Assessment of Preoperative Left Ventricular Function in Patients with Mitral Regurgitation: Value of the End-systolic Wall Stress–End-systolic Volume Ratio

Blase A. Carabello, M.D., Stanton P. Nolan, M.D., and Lockhart B. McGuire, M.D.

Summary

Twenty-one patients with symptomatic, chronic, severe mitral regurgitation (MR) but without other valvular heart disease or coronary disease were evaluated to determine which hemodynamic and angiographic factors might be prognostic of surgical outcome. Sixteen patients were in New York Heart Association functional classes I or II postoperatively and formed group A. One patient remained in class III postoperatively and four patients died perioperatively; they constitute group B. End-diastolic volume index (EDVI) was less for group A than for group B, 119 ± 25 ml/m² vs 170 ± 28 ml/m² (p < 0.001). End-systolic volume index (ESVI) was also lower in group A, 39 ± 19 ml/m² vs 72 ± 32 ml/m² for group B (p < 0.01).

The ratio of end-systolic wall stress to end-systolic volume index (ESWS/ESVI) was examined in normal persons and in groups A and B. This ratio was significantly lower in both groups than in normal persons, indicating relatively greater end-systolic volume at a given wall stress, suggesting left ventricular dysfunction. The ESWS/ESVI ratio in group B, 2.2 ± 0.2, was significantly less than in group A, 3.3 ± 0.4 (p < 0.001). The variables of age, pulmonary capillary wedge pressure, EDVI, ESVI, ejection fraction and the ESWS/ESVI ratio were subjected to stepwise discriminant multivariate analysis to determine if any were independent predictors of outcome. The only independent predictor determined by this method was the ESWS/ESVI ratio (p < 0.001). We conclude that the ESWS/ESVI ratio may be helpful in evaluating left ventricular function and operative risk in patients with chronic, symptomatic MR.

Left Ventricular Performance

Assessed by measurement of ejection fraction (EF) has been shown to worsen after mitral valve replacement (MVR) for chronic mitral regurgitation (MR). This may be because the regurgitant mitral valve is an unloading device that reduces mean systolic wall stress. Wall stress is an important determinant of ventricular shortening, and reduction in wall stress facilitates ventricular emptying. The imposition of a competent mitral valve removes this method of unloading, and thus might reduce ventricular shortening and EF. Although EF is frequently used to quantitate left ventricular function, it might overestimate left ventricular function in patients with MR.

Many authors have advocated the use of the end-systolic volume/end-systolic wall stress (ESV/ESWS) relationship to better define left ventricular function. EF is affected by changes in preload and afterload; ESV is relatively independent of preload and varies linearly with afterload. Afterload has been approximated by measuring either end-systolic pressure (ESP) or ESWS. By altering systolic ventricular pressure, ventricular volume vs pressure or wall stress may be plotted to describe left ventricular function. A relatively large ESV for a given ESP or ESWS indicates relatively less ventricular shortening for a given afterload, and therefore decreased myocardial contractility. However, with this method, an intervention must be performed at the time of volume measurements to measure volume changes at different afterloads. It seemed possible to us that simple examination of the ESWS/ESVI index ratio (ESWS/ESVI) in patients with MR might contain useful prognostic information about left ventricular function. A higher ESWS/ESVI ratio would indicate relatively greater left ventricular shortening at a given afterload, and a lower ESWS/ESVI would indicate less shortening for a given afterload and thus relatively poorer left ventricular function. We believed some patients with MR had an unsatisfactory surgical result despite a normal preoperative EF. We undertook this study to examine whether the ESWS/ESVI ratio and other hemodynamic measurements might be helpful in evaluating preoperative surgical risk in patients with MR undergoing MVR.

Materials and Methods

Catheterization reports of all patients with MR catheterized at the University of Virginia Hospital from January 1, 1975 to January 1, 1980 who subsequently underwent MVR were reviewed. Of 106 such patients, 28 had pure MR without significant mitral stenosis, other valvular lesions or coronary artery disease. Of these 28 patients, 21 had pressure tracings and ventriculograms of adequate quality to allow for wall stress analysis. Adequate pressure tracings were defined as those in which the dicrotic notch was clearly present. Adequate angiograms were defined as those in which end-diastolic wall thickness and end-diastolic and end-systolic chamber size could be clearly demarcated.

Assessment of preoperative functional class was made by review of the patients' symptoms described in the hospital record. One patient underwent intra-aortic balloon pumping during catheterization. All pa-
tients were taking digoxin and furosemide at the time of study. No patient was taking vasodilators.

Right atrial pressure, pulmonary capillary wedge mean pressure, pulmonary capillary wedge V-wave pressure, aortic pressure and left ventricular pressure were recorded. Confirmation of the pulmonary capillary wedge pressure was made using the criteria that the V wave peaked after the ECG T wave and that mean pulmonary artery pressure was greater than mean pulmonary capillary wedge pressure. In questionable cases, confirmation was also made by oximetry. Cardiac output was determined by the Fick method. Left ventricular pressures and ventriculograms were obtained using standard fluid-filled angiographic catheters. Left ventricular volumes were calculated from single-plane, right anterior oblique ventriculograms using the area-length method.\textsuperscript{18} Volumes were calculated using the regression equation for the right anterior oblique position derived by Wynne et al.\textsuperscript{20} Volumes were indexed by dividing by body surface area. Twelve patients were in atrial fibrillation and nine were in sinus rhythm at the time of the catheterization. For patients in atrial fibrillation, the angiographic volumes of three consecutive cardiac cycles were calculated and averaged. Pressures and volume were obtained nonsimultaneously. To minimize error in stress calculations that might have occurred because of nonsimultaneous pressure and volume measurements in patients with atrial fibrillation, the RR intervals preceding the beats used to calculate volumes were obtained from ECG recordings made during angiography. These RR intervals were matched to RR intervals of beats from pressure recordings made just before angiography. The pressure recordings and volume determinations were thus matched by RR interval. We have validated this method in five patients in atrial fibrillation in whom simultaneous pressure and volume recordings were made. Dicrotic notch pressure, which was used to calculate end-systolic stress, did not vary by more than 5 mm Hg from beats during angiography to beats matched for RR interval just before angiography.

In patients in sinus rhythm, volumes were calculated from one cardiac cycle. Post extrasystolic beats were avoided. End-systolic circumferential midwall stress (ESWS) was calculated from Mirsky's variation of the LaPlace relationship as it pertains to the left ventricle:\textsuperscript{21}

\[
\text{Stress} = \frac{p \cdot b}{h} \cdot (1 - \frac{h}{2b} - \frac{b^2}{2a^2})
\]

where \(p\) = pressure measured at the dicrotic notch of the aortic pressure tracing, \(h\) = wall thickness, \(a = \frac{L}{2}\) = midwall semi-major axis (\(\frac{L}{2} + \frac{h}{2}\)) at end-systole and \(b = \frac{D}{2}\) = midwall semi-minor axis (\(\frac{D}{2} + \frac{h}{2}\)) at end-systole.

The result obtained by this formula was converted to \(\text{dyn} \times 10^5/\text{cm}^2\) by multiplying by a conversion factor of 1332 dyn/cm\(^2\)/mm Hg. Wall thickness was obtained using the method of Hugenholtz et al.\textsuperscript{22} Thus, determination of ESWS and ESVI allowed for calculation of the ESWS/ESVI ratio.

All patients underwent MVR within 3 weeks of catheterization with porcine bioprostheses. Of the 21 patients, 18 received cold cardioplegia during surgery; all five group B patients were in this group. Of the 19 patients who were successfully weaned from cardiopulmonary bypass, none had ECG or enzymatic evidence of operative myocardial infarction. The duration of aortic cross-clamping for group A (44 ± 11 minutes) was not significantly different from that for group B (51 ± 16 minutes).

Normal Subjects

Twenty patients who underwent cardiac catheterization in whom no abnormality was detected permitted the evaluation of the normal ESWS/ESVI ratio. No normal subject was receiving digitalis or propranolol at the time of the study. Angiographic and wall stress calculations were performed using the same method in all subjects, normal and abnormal.

Statistics

Statistical inference for attributes was made using the exact probability test.\textsuperscript{23} Differences in the mean (± SD) of measurements between the groups was determined by the \(t\) test. Comparison of differences in means of more than two variables were evaluated by performing analysis of variance, followed by Scheffe's multiple comparison test. The significance of variables as independent predictors of surgical outcome was determined by stepwise discriminant multivariate analysis.

Results

Among the 28 patients who received porcine mitral valve prostheses for "pure" mitral regurgitation, two patients could not be weaned from cardiopulmonary bypass and died. Two died perioperatively in a low-output state. The average follow-up period for surviving patients was 12 ± 8 months. All four of the patients who died were among the group of 21 whose ventriculograms were technically adequate to permit study of ventricular volumes and left ventricular wall stress.

Before operation, all patients had congestive symptoms equivalent to functional class II or greater, and 15 of 21 were class III or class IV (fig. 1). Group A included the 16 patients who improved postoperatively; group B included the five patients who either died or did not improve after operation. There was no significant difference in the average age of the two groups. Nine of the 12 patients (75%) in atrial fibrillation survived vs eight of nine patients (89%) in sinus rhythm (NS). Six of six patients (100%) who were preoperative class II survived, compared with 11 of 15 (74%) class III or IV patients (NS).

The hemodynamic and angiographic data of both groups are presented in table 1. There was no significant difference in cardiac index or pulmonary artery
NYHA CLASS

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FIGURE 1. Preoperative and postoperative New York Heart Association (NYHA) functional classification of symptomatic patients with chronic mitral regurgitation.

TABLE 1. Hemodynamic and Angiographic Data

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<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>PCWP (mm Hg)</th>
<th>EDVI (ml/m²)</th>
<th>ESVI (ml/m²)</th>
<th>EF</th>
<th>ESWS/ESVI</th>
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<td>±0.4</td>
<td>±0.8</td>
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</tbody>
</table>

| Group B |     |             |              |              |    |           |          |
| 17       | 68   | 22           | 139          | 58           | 0.58| 2.4       | 2.0      |
| 18       | 62   | 32           | 184          | 115          | 0.38| 2.2       | 0.8      |
| 19       | 48   | 26           | 201          | 69           | 0.66| 2.3       | 1.3      |
| 20       | 67   | 30           | 185          | 90           | 0.51| 1.9       | 1.1      |
| 21       | 53   | 18           | 140          | 29           | 0.80| 2.4       | 1.9      |
| Mean     | 60   | 26           | 170          | 72           | 0.59| 2.2       | 1.4      |
| ± SD     | ±9   | ±6           | ±28          | ±32          | ±0.16| ±0.2     | ±0.5     |
| p        | 0.52 | 0.06         | 0.001        | 0.009        | 0.192| 0.001    | 0.009    |

The p values refer to univariate comparison of group A and group B.

*Patient underwent intraaortic balloon pumping during catheterization.

Abbreviations: PCWP = pulmonary capillary wedge pressure; EDVI = end-diastolic volume index; EF = ejection fraction; ESWS/ESVI = end-systolic wall stress–end systolic volume index ratio; ESP/ESVI = end-systolic pressure–end systolic volume index ratio.
Discussion

The ESWS/ESVI ratio was more sensitive than EF or other hemodynamic variables in predicting surgical outcome in symptomatic patients with chronic MR. This may be because the ESWS/ESVI is more accurate in assessing left ventricular function. Thus, group A patients, who had a mean EF of 0.67 (range 0.45–0.85), had a significantly lower ESWS/ESVI ratio than normal subjects, indicating left ventricular dysfunction. For any given wall stress they had a greater ESVI than normal. That left ventricular dysfunction was present is also suggested by a higher-than-normal mean pulmonary capillary wedge pressure and a lower-than-normal cardiac index. Even greater left ventricular dysfunction was suggested by the ESWS/ESVI ratio in group B. In this group, the mean EF, 0.59, would be considered in the normal range, and only one patient in this group had an EF of less than 0.5. That EF might be an unreliable indicator of left ventricular function is not surprising. EF is sensitive not only to changes in contractility, but also to changes in preload and afterload.8 In MR, preload is increased by the volume overload in that condition. Afterload as approximated by wall stress, however, is decreased in the later part of systole in MR.4 These changes in preload and afterload which are present in MR tend to normalize EF, even in the presence of left ventricular dysfunction.6

ESV is independent of preload, but is influenced by afterload.10–18 Borow et al. found ESVI more sensitive than EF in determining surgical outcome in patients with MR.26 We also found a greater ESVI and EDVI in group A patients than in normal persons and a greater EDVI and ESVI in group B than group A; however, there was overlap between groups, and ESVI or EDVI alone did not separate the two groups. Multivariate analysis demonstrated the ESWS/ESVI ratio to be an independent predictor of outcome in this study. Although the other factors were not significant independent predictors, this may have been because of our small sample size. The present study supports the hypothesis that the ESWS/ESVI ratio may be more useful than EF or ESVI or EDVI in assessing surgical risk for MVR. An example is patient 21 (fig. 4), who had a history of chronic MR with apparent acute worsening of his clinical condition. He was catheterized during intraaortic balloon pumping. The EF was 0.80, ESVI was normal and EDVI was moderately enlarged. However, the ESWS/ESVI was well below normal. We postulate the unloading effect of both the patient's MR and the intraaortic balloon pumping provided a very low ESWS, allowing for a normal ESVI and a supranormal EF. Yet, the severity of his left ventricular dysfunction was detected by examination of his ESWS/ESVI ratio. The patient underwent MVR and subsequently died perioperatively in a low-output state.

The relationship between ESV and either ESP or ESWS have been used in other studies to evaluate left

**Figure 2.** Preoperative ejection fractions (EF) for members of group A (circles) and B (triangles). Although EF tended to be higher in group A, there is considerable overlap between groups. EF alone was not a good predictor of surgical outcome.

for groups A and B is shown in figure 4. The average ESWS/ESVI ratio for normal persons was 5.6 ± 0.9, which is significantly greater than that for group A, 3.3 ± 0.4 (p < 0.025). The mean ESWS/ESVI ratio was significantly higher for group A than for group B, 3.3 ± 0.4 vs 2.2 ± 0.2 (p < 0.025).

The ESP/ESVI ratio was also examined. For group A, the average ESP/ESVI ratio was 2.6 ± 0.8 mm Hg/ml/m², which was significantly higher than that for group B, 1.4 ± 0.5 mm Hg/ml/m² (p < 0.025). However, the ESP/ESVI for both groups overlapped significantly. Age, pulmonary capillary wedge pressure, EDVI, ESVI, EF, ESWS/ESVI and ESP/ESVI were then subjected to stepwise discriminant variable analysis. The only independent predictor of an unfavorable outcome was the ESWS/ESVI ratio (p < 0.001).
ventricular function. In these studies, an intervention was used to produce a change in systolic pressure or wall stress to create two or three different volume-pressure or volume-stress points to form a line. The slope of this line has been used to assess left ventricular function. In this study, the ESWS/ESVI ratio in normal persons was 5.6 ± 0.9. A progressively smaller ratio would seem to indicate progressively greater left ventricular dysfunction as there is progressively less left ventricular shortening (greater left ventricular volume) for any given afterload. For both ESV and ESWS, the end-systolic left ventricular radius (dimension) is used in their computation. Thus, they are likely to vary directly with one another. However, the calculation of ESWS further defines left ventricular afterload and is useful for evaluating the load against which the ventricle must shorten. Although in our small series the patients fell into distinct groups, in a larger population there could be a continuum of ESWS/ESVI ratios that indicates varying degrees of dysfunction.

We did not find as strong a predictive value for the ESP/ESVI ratio as for the ESWS/ESVI ratio. This is not surprising and does not necessarily contradict other studies. ESWS varies directly with pressure and radius and inversely with wall thickness. Acute

**Figure 3.** End-diastolic volume index (EDVI) and end-systolic volume index (ESVI) for group A (circles) and group B (triangles). Both mean EDVI and ESVI were significantly higher in group B than in group A.

**Figure 4.** End-systolic wall stress/end-systolic volume index ratio (ESWS/ESVI) for normal subjects (open circles), group A (closed circles) and group B (triangles). ESWS/ESVI was significantly lower in group A than in normal persons and lower in group B than in group A, suggesting left ventricular dysfunction in group A and more severe left ventricular dysfunction in group B. The asterisk denotes patient 21, who had an ejection fraction of 0.8 but in whom severe left ventricular dysfunction is suggested by the ESWS/ESVI.
changes in pressure in a given ventricle vary directly with wall stress, and therefore pressure can be successfully substituted for stress in constructing an afterload-volume relationship. However, when several ventricles are compared, ESWS probably more accurately estimates afterload than pressure alone because of patient-to-patient variation in ventricular radius and thickness.28 Thus, ESWS is more precise in constructing the afterload-volume relationship.

Our results suggest that many symptomatic patients with chronic MR have left ventricular dysfunction. We infer chronicity from the fact that symptoms and a murmur were present for at least 5 months before the study. Our results might not relate to acute MR, such as that secondary to rupture of chordae tendineae, in which a sudden volume overload may result in symptoms that are related to acute regurgitation and not necessarily to left ventricular dysfunction. All of our patients were symptomatic; thus, our results may not relate to asymptomatic patients with chronic MR.

Other limitations of our study should be noted. Our pressure and volume measurements were non-simultaneous. Because ventricular ejection may continue in mitral regurgitation after aortic valve closure, errors in pressure and volume matching may have occurred. It is doubtful, however, that these errors were so large that they would invalidate our study.

In addition, our group of patients, particularly group B, was small. Factors other than left ventricular function could have resulted in a poor outcome in that group. However, the groups had no obvious differences in operative or postoperative surgical factors. Further prospective studies to validate the value of the ESWS/ESVI ratio for evaluating left ventricular function and as predictor of surgical outcome in patients with MR seem justified. Comparison of the ESWS/ESVI ratio with other measurements of contractility would be useful.

In summary, standard hemodynamic and angiographic measurements may be unreliable for evaluating left ventricular function and surgical outcome in patients with chronic MR. Patients with normal EF may have significant impairment of left ventricular function. Left ventricular function might be better quantified by the ESWS/ESVI ratio than by EF alone. Relatively lower ESWS/ESVI ratios may indicate relatively more impairment in left ventricular function and, presumably, greater surgical risk.

References

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