The Mitral Valve Orifice Method for Noninvasive Two-dimensional Echo Doppler Determinations of Cardiac Output

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SUMMARY We developed and validated a mitral valve orifice method for Doppler cardiac output determination. In 15 open-chest dogs, cardiac output was controlled and measured by a roller pump interposed between the right atrium and pulmonary artery as a right-heart bypass. Left heart flows were measured in the open-chest dog model by Doppler measurements at the mitral valve orifice and compared not only to volume flow measured by the roller pump, but to electromagnetic flow meters as well. The maximum mitral valve orifice area was measured off short-axis two-dimensional echocardiographic views by planimetry. The maximal orifice was then adjusted for its diastolic variation in size by calculating a ratio of mean-to-maximal mitral valve separation on a derived M-mode echocardiogram. Flow was sampled parallel to mitral valve inflow in a four-chamber plane. The multiplication of mean flow throughout the cardiac cycle by the mean mitral valve area after correction for diastolic size variation yielded a cardiac output determination that could be compared to the roller pump measurement. Fifty-two cardiac output determinations over roller pump values of 1–5 l/min yielded a high correlation between roller pump flows and Doppler (r = 0.97 ± 0.23/min). Our study shows that the mitral valve orifice provides an accurate site for Doppler cardiac output measurements.

A MAJOR DIFFICULTY in determining cardiac output using quantitative Doppler echocardiography is an inability in many cases to adequately visualize and quantitate internal aortic diameter in the area of Doppler sampling.1–3 In normal Doppler flow calculations, small errors in internal diameter measurement for vessels are raised to the second power when calculating cross-sectional area. Moreover, suprasternal notch aortic imaging tends to optimize Doppler flow recordings, but produces significant difficulties for determination of ascending aortic cross-sectional area. Even when aortic diameter can be accurately measured, it is unclear in the curved ascending aorta what portion of the anatomical flow cross section has a flat flow profile.5

We studied a method for Doppler quantitation of transmural flow using echocardiographic views of the mitral valve that are reliably obtained in clinical two-dimensional echocardiographic examinations of adult patients. We validated this method in an open-chest animal model in which flow could be tightly controlled and accurately measured.

Methods
Validation Studies: Surgical Techniques and Animal Model
Fifteen dogs that weighed 20–25 kg were given pentobarbital, 30 mg/kg, and ventilated using a Harvard respirator. A midline sternotomy was performed and the aorta and its branch vessels were isolated and cleaned of adventitia and fat. The azygous vein was then ligated and the pericardium opened. Stab incisions were made in the lateral right atrial wall and right atrial appendage, through which retrograde cannulation of the venae cavae using ½-inch tubing was achieved. This technique has been described.5 These cannulas drained by gravity to a 5-liter reservoir from which a ¼-inch tube passed through a mechanical roller pump, and the return tube from the pump was sutured to the right atrial free wall and passed through the tricuspid valve into the pulmonary artery. Heparin (5000 U) was given in a bolus and the reservoir primed with 1 liter of Ringer’s lactate. Ligatures around the venae cavae and pulmonary artery were tightened as right-heart bypass was instituted. The roller pump, which had been calibrated using a stopwatch and graduated cylinder, could then be set to achieve and maintain left cardiac output within strict limits. When venous return did not keep up with forward flow, a maximum of 1 liter of Ringer’s lactate was added to the reservoir. Cardiac output using the roller pump could be varied between 0.5 and 6 l/min and Doppler flow measurement made over flows varying in increments of 0.5 l/min. Calibrated electromagnetic flow probes (Gould-Statham SP2204) were periodically also placed 2 cm distal to the aortic valve to verify roller pump accuracy, and were used in each of the dogs over two to three cardiac outputs, but not for every roller pump setting.

Ultrasound and Doppler Method
A prototype two-dimensional sector scanner with range-gated Doppler capability (Electronics Medicine/Honeywell) was used for both imaging and Doppler flow studies. The instrument has a 3.5-MHz mechanical transducer that is oscillated through an angle of 60–75°. A movable Doppler sample cursor allows
sampling along any line within the image when the oscillating transducer system is stopped and set into Doppler mode. The depth of the sample volume is variable to a maximum of 16 cm from the transducer and sample volume length is adjustable from 2 mm to 2 cm. The Doppler shift is detected only from the region specified within the sample volume. Doppler signals were sampled at a rate of 19,500 samples/sec at 0–4 cm depth, 9750 samples/sec at 4–8 cm, and 6500 samples/sec at more than 8 cm. Fast Fourier transform spectral analysis of the flow velocities within the sample volume was performed at 5-msec intervals. Sampling position was easily checked by switching the instrument from Doppler to real-time imaging mode.

Two-dimensional images of the mitral valve orifice were obtained by placing the transducer directly on the heart in a standard short-axis orientation. The view was adjusted to record both leaflet tips at a level just above that at which the “fishmouth” becomes incomplete as the leaflets merge with chordal structures.

Maximal mitral valve orifice size at the level of the leaflet tips was then obtained by ECG gating to the greatest mitral valve leaflet separation at either the E or A point on the derived M-mode echocardiogram (figs. 1 and 2). The maximal area by the stop-frame was later checked against frame-by-frame analysis of the videotaped real-time images. A derived M-mode mitral echocardiogram hard copy at 100 mm/sec paper speed was obtained across the middle of the leaflets at the same level as the two-dimensional image and was later used to correct for variations in mitral valve orifice size during diastole (fig. 2). The transducer was then repositioned and placed lightly on the cardiac apex to obtain two- or four-chamber views, and the Doppler sample volume was placed parallel to the left ventricular inflow tract just inferior to the tips of the mitral valve leaflets (fig. 3A). The angle between Doppler sampling direction and assumed direction of mitral inflow was estimated by an angle cursor on the sample line and the view was adjusted so that this angle was always less than 15°. Although the direction of flow in the plane perpendicular to the image, the azimuthal plane, could not be determined, we attempted to maximize Doppler shift by small positional changes so as to be as close as possible to parallel to mitral inflow. Lateral beam characteristics in a water bath for this system suggest that the 6-db attenuation at 4 cm depth is ± 2 mm, which may be assumed to be the lateral dimension of the Doppler sample volume. The sample volume length was usually set at 0.5–1 cm. Two-dimensional mitral orifice size, M-mode mitral separation during diastole and ECG and Doppler flow (recorded on an LS-8 hard-copy recorder at 100 mm/sec) (fig. 3B) were each recorded for each cardiac output determination after 5 minutes of stabilization after any changes in roller pump speed.

Data Analysis

Analysis of records and calculations of cardiac flow were performed by one examiner, who was blinded to the roller pump settings. Twenty selected records were checked by another observer whose determinations of

Figure 1. Short-axis view shows the mitral valve orifice (MVO) in an open-chest dog. The orifice almost fills the left ventricular cavity at this level.

Figure 2. Derived M-mode echocardiogram through the middle of the mitral valve orifice shows the technique for measuring mean-to-maximal (max) leaflet separation. Mean was determined by adding all lines and dividing by the number of lines spaced equidistantly through the M-mode trace in diastole. MV = mitral valve; SEP = separation. In the greyhound dogs we used, it is not uncommon for the posterior leaflet to have an exaggerated motion pattern.
cardiac output never differed from the first observer by more than 5%.

For flow calculations, mitral inflow Doppler velocity flow curves from three sequential beats were digitized using a programmable graphics analyzer (Numonics) in order to obtain a mean mitral flow over time for the entire cardiac cycle. Although the scanner provides spectral analysis for quantitating all the velocities within the sample volume, the spectral output relates the number of times a particular velocity appears in the spectral determinations to the darkness of the lines during any 5 msec sampling period. The modal velocity on the printout can be approximated with a line drawn through the densest portion of the velocity trace (fig. 3B). Using this modal velocity from the spectral wave form, the area under the curve was digitized over two to three entire sinus beats at a regular heart rate to determine the mean temporal velocity of transmitral flow throughout the cardiac cycle. In obtaining the records, we avoided, as much as possible, flow in the left ventricular outflow tract, and if flow away from the transducer was recorded, it was ignored during flow tracing, as all flow curves were brought to zero during systole (fig. 3B).

An effective mean diastolic cross-sectional orifice area for the mitral valve was determined by multiplying the maximal mitral valve orifice area (obtained by planimetry of the stop-frame two-dimensional valve orifice image through the middle of the leaflets) by the ratio of mean-to-maximal mitral valve leaflet separation on the derived M-mode echocardiogram. The purpose of using this ratio was to correct for variations in mitral valve orifice size during diastole (fig. 2). To obtain the mean/maximal ratio, the diastolic portion of an M-mode beat was divided into 0.05-second segments and leaflet separation measured and averaged to obtain the mean. Maximal separation was determined either at an E or an A point, whichever corresponded to the two-dimensional mitral orifice view.

Cardiac output using the mitral valve orifice method could then be determined using the formula RGD-CO = (V × CSA × 60)/cos θ, where RGD-CO = range-gated Doppler cardiac output (l/min), V = mean velocity throughout the entire cardiac cycle uncorrected for angle (cm/sec), CSA = the effective mean diastolic mitral valve orifice area corrected for diastolic variations (cm²), and cosine θ = the angle between the Doppler beam and blood flow.

Statistical Analysis

Doppler cardiac outputs derived from the animal studies were compared with the roller pump cardiac outputs using linear regression. When electromagnetic flowmeter and roller pump values were simultaneously obtained in the animal model, the roller pump value was used for the statistical analysis. Maximal and mean mitral valve orifice sizes were also compared to roller pump flow using regression analysis individually in five dogs.

Animals

Fifty-two cardiac output values derived from Doppler velocity information were compared to simultaneous roller pump values in the dogs. For each dog, two to five cardiac output comparisons between roller pump and Doppler values were made. Not all dogs had all levels of roller pump cardiac outputs evaluated. Roller pump values ranged from 1.0 to 5.0 l/min and Doppler-derived flow values from 0.91 to 5.2 l/min. Stroke volumes calculated from Doppler information

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**Figure 3.** (A) Apical two-chamber view shows sampling of mitral valve inflow at the level of the leaflet tips in a direction almost parallel to flow. SV = sample volume; LA = left atrium; LV = left ventricle; AO = aorta. (B) Mitral valve (MV) Doppler flow record obtained in the same open-chest dog as in figure 3A at a paper speed of 100 mm/sec. The dots superimposed on the last beat show the method of tracing through the modal velocities throughout one cardiac cycle to determine mean temporal flow.
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ranged from 6.6 to 63 ml/beat. Doppler transmural temporal mean velocity corrected for angle ranged from 5–23.4 cm/sec and peak velocity corrected for angle ranged from 27–117 cm/sec. An angle of 0° was calculated between the sampling direction and the direction of mitral flow for 80% of data points, and all other sampling angles were less than 15°. A linear correlation (r = 0.97) with a standard error of the estimate of 0.23 l/min was obtained between Doppler output and roller pump determinations (fig. 4).

Mitral Valve Orifice Area vs Cardiac Output

The effect of various roller pump settings on maximal mitral valve orifice size was studied in five dogs. Within the range of 1.0–5.0 l/min, maximal mitral valve orifice size and cardiac output were highly correlated (r = 0.90, 0.98, 0.94, 0.85 and 0.99) in each of the five dogs in whom we rapidly and sequentially performed mitral imaging while changing the cardiac output (fig. 5).

Spectral Dispersion

Spectral width for mitral flow (± 6 db) in the dogs (even at high flows) was less than ± 10 cm/sec.

Mean to Maximal Mitral Valve Leaflet Separation

The ratio of mean to maximal mitral valve separation used for correction of the two-dimensional echocardiographic orifice area on derived M-mode echocardiograms was 0.70–0.85 (mean 0.81).

Discussion

We¹, 4, 5 and others², 3, 6, 7 have used Doppler-derived flow from the aorta to quantitate cardiac output. Although the results using ascending aortic measurements have been encouraging, difficulty in the accurate determination of internal aortic cross-sectional area by echocardiography represents a major problem for accurate flow prediction.¹ Significant echo dropout occurs in suprasternal aortic imaging as a result of the aortic walls being parallel to the ultrasound beam, and the aorta remains the same size, even in low cardiac output states, where only a central stream may emerge from a partially opened aortic valve.

Imaging and Doppler flow recording at the mitral valve orifice offers a number of advantages over suprasternal recording. Short-axis views allow the mitral valve leaflet tips to be imaged in a plane roughly perpendicular to the ultrasound beam, while in the four-chamber view, Doppler flow into the left ventricle is recorded parallel to the interrogating ultrasound beam. Using this method, ambiguity in determination of cross-sectional area is therefore minimized, while Doppler flow velocities are optimized. Also, by using the cross-sectional short-axis orifice view, the mitral orifice area could be determined by planimetry, avoiding the need to raise a diameter to the second power in the calculation of cardiac output. Further, the change in mitral valve orifice size with roller pump flows suggests that the mitral valve orifice adapts to encompass the flow stream passing through it. In this respect, our data confirmed work by Rasmussen and co-workers, who demonstrated a method for calculating stroke volume in humans using mitral valve motion.⁸ In the individual dogs the correlation between maximal mitral valve orifice size and roller pump flow was 0.85–0.99. The implication of this finding for clinical use suggests that it is not enough to follow serial changes in left ventricular inflow velocities without also obtaining corrected mitral valve orifice sizes, nor is it enough to record mitral orifice size alone as an estimate of cardiac output, because presumably, the maximal orifice available plateaus at high cardiac output and is ultimately limited by left ventricular cavity dimensions. In the two smallest of the five dogs studied in this fashion, a leveling off of mitral valve orifice size was seen at cardiac outputs approaching 5 l/min, the highest roller pump setting we used. Individual data points are shown on figure 5 for one of those dogs.
Our animal results in which rigidly controlled roller pump cardiac output was compared to Doppler flow using the mitral valve orifice method achieved excellent correlation \((r = 0.97)\). These results may be explained in part by the simultaneous measurements, lack of beat-to-beat variation, and consistency of heart rates, since all the necessary views could be obtained in 1–2 minutes. The technique of using the roller pump as a right-heart bypass to control left-heart inflow and outflow further avoids the 10–15% variations inherent in thermodilution techniques9 and also probably contributed to the accuracy of the results.

We recently attempted to apply this method in 18 adult patients who were studied in the coronary care unit to determine the clinical value of the mitral valve method. Admission diagnoses included myocardial infarction in 12 patients, pulmonary embolism in one patient and sepsis in one patient. Four patients had undergone coronary artery bypass grafting. None had mitral valve disease or mitral insufficiency. The criteria for inclusion in the clinical study were previous clinically indicated placement of Swan-Ganz thermodilution catheter and the ability to image the mitral valve orifice and to record Doppler flow from apical views. In this unstable and critically ill population, 15 of the 18 patients were successfully imaged. Examinations lasted 10–15 minutes. The procedure for obtaining flow data and orifice imaging data was similar to that used in the animal studies, but a sample length of 1–2 cm was used in human studies (fig. 6). Mitral valve flow measurements by Doppler were compared to standard thermodilution cardiac outputs performed with a thermodilution computer system (Edwards Instruments, 9510-A) as an average of five injections. In this preliminary study in humans, though on a small number of patients, the correlation between Doppler and thermodilution cardiac outputs was 0.94, with a standard error of the estimate of \(\pm 0.38\) l/min. Twelve of the 15 values of Doppler cardiac output were within 10% of the thermodilution determination. These encouraging preliminary results were obtained over thermodilution cardiac outputs of 2–8.4 l/min.

That mean diastolic mitral valve orifice size may be used to determine cross-sectional flow area is an empirical finding. Our attempts to use the mitral valve annulus10 cross-sectional area measured from the echo

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**Figure 6.** (A) Short-axis view in a patient with a dilated left ventricle and poor left ventricular function shows the mitral valve orifice area. The mitral valve sits in the middle of the dilated cavity and does not appear completely open, but this was in fact the widest opening of the valve in this patient. (B) Four-chamber view shows placement of a 1/2-cm-long sample volume (SV) in the left ventricular inflow tract parallel to the direction of mitral flow. LV = left ventricle; LA = left atrium; RV = right ventricle; RA = right atrium. (C) Mitral Doppler flow curve from a human subject shows the characteristic wave form of the mitral valve velocities and the method of tracing velocities throughout a complete cardiac cycle to determine mean velocity over time.
recording was to avoid the left ventricular outflow area in which flow moves away from the transducer in systole. This problem could be minimized by directing the sampling volume as laterally as possible while still maximizing forward flow. Determining whether systolic negative flow observed in the mitral trace is mitral regurgitation or merely recording of a portion of the left ventricular outflow tract is important because the mitral valve orifice technique for calculating cardiac output presupposes that all left ventricular inflow will leave the left ventricular outflow, which will not occur in patients with mitral regurgitation.

Digitization of maximal mitral valve two-dimensional orifice size required practice and internal laboratory validation. Small differences in planimetry of mitral valve orifice size greatly affect resulting hemodynamic predictions. By using a roller pump to rigidly control left ventricular inflow and outflow, we could, in effect, work backwards to determine the appropriate place to digitize images. Digitizing through the middle of the normal mitral valve leaflet echocardiograms once optimal gain settings were established attained the best results. Martin et al. determined that the internal edges of the mitral valve orifice correlated best with Gorlin formula valve areas in mitral stenosis patients. We do not consider our method of tracing area to be significantly in conflict, as we did not deal with any abnormally thickened valves.

We would conclude from our studies that cardiac output may be determined noninvasively by Doppler echocardiography using the mitral valve orifice method and that the results correlates well with other methods of cardiac output measurement. Moreover, some of the problems inherent in suprasternal aortic imaging are circumvented using this technique, and the views necessary can usually be obtained without discomfort in most adult patients and almost all children and infants. In addition to validating the technique against a highly accurate roller pump model in animals, we believe, based on our preliminary experience, that our method can accurately predict thermodilution cardiac output values in critically ill patients. We would expect that this method will enhance the clinical value of two-dimensional Doppler echocardiography for providing noninvasive measurements of cardiac output.

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