Accurate Measurement of the Transmirtal Gradient in Patients With Mitral Stenosis: A Simultaneous Catheterization and Doppler Echocardiographic Study

RICK A. NISHIMURA, MD, FACC, CHARANJIT S. RIHAL, MD, A. JAMIL TAJIK, MD, FACC, DAVID R. HOLMES, Jr., MD, FACC
Rochester, Minnesota

Objectives. This study compared the accuracy of Doppler echocardiography with that of conventional cardiac catheterization in the measurement of transmitral gradients in patients with mitral stenosis.

Background. Simultaneous measurement of left atrial and left ventricular pressures is the most accurate method for determination of the mean mitral valve gradient in patients with mitral stenosis. Because of the inherent risks of transseptal catheterization, pulmonary capillary wedge pressure has been used in many invasive laboratories for determination of the mean mitral valve gradient. Recent studies have observed significant errors when pulmonary capillary wedge pressure was used for these measurements. Doppler echocardiography provides a noninvasive alternative for measurement of the transmitral gradient, but its relative accuracy has remained unclear.

Methods. Seventeen patients with mitral stenosis who underwent transseptal cardiac catheterization had simultaneous measurement of 1) transmitral gradient by direct left atrial and left ventricular pressures, 2) transmitral gradient by pulmonary capillary wedge and left ventricular pressures, and 3) transmitral gradient by Doppler echocardiography.

Results. Transmirtal gradient measured by pulmonary capillary wedge and left ventricular pressures significantly overestimated the gradient obtained by direct measurement of left atrial pressure, with a mean (±SD) difference of 3.3 ± 3.5 mm Hg (or 53%). Correcting the pulmonary capillary wedge pressure for the phase shift resulted in better correlation, but a consistent overestimation still remained, with a mean difference of 2.5 ± 2.9 mm Hg (or 43%). The best correlation with the smallest variability was comparison of the Doppler-derived mean gradient with the gradient from direct measurement of left atrial and left ventricular pressures, with a mean difference of 0.2 ± 1.2 mm Hg.

Conclusions. Compared with the transmitral gradient obtained by direct measurement of left atrial and left ventricular pressures, the Doppler-derived gradient is more accurate than that obtained by conventional cardiac catheterization and should be considered the reference standard.

(J Am Coll Cardiol 1994;24:152-8)
illary wedge pressure) for determination of the transmitial
gradient in patients with mitral stenosis, comparing each
method with simultaneous, direct measurements of left atrial
and left ventricular pressures.

Methods

Patients. The study group included 17 patients with mitral
stenosis who underwent transseptal catheterization (14
women, 3 men; mean age 62 years, range 34 to 82). Of these,
12 patients had a percutaneous mitral balloon valvuoplasty
procedure, and five had the transseptal procedure as part of
diagnostic catheterization study. The study was approved
by the Institutional Review Board of this institution, and
informed consent was obtained from each patient. All pa-
tients had the previous diagnosis of mitral stenosis by
physical examination and echocardiography, and all had
transesophageal echocardiography to exclude left atrial
thrombus before transseptal catheterization. Nine patients
were in atrial fibrillation, and the remaining eight patients
were in normal sinus rhythm.

Catheterization procedure. Catheterization was per-
formed in the fasting state. A right femoral access site was
used in all patients, and a 6F or 7F pigtail catheter was
placed retrogradely into the left ventricle for fluid-filled
catheter measurement of left ventricular pressure. Care was
taken to avoid catheter overdamping and underdamping,
and the shortest possible transducer connection was
used. Pulmonary capillary wedge pressure was measured
with a balloon-tipped thermodilution catheter in 12 patients
and a 7F Lehmann catheter in the remaining five patients.
For each patient, the catheter was placed into the most
peripheral portion of the pulmonary artery tree until a
pulmonary capillary wedge pressure contour was obtained
(6). In the five patients undergoing right heart catheteri-
ization with the Lehmann catheter, confirmation of the wedge
position was obtained with a saturation >95% (6). In the 12
patients undergoing right heart catheterization with the
balloon-tipped catheter, saturations were not obtained be-
cause of concern for potential pulmonary artery erosion (12).

The Brockenbrough technique (13) was used to perform
transseptal catheterization in all patients. An 8F transseptal
sheath was used, and the transseptal puncture was per-
formed under fluoroscopic biplane imaging. After confirma-
tion that the transseptal catheter tip was in the left atrium,
5,000 U of heparin was given, and left atrial pressure
measurements were made directly from the sheath placed in
the midportion of the left atrium. All three pressures (left
atrial, pulmonary capillary wedge and left ventricular) were
recorded simultaneously.

Doppler echocardiography. A continuous wave Doppler
echocardiographic procedure was performed during the
catheterization with use of either a Hewlett-Packard or an
Acuson echocardiographic instrument. A small, nonimaging,
2.0-MHz continuous wave transducer was placed at the left
ventricular apex, and the continuous wave Doppler beam
was directed through the mitral valve apparatus until the
highest velocity with the cleanest spectral display envelope
was obtained. The left ventricular, left atrial and pulmonary
capillary wedge pressures were recorded simultaneously on
the Doppler spectral display, and a hard-copy printout was
made at a speed of 100 mm/s.

Analysis. A blinded, off-line analysis was performed of
the catheterization pressures and Doppler velocity curves
from the hard-copy printout with use of a Jandel scientific
digitizing tablet (14). One cardiac cycle with a clean Doppler
spectral display was selected from which the simultaneous
pressures and Doppler velocities were digitized. Left atrial,
pulmonary capillary wedge and left ventricular pressures
were digitized at 20-ms intervals. The left atrial/left ventricu-
lar mean diastolic gradient was determined by obtaining the
average of the difference between the instantaneous left
ventricular and left atrial pressures at each interval. The
pulmonary capillary wedge pressure/left ventricular mean
diastolic gradient was determined by the average of the
difference between the instantaneous left ventricular and
instantaneous pulmonary capillary wedge pressures at each
interval. A corrected mean gradient was obtained by cor-
recting for the time delay of the pulmonary capillary wedge
pressure, time shifting the pulmonary capillary wedge pres-
sure so that the peak of the v wave coincided with the
descending left ventricular pressure curve (6). A mean
gradient was then calculated by the average of the difference
between the instantaneous left ventricular pressures and the
time-shifted instantaneous pulmonary capillary wedge pres-
sure at each time interval.

The descending limb of the v wave on both the left atrial
and the pulmonary capillary wedge pressures was digitized at
20-ms intervals with use of the transmitral Doppler velocity
curve of the same beat from which the catheterization
pressures were traced. The modified Bernoulli equation
(pressure gradient = 4 \times v^2) was applied to the
instantaneous velocities to derive instantaneous pressures
at each time interval, and a mean gradient was calculated. The
Doppler curves were traced independently without knowl-
dge of the pressure curves.

Statistical analysis. Comparison of the mean gradients by
the different methods was done by use of the method of
Bland and Altman (15), in which the difference between two
measurements is plotted against the average of the two
measurements for each data point. A linear regression
analysis was performed to compare the mean gradients. Com-
parison of the mean absolute pressures and the slope of the
v wave was made with a paired t test, and p < 0.05 was
considered significant.

Intraobserver variability was determined for the digitiza-
tion of the transmitral Doppler flow velocity curves. Two
random beats from 12 consecutive patients were digitized
from the Doppler strip recordings. The mean observer variability was ±1 mm Hg.

**Results**

The absolute mean pressure, maximal and minimal pressures, total difference in maximal and minimal pressures and slope of the v wave for left atrial and pulmonary capillary wedge pressures are shown in Table 1. There was no significant difference between the absolute mean left atrial and mean pulmonary capillary wedge pressures. However, there was a significantly greater change in the magnitude of the difference between maximal and minimal pressures in the left atrial tracing (22 ± 9 mm Hg [mean ± SD]) than in the pulmonary capillary wedge pressure tracing (17 ± 8 mm Hg, p < 0.01). The slope of descent of the v wave was steeper in the left atrial pressure than in the pulmonary capillary wedge pressure (0.18 ± 0.08 mm Hg·s⁻¹ compared with 0.08 ± 0.05 mm Hg·s⁻¹, p < 0.001).

The left atrial/left ventricular transmitral pressure gradient was compared with 1) the mean transmural gradient measured by Doppler echocardiography and 2) the pulmonary capillary wedge pressure (both uncorrected and corrected pulmonary capillary wedge pressure/left ventricular gradients) (Fig. 1 and 2). The pulmonary capillary wedge pressure/left ventricular gradient was consistently larger than the left atrial/left ventricular gradient (Fig. 3). The average difference between the mean gradients when the pulmonary capillary wedge and left atrial pressures were used was 3.3 ± 3.5 mm Hg. The corrected pulmonary capillary wedge pressure/left ventricular gradient demonstrated less scatter than the uncorrected pulmonary capillary wedge pressure/left ventricular gradient compared with the left

| Table 1. Comparison of Left Atrial and Pulmonary Capillary Wedge Pressures |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| **Absolute Mean**           | **Maximal Pressure**        | **Minimal Pressure**        | **Maximal minus Minimal Pressure** | **Slope of v Wave** |
| Pressure (mm Hg)            | (mm Hg)                     | (mm Hg)                     | (mm Hg)                     | (mm Hg/s)                  |
| LA pressure                 | 29.0 ± 7.0                  | 43.0 ± 11.0                 | 21.0 ± 5.0                  | 12.0 ± 9.0                 | 0.18 ± 0.08               |
| PCWP                        | 30.0 ± 7.0                  | 39.0 ± 11.0                 | 22.0 ± 7.0                  | 17.0 ± 8.0*                | 0.08 ± 0.05*              |

Data are presented as mean values ± 1 SD. *p < 0.01 compared with left atrial (LA) pressure. tp < 0.001 compared with left atrial pressure. PCWP = pulmonary capillary wedge pressure.
atrial/left ventricular transmitral gradient. However, there still was a consistent overestimation by the corrected gradient (Fig. 4). The average difference between the mean gradients when the corrected pulmonary capillary wedge and left atrial pressures were used was 2.5 ± 2.9 mm Hg.

Figure 3. A, Mean gradient compared with difference of the transmitral gradient when the pulmonary capillary wedge (PCWP) or left atrial (LA) pressure is used. B, Scattergram demonstrating the relation of the transmitral gradient when pulmonary capillary wedge or left atrial pressure is used.

Figure 4. A, Mean gradient compared with difference of the transmitral gradient when the corrected pulmonary capillary wedge (CPCWP) or left atrial pressure is used. B, Scattergram demonstrating the relationship of the transmitral gradient when corrected pulmonary capillary wedge or left atrial pressure is used. Other abbreviations as in Figure 1.

Overall, there was an average 53% overestimation of the mean gradient when the pulmonary capillary wedge pressure was used and a 43% overestimation when the corrected pulmonary capillary wedge pressure was used. There was no significant difference in the mean differences between the pulmonary capillary wedge and left atrial pressures when a balloon-tipped catheter or an end-hole catheter was used (p = NS).

The best correlation with the smallest variability was the comparison of the Doppler-derived mean gradient with the left atrial/left ventricular gradient (Fig. 5). The mean difference between the Doppler gradient and the gradient using simultaneous left atrial/left ventricular pressures was 0.2 ± 1.2 mm Hg.

Discussion
Catheter-based measurement of transmitral gradient. Accurate measurement of the transmitral gradient is essential in assessing the hemodynamic consequence of the obstruction to left ventricular inflow in patients with mitral stenosis. Although direct measurement of left ventricular and left atrial pressures simultaneously is the most accurate method for determination of the mean mitral diastolic gradient, this
1.56 NISHIMURA ET AL. ACCURATE TRANSMITRAL GRADIENT MEASUREMENT

![Graph A]

**Figure 5. A.** Mean gradient compared with difference of the transmitral gradient when Doppler (Dopp) velocity or left atrial (LA) pressure is used. B. Scattergram demonstrating the relation of the Doppler-derived transmitral gradient with the transmitral gradient from left atrial pressure. LV = left ventricular.

necessitates transseptal catheterization with its inherent associated risks (2). These risks are increased in the patient with mitral stenosis who frequently has a distorted atrial anatomy and an increased incidence of left atrial thrombi.

The pulmonary capillary wedge pressure is used by many clinical catheterization laboratories as an indirect measurement of left atrial pressure (6). The mean gradient between the pulmonary capillary wedge and left ventricular pressures both at rest and with exercise has thus become a well accepted measurement of the transmitral gradient in patients with mitral stenosis. Recent reports, however, have questioned the reliability of this technique for assessment of the transmitral gradient both in patients with native mitral stenosis and in those with prosthetic mitral valves (7–9). These reports have shown a consistent overestimation of the true mitral gradient when the pulmonary capillary wedge and left ventricular pressures are used, and this may result in erroneous clinical assessment of the severity of mitral stenosis. On the basis of these studies, it has been recommended that transseptal catheterization be used for the evaluation of transmitral gradients when critical pressure measurements are required (9). Others have suggested that these errors could be reduced by 1) use of an end-hole catheter for measurement of pulmonary capillary wedge pressure, 2) oximestry confirmation, and 3) use of a time correction for the delay of transmission of pressure through the lungs (6,6).

**Doppler-derived transmitral gradient.** These controversies are academic, however, because noninvasive Doppler echocardiography now can provide a highly accurate measurement of the transmitral gradient. As demonstrated herein, the Doppler-derived mean gradient is more accurate than conventional catheter-derived transmitral gradients with use of the pulmonary capillary wedge pressure compared with simultaneous gradients from direct left atrial pressure. This finding remained true even after correction for the time delay in the pulmonary capillary wedge pressure (6,6). The use of an end-hole catheter with oximetry saturation did not improve the accuracy of the pulmonary capillary wedge pressure for determination of the transmitral gradient.

The Doppler-derived mean gradient is easily and reproducibly obtained in all patients with mitral stenosis. In contrast to other stenotic valvar lesions, the significant errors that could result from a large angle of incidence between the Doppler beam and the stenotic jet do not exist because the jet of mitral stenosis is usually directed centrally toward the apex of the left ventricle. In laboratories not well experienced in the use of the small nonimaging probe, continuous wave Doppler echocardiography guided by two-dimensional and color flow imaging can be performed to ensure that there is a small angle of incidence for the more eccentric stenotic jets. The initial studies that examined the accuracy of Doppler echocardiography in determination of the transmitral gradient in patients with mitral stenosis showed an acceptable correlation with the mean transmitral gradient obtained from the pulmonary capillary wedge and left ventricular pressures from catheterization, although there was a consistent underestimation of the transmitral gradient by Doppler echocardiography (10,11,17).

With the inherent problems of pulmonary capillary wedge pressure in measurement of the transmitral gradient discussed earlier, the true accuracy of Doppler echocardiography has been unclear. Holen et al. (10) suggested that "the ultrasound technique may well determine the actual gradient more accurately than catheterization," and a subsequent study showed an excellent correlation of the transmitral Doppler gradient with catheter gradients when a direct left atrial pressure measurement was used (18). As demonstrated in this prospective, simultaneous study, the Doppler-derived transmitral gradient is indeed more accurate than conventional catheterization. We have previously shown that this superior accuracy of Doppler echocardiography over conventional cardiac catheterization in determination of the transmitral gradient is also seen in patients with prosthetic mitral valves (19).

**Limitation of pulmonary capillary wedge pressure measurements.** The use of the pulmonary capillary wedge pressure for indirect assessment of left atrial pressure was first introduced almost five decades ago (3–5). Early studies demonstrated excellent correlation between the mean pul-
monary capillary wedge and mean left atrial pressures (3-5,20-23). Although there have been conflicting reports subsequent to this relation (24-28), if a proper end-hole catheter is used and high saturation is confirmed by oximetry, the pulmonary capillary wedge pressure is an accurate measurement of the mean left atrial pressure at low and moderately increased pulmonary artery pressures (6,29). The accuracy is less at very high pulmonary artery pressures because of the change in the ratio of pulmonary arterial and pulmonary venous compliance, which promotes asymmetric transmission of pressure waves across the pulmonary bed (29,30).

With the balloon-tipped wedge catheter, developed several decades ago, a technically easier method became available to obtain pulmonary capillary wedge pressure (31,32). After thermodilution cardiac output capabilities were added on the same catheter, it became widely used in many institutions for all right heart catheterizations. However, the balloon-tipped catheter is less reliable than an end-hole catheter for determining the true pulmonary capillary wedge pressure (6,16), and the position is harder to confirm by oximetry.

Although the mean pulmonary capillary wedge pressure may reflect the pressure, the pulmonary capillary wedge pressure has several limitations for determination of the mean transmitral gradient in mitral stenosis. The pulmonary capillary wedge pressure is delayed in temporal sequence as a result of the transmission of the waveform through the pulmonary circulation (33). The degree of delay varies from patient to patient but is usually from 60 to 140 ms. Without correction for this time delay, there was a 53% overestimation of the mean transmitral gradient, a finding observed by others (16). Correction for this delay decreased the error, but there was still a 43% overestimation of the transmitral gradient related to the contour of the pulmonary capillary wedge tracing. The occurrence of a dampened contour was noted several decades ago during the first clinical studies investigating pulmonary capillary wedge pressure, although at that time, the major emphasis was on the ability of the pulmonary capillary wedge pressure to measure mean left atrial pressure (21,26,30). In the current study, this change in contour and dampening of the pulmonary capillary wedge pressure was noted to be the cause of the greatest discrepancy in the transmitral gradient when it was compared directly with the gradient measured by left atrial pressure. There was a smaller difference between the maximal and the minimal pulmonary capillary wedge pressures than between the direct left atrial maximal and minimal pressures. The slope of the decrease in pressure after mitral valve opening, that is, the slope of the Y descent, was less rapid in the pulmonary capillary wedge than in the left atrial pressure, resulting in an overestimation of the transmitral gradient. These errors did not occur in all instances in which the pulmonary capillary wedge pressure was used (Fig. 2), but it was not possible to differentiate which were accurate from the pressure contour alone.

Study limitations. There are limitations to this study. The left atrial/left ventricular pressure gradients were used as the standard with which the other gradients were compared. High fidelity manometer-tipped catheters would have been ideal for pressure measurements but were not used. The pressures were measured with fluid-filled catheters, which have intrinsic errors as a result of potential overdamping and underdamping as well as catheter whip. Care was taken to try to avoid these errors by using the shortest extenders and catheters with the largest bore possible. The number of patients who had pulmonary capillary wedge pressure measured with a large-bore catheter with concomitant oximetry saturation was relatively small, and a larger number might have shown a closer correlation with the left atrial pressure measurements (6,16). However, the balloon-tipped wedge catheter has been widely accepted because it is easy to use and can obtain thermodilution cardiac outputs, and these results are thought to be representative of the methods used today.

Conclusions. In summary, compared with the transmitral gradient obtained by direct measurement of left atrial and left ventricular pressures, the Doppler-derived gradient is the most accurate method available. The Doppler gradient is more accurate than that obtained by conventional cardiac catheterization with use of pulmonary capillary wedge pressure, even after correction for the time delay. For the patient in whom accurate measurement of the transmitral gradient is required, the Doppler-derived gradient should be considered the reference standard if performed by experienced operators in laboratories with careful quality control checks.

References


