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The Mitral Regurgitation Index: An Echocardiographic Guide to Severity

Liza Thomas, MD, Elyse Foster, MD, FACC, Julien I. E. Hoffman, MD, Nelson B. Schiller, MD, FACC
San Francisco, California

OBJECTIVES The purpose of this study was to develop a semiquantitative index of mitral regurgitation severity suitable for use in daily clinical practice and research.

BACKGROUND There is no simple method for quantification of mitral regurgitation (MR). The MR Index is a semiquantitative guide to MR severity. The MR Index is a composite of six echocardiographic variables: color Doppler regurgitant jet penetration and proximal isovelocity surface area, continuous wave Doppler characteristics of the regurgitant jet and tricuspid regurgitant jet-derived pulmonary artery pressure, pulse wave Doppler pulmonary venous flow pattern and two-dimensional echocardiographic estimation of left atrial size.

METHODS Consecutive patients (n = 103) with varying grades of MR, seen in the Adult Echocardiography Laboratory at UCSF, were analyzed retrospectively. All patients were evaluated for the six variables, each variable being scored on a four point scale from 0 to 3. The reference standards for MR were qualitative echocardiographic evaluation by an expert and quantitation of regurgitant fraction using two-dimensional and Doppler echocardiography. A subgroup of patients with low ejection fraction (EF $<$50%) were also analyzed.

RESULTS The MR Index increased in proportion to MR severity with a significant difference among the three grades in both normal and low EF groups (F = 130 and F = 42, respectively, $p < 0.0001$). The MR Index correlated with regurgitant fraction ($r = 0.76$, $p < 0.0001$). An MR Index $\geq$2.2 identified 26/29 patients with severe MR (sensitivity = 90%, specificity = 88%, PPV = 79%). No patient with severe MR had an MR Index $<$1.8 and no patient with mild MR had an MR Index $>$1.7.

CONCLUSIONS The MR Index is a simple semiquantitative estimate of MR severity, which seems to be useful in evaluating MR in patients with a low EF. (J Am Coll Cardiol 1999;33:2016–22) © 1999 by the American College of Cardiology

Echocardiography is the most commonly used noninvasive method for detection and estimation of mitral regurgitation (MR) severity. Although the echocardiographic finding of MR is ubiquitous in adults, evaluating its severity remains a clinical challenge. Numerous echocardiographic techniques, both qualitative and quantitative, have been developed. However, no single precise method is routinely used as a "reference standard" (1) and previous studies have demonstrated that existing measures of MR severity correlate poorly with clinical signs and symptoms (2,3).

Quantitative echocardiographic measures include calculation of regurgitant volume, regurgitant fraction (RF) and effective regurgitant orifice area by two-dimensional and Doppler echocardiography (4–8) and the proximal isovelocity surface area (PISA) technique, respectively (9–11). These quantitative methods are cumbersome and time consuming and, hence, infrequently used for routine clinical evaluation. Qualitative evaluation is based on a number of variables: color Doppler jet characteristics including jet entrainment, jet width and area, continuous wave (CW) Doppler intensity and character of the regurgitant jet, pulmonary venous flow pattern and left atrial (LA) dynamics (12). The qualitative nature of these variables leads to a high degree of interobserver variability that may adversely influence clinical decision making. Hence, a simple yet accurate reproducible and clinically applicable guide is desirable to identify and follow up patients with hemodynamically significant MR.

We hypothesized that the systematic application of a combination of qualitative and quantitative echocardiographic variables would provide an index of MR that would be more reproducible than a qualitative estimate alone and less time intensive than existing quantitative methods. The specific aims of this study were to develop a new "MR Index" and to test the hypotheses that the MR Index would:

1) correlate with the qualitative assessment of severity of MR; and
2) correlate with a quantitative measure of MR, in this instance the RF.

From the Division of Cardiology, University of California, San Francisco, California.
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Abbreviations and Acronyms

CW	=	continuous wave
EF	=	ejection fraction
LA	=	left atrium
LV	=	left ventricular
MR	=	mitral regurgitation
PISA	=	proximal isovelocity surface area
RF	=	regurgitant fraction

METHODS

We retrospectively studied 103 consecutive patients (54 men and 49 women) between the ages of 25 and 89 years with echocardiographically diagnosed native valve MR, examined and entered into the UCSF Adult Echocardiography Database between January 1994 and December 1996. Approval for this study was obtained from the Committee for Human Research at UCSF. Inclusion criteria were:

1) "isolated MR,"
2) sinus rhythm,
3) heart rate <110 bpm,
4) no more than trivial or mild aortic regurgitation, and
5) concurrent tricuspid regurgitation regardless of severity.

Exclusion criteria were:

1) trivial or trace MR,
2) associated mitral or aortic stenosis (n = 6),
3) moderate or severe aortic regurgitation (n = 4), qualitative
4) atrial fibrillation or sinus tachycardia >110 beats/min (n = 3), and
5) previous mitral valve repair surgery (n = 1).

Four patients (one with mild MR, two with moderate MR and one with severe MR) were excluded from the total of 89 patients with MR for technical reasons such as an inadequate pulmonary venous flow signal. In addition to patients with MR, ten age-matched normal subjects from the same population were also analyzed.

In our laboratory, the routine evaluation and assignment of a qualitative grade of MR is based on a number of echocardiographic and Doppler parameters (12) and are reported using standard phrases from a dictionary database as mild, mild to moderate, moderate, moderate to severe and severe. Patients were divided into three categories on the basis of the expert reader's grading of MR severity: MILD MR—included patients graded as mild MR, MODERATE MR—included patients graded as mild-moderate and moderate MR, SEVERE MR—included patients graded as moderate-severe and severe MR. As a quantitative expression of MR, RF was retrospectively calculated in all patients by two dimensional and Doppler echocardiography as described below.

The left ventricular (LV) end diastolic volume and the LV end systolic volumes were measured using the biplane method of discs using the orthogonal four and two chamber apical views and the ejection fraction (EF) was calculated as described below. Subgroup analysis by EF compared patients as those with normal or near normal EF (EF > 50%) (n = 50) with those with moderate or severely decreased EF (EF < 50%) (n = 36). The EF in the <50% group ranged from 8% to 49%. Furthermore, the 36 patients were classified into those with moderately decreased EF (EF > 30%) (n = 18) and those with severely decreased EF (EF < 30%) (n = 18). These were evenly divided as six patients in each category of mild, moderate and severe MR.

Echocardiographic study. Doppler, M mode and two-dimensional echocardiography were performed according to the established clinical laboratory practice using commercially available instruments routinely used in the Echocardiography Laboratory (Hewlett-Packard Sonos 1500 and 2500 and the Acuson XP 128, Andover, Massachusetts) with 2.5 or 3.5 MHz phased array transducers.

The Mitral Regurgitation Index. The MR Index was derived from six frequently applied echocardiographic variables. Three of the variables were significantly influenced by the severity of MR; these included jet penetration into the LA, PISA, CW regurgitant jet character and intensity. Three variables related to the compensatory changes in the heart secondary to MR were: pulmonary artery pressure by tricuspid regurgitation velocity, pulmonary venous inflow pattern and LA size. Each parameter was scored on a four point scale from 0–3 (refer to Table 1) and the total was divided by the number of variables. Thus, a grade of 3.0 represents the most extreme degree of MR and a grade of 0 represents the absence of MR.

Jet penetration was studied in the parasternal long axis and apical four and two chamber views. A jet was considered to be eccentric if it impinged on the lateral wall or the interatrial septum in any of the above views. Because this was a retrospective study, not all echocardiograms reviewed did include a magnified view with a lowered Nyquist for measurement of PISA and the radius was therefore measured in the apical four chamber view (Nyquist setting in all patients ranged between 50 and 64). The PISA radius was measured as the distance from the first alias to a point at the trailing edge of the mitral leaflets nearest the regurgitant orifice along a vector parallel to the direction of interrogation at a point in midsystole. The CW jet intensity and character were evaluated from spectral recordings obtained either in the apical four chamber view or with the standard lone CW transducer positioned at the apex.

The systolic pulmonary artery pressure was estimated as the sum of the gradient across the tricuspid valve (calculated from the modified Bernoulli equation as gradient $= 4\ v^2$ where v = peak velocity) and the right atrial pressure. Right atrial pressure was estimated using the size and respiratory response of the inferior vena cava in the subcostal view as

Table 1. The Mitral Regurgitation Index: Grading of Its Six Constituent Variables

1) Jet Penetration:
 0 = no jet
 1 = central jet; jet does not impinge on lateral wall in any view
 2 = eccentric jet which extends up to the first pulmonary vein
 3 = eccentric jet which encircles the atrium extending beyond the pulmonary vein
2) PISA:
 0 = No PISA
 1 = PISA ≤0.5 cm
 2 = PISA = 0.5–1.0 cm
 3 = PISA ≥1.0 cm
3) CW Jet Intensity and Character:
 0 = No jet
 1 = Incomplete jet envelope
 2 = Complete jet envelope; jet density 20–50% of inflow
 3 = Complete envelope; jet density 50–70% of inflow
4) Pulmonary Artery Pressure (PAP)*:
 0 = PAP <25 mm Hg
 1 = PAP = 25–30 mm Hg
 2 = PAP = 31–45 mm Hg
 3 = PAP >45 mm Hg
5) Pulmonary Venous Flow Pattern:
 0 = systolic dominant flow; systolic impulse exceeds diastolic impulse by 50% or more
 1 = systolic dominant flow; systolic impulse exceeds diastolic impulse by <50%
 2 = diastolic dominant flow
 3 = systolic flow reversal
6) Left Atrial Size:
 0 = normal
 2 = mild enlargement
 2 = mild to moderate and moderate enlargement
 3 = moderate to severe and severe enlargement

MR INDEX = Total Score/number of variables (6). PISA = proximal isovelocity surface area.

previously described (13) (Appendix, Table 1). In three patients, an adequate tracing was not obtained of the tricuspid regurgitant jet. In all these patients, however, there was only trivial to mild tricuspid regurgitation on color Doppler, normal right atrial and right ventricular dimensions, left to right bulging of the interatrial septum and inferior vena cava pressure of 5 mm Hg. The pulmonary artery pressure was inferred to be 25 mm Hg in these three patients from these other corroborative signs. Pulmonary venous flow pattern was obtained from Doppler interrogation of the right upper pulmonary vein. Left atrial size was judged subjectively from the parasternal long axis and apical four and two chamber views.

Assessment of severity of mitral regurgitation. The qualitative assessment of MR severity was done by an expert reader at the time the study was initially performed and was based on a number of variables (12). In addition to this qualitative grading, measured RF provided an independent measurement of the severity of MR.

Table 2. Clinical, Doppler and Echocardiographic Variables (Mean ± SD) Among the Three Grades of Mitral Regurgitation

Variables	Mild MR	Moderate MR	Severe MR
Age	65 ± 12 yr	60 ± 17 yr	62 ± 16 yr
Number	29	27	29
Regurgitant volume	12 ± 10 ml*	31 ± 12 ml†	59 ± 26 ml
Regurgitant fraction	20 ± 11%*	40 ± 11%†	57 ± 13%
Ejection fraction	50 ± 20%	48 ± 17%	49 ± 18%
MR Index	1.1 ± 0.3*	1.8 ± 0.3†	2.4 ± 0.3

* = $p < 0.05$ versus moderate and severe. † = $p < 0.05$ versus severe. MR = mitral regurgitation.

Measurement of regurgitant fraction. Left ventricular stroke volume was measured as recommended by the American Society of Echocardiography (14). The LV stroke volume was computed as the difference between the LV end diastolic volume and LV end systolic volume measured by applying the biplane method of discs as described above. An average of three measurements was used. Forward stroke volume in patients with MR was calculated as the product of the left ventricular outflow tract velocity time integral and the LVOT area (regurgitant volume = LV stroke volume − forward stroke volume; Regurgitant fraction (RF) = Regurgitant volume/LV stroke volume).

Observer agreement. In 30 randomly selected studies, two experts independently estimated the degree of mitral regurgitation as mild, moderate and severe. In the same 30 cases, the MR Index was independently scored by the two experts. The same studies were also reexamined by one observer at a separate time to determine intraobserver agreement of the MR Index.

ANALYSIS

All values are expressed as a mean ± standard deviation. The differences among groups were examined by analysis of variance, and the post hoc tests applied were the Fisher PLSD test, Scheffe F-test and Dunnett *t* test. Simple and multiple regression was used to examine the relationship between the RF, the MR Index and the six variables. Spearman Rank correlation was used to determine the relationship between RF and each variable, and the Kruskal-Wallis test was used to correlate the MR Index to the qualitative grade of MR. Student *t* test was used to study differences between unpaired groups. Data were analyzed using the Statview Student package and Statview 4.02 (Abacus Concepts, Sunnyvale, California).

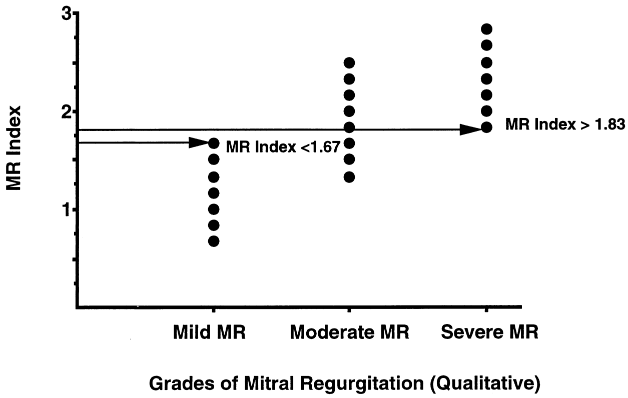

Figure 1. Correlation graph of the study population of 85 patients, of the Mitral Regurgitation Index versus the three grades of mitral regurgitation (MR): mild MR (n = 29), moderate MR (n = 27), severe MR (n = 29). All patients with severe MR had an MR Index >1.83 and all those with mild MR had an MR Index <1.67.

RESULTS

We studied four groups: normal (n = 10), mild MR (n = 29), moderate MR (n = 27) and severe MR (n = 29). The mean values for the clinical, Doppler and echocardiographic variables measured are listed (Table 2).

The MR Index. The MR Index was observed to increase in proportion to MR severity with significant differences among the four groups (F = 130.3, $p = 0.0001$). Post hoc tests showed that there was a significant difference between mild MR versus moderate MR, mild MR versus severe MR and moderate MR versus severe MR ($p < 0.05$).

An MR Index of greater than ≥2.17 identified 26/29 patients with severe MR (sensitivity of 90%, specificity of 88%, positive predictive value of 79%, negative predictive value of 94%). No patient with severe MR had an MR Index that was less than 1.83, and no patient with mild MR had an MR Index greater than 1.67 (Fig. 1).

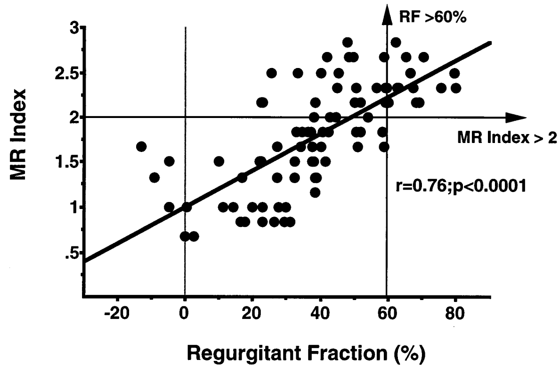

Figure 2. Regression plot of correlation between the Mitral Regurgitation Index and the regurgitant fraction in 85 patients with varying grades of mitral regurgitation ($r = 0.76$, $p < 0.0001$). In patients with a regurgitant fraction greater than 60%, the MR Index was noted to exceed 2.0 in all cases.

Table 3. The MR Index (Mean ± SD) of Normal and Low Ejection Fraction (EF) Subgroups

Category	Mild MR	Moderate MR	Severe MR
MR Index Normal EF	1.1 ± 0.3*	1.9 ± 0.3†	2.4 ± 0.3
MR Index Low EF	1.2 ± 0.4*	1.8 ± 0.4†	2.4 ± 0.3

* = $p < 0.05$ versus moderate and severe. † = $p < 0.05$ versus severe. EF = ejection fraction; MR = mitral regurgitation.

Univariate analysis of the RF to the MR Index showed good correlation ($r = 0.76$, $p = 0.0001$) (Fig. 2). Furthermore, all patients with an RF >60% had an MR Index >2.

Regurgitant fraction and the MR Index. The RF increased with the severity of mitral regurgitation, and there was a significant difference between normals and the three grades of MR severity (F = 57, $p = 0.0001$). Post hoc tests showed a significant difference ($p < 0.05$) between normal versus mild, moderate and severe MR, mild MR versus moderate and severe MR; and moderate MR versus severe MR. Spearman-Rank correlation of the six variables in the MR Index showed that each of the variables were univariate predictors of RF ($p < 0.001$) and the MR Index ($p < 0.001$).

When each of the six variables was entered into a multiple regression, jet penetration and CW density and character were significant predictors of the RF ($r = 0.82$, $p < 0.0001$) and this was confirmed in stepwise forward and backward regression analysis ($r = 0.81$, $p < 0.0001$). Multiple regression analysis of the six variables to the MR Index showed that all variables except pulmonary artery pressure were significant in predicting the MR Index ($r = 0.95$, $p < 0.0001$). Stepwise forward and backward regression analysis confirmed these findings ($r = 0.95$, $p < 0.0001$).

Subgroup analysis of patients with a low EF. There was a significant difference in the MR Index among the three groups of patients with MR in the subgroup with a low EF (F = 42, $p = 0.0001$). This was also noted with the RF (F = 31, $p = 0.0001$). Unpaired Student *t* test showed no significant difference in the three grades of MR between the subgroups with a normal and low EF (Table 3). Using an MR Index ≥2.17 identified patients with severe MR with a sensitivity of 92%, specificity of 87%, positive predictive value of 79% and a negative predictive value of 95%.

Observer variability. The interobserver variability for the estimation of the qualitative grade of MR by two expert readers showed a concordance of 100%. In the testing of the interobserver variability in evaluation of the MR Index, the Index was identical in 21/30 patients (the score for each patient could vary between 0–18 [i.e., a total of six parameters each scored on a four point scale]). Furthermore, in the nine patients with a difference in the MR Index, there was a difference of only one grade for any variable, and the

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difference noted in the MR Index between observers was ±0.3.

Intraobserver variability in the MR Index for the same group of 30 patients showed a difference in 4 patients. Once again, there was a difference of only one grade for any single variable and the difference in the MR Index was ±0.3.

DISCUSSION

Evaluation of MR. The evaluation of MR must encompass the anatomy of the responsible lesion (i.e., the size of the regurgitant orifice) as well as the hemodynamic impact of the volume of regurgitant blood flow. Thus, to date, there has been no single satisfactory or reliable means of evaluating MR severity. Until a decade ago, angiographic grading of MR was considered the reference standard (15). However, its highly variable and subjective nature and the decreasing use of LV angiography has diminished its role (7,16,17). With the development and recent advances in echocardiography, noninvasive estimation of MR severity, (both quantitative and qualitative) has been gaining favor.

Quantitative echocardiographic measurements by two-dimensional Doppler flow imaging technique (18), calculation of regurgitant volume, fraction (4–8) and effective regurgitant orifice area (9–11) are well-documented methods. However, these techniques, although the mainstay of research studies, are seldom used clinically. In an era of cost containment in health care management, these time consuming and cumbersome techniques have even less likelihood of being incorporated into routine clinical practice.

As a standard practice, cardiologists rely on a qualitative estimation of MR severity that is often largely based on color flow characteristics of the regurgitant jet. Several other variables, including CW jet intensity and character, pulmonary venous flow patterns, left atrial dynamics and pulmonary artery pressure, are less often used. Qualitative assessment by expert readers has been used in several clinical studies as a reference standard and, though accurate, is inherently difficult to standardize (5,19).

Current practice for management of MR is aimed at early detection of hemodynamically significant MR with an aim towards surgical repair before development of significant left ventricular dysfunction (20–23). For all the previously cited reasons, the need to develop a relatively simple, easily reproducible and clinically applicable technique seems compelling.

The MR Index and the six variables used. In this study we developed a semiquantitative index that incorporates commonly recognized echocardiographic signs of MR severity. The MR Index is a composite of variables that reflect regurgitant volume (color jet penetration into the LA, CW regurgitant jet morphology and intensity); the PISA and the hemodynamic impact of MR (pulmonary artery pressure, pulmonary venous inflow pattern and LA size) (Table 1). Theoretically, this index could provide a more comprehensive evaluation of MR severity than obtained with any existing method. Color jet characteristics such as jet width (19,24–26), entrainment (27) and jet area (28,29) have previously been used as estimates of MR severity. Jet area, the parameter most commonly used in routine clinical practice, has not been found to be reliable (30,31). In recent years, the estimation of PISA and calculation of the effective regurgitant orifice area have been established as useful estimates of MR severity (9–11,32–34). However, there has been considerable variability in measurements with a noncircular orifice and with an eccentric jet (35,36) because of the geometric assumptions on which the calculations of regurgitant orifice area are based. The CW density of the regurgitant jet provides a qualitative estimation of regurgitant volume, but is highly subject to Doppler interrogation axial to the MR jet (37,38). Pulmonary artery pressure (39), pulmonary venous inflow patterns (40–44) and LA dynamics (45,46) have also been previously studied in estimating MR severity but are influenced by other conditions that affect LV diastolic pressure and compliance.

An important consideration in the development of the MR Index was to create a measure that could be easily applied. Thus, specific quantitative measurements like left atrial diameter or volume and systolic to diastolic pulmonary venous flow ratio were kept at a minimum. Although minimizing quantitation, objectivity was sought by using four precisely defined grades for each of the six variables (Table 1). This composite MR Index, by containing variability, attempts to standardize and quantitate an otherwise qualitative estimate as was demonstrated by the low interobserver variability. Thus, the index would facilitate comparison of serial studies when interpreted by different readers on different occasions.

Applying the MR Index. This study has shown that the proposed MR Index is an accurate reflection of MR severity. The MR Index increased with increasing severity of MR and showed significant differences among the three groups. Furthermore, a score greater than 2.17 identified patients with severe MR with a sensitivity of 90%, specificity of 88%, positive predictive value of 79% and negative predictive value of 94%. These predictive values were not affected by poor LV contractility (EF $<$ 50%). Each of the six variables were univariate predictors of the MR Index. However, on multiple regression analysis, pulmonary artery pressure was not a significant predictor, probably because it is influenced by additional factors independent of MR severity such as LA pressure and pulmonary vascular reactivity. Thus, although a univariate predictor, pulmonary artery pressure was not significant in a multiple regression analysis with factors that are influenced exclusively by the severity of MR. However, in clinical practice, the pulmonary artery pressure is an important factor taken into consideration for both the management and evaluation of MR. Hence, we retained this factor as part of the MR Index.

Reference standards. The reference standards used in this study were the qualitative grading of MR by an expert and the RF. Accuracy of qualitative estimations by an expert reader have been used previously (5,19) and have proved reliable. As a further indication of the validity of expert grading, 9 out of the 29 patients grouped in the severe MR category have gone on to have valve repair or replacement in the following one to two years, whereas none in the categories of mild or moderate MR (n = 56) required surgery. The RF is a well-accepted quantitative reference standard. The RF showed a significant difference among the three groups and post hoc tests showed significant differences among them. Thus, the new MR Index correlated significantly with both the qualitative and quantitative grades of MR used as reference standards in this study.

The results of the retrospective analysis of the MR Index are promising and suggest that it might be a useful tool in routine clinical practice. Its utility, however, needs to be further validated in prospective and longitudinal studies.

Study limitations.

1) There is no accessible nonechocardiographic method to quantify MR; as is common practice, we used qualitative echocardiographic grading by an expert reader and echocardiographic quantitation of RF as reference standards;
2) We were unable to make comparisons between the MR Index and the effective regurgitant orifice area as there was inadequate data for PISA measurement in patients with mild MR;
3) This study was retrospective and, as such, has inherent limitations;
4) Only patients with chronic MR were studied. The hemodynamics of acute MR may lead to different results and require further study;
5) All the patients studied were in sinus rhythm and therefore the applicability of the MR Index in patients with atrial fibrillation is not known;
6) We did not have an opportunity to compare reproducibility among echocardiographic instruments from different vendors;
7) This analysis consisted only of a study of MR in a resting patient at a particular point in time. Serial and exercise studies should provide additional dimensions to this index.

Conclusions. There is no single precise method for evaluation of MR. In patients with severe MR, particularly those with an eccentric jet, the commonly used parameters are difficult to obtain. The MR Index is a relatively simple semiquantitative estimate of MR severity which is potentially widely applicable in clinical practice as a simple technique for evaluating patients with hemodynamically significant MR and, more important, in their follow up over a period of time. Furthermore, with the Index expressly being a composite of six factors, it seems that errors in estimation of a single variable would be obviated by the other factors. The MR Index also appears to be useful, both in evaluating MR in patients with a low EF and also in those with an eccentric jet. Further longitudinal and clinical studies are needed to show if this index provides information useful in predicting the clinical course of patients with MR.

APPENDIX

PAP = TR gradient + right atrial pressure
RAP = 5 mm Hg: Diameter of IVC less than 18 mm but decreased by more than 50% with inspiration.
RAP = 10 mm Hg: Diameter of IVC more than 18 mm but decreased by more than 50% with inspiration.
RAP = 15 mm Hg: Diameter of IVC more than 18 mm but did not decrease by more than 50% with inspiration.
CW = continuous wave; PISA = proximal isovelocity surface area; PAP = pulmonary artery pressure; RAP = right atrial pressure; TR = tricuspid regurgitation.

Reprint requests and correspondence: Dr. Nelson B. Schiller, Moffitt Hospital, 505 Parnassus Avenue, University of San Francisco, San Francisco, California 94143-0214. E-mail: schiller@cardio.ucsf.edu.

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