Doppler Evaluation of Severity of Mitral Regurgitation: Relation to Pulmonary Venous Blood Flow Patterns in an Animal Study

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**Objectives.** This study examined the influence of regurgitant volume on pulmonary venous blood flow patterns in an animal model with quantifiable mitral regurgitation.

**Background.** Systolic pulmonary venous blood flow is influenced by atrial filling and compliance and ventricular output and by the presence of mitral regurgitation. The quantitative severity of the regurgitant volume itself is difficult to judge in clinical examinations.

**Methods.** Six sheep with chronic mitral regurgitation produced by previous operation to create chordal damage were examined. At reoperation the heart was exposed and epicardial echocardiographic performance. Pulmonary venous blood flow waveforms were recorded by pulsed Doppler under color flow Doppler guidance using a Vingmed 750 scanner. The pulmonary venous systolic inflow to the left atrium was expressed as a fraction of the total inflow velocity time integral. Flows across the aortic and mitral valves were recorded by electromagnetic flowmeters balanced against each other. Pressures in the left ventricle and left atrium were measured directly with high fidelity manometer-tipped catheters. Preload and afterload were systematically manipulated, resulting in 24 stable hemodynamic states.

**Results.** Simple logarithmic correlation between the regurgitant volume and size of a positive or negative pulmonary venous inflow velocity time integral during systole was good (r = -0.841). By stepwise linear regression analysis with pulmonary venous negative systolic velocity time integral as a dependent variable compared with the regurgitant volume, fractional shortening, left atrial v wave size, systemic vascular resistance and left ventricular systolic pressure, only contributions from v wave size and regurgitant volume (r = 0.80) reached statistical significance in determining pulmonary venous negative systolic flow.

**Conclusions.** Evaluation of systolic pulmonary venous blood flow velocity time integral can give valuable information helpful for estimating the regurgitant volume secondary to mitral regurgitation.

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were recorded simultaneously. All hemodynamic recordings were performed during angiographic studies. After baseline measurements, the severity of mitral regurgitation was changed by altering preload or afterload, or both (blood transfusion or angiotensin infusion, or both). Before each and every hemodynamic/Doppler study state, the animals' hematocrits were determined. The calibrations of the flow probes were readjusted, compensating for any changes in hematocrits by insensible fluid loss, blood loss or alterations of the preload by the blood transfusions. Approximately 1 h time lapsed after termination of cardiopulmonary bypass, permitting stabilization of the animals' hemodynamic status before initiating hemodynamic and echocardiographic studies. For each hemodynamic study state, angiotension infusions and blood transfusions were titrated to end points such that stable mean left atrial pressure elevations of 3 to 5 mm Hg were obtained. Left atrial pressures were monitored continuously. A total of 24 stable hemodynamic states (3 to 5/sheep) were obtained.

**Doppler echocardiography.** All Doppler recordings were performed with a Vingmed 750 system interfaced with a Macintosh Iici computer (Vingmed Sound A/S, Oslo, Norway). Epicardial scanning was performed with a 5-MHz transducer. The probe was positioned at the posterior and lateral wall of the left atrium, taking care not to compress the atrium. The venous blood flow patterns from the right pulmonary veins were recorded by pulsed wave Doppler with the 2-mm long sampling volume placed 5 to 10 mm inside a pulmonary vein orifice (Fig. 1). In all sheep the pulmonary venous blood flow waveforms from the right-sided pulmonary veins could be recorded. Spectral velocity records were traced through the modal velocities for measurements. To quantitate pulmonary venous flow we developed an index wherein the systolic pulmonary flow velocity time integral was expressed as a fraction of the total forward pulmonary vein flow velocity time integral (Fig. 2). In sheep with primarily positive pulmonary vein inflow during systole, the velocity time integral of the systolic inflow was divided by the total velocity time integral to produce a systolic inflow index. In sheep with a period of primarily reversed pulmonary vein systolic flow, the index was given a negative value and expressed as the systolic inflow divided by the diastolic inflow (Fig. 2). Left ventricular shortening fraction was estimated from short axis two-dimensional echocardiographic recordings of the left ventricle. The echo scanner system settings remained constant during the study. All ultrasound recordings were digitally transferred to the Macintosh computer using the system Asta Port for off-line analysis. For all values, 3 beats were averaged.

**Interobserver variability.** The ratios of the velocity time integral of the systolic inflow to the total velocity time integral were calculated by two observers. Interobserver differences were calculated as the difference between the two observers divided by the mean of the observers.

**Statistical analysis.** To evaluate quantitative changes, mean values and standard deviations were calculated to express descriptors of mitral regurgitation severity. Simple linear and stepwise linear and logarithmic regression analyses were used to relate pulmonary vein flow patterns to the severity of mitral regurgitation. To investigate the least subset of statistically significant contributing factors to the systolic inflow ratio,
we used a forward stepwise regression procedure from a statistical computer program (Stat View 1988, Abacus Concepts, Inc.). The systolic inflow ratio was used as the dependent variable (Y), and the regurgitant volume, fractional shortening, magnitude of the v wave, pulmonary and systemic vascular resistance and left ventricular peak systolic pressure were used as independent variables (X₁₋₆). The value of $F$ to enter was set at 4.0.

**Results**

Quantitation of regurgitation with the electromagnetic flow probes indicated clinically relevant regurgitant flows: Mean regurgitant flow rates ranged from 0.19 to 2.41 liters/min (mean 1.18, SD 0.59), regurgitant volume/beat ranged from 1.8 to 29.0 ml/beat (mean 11.0, SD 6.2); peak regurgitant flow rates were from 1.0 to 8.1 liters/min (mean 3.5, SD 2.1); regurgitant fractions varied from 0.08 to 0.54 (mean 0.29, SD 0.12). A moderate negative correlation was found between mean left atrial pressure and pulmonary systolic inflow ratio ($r = -0.52$). However, there was a close correlation between the mean left atrial pressure and v wave size ($r = 0.95$).

Using a logarithmic regression between the regurgitant volume/beat and pulmonary systolic inflow index, a strong negative correlation with a correlation coefficient of $-0.81$ (SEE 0.08) was found, ranging from those hemodynamic states with a positive flow fraction extending to those sheep with reversed systolic flow (Fig. 3).

Correlations between pulmonary venous flow index and left atrial v wave, pulmonary vascular resistance, left ventricular systolic pressure and forward stroke volume were poor ($r = 0.52$ [p = 0.009], 0.48 [p = 0.02], 0.03 [p = 0.9] and 0.40 [p = 0.05], respectively).

By stepwise linear regression analysis with the systolic inflow ratio as the dependent variable compared with regurgitant volume, fractional shortening, magnitude of the v wave, pulmonary and systemic vascular resistance and left ventricular peak systolic pressure, only regurgitant volume and v wave magnitude were significantly related ($r = 0.80$). The mean...
percent interobserver variability for measurement of the pulmonary venous systolic inflow index was 4%.

Discussion

A critical problem in the evaluation of mitral regurgitation is that there is no clinically applicable method whereby regurgitant volume itself can be measured reliably. Left ventricular angiography has achieved the role of a reference standard despite it being obviously a semiquantitative method (1). Comparison of any noninvasive index of regurgitation (e.g. Doppler echocardiography and ventriculography) is therefore problematic. Several studies of Doppler-derived pulmonary venous blood flow patterns in patients with mitral regurgitation or mitral stenosis, or both, have recently been reported (7-11). In some studies only a part of the study group was examined invasively; in others the interval between invasive and noninvasive measurements was prolonged (6-12). Patterns of pulmonary venous blood flow are influenced by several factors, including regurgitant volume, left atrial compliance, left ventricular systolic and diastolic function, systolic blood pressure and peripheral vascular resistance. In one study (13) a relation between Doppler-derived pulmonary venous blood flow patterns and mean pulmonary wedge pressure was found. In the present study a moderately negative correlation between mean left atrial pressure and systolic inflow index was found. However, left atrial v wave pressure, which was closely related to mean left atrial pressure (r = 0.95), still correlated poorly with degree of mitral regurgitation (14).

Pulmonary venous blood flows from the pulmonary veins into the left atrium during both ventricular systole and diastole (15,16). The ratio of flow during ventricular systole to that during ventricular diastole is approximately 2:1 under normal conditions (3). In patients with severe mitral regurgitation, reversed systolic flow can be seen by angiography, providing a criterion for grade 4 regurgitation (17). In patients with moderate regurgitation, the total flow into the left atrium during ventricular systole is reduced (11,12). These flow alterations can be determined by Doppler echocardiographic examinations. However, recording pulmonary venous blood flow by pulsed Doppler techniques using the transthoracic approach is difficult in a large proportion of adult patients. With transesophageal echocardiography using transverse plane probes, the pulmonary venous blood flow patterns from the left upper vein can be recorded in nearly all patients. With biplane or multiplane transesophageal transducers, recordings of the flow from the other veins is also possible, and differences in right versus left pulmonary vein patterns have been reported (8) with eccentric mitral regurgitant jets. The influence of the direction of the regurgitant jet on the pulmonary blood flow patterns was not systematically examined in the present study. Our access to placing the transducer on the heart in this study provided best sampling of mainly the right pulmonary veins. The mitral regurgitant jets by color Doppler had variable directions. However, in one sheep, where we extended the incision late in the experiment, the jet was observed by color Doppler to enter directly into the orifice of a left pulmonary vein, and a prominent short reversed systolic flow could be recorded in that vein. At the same time there was continued low velocity systolic inflow from the right pulmonary veins into the left atrium such that a decreased index, but with a positive value, was calculated. The distortion of the atrium necessary to
image the left pulmonary veins precluded our making quantitative measurements during left vein sampling.

**Present study.** We used an animal model to directly compare a Doppler index of mitral regurgitation with regurgitant volume measured by intracardiac and extracardiac electromagnetic flow probes. By calculating the index as shown in Figure 2, a descriptor of the pulmonary venous inflow was available, which varied from dominant positive systolic inflow in minimal regurgitation to reversed systolic flow with forward inflow only in diastole in severe mitral regurgitation. A close negative correlation was found between the regurgitant volume and systolic pulmonary venous blood flow index using logarithmic correlation. The use of logarithmic correlation seemed reasonable because the index can be expected to approach −1 as the volume of regurgitation increased. The finding of systolic inflow indexes approaching −1 (indicating that the pulmonary vein reversed flow approaches the forward flow) has two possible explanations: 1) In situations of reversed systolic flow, the cross-sectional area of the pulmonary veins may increase during ventricular diastole when the total inflow to the left atrium occurs; and 2) the angle between the Doppler beam and the direction of flow may change during the cardiac cycle. Otherwise, if reversed flow equaled forward flow in all veins, there would be no significant net forward inflow.

By stepwise linear regression analysis, using the negative pulmonary vein systolic velocity time index as the dependent variable, regurgitant volume and magnitude of the v wave were found to be significantly correlated. The magnitude of the v wave, besides reflecting volume of regurgitant flow, reflects left atrial compliance. Left ventricular function expressed as fractional shortening, systolic arterial blood pressure and systemic vascular resistance was found not to influence the index significantly.

**Study limitations.** Ventricular compliance data were not obtained in this study, although such data may obviously affect the pulmonary venous flow patterns (13). Although our sheep did have chronic mitral regurgitation with the adaptive changes commensurate with compensated hemodynamic states, it is true that multiple data points for each individual animal were obtained by acute hemodynamic alterations. Thus, a poorer correlation between pulmonary venous flow index and severity of mitral regurgitation might be obtained after long-term adaptation.

We created mitral regurgitation in sheep by severing the anterior or posterior chords, resulting in eccentric jets directed posteriorly or anteriorly rather than rightward or leftward directly into veins. For technical reasons of Doppler ultrasound alignment, the Doppler flow velocities were sampled only in the right pulmonary veins. However, we cannot rule out effects due more directly to jet direction on pulmonary vein flow patterns.

**Conclusions.** Pulmonary vein systolic inflow index closely reflects regurgitant volume in mitral regurgitation. This index may be determined from Doppler measurements recorded by transesophageal and, sometimes, transthoracic techniques, and it should be included in the clinical evaluation of patients with mitral regurgitation. Because the recordings are performed with pulsed Doppler, it should be less system and operator dependent than color flow mapping.

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**References**


