LABORATORY INVESTIGATION
CONGENITAL HEART DISEASE

A two-dimensional Doppler echocardiographic method for calculation of pulmonary and systemic blood flow in a canine model with a variable-sized left-to-right extracardiac shunt

ERIK J. MEIBOOM, M.D., LILLIAM M. VALDES-CRUZ, M.D., SUZANA HOROWITZ, B.S., DAVID J. SAHN, M.D., DOUGLAS F. LARSON, M.S., KENT A. YOUNG, CARLOS OLIVEIRA LIMA, M.D., STANLEY J. GOLDBERG, M.D., AND HUGH D. ALLEN, M.D.

ABSTRACT The purpose of this study was to validate a two-dimensional range-gated Doppler echocardiographic method for measurement of pulmonary and systemic blood flow in a canine model with a surgically created extracardiac systemic-to-pulmonary shunt, the size of which could be varied. In five anesthetized open-chest dogs, a previously calibrated electromagnetic (EM) flowmeter was placed around the ascending aorta, and the femoral artery was dissected, cannulated, and connected to a previously calibrated roller pump. The return tubing from the roller pump was inserted into the main pulmonary artery to create a variable-sized systemic-to-pulmonary artery shunt. In this preparation with intact ventricular and atrial septa, pulmonary blood flow volume was measured as flow from the ascending aorta with the EM flowmeter probe; left-to-right shunt volume was measured from the calibrated roller pump flow, and systemic flow was measured by subtraction of roller pump flow from the EM flowmeter reading of the ascending aorta. In two additional dogs, a 16 mm diameter, 12 cm long Teflon graft was placed between the descending aorta and the main pulmonary artery to mimic more closely a patent ductus arteriosus. Flow through the shunt was measured with an EM flowmeter probe placed around the graft. Systemic and pulmonary flows were then calculated by a Doppler echocardiographic method from RR interval-matched beats and compared with simultaneously recorded EM flowmeter measurements from the ascending aorta, and left-to-right shunt flows to permit comparison of pulmonary and systemic flows and their ratios (QP:QS) by both methods. Doppler systemic flow was measured as systemic venous return at the right ventricular outflow tract. The size of the outflow tract and mean flow as a function of time were obtained by echocardiographic imaging and interrogation of the outflow tract from a short-axis view. Pulmonary blood flow could not be measured at the pulmonary artery because of high multidirectional velocities and spectral broadening of the flow curves similar to those obtained in children with patent ductus arteriosus. Therefore, pulmonary blood flow was measured as pulmonary venous return through the mitral valve. The mitral orifice was measured from a short-axis view, and Doppler flow curves were recorded from the apical four-chamber view. For 26 left-to-right shunts, excellent correlations were obtained between Doppler echocardiographic and EM flowmeter measurements of pulmonary flows (range 1.2 to 7.7 l/min; r = .99, SEE = ± 0.16 l/min), systemic flows (range 0.6 to 5.7 l/min; r = .99, SEE = ± 0.13), and QP:QS ratios (range 0.9:1 to 4.2:1; r = .96, SEE = ± 0.21:1). Our study validates the accuracy of this Doppler echocardiographic method to measure pulmonary and systemic flows and their ratios in the presence of extracardiac aortic-to-pulmonary artery shunts.


From the Department of Pediatrics, University of Arizona, Health Sciences Center, Tucson, and the Department of Pediatrics, University of Groningen, Groningen, The Netherlands. Supported in part by a grant from the Jan Kornelis de Cock Foundation, The Netherlands. 
Address for correspondence: Lilliam Valdes-Cruz, M.D., Department of Pediatrics (Pediatric Cardiology), University of California San Diego University Hospital, CTF B102, 225 West Dickinson St., San Diego, CA 92103.
Received Feb. 4, 1983; revision accepted April 25, 1983.

OUR PREVIOUS STUDIES and those of other investigators have demonstrated that two-dimensional Doppler echocardiographic methods are accurate for noninvasive calculation of cardiac flows in the intact circulation in man.1-10 Our own work has also shown that Doppler echocardiography accurately measures pulmonary and systemic flows and their ratios, even in
the presence of large intracardiac shunts in animal models.11 Our purpose was to assess the accuracy of systemic and pulmonary flows measured with a quantitative two-dimensional range-gated Doppler flowmeter in an open-chest canine model with a variable-sized, surgically created, extracardiac aortic-to-pulmonary shunt.

Methods

Surgical technique and animal model. Seven mongrel dogs weighing 20 to 30 kg were anesthetized with pentobarbital sodium (30 mg/kg), intubated, and ventilated with a standard volume pump. A median sternotomy was performed and the pericardium was opened. The ascending aorta and the main pulmonary artery were dissected, cleaned of fat and adventitia, and a previously calibrated electromagnetic (EM) flowmeter probe of appropriate size (Gould-Statham SP2204) was placed around the ascending aorta 2 cm above the aortic valve. Adequate contact of the flowmeter cuff was verified by recording phasic aortic flow tracings.

In five dogs, the right femoral artery was dissected, cannulated, and connected to a roller pump by ¼ inch tubing. The return end of the roller pump tubing was attached to a cannula inserted and fixed into the main pulmonary artery through a purse-string suture (figure 1). The roller pump had been previously calibrated by measurement of flow rates with a stopwatch and a graduated cylinder. In this model with intact atrial and ventricular septa, pulmonary blood flow was measured as the flow from the ascending aorta by the EM flowmeter reading; left-to-right shunt volume was the measured flow through the roller pump, and systemic blood flow was equal to the flow from the ascending aorta as determined by the EM flowmeter minus the roller pump volume.

In an additional two dogs, a 16 mm diameter, 12 cm long Gortex shunt was sewn between the descending aorta and the main pulmonary artery within the thorax to simulate more closely a ductus arteriosus or the surgically created, palliative, systemic-to-pulmonary artery shunts used clinically. An EM flowmeter probe was placed around the ascending aorta as described above, and another one was placed snugly around the Gortex tubing close to the pulmonary-arterial end. Selective constriction of the tubing at the aortic end allowed variations of shunt size. As before, pulmonary blood flow equaled flow from the ascending aorta as determined by EM flowmeter values; left-to-right shunt volume was measured by the flowmeter probe at the Gortex shunt, and systemic flow was determined by pulmonary blood flow minus left-to-right shunt flow.

Continuous EM flowmeter recordings were obtained throughout the study for comparison with Doppler-determined flows. After each step-by-step change in shunt size, achieved by an alteration of pump setting or by degree of Gortex-shunt constriction, a stabilization period of 2 min was allowed and constancy of EM flowmeter readings was observed before any Doppler echocardiographic recordings were made. Doppler measurements of pulmonary and systemic flow were performed as described below for each shunt size, and were matched to each other, to the simultaneous EM flowmeter measurements, and to the roller pump settings to permit calculation of pulmonary/systemic ratios (QP/QS) by both Doppler echocardiography and EM flowmeter measurements.

Ultrasound and Doppler methods. Ultrasound imaging and Doppler echocardiographic studies were performed with a commercially available range-gated pulsed Doppler unit (E for M/Honeywell). The unit contains a 3.5 MHz single-element transducer that mechanically sweeps through a 30 to 75 degree arc to achieve real-time two-dimensional echocardiographic imaging at 30 frames/sec. The scanner can be stopped along any line within the image and a Doppler sample volume can be positioned at any depth along that line; this permits localization of the sample volume and estimation of the angle between the direction of Doppler sampling and the direction of flow within the plane of imaging. The sampling angle relative to the direction of the flow within the elevational or azimuthal plane, that is, the plane perpendicular to the plane of imaging, could not be determined; however, small deviations from sampling exactly parallel to flow (angles = 0 or 180 degrees) were of no practical importance, since the cosine of the sampling angle would still be close to unity (see formula 1). Sample-volume length was variable between 2 mm and 2 cm and was usually set at 5 mm in

FIGURE 1. Diagram of the extracorporeal shunt model that demonstrates the interposition of the roller pump between the femoral artery and the main pulmonary artery. SVC = superior vena cava; IVC = inferior vena cava; RA = right atrium; LA = left atrium; RV = right ventricle; LV = left ventricle; PA = pulmonary artery; Ao = ascending aorta; Femoral A = femoral artery.
these studies. Sample-volume width in a water tank (that is, the lateral displacement of a transducer required to produce an amplitude fall-off to half-maximum intensity for the returning Doppler signal [6 dB] from a moving string target) was ± 1.8 mm between 2 and 4 cm in depth and ± 2 mm at 4 to 8 cm in depth. Sample-volume width was not variable. The operational mode of the scanner could be switched rapidly from real-time imaging to spatially oriented Doppler sampling. In Doppler mode, signals were sampled at a pulse repetition frequency of 19,500 samples/sec when the signal was obtained from a depth less than 4 cm, which results in a maximal nonambiguously detectable velocity of 220 cm/sec. Signals were sampled at a frequency of 4,500 samples/sec at a depth of 4 to 8 cm, which results in a maximal nonambiguously detectable flow velocity of 110 cm/sec at the 0 degree sampling angle. Two outputs of the Doppler frequency shift were available: an audio signal and a quantitative fast Fourier transform spectral analysis of the Doppler frequency shift sampled at 200 times/sec. The Doppler spectral output was converted automatically by the scanner to flow velocity in centimeters per sec with the formula:

\[
\text{flow velocity} = \frac{\text{frequency shift} \times \text{velocity of sound in medium}}{2 \times \text{transmitted frequency} \times \cos \theta}
\]

(1)

(where \(\cos \theta = \) angle between the direction of Doppler sampling and the direction of blood flow. Correction for \(\cos \theta\), however, was not applied automatically by the unit; rather, it was done manually in formula 2, which calculates volume flow as described below.)

**Measurements of blood flow volumes.** Pulmonary and systemic blood flow volumes were calculated from the two-dimensional echocardiographic images and the flow-velocity curves with the general formula:

\[
\text{Blood flow/min} = \frac{\text{mean flow velocity} \times \text{cross-sectional area} \times 60 \text{ sec/min}}{\cos \theta}
\]

(velocity throughout the cardiac cycle uncorrected for angle is in centimeters per sec and cross-sectional area is in square centimeters).

The sampling angle \(\theta\), that is, the angle of incidence between direction of flow and the Doppler sample volume, was determined manually with a protractor directly from the freeze frame of the two-dimensional echocardiographic image, which showed the sample-volume position relative to the imaged cardiac structures (figure 2). Correction for angle \(\theta\) was applied manually in formula 2 rather than in formula 1.

**Calculation of systemic flow by Doppler echocardiography.** Systemic flow was measured as systemic venous return at the right ventricular outflow tract. We obtained a two-dimensional echocardiographic image of the right ventricular outflow tract by positioning the transducer over the right ventricular body, aiming superiorly in a short-axis plane (figure 2). The Doppler sample volume was positioned within the outflow tract, below the pulmonic valve, as parallel as possible to the assumed direction of flow as determined by visual examination within the plane being imaged. Once the optimal two-dimensional echocardiographic image and Doppler flow curves were obtained and the sample volume was confirmed to be as parallel as possible to the assumed direction of flow (angle \(\theta = 0\) degrees), a still frame of the two-dimensional echocardiographic image and the fast Fourier output of the Doppler frequency shift were recorded on a strip chart at a paper speed of 100 mm/sec and on video tape (figure 2). We obtained mean Doppler flow velocity over time by digitizing and integrating the area under the Doppler waveform over three complete cardiac cycles with a Nonumics minicomputer (see below). The cross-sectional area of the right ventricular outflow tract was derived from the maximal systolic inner diameter of the outflow tract in a direction parallel to the plane of the pulmonic valve and at a point just proximal to it. The measurement was not corrected for variation of right ventricular outflow tract size during the cardiac cycle.

**Calculation of pulmonary flows by Doppler echocardiography.** The pulmonary artery could be imaged, but pulmonary flows could not be quantitated within the main pulmonary artery because the left-to-right shunt that occurred in this area caused spectral broadening of the Doppler flow signals, multidirectional flows, and velocities above the Nyquist limit; this precluded pulmonary artery flow measurement by the Doppler technique. In other sites within the pulmonary artery, a bidirectional pattern with reverse shunt flow toward the pulmonary valve was obtained; however, it was unclear over which flow area of the pulmonary artery this flow pattern would be integrated (figure 3). This pulmonary flow pattern closely mimicked patterns found in children with patent ductus arteriosus. Pulmonary flow determined by Doppler echocardiography was therefore measured as pulmonary venous return, that is, flow through the mitral valve orifice.

We calculated transmural flow by placing the transducer at the cardiac apex and by echocardiographic imaging in a four-chamber view. The Doppler sample volume was placed within the left ventricular inflow tract distal to the mitral valve leaflets and lateral to the outflow tract. Once the optimal two-dimensional echocardiographic image and Doppler wave curves were obtained, they were recorded on a strip chart at a paper speed of 100 mm/sec and on video tape (figure 4). The Doppler flow curves obtained from the mitral valve were digitized and integrated with the minicomputer to calculate the mean temporal flow velocity in the mitral valve (see below).

We obtained flow area of the mitral valve by positioning the transducer over the atrioventricular ring and scanning in a short-axis plane. A gated stop frame of the maximal diastolic mitral valve orifice on a two-dimensional echocardiographic image was recorded. Maximal orifice area was digitized along the inner contours of the two-dimensional echocardiographic image of the mitral leaflet. Since the mitral valve is not maximally opened during the entire diastolic time, a correction factor for the phasic diastolic movement of the valve was calculated as the mean-to-maximal leaflet separation from the derived M mode tracing. The maximal two-dimensional echocardiographic image of the mitral valve orifice was multiplied by the mean-to-maximal leaflet separation ratio to arrive at the effective mitral valve orifice throughout the entire period of diastole.\(^2\),\(^4\),\(^11\)

**Digitizing methods: calculation of mean temporal flow.** The mean flow velocities as a function of time for the right ventricular outflow tract and mitral valve were obtained by digitization and integration of the area under the Doppler flow velocity curves over three consecutive RR interval–matched beats. To accomplish this, the middle of the densest portion of the gray scale spectral display of the Doppler velocity curves was traced (this is the modal velocity shift that is most frequently present in the returning signal). The minicomputer divided the velocity-time integral from the three complete beats by the time of the three beats to obtain mean right ventricular outflow tract flow velocity or mitral flow velocity as a function of time. Diastolic flow velocities above the zero line for the right ventricular outflow tract and systolic flow velocities below the zero line for the mitral traces were minimized by changes in transducer position and sample-volume sizes. These flow patterns, which potentially represent reverse flow when present, were neglected when the curves were traced; that is, curves were traced only down to the zero lines in systole for mitral
FIGURE 2. Top, Parasternal short-axis image of the right ventricular outflow tract with the Doppler sample volume (SV) positioned proximal to the pulmonary valve (PV). Ao = aorta. Bottom, Doppler velocity curve derived from the outflow tract.

valve and in diastole for the outflow tract. All curves used for comparison of pulmonary blood flow and systemic blood flow were obtained at equivalent heart rates.

As a measure of the presence or absence of turbulence, spectral width of the Doppler curves (cm/sec) were measured with the minicomputer at the time of peak flow, in systole or diastole. The measurement included the width of the gray scale spectrum at peak flow and was cross-checked against a quantized log spectral display that allocates the darkest gray scale to the entire range of velocity present within ±6 dB of the spectral mean (figure 5).

Reproducibility of measurements. To determine reproducibility, all measurements were made in duplicate on the same tracing by the same investigator. To test interobserver variability, all measurements were made independently by investigators who were unaware of the simultaneous EM flowmeter readings or of each other's results.

Statistical analysis. Linear correlation was used to compare Doppler pulmonary and systemic flows and QP:QS ratios with those obtained by the combination of EM flowmeters and roller pump. A paired t test was used to assess interobserver variability and errors in reproducibility.

Results
In the seven experimental animals, 26 different sized shunts were obtained. Each animal had a minimum of two and a maximum of eight different shunt magnitudes recorded. We derived 22 shunts from the five dogs with the femoral artery-to-pulmonary artery shunts and four shunts from the two animals with the Gortex shunts.

Systemic blood flows derived from the combined EM flowmeter–roller pump measurements ranged from 0.6 to 5.7 L/min; pulmonary flows determined by
the EM flowmeter probe around the ascending aorta ranged from 1.2 to 7.7 l/min, and QP:QS ratios ranged from 0.9:1 to 4.2:1.

One Doppler measurement of the right ventricular outflow tract was discarded because of an inadequate two-dimensional echocardiographic image. All Doppler measurements of the mitral valve were acceptable. This resulted in 26 Doppler pulmonary flows that ranged from 1.2 to 7.6 l/min, 25 Doppler systemic flows that ranged from 0.7 to 5.6 l/min, and 25 Doppler QP:QS ratios that ranged from 0.8:1 to 4.2:1.

All flow measurements were attempted within 0 to 4
cm sampling depth; however, occasional adjustments of transducer and sample-volume position were necessary to maximize flow curves and to avoid valve and wall motion artifacts. Therefore, at times, records were obtained between 4 to 6 cm in depth if the maximal signal was easier to record at that greater depth and the velocities were still within the Nyquist limits. Peak Doppler flow velocities measured over the mitral valve ranged from 31 to 118 cm/sec with a mean spectral width at ± 6 dB of 9.2 ± 0.5 cm/sec (SE). Peak Doppler flow velocities in the right ventricular outflow tract varied from 24 to 88 cm/sec with mean spectral width at ± 6 dB of 11.6 ± 0.6 cm/sec. Peak flow velocities within both areas of investigation remained within the Nyquist limit of the ultrasound system, even in the presence of large shunts.

Correlation of Doppler and EM flowmeter–roller pump flows. Figure 6 summarizes our results. Doppler pulmonary flows derived at the mitral valve orifice correlated extremely well with those measured in the ascending aorta by the EM flowmeter (r = .99, SEE = ± 0.16 l/min). The linear correlation for pulmonary flow measurement, with the highest point eliminated, yielded a correlation coefficient of .98, SEE = ± 0.16. Doppler systemic blood flows obtained at the right ventricular outflow tract also correlated well with those measured from the aortic flow minus the roller pump or the Gortex shunt flow (r = .99, SEE = ± 0.13). Eliminating the highest point, we obtained a correlation coefficient of r = .96, SEE = ± 0.14. Finally, Doppler QP:QS ratios also correlated well with the reference standards (r = .96, SEE = 0.21:1).

No qualitative or quantitative differences were found between results obtained with the roller pump and the smaller number of determinations obtained from the Gortex shunt model.

Interobserver variability and errors of reproducibility. All measurements were highly reproducible. The SEM
to test reproducibility was less than 5% when duplicate measurements by one observer on a given record were compared. Further, interobserver variability was also less than 5%.

Discussion

Previous studies have shown that range-gated two-dimensional Doppler echocardiography with fast Fourier transform spectral analysis of the Doppler frequency shift is a reliable, noninvasive method for calculation of cardiac output and assessment of the magnitude of intracardiac left-to-right shunts. These earlier studies included validation of these measurements in animal models with shunts and in children with heart disease. Our present study further validates two-dimensional Doppler echocardiography for calculation of flows in the presence of both small and large systemic arterial-to-pulmonary artery left-to-right shunts.

In this study, as in shunts through a patent ductus arteriosus encountered in the clinical setting, the shunt stream was directed into the main pulmonary artery, which resulted in increased velocities above the Nyquist limit and multidirectional nonlaminar flow patterns that precluded Doppler pulmonary blood flow measurements in the main pulmonary artery. Therefore, we measured pulmonary flow by Doppler echocardiography as pulmonary venous return through the mitral valve orifice, a technique that had already been validated and proved reliable in our laboratory.

In contrast to intracardiac shunts, in the presence of extracardiac shunts distal to the take-off of the vessels to the head and upper extremities, systemic blood flow could not be measured over the ascending aorta by

FIGURE 6. Regression analyses that correlate Doppler flows to the simultaneous reference flows for systemic (A) and pulmonary (B) blood flows, and derived QP:QS (C). The 95% confidence limits for the data points are shown by the dotted lines (see text for details).
either Doppler echocardiography or by the EM flowmeter, since the aorta also carries shunt flow later diverted into the pulmonary circulation. Therefore, systemic blood flow in our model was calculated by Doppler echocardiography as systemic venous return in the right ventricular outflow tract proximal to the pulmonary valve. At this site, peak flow velocities were never above the Nyquist limit, and no increase in spectral width was encountered, which indicates no significant turbulence. The measurement of the right ventricular outflow tract was obtained on two-dimensional echocardiographic images at a level just proximal to the pulmonary valve, because that is the area above the crista that has little variation in size throughout the cardiac cycle and is where the walls can be easily defined.

The mitral valve orifice method that we used in this study has the advantage of providing a two-dimensional echocardiographic image from which we can measure cross-sectional flow area directly by planimetry, instead of having to calculate it by squaring a diameter measurement. It has proved to be highly accurate in our previous studies, both in humans and animals who have intact circulation, as well as for an estimation of pulmonary blood flow in the presence of shunts at the ventricular level.11, 13

The two models used in our study enabled us to obtain variable and measurable shunt magnitudes in experimental animals and closely simulated ascending aortic and main pulmonary flow patterns of a patent ductus or other systemic arterial-to-pulmonary arterial shunts encountered in the clinical setting. Doppler tracings obtained in both models were identical and also very similar to those obtained in patients with patent ductus arteriosus.

We have recently completed a pilot study to assess the capability of the Doppler echocardiographic method to measure QP:QS ratios in children with isolated patent ductus arteriosus. We studied 11 patients, ages 3 to 37 months, with isolated patent ductus arteriosus. QP:QS determinations were performed by indicator-dilution techniques in the cardiac catheterization laboratory and the results were compared with simultaneously obtained Doppler echocardiographic measurements. In this small group of patients, an encouraging result was obtained in that Doppler QP:QS determinations correlated well with dye-curve QP:QS measurements (r = .89; SEE = ± 0.3:1). Neither cardiac motion with reference to the chest wall nor distortion of the ultrasound energy that passed through the chest wall prevented us from obtaining good Doppler echocardiographic studies in these young children or clear images of the right ventricular outflow tract and mitral valve flow areas. Nonetheless, in older patients, echocardiographic imaging of the right ventricular outflow tract may prove difficult; the technique may also prove to have limited applicability in very young infants and premature babies in whom large ductal shunts are often accompanied by left-to-right shunting at the foramen ovale, which precludes the use of mitral flow as a measure of total pulmonary flow.

In conclusion, our study demonstrates that extracardiac left-to-right shunts can be quantitated accurately by the two-dimensional Doppler echocardiographic method described in this open-chest animal model. Our initial pilot studies in young children suggest that in patients with isolated patent ductus arteriosus and no other intracardiac shunts, the technique may prove clinically useful as a measurement of the overall magnitude of the left-to-right shunting.

References

CIRCULATION
A two-dimensional Doppler echocardiographic method for calculation of pulmonary and systemic blood flow in a canine model with a variable-sized left-to-right extracardiac shunt.

E J Meijboom, L M Valdes-Cruz, S Horowitz, D J Sahn, D F Larson, K A Young, C Oliveira Lima, S J Goldberg and H D Allen

doi: 10.1161/01.CIR.68.2.437

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1983 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/68/2/437.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation* is online at:
http://circ.ahajournals.org//subscriptions/