undergone mitral valve replacement portends a poor prognosis (23). Similarly, Reed and colleagues (7) reported that the size of the left atrium determined by 2-D echocardiography predicted outcome in 176 patients who underwent mitral valve replacement. It appeared to be equally as important a predictor of outcome as was left ventricular function. Left atrial size reflects the natural history of MR, and the more severe and chronic the MR the larger the left atrium. Left atrial size does not change significantly with loading conditions, whereas left ventricular dimensions and wall stress are affected when afterload and preload are acutely altered (24). In addition, the degree of MR may in itself be influenced by the compliance of the left atrium. Also, in patients with stiffer left ventricles, as can occur in chronic MR, the larger the left atrium (25).

Three phases of left atrial volumetric changes have been described (26). The reservoir phase begins with mitral valve closure and continues through ventricular systole. Blood enters the left atrium through the pulmonary veins, and the maximal left atrial volume is reached at ventricular end-systole. In patients with mitral regurgitation, the maximal left atrial volume can increase significantly with MR and represents the combination of the regurgitant volume of MR and the volume of blood contributed by the pulmonary veins. The conduit phase begins with mitral valve opening and lasts until atrial systole begins. The contraction phase begins with atrial systole and continues through mitral valve closure. During this phase, further reduction in left atrial volume occurs until it reaches its smallest size.

Left atrial filling or left atrial emptying volume can be readily determined by 2-D echocardiography and represents the difference between the largest left atrial area measured at end-systole and the smallest left atrial area measured at end-diastole (27). This index was previously utilized as a noninvasive method in quantifying the severity of mitral regurgitation (28).

Pulmonary vein velocity profiles as determined by pulsed-wave Doppler consist of a systolic antegrade wave followed by a smaller diastolic antegrade wave and a terminal small negative wave due to reversal of flow during atrial systole. Systolic pulmonary venous blood flow is influenced by atrial filling and compliance and ventricular output and by the presence of mitral regurgitation (29,30). In an experimental study involving sheep, the pulmonary venous systolic inflow expressed as a fraction of the total inflow velocity time integral correlated with the severity of MR (31).

The Present Study

The present study consisted of 30 patients, average age 59 ± 13 years (20 male and 10 female); 8 patients had organic MR, 10 ischemic MR, 5 functional MR, and 7 patients had no mitral regurgitation (32). Only four patients had atrial fibrillation. Patients with aortic regurgitation were excluded. Left atrial filling (LA filling) was calculated according to the method of Ren et al. (28) using 2-D echocardiography and a biplane area-length formula. The systolic component of the pulmonary venous inflow pattern was expressed as a percentage of the total (systolic + diastolic) velocity time integral (PVs%). When systolic reversal of flow was present in the pulmonary vein, indicative of severe MR, an assignment of zero was made. Doppler regurgitant volume was determined in all 30 patients by the method of Rockey and associates (13), which utilizes mitral and aortic stroke volumes by calculating the product of the annulus area and the mitral and aortic time-velocity integral. Regurgitant volume was determined by subtracting aortic stroke volume from the mitral stroke volume. In the present study, no angiographic or hemodynamic determinants of regurgitant volume were obtained, and the Doppler regurgitant volume was considered the gold standard.

By linear regression analysis, PVs% had the highest correlation with Doppler regurgitant volume ($R^2 = 0.56; p < 0.001$) followed by LA filling ($R^2 = 0.48; p < 0.0001$). A linear combination of the two parameters PVs% and LA filling gave the highest correlation coefficient ($R^2 = 0.88$ SEE [Standard Error Estimate] 10.6; $p < 0.0001$) using the equation Doppler R Vol = 6.18 + (1.01 × LA fill) − (0.783 × PVs%). On the basis of their high correlation using the two measured variables, Rossi and colleagues (32) evaluated 54 patients prospectively. The average age was 56 ± 14 years; 26 patients had organic MR, 14 ischemic, 4 functional and 10 no MR. Only four patients had atrial fibrillation. In this cohort of patients the correlation between Doppler R Vol and estimated regurgitant
volume was good ($R^2 = 0.90$; SEE 12.1 ml; $p < 0.0001$). When the regurgitant volume was higher than 55 ml, implying severe mitral regurgitation, the sensitivity of the equation was 100% and specificity was 98%; positive predictive value was 91% and negative predictive value was 100%.

The advantage of Rossi’s (32) methodology of assessing the severity of mitral regurgitation is that all measurements can be obtained using 2-D echocardiography and Doppler-determined pulmonary flow velocities. The present study also used single-plane atrial volume for determination of regurgitant volume with a high degree of accuracy although somewhat less than the biplane method. With new automatic border technology, rapid estimation of atrial regurgitant volume can be determined.

**Study limitations.** Using the four-chamber views, the Doppler flow velocities can only be obtained from the right superior pulmonary vein. Because the left pulmonary vein is generally not sampled in this view, eccentric jets may not always be sampled in the right superior pulmonary vein. In Rossi’s study (32), no breakdown is given with regard to those patients with organic mitral regurgitation (anterior versus posterior leaflet). In addition, it appears that patients with acute MR were excluded from the study.

Pulmonary veins cannot always be sampled by Doppler echocardiography in all patients owing to a variety of factors. Although the pulmonary veins may be dilated in severe mitral regurgitation, Rossi and colleagues (32) were unable to sample satisfactorily the right superior pulmonary vein in seven patients (7.6%). The pulmonary veins are far-field structures and their entrance into a markedly dilated left atria as occurs in severe MR is not always apparent as anatomical distortion can occur with grossly enlarged left atria. Although transesophageal echocardiography is consistently more reliable in detecting the pulmonary veins it was not employed by Rossi and associates. Only a handful of patients with atrial fibrillation were included in the present study, and no breakdown analysis was provided with this subgroup of patients.

In patients with atrial fibrillation and without MR, a decreased PV is% occurs, and how this finding would affect the equation remains to be determined. Because Rossi and associates assigned a zero to those patients with severe MR, underestimation of the severity of MR did occur. Nevertheless, all patients with severe MR were correctly characterized by their equation despite the underestimations. However, Rossi and colleagues point out that, in severe acute MR (because the regurgitant jet frequently has an eccentric course) their equation may truly underestimate the severity of regurgitation. The investigators did not employ ventriculography as a gold standard to compare their derived equation although semiquantitative ventriculography does have limitations (33). Had calculations for regurgitation volume or regurgitant fraction used the Fick principle for forward cardiac index and the ventriculographic determination of stroke volume, the authors would have had a more reliable gold standard with which to compare their equation.

The clinician is now faced with a variety of Doppler echocardiographic techniques in estimating the severity of MR. Each one has imperfections. Clinical judgment, overall evaluation of left ventricular size and function, left atrial size, presence or absence of atrial fibrillation, etiological causes of MR, presence or absence of pulmonary hypertension and newer Doppler echocardiographic indices such as described by Rossi and colleagues (32) should go a long way in helping decide when to intervene in asymptomatic patients with severe MR.

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