Factors Influencing Pulmonary Venous Flow Velocity Patterns in Mitral Regurgitation: An In Vitro Study

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Objectives. The aim of this study was to investigate factors affecting pulmonary venous flow patterns in mitral regurgitation.

Background. Although pulmonary venous flow velocity patterns have been reported to be helpful in assessing the severity of mitral regurgitation, the influence of regurgitant jet direction, pulmonary venous location and left atrial pressures on pulmonary venous flow patterns has yet to be clarified.

Methods. The mitral regurgitant jet was produced by a pulsatile piston pump at 10, 30 and 40 ml/beat through a circular orifice, whereas the pulmonary venous flow was driven by gravity. Four different patterns of pulmonary venous flow and mitral regurgitation were examined. The V wave pressure was set at 10, 30 and 50 mm Hg and pulmonary venous flow velocity at 30 cm/s. Color and pulsed Doppler recordings were obtained with a VingMed 800 scanner interfaced with a computer facilitating digital analysis.

Pulmonary venous flow velocity patterns obtained by pulsed wave Doppler echocardiography have been reported to be helpful in assessing the severity of mitral regurgitation (1-7). Unfortunately, no truly quantitative study comparing pulmonary venous flow with regurgitant severity has been reported, and the influence of regurgitant jet direction, pulmonary vein location and left atrial pressures on pulmonary vein flow patterns still remain to be clarified. Initially, some investigators have suggested (1) that the direction of the mitral regurgitation jet in severe mitral regurgitation relative to the pulmonary vein does not significantly influence systolic pulmonary venous flow pattern and stressed the applicability of this method mainly for predicting severe mitral regurgitation. However, others (3.5) have stated that the effect of the mitral regurgitant jet on the pulmonary venous flow pattern in individual veins depends on the direction of mitral regurgitation.

To our knowledge, no in vitro studies on the relation between pulmonary vein flow pattern and direction of mitral *Results.* The decrease in the velocity time integral of pulmonary venous flow was more prominent for any given volume of mitral regurgitation at higher left atrial pressure. When the mitral regurgitant jet was directed toward the pulmonary vein, a more prominent decrease in the velocity time integral was seen, especially for severe mitral regurgitation (40 ml) with high left atrial pressure (95% vs. 55%, p < 0.001); and the time to peak deceleration of forward flow was significantly shorter (485 vs. 523 ms, respectively, p < 0.01). Also, two different types (laminar and turbulent) of reversed pulmonary venous flow were observed.

Conclusions. Multiple factors, including jet direction, mitral regurgitant volume and left atrial pressure, determine the effect of mitral regurgitation on pulmonary venous flow velocity patterns. (J Am Coll Cardiol 1995;26:1333-9)

regurgitation have been performed to clarify these issues. Thus, we undertook the present study to investigate the effect of mitral regurgitant jet direction relative to the location of pulmonary veins on pulmonary venous flow velocity and also to study other factors that might influence mitral regurgitant flow-pulmonary vein flow interactions.

Methods

In vitro flow model. The model consisted of a rigid acrylic chamber designed to serve as the left atrium. The left atrial chamber was in the shape of a cylinder of 7.6 cm in diameter with height of 13 cm and a volume of 320 ml. A circular window made of polycarbonate in the chamber allowed imaging by color Doppler echocardiography (Fig. 1). The flexible outflow tubing could be variably constricted to vary outflow resistance and to change left atrial chamber pressure. The effect of left atrial chamber peak V wave pressure of 10, 30 and 50 mm Hg on pulmonary venous flow and mitral regurgitant jet flow interactions was examined. This pressure is hereinafter referred to as *left atrial pressure*.

The pulmonary vein orifice was circular in shape, with a 1.0-cm diameter (0.79-cm² orifice area), and pulmonary venous flow could be directed toward the mitral valve, as in a lower pulmonary vein, or away from the mitral valve, as in an upper pulmonary vein. Pulmonary venous flow was at an angle of 30° from the left atrial chamber wall. The mitral

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Figure 1. Diagram of the experimental model: gravity-driven pulmonary flow system.

valve regurgitant orifice was circular in shape, with a 0.15-cm² area. The pulmonary vein and mitral regurgitant orifice were located 7 cm apart from each other along the round left atrial wall at the same level. Figure 2 shows the horizontal cut plane of this level of the model. Mitral regurgitant flow was directed toward or away from the pulmonary vein. Four different conditions with respect to the relative directions between pulmonary venous flow and the mitral regurgitant jet were studied in the in vitro model (Fig. 2).

We produced three different mitral regurgitant volumes (10, 30 and 40 ml) with similar pulsatile waveforms for mimicking mild, moderate or severe mitral regurgitation using a pulsatile flow pump (Harvard piston pump, model 1423). The mitral regurgitant peak velocity ranged from 2.5 to 8.0 m/s. The frequency (heart rate) was kept constant (68 beats/min, 882-ms cycle length). The reservoir contained 1% cornstarch particle/water solution to produce physiologic ultrasound reflections.

Pulmonary venous flow was driven by gravity by placing a reservoir 120 cm above the pulmonary vein orifice, which was connected to a steady flow pump. Baseline pulmonary venous flow velocity was kept constant at 30 cm/s using the steady flow pump to fill the reservoir to a level that would maintain baseline flow velocity constant when the left atrial chamber pressure was altered.

Color and pulsed Doppler echocardiography. Flow patterns in the pulmonary vein were examined and recorded using a VingMed 800 scanner with a 5.0-MHz transducer. The echocardiographic system was interfaced with a Macintosh IIci computer that facilitated digital analysis. Pulsed wave Doppler echocardiography was used to determine the pulmonary venous flow pattern with the sample volume placed 2.0 cm inside the pulmonary vein. The sample volume length was 0.1 cm.

The timing of the ejection phase of the pulsatile pump was displayed and recorded by generating an electric signal—a simulated electrocardiogram that was superimposed on the pulsed wave Doppler record to determine the relation between mitral regurgitant timing and pulmonary venous flow changes.

To analyze pulmonary venous flow patterns (Fig. 3), we

Figure 2. Diagram showing four different combinations of mitral regurgitation and pulmonary venous flow directions in the horizontal plane of the in vitro left atrial model.





Figure 3. Illustration of method for measuring the lowest value of pulmonary vein flow velocity (arrows). DT = deceleration time; t = time; v = velocity; VTI = velocity time integral.

evaluated the lowest value of the pulmonary venous flow velocity during the cycle and the velocity time integral of the pulmonary venous flow and measured the percent change compared with the baseline pulmonary venous flow velocity time integral (without mitral regurgitation). We measured also the time to peak deceleration of pulmonary venous flow to its lowest value of reversed velocity as a measure to investigate the effect of mitral regurgitant direction on the timing of the maximal influence of mitral regurgitation on pulmonary venous flow (Fig. 3). At least three tracings were measured and averaged for each measurement point.

Interobserver and intraobserver variability. Doppler tracings of pulmonary venous flows were measured by two independent observers. Two days later, one observer remeasured the same images without reviewing the first measurements. Interobserver and intraobserver variability was calculated as the difference between the two observations divided by the mean of the two observations.

Statistical analysis. The difference in pulmonary venous flow velocity change due to the direction of pulmonary venous flow and mitral regurgitant jets, changes in left atrial pressure, mitral regurgitant volume, pulmonary venous flow velocity and sample volume distance into the pulmonary vein orifice were analyzed by one-way analysis of variance and a Bonferroni *t* test for matched conditions. Statistical significance was defined as p < 0.05.

Results

Effect of mitral regurgitant volume on pulmonary venous flow (Table 1). Summary of data from conditions 1 and 2 averaged. At a left atrial chamber V wave pressure of 10 mm Hg for the smallest mitral regurgitant volume (10 ml), the velocity time integral decreased only $4.1 \pm 0.6\%$ (mean \pm SD) from baseline. At the same left atrial pressure, the decrease in velocity time integral was significantly greater when mitral regurgitant volume was increased to 30 or 40 ml (12 \pm 1.2% and 17 \pm 1.8%, respectively). At atrial chamber pressures of both 30 and 50 mm Hg, progressive increases in regurgitant volume led to progressive decreases in the velocity time integral and the velocity of the pulmonary venous flow (Tables 1 and 2).

Effect of left atrial pressure on pulmonary venous flow velocity. A statistically significant difference (p < 0.0001) between left atrial pressures of 10, 30 and 50 mm Hg with respect to both the lowest value of velocity and the decrease in the velocity time integral of pulmonary venous flow velocity was observed (Tables 1 and 2). The higher the left atrial pressure, the more severe the effect on the decrease in velocity and on the velocity time integral of pulmonary venous flow.

Effect of mitral regurgitant jet directions on pulmonary venous flow velocity. Of the four spatial conditions of pulmonary venous flow and regurgitant jet direction, a greater decrease in the velocity time integral was observed when mitral regurgitation was aimed at the pulmonary vein orifice, especially when the higher volume of mitral regurgitation (40 ml) was combined with high left atrial pressure (conditions 1 and 2), than when it was directed away from the pulmonary vein (conditions 3 and 4) (95 \pm 4.6% for conditions 1 and 2 vs. $55 \pm 3.4\%$ for conditions 3 and 4, p < 0.001). Furthermore, the time to peak deceleration in the pulmonary vein was also significantly shorter in conditions 1 and 2 (485 \pm 12 vs. 523 \pm

MR Volume (ml)	LA Pressure (mm Hg)	Condition 1 (%)	Condition 2 (%)	Condition 3 (%)	Condition 4 (%)
10	10	4.1 ± 0.7	4.2 ± 0.5	6.3 ± 1.2	3.7 ± 0.5
	30	8.0 ± 0.9	11 ± 0.8	10 ± 1.1	13 ± 1.2
	50	30 ± 1.5	26 ± 1.2	22 ± 1.1	23 ± 1.2
30	10	10 ± 0.9	14 ± 1.6	8.1 ± 1.0	13 ± 1.2
	30	22 ± 2.0	19 ± 2.0	18 ± 1.6	21 ± 1.9
	50	68 ± 2.5	54 ± 2.2	49 ± 2.1	50 ± 2.2
40	10	16 ± 1.3	19 ± 2.0	17 ± 1.6	16 ± 1.0
	30	26 ± 1.1	24 ± 1.4	25 ± 2.1	24 ± 1.9
	50	96 ± 4.2	93 ± 4.8	54 ± 3.1	56 ± 3.5

 Table 1. Percent Decrease in Velocity Time Integral of Pulmonary Venous Flow Caused by Mitral Regurgitation*

*Values given in text highlight conditions 1 and 2 and may differ from table averages as a function of variable number of observations. Data presented are mean value \pm SD, unless otherwise indicated. LA = left atrial; MR = mitral regurgitation.

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AR Volume (ml)	LA Pressure (mm Hg)	Condition 1 (cm/s)	Condition 2 (cm/s)	Condition 3 (cm/s)	Condition 4 (cm/s)
10	10	29 ± 1.0	29 ± 3.9	28 ± 2.1	29 ± 2.0
	30	26 ± 1.3	25 ± 2.0	25 ± 1.8	23 ± 1.3
	50	10 ± 1.2	11 ± 1.0	13 ± 1.2	13 ± 1.0
30	10	25 ± 1.8	20 ± 1.2	26 ± 1.9	21 ± 1.0
	30	17 ± 1.7	18 ± 1.0	19 ± 1.2	18 ± 1.3
	50	3.2 ± 0.9	5.5 ± 0.5	6.3 ± 0.9	6.2 ± 0.5
40	10	21 ± 1.8	18 ± 1.9	21 ± 2.0	20 ± 2.5
	30	15 ± 1.4	17 ± 1.5	16 ± 1.3	15 ± 1.9
	50	-60 ± 4.1	-55 ± 3.2	5.0 ± 0.9	4.1 ± 0.7

 Table 2. Lowest Value of Pulmonary Venous Flow Velocity in the Presence of Mitral Regurgitation for All Combinations

Data presented are mean value \pm SD, unless otherwise indicated. Abbreviations as in Table 1.

18 ms for conditions 3 and 4, p < 0.01) (Table 3). However, no significant difference in the pulmonary vein flow patterns resulted from the direction of pulmonary venous flow with respect to the mitral regurgitant jet (i.e., conditions 1 and 3 vs. conditions 2 and 4).

Reversed pulmonary venous flow. Significantly prolonged reversed pulmonary venous flow was observed only in conditions 1 and 2, in which mitral regurgitation was directed toward the pulmonary vein with the largest mitral regurgitant volume and highest left atrial pressure. As demonstrated in Figure 4, two different types of reversed pulmonary venous flows were observed: 1) Laminar flow appeared early in "systole," seemingly coincident with the V wave pressure increase (Fig. 4, panel 6); and 2) turbulent and variance-encoded flow due to direct penetration of mitral regurgitant flow into the pulmonary vein (Fig. 4, panels 7 and 8).

Position of sample volume. When the pulsed wave Doppler sample volume was positioned further inside the pulmonary vein, the magnitude of changes in pulmonary venous flow velocity due to the mitral regurgitant jet decreased significantly (p < 0.0001). At 50-mm Hg left atrial chamber pressure, an inverse linear relation between the distance of the sample volume from the pulmonary vein orifice into the pulmonary vein and the percent decrease in the velocity time integral was seen (r = 0.98).

Variability of measurements. The interobserver variability for pulsed wave Doppler pulmonary venous flow velocity time

Table 3. Deceleration Time of Conditions 1 and 2 and Conditions 3 and 4^*

MR Volume (ml)	Conditions 1 and 2 (mean \pm SD)	Conditions 3 and 4 (mean ± SD)
10	$375 \pm 18 \text{ ms}$	395 ± 19 ms
30	$390 \pm 24 \text{ ms}$	$415 \pm 19 \text{ ms}$
40	$485 \pm 12 \text{ ms}^{\dagger}$	$523 \pm 18 \text{ ms}$

*Times are for pulmonary venous flow for variably directed mitral regurgitation (MR) at 50-mm Hg peak V wave pressure. $\dagger p < 0.01$ versus conditions 3 and 4.

integral measurements was 5.6 \pm 3.6%; intraobserver variability was 4.7 \pm 3.4%.

Discussion

Although pulmonary venous flow can be sampled from precordial studies, transesophageal echocardiography has increased the yield rate of high quality traces, providing the opportunity to assess pulmonary venous flow in normal subjects (8) and in patients with various cardiac conditions (1,3,5-7,9-12). Several studies (2,3,5,7) have reported the importance of reversed systolic flow in identifying severe mitral regurgitation.

Effect of left atrial pressure on pulmonary venous flow. Klein et al. (3), using transesophageal echocardiography, reported that patients with mitral regurgitation showed an inverse relation between the systolic/diastolic flow ratio and left atrial V-wave pressure. The same study (3), as well as other studies by Chen et al. (9) and Klein et al. (10) using transesophageal echocardiography in patients with mitral stenosis, also demonstrated an inverse relation between left atrial pressure and systolic pulmonary flow velocity. However, in the original study by Klein et al. (3), it was impossible to separate the two factors influencing the pulmonary venous flow pattern (i.e., mitral regurgitant volume and left atrial pressure) because as usually observed in clinical conditions, patients with severe mitral regurgitation often had a higher left atrial pressure. In the study by Chen et al. (9), no patient had severe or even moderate mitral regurgitation. Therefore, the relation between mitral regurgitant volume and left atrial pressure with respect to the influence on the pulmonary venous flow pattern could not be studied. To our knowledge, no in vitro study has been performed to investigate this issue. The present in vitro study demonstrated that when left atrial ambient pressure, and, accordingly V wave pressure, was increased from 10 to 30 and to 50 mm Hg, the decrease in the velocity time integral was more prominent for any given volume of mitral regurgitation. The results of the present study therefore aid understanding of these clinical reports.

Direction of mitral regurgitant jet. Some investigators initially reported that the direction of the mitral regurgitant jet



Figure 4. Pulsed and color Doppler echocardiographic images of pulmonary venous (PV) flow and mitral regurgitant (MR) jet (condition 2) in severe mitral regurgitation, with highest left atrial pressure at 10 sequential points in a cycle, showing two different types of reversed pulmonary venous flows (sequences 7 and 8). See text for further discussion.



Figure 5. Clinical transesophageal echocardiographic recordings of left (top) and right (bottom) upper pulmonary venous flow velocity patterns in a patient with moderate to severe mitral regurgitation directed toward the left. Note the difference in deceleration time. Earlier deceleration and reversal of systolic flow were observed only in left upper pulmonary venous flow when mitral regurgitation was directed toward the left. Top, mitral regurgitation directed toward the pulmonary vein; bottom, mitral regurgitation directed away from the pulmonary vein.

in severe mitral regurgitation did not significantly influence the systolic pulmonary venous flow pattern, whereas Klein et al. (7) first demonstrated that the effect of the mitral regurgitation jet on the pulmonary venous flow pattern depended on the direction of the mitral regurgitation. In the clinical setting, it is sometimes difficult to visualize the actual direction of eccentric mitral regurgitant jets in relation to the pulmonary veins (7). Thus, we thought that an investigation using an in vitro setting might be helpful in understanding the effect of mitral regurgitant jet direction. In our study, the direction of the mitral regurgitant jet had a statistically significant influence on the velocity time integral of pulmonary venous flow velocity only when mitral regurgitation was more severe (40 ml). This more prominent decrease in the velocity time integral could be explained by "asymmetry" of left atrial pressure adjacent to the pulmonary vein caused by the mitral regurgitant jet moving toward the pulmonary vein orifice. In addition, when the mitral regurgitant jet was directed toward the pulmonary vein, the

peak effect of the decrease in pulmonary venous velocity occurred earlier than when mitral regurgitation was directed away from the pulmonary vein. To our knowledge, the observation of this time delay of the peak effect in deceleration has not been reported in the clinical setting. However, using transesophageal echocardiography, we found clinical examples of this time delay, as shown in Figure 5. The delay of the peak effect of the mitral regurgitant jet on the decrease in pulmonary venous flow velocity could be explained by the localized differences in pressure distribution of short duration inside the left atrium during systole.

Importance of reversed pulmonary venous flow. Reversed pulmonary venous flow has been reported (2,3,5,7) to be helpful in identifying severe mitral regurgitation. However, in our in vitro study significant reversed flow was observed only when mitral regurgitation was directed toward the pulmonary vein, with the largest mitral regurgitant volume and highest left atrial pressure. In clinical settings, severe mitral regurgitation is closely associated with higher left atrial pressure (3,6,7). Thus, it could be difficult to separate these two factors. From our results, one might conclude that when a reversed systolic flow was observed clinically, the patient would be expected to have both severe mitral regurgitation and a high left atrial V wave pressure.

Two different types of reversed pulmonary venous flows were observed in our model. Figure 4 shows the phase change of pulmonary venous flow during the whole cycle and shows these two reversed flows: Early laminar backflow was caused by the high left atrial pressure, and the other, later, turbulent reversed flow was caused by the direct intrusion of the mitral regurgitation jet into the pulmonary vein. This finding may be helpful in identifying the relative contributions of direction and severity of mitral regurgitation.

Our study showed that left atrial pressure and the direction of the mitral regurgitant jet were significant factors in decreasing pulmonary venous flow velocity when mitral regurgitation was significant. Evaluation of the pulmonary venous flow velocity pattern by Doppler echocardiography may thus be applicable both for estimating left atrial pressure and for assessing the severity of mitral regurgitation in clinical situations.

Limitations of the study. Some oversimplification of physiology was inevitable in our in vitro model: 1) Because the left atrial chamber did not relax or contract, compliance of the left atrial chamber was unphysiologic, and there was no suctioning from the left ventricle. Thus, a physiologic pressure-volume curve could not be obtained with this model. However, the present in vitro model may simulate a patient with chronic mitral regurgitation and a left atrium that is dilated but still relatively noncompliant. 2) In our study, only one pulmonary vein entered the left atrium, and this flow was a steady flow driven by gravity. Clinically, normal pulmonary venous flow without mitral regurgitation has two or three peaks per cardiac cycle (2,8). It would have been ideal to have at least two pulmonary veins, both with pulsatile flow. However, two pulsatile flows at the same time, would be difficult to simulate physiologically, especially because pulmonary vein flow is both

driven and "sucked" forward. Even though the pulmonary venous flow was driven by gravity, the waveforms observed in our in vitro pulmonary veins were physiologic in the presence of mitral regurgitation. Because the mitral regurgitant velocity and volume and pulmonary venous flow velocity were similar to those in the clinical setting, the effects of mitral regurgitation on the pulmonary venous flow observed in our study should not be very different from those observed clinically. 3) We used only a simple, single circular orifice to simulate mitral regurgitation. Because the direction and propagation of the jet would be affected by the orifice geometry, and a wide variety of orifice geometries are encountered clinically, our model might be too simple to simulate the wide variety of patterns found in clinical conditions. However, the results from our study model could be useful in understanding the basic effects of the mitral regurgitant jet on pulmonary vein flow pattern.

Conclusions. The present in vitro study demonstrated that multiple factors, including jet direction, mitral regurgitant volume and left atrial pressure, determine the effect of mitral regurgitation on pulmonary venous flow velocity. These factors compound simple assessment and require some sampling of pulsed Doppler patterns in multiple pulmonary veins when performing clinical studies.

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