An Enhanced Method for Measuring Cardiac Output Using Doppler Color Flow Echocardiography

Hiromi Seo, MD; Masakazu Yamagishi, MD; Syed Azilzul Haque, M.B.B.S; A.K.M. Mohibullah, M.B.B.S; Abdullah Al-Shafi Majumder, MD; Satoshi Nakatani, MD; Oi Ling Kwan, RDMS*; Anthony N. DeMaria, MD*; Kunio Miyatake, MD

An enhanced method for determining cardiac output using Doppler color flow imaging techniques to measure mitral orifice diameter was developed and validated in an experimental model and in clinical patients. In an in vitro circuit model, color jet width correlated well with actual orifice dimension from 12 to 24 mm ($r=0.99$). In the clinical application, mitral valve area was calculated as $a \times b \times \pi/4$ where $a$ and $b$ represent the width of the color flow stream in the mitral orifice just distal to the annulus in apical long-axis (short-diameter) and 4-chamber (90° rotated, long-diameter) views, respectively. Cardiac output was then computed as the product of mitral valve area and time-velocity integral of transmural flow from the same site. Cardiac output was also measured by thermodilution and conventional echocardiographic methods using diameters and time-velocity integrals from the left ventricular outflow tract. In 30 patients with nonvalvular heart disease, cardiac output measured by thermodilution ranged from 3.40 to 8.40 L/min. Cardiac output was determined in 28 of 30 patients (93%) by the Doppler color flow imaging technique; it ranged from 3.00 to 8.36 L/min and correlated well with thermodilution: $y=0.90x+0.63$, $r=0.91$. Cardiac output was determined in 24 of 30 patients by the conventional left ventricular outflow method (80%). The cardiac output measured by the conventional method correlated less closely with thermodilution ($r=0.84$), although there was no statistical difference in correlation coefficients between the 2 methods. These results indicate that the Doppler color flow imaging technique can be used to enhance the determination of cardiac output by echocardiography, particularly when the conventional method has resulted in technically inadequate recordings.

*(Jpn Circ J 1997; 61: 905–911)*

**Key Words:** Cardiac output; Doppler color flow echocardiography; Mitral orifice

Determination of cardiac output plays an important role in assessing cardiac function in patients with various kinds of heart disease. Although thermodilution methods using a balloon flotation catheter have been widely used to measure cardiac output at the bedside, complications may occur, particularly when using this catheter long term. Thus, noninvasive measurements of cardiac output can be of clinical value. Doppler echocardiographic methods of measuring cardiac output by multiplying the area and time-velocity integral of flow in the left ventricular outflow tract or the mitral annulus have been developed. However, it is sometimes difficult to obtain images that are good enough to allow determination of the diameter of the left ventricular outflow tract and the mitral annulus, thus limiting the applicability of these techniques in clinical practice.

Measurement of the width of the color flow signal from the left ventricular outflow tract or mitral orifice may enable calculation of the functional area of blood flow. We previously reported that, in an experimental model and in an in vivo study, the width of a color jet could accurately represent the diameter of the actual mitral orifice. This suggests that, when combined with flow velocity measurement, determination of color width of the mitral inflow jet can provide an accurate measurement of cardiac output, even in patients with inadequate 2-dimensional echocardiography.
graphic images. In this study, we have developed an enhanced method of measuring cardiac output using Doppler color flow echocardiography and compared the results obtained with those obtained by thermodilution and conventional Doppler echocardiographic methods. The study design consisted of (1) a feasibility study in an in vitro model and (2) clinical measurements.

**Experimental Study**

**Experimental Apparatus**

The circuit model used in this experiment has been described previously. Additional studies were carried out as part of this protocol to validate color Doppler measurements of larger flow streams, such as would be encountered across a normal mitral valve. Briefly, a glycerin solution containing Sephadex (at a viscosity of 3.8 centipoise, similar to the viscosity of blood) was rhythmically squirted into a water bath as a jet through a circular and sharp-edged orifice with a cross-sectional diameter of 12–24 mm. The driving pressure was 10 mmHg, the ejection time 500 msec, and the rate at which the jets were delivered 60/min. Each jet was examined with a Toshiba SSH-160A system using a 2.5-MHz phased array transducer. The pulse repetition frequency and color filter were set at 4.5 kHz and 400 Hz, respectively. Color gain was standardized by starting at maximal gain and then adjusting the gain downward until background noise just disappeared.

To obtain high-quality color images, the number of scan lines and the frequency of the ultrasonic interrogating bursts per scan line were increased. Each examination was performed using the narrowest sector angle (a sector arc of 30°) capable of displaying a flow jet at the orifice. Line density was set at 30 lines/frame at this sector arc. The frame rate in this setting was 10 frames/sec and the frequency of bursts per scan line was calculated from these variables.

**Experimental Procedures**

The transducer was placed parallel to the flow jet and a damper was used to obtain the same decrement of the Doppler signal that occurs during imaging in patients. The distance between the transducer and the orifice was set at 7 cm, and the transducer was moved and angled to obtain the clearest color jet. Orifice diameter was varied from 12 to 24 mm in 2-mm steps, and the color jet width for each orifice was defined as the width of color signal appearing through the hole. Jet width data were recorded as the mean value of 5 measurements and were compared with the actual diameter (Fig 1).

**Clinical Study**

**Study Patients**

In the cardiac care units of the University of Kentucky Medical Center, Lexington, or the National Cardiovascular Center, Suita, we studied 30 patients who had had a Swan-Ganz balloon flotation catheter inserted (93A-131H-7F, Edward Critical Care Division, Irvine, CA, USA) to monitor cardiac hemodynamics. These patients consisted of 19 with myocardial infarction, 7 with unstable angina pectoris, 2 with hypertensive heart disease, and 2 with cardiomyopathy. There were 23 men and 7 women ranging in age from 42 to 77 (mean 61) years. Six patients exhibited atrial fibrillation, while the others were in sinus rhythm.

The body surface area ranged from 1.53 to 2.32 (mean 1.83) m². Patients who showed moderate to severe valvular regurgitation (>grade 3 and 4) on Doppler color echocardiography were excluded from the examination. However, 24 patients with mild regurgitation were included, because the presence of mild regurgitation was considered to have little effect on the clinical measurement of cardiac output.

**Doppler Echocardiography Equipment**

We used a Doppler color echocardiography system (SSH-140A or -160A, Toshiba, Tustin, CA, or Tokyo), which was equipped to perform conventional 2-dimensional echocardiography, pulsed Doppler and Doppler color flow imaging. The system has a steerable cursor that allows Doppler sampling anywhere along the plane of the image. In the measurement of color width in patients, the settings for pulse repetition frequency, high pass filter, line density, number of bursts per scan line, and color gain were the same as in the experimental study. Echocardiographic images, Doppler velocity spectra, and simultaneous single-lead ECG were recorded on VHS video-tape and/or photos.

**Measurement of Cardiac Output by the Color Doppler Method**

There is substantial evidence to indicate that the mitral annulus is neither fixed nor circular and, therefore, approximation of the mitral orifice as an ellipse provides the most accurate measurement of transmural flow. The measurement of color width was carried out at the time of the peak E wave in the mitral flow velocity pattern during early diastole, because during this phase the mitral orifice could be fully occupied by color flow images. One of the reasons why we chose the mitral orifice just distal to

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Japanese Circulation Journal  Vol.61, November 1997
the annulus was that the flow velocity pattern at the orifice is less turbulent than at the annulus.\textsuperscript{15}

The width of the color jet was measured at the mitral valve orifice just distal to the annulus in the apical long-axis view, and was defined as an anteroposterior dimension [short diameter (a)] of an ellipse (Fig 2A). The transducer was then rotated clockwise 90° and the mitral inflow jet was observed. The transducer was moved meticulously to obtain the widest color jet. The jet width measured in this view was defined as the mediolateral dimension [long diameter (b)] of the mitral orifice (Fig 2B). Under these conditions, the 2-dimensional gain was adjusted downward so that visualization of the cardiac structures was just possible, because excessive gain on the anatomic image can obscure flow in the color display and lead to underestimation of the color flow width. Mitral orifice area was calculated according to the formula of $a \times b \times \pi/4$. Each color jet width was measured by the computer analyzing system and was represented by the mean value of 3 measurements.

Flow velocity of the mitral inflow was determined by the pulsed Doppler method from the apical 4-chamber view. Sample volume, which was 2 mm in depth and in width, was set at the same level as that at which the long diameter of the orifice was determined. The time-velocity integral was measured by tracing through the modal components of the velocity spectrum (Fig 2C). No angle correction was performed, because the angle between the direction of flow and the Doppler beam on the 2-dimensional image was negligible, as already reported by Lewis et al.\textsuperscript{6} Cardiac output was then calculated by multiplying mitral orifice area, time-velocity integral, and heart rate.

\textbf{Measurement of Cardiac Output by Conventional Methods}

Left Ventricular Outflow Method. In order to record the dimension of the left ventricular outflow tract (c) by conventional 2-dimensional echocardiography, the transducer was placed in the parasternal position to obtain a long-axis view of the left ventricle and the aortic valve. The area of the left ventricular outflow tract was calculated by assuming that it was circular: $c \times c \times \pi/4$, as proposed by Lewis et al.\textsuperscript{6}

To record flow velocity at this portion, the apical long-axis view was used. From the apical window, the
transducer was rotated slightly with a superior tilt until the aortic valve and ascending aorta were visualized and the sample volume was placed in the middle of the left ventricular outflow just proximal to the aortic valve leaflet where the dimension was determined. Cardiac output was determined as the product of the area, time-velocity integral, and heart rate.

Mitral Annular Method. The mitral annular method was performed in 18 patients who were admitted to the University of Kentucky Medical Center. Two-dimensional echocardiographic images of the mitral annulus were recorded in a parasternal long-axis view, in which insertion of the mitral leaflets into the annulus could be visualized (anteroposterior annular dimension, d), and in an apical 4-chamber view (medialateral annular dimension, e). The mitral annular area was computed for early diastole, also assuming an elliptical configuration: \(A = d \times e \times \pi/4\).

From the apical 4-chamber view, the Doppler cursor was aligned parallel to the apparent direction of mitral flow and the sample volume placed at the level of the mitral annulus in diastole. Cardiac output was calculated by multiplying area, time-velocity integral, and heart rate.

Thermodilution Method. Just after noninvasive measurements of cardiac output, thermodilution cardiac outputs were obtained by a cardiac output instrument (Model COM-2, Edwards Critical Care Division) by injecting 10 ml of 5% dextrose in water at room temperature through the proximal portion of a thermodilution Swan-Ganz catheter placed in the main pulmonary artery. Cardiac output was computed as the average of 3 determinations.

Reproducibility of Doppler Echocardiographic Measurement. To examine the reliability of color Doppler measurement, we randomly selected 10 patients with cardiac output of 4.28±0.45 L/min, and determined cardiac output by 1 observer on 2 occasions (intraobserver variability). Another observer independently performed the determination for the same 10 patients (interobserver variability). The means and standard deviations of differences between observations were 0.32±0.21 L/min (intraobserver) and 0.45±0.33 L/min (interobserver).

Statistics. Data were expressed as means±SD. The standard Student’s t test was used to compare the short and long dimensions of the mitral annulus. Simple regression analysis was used for comparisons of thermodilution and each Doppler echocardiographic method.

Results

Experimental Study

Measurement of a color width of a representative jet in the circuit model is shown in Fig 1. The width of the color jet at the orifice correlated well with the actual diameter \([r=0.99, y=1.07x-0.54]\), standard error of the estimate (SEE)=0.03 mm; \(p<0.01\) [Fig 3]. The mean absolute difference between the color jet width and actual diameter was 0.61 mm.

Clinical Study

Cardiac Output by Thermodilution Method. We were able to apply the thermodilution method in all patients examined. Cardiac output ranged from 3.40 to 8.40 L/min (mean 4.98 L/min).

Color Doppler Method and Thermodilution Method. The color Doppler method was successfully applied in 28 of 30 patients examined. The color width of transmitral flow ranged from 2.00 to 2.93 (mean 2.35) cm in short the diameter and from 2.01 to 3.14 (mean 2.59) cm in the long diameter. The mean velocity of the transmitral inflow, which is the determining factor for visualizing the well-defined border of the color jet, ranged from 22 to 62 (mean 38) cm/sec. Under these conditions, cardiac output ranged from 3.00 to 8.36 (mean 4.79) L/min. In 2 patients who had a history of chronic obstructive lung disease, color flow images of mitral inflow of adequate quality could not be obtained. When the cardiac output obtained by this method was compared with the values obtained by the thermodilution method, there was good correlation between them \((r=0.91, \text{SEE}=0.08 \text{ L/min}, p<0.001)\). There was no consistent over- or underestimation of cardiac output by either the thermodilution or color Doppler method \((y=0.90x+0.63)\) (Fig 4A).

Conventional Doppler Methods and Thermodilu-
tion. The left ventricular outflow method could be applied in 24 of 30 patients (80%) in whom 2-dimensional echo images were sufficiently accurate to allow measurement of the diameter of the left ventricular outflow. The dimension of the left ventricular outflow tract ranged from 1.65 cm to 2.48 cm, mean 2.01 cm. Under these conditions, there was a good correlation between cardiac output determined by this method (from 2.82 to 8.70 L/min, mean 4.58 L/min) and those obtained by thermodilution (r=0.84, SEE=0.13 L/min, p<0.0001). Regression equation was y=0.75x+1.48 (Fig 4B).

We were able to apply the mitral annular method in 12 of 18 patients (67%). Measured dimensions ranged from 2.20 to 3.40 (mean 2.86 cm) in the short diameter and from 2.70 to 4.20 (mean 3.24 cm) in the long diameter (p<0.05). There was also good correlation between the data obtained by this method (from 3.20 to 7.91 L/min, mean 5.36 L/min) and those obtained by the thermodilution method (r=0.86, SEE=0.16 L/min, p<0.0003), and the regression equation was y=0.86x+0.80.

Discussion

Previous Studies

Several methods have been established for noninvasive determination of cardiac output in experimental and clinical studies. Among them, Asch et al reported a technique in which cardiac output was accurately calculated in the experimental model by measuring both long and short diameters of the mitral annulus from the apical approach. Lewis et al demonstrated that Doppler methods using left ventricular outflow tract and mitral annular measurements could accurately determine cardiac output in patients. We also observed good correlations between thermodilution cardiac output and calculations derived from the left ventricular outflow tract and mitral annulus by conventional Doppler echocardiography, although calculations could not be performed for all the patients examined (80% and 67%, respectively).

The primary cause of the technical difficulties encountered in these cardiac patients was the presence of pulmonary disease, such as emphysema. Pulmonary disease impeded transmission of ultrasonic energy and yielded inadequate images of the mitral annulus (anterioposterior) and/or the left ventricular outflow tract from the parasternal long-axis view. Lewis et al proposed an alternative method in which cardiac output was measured at the mitral annulus from the apical approach. However, in that method, determination of both short (anterioposterior) and long (mediolateral) diameters was difficult because of the inadequate quality of 2-dimensional echocardiographic images from the apical window. Indeed, only the short diameter was used to calculate the mitral annular area, which was assumed to be a circle, although an ellipse appears to be the most appropriate model for the mitral annulus. Thus, when adequate 2-dimensional images of mitral annulus or left ventricular outflow tract cannot be obtained from the parasternal long-axis view, another method, which allows determination of both long and short diameters of the mitral orifice from the apical approach, should be applied.

Advantage of Color Doppler Echocardiography

The primary advantage of this method is the higher yield of technically satisfactory images in difficult patients, as the apical window allows visualization of the mitral inflow stream used in the measurements and provides an optimal angle between the Doppler beam
and flow direction.

It was essential to examine whether the measurement of color flow width could represent the actual diameter of the orifice from which flow emanates. We have previously reported that the measured color flow width correlates well with the actual diameter of the tube orifice of 4–16 mm in an in vitro model. Similar studies were performed by Thomas et al. and Baumgartner et al., who demonstrated that there was good correlation between the color Doppler-derived orifice dimension and the actual dimension in both in vitro and in vivo studies. In the present study, we performed additional correlations of color width using larger orifices, because the size of the normal mitral orifice at the level of the annulus falls within this range. Under these conditions, we found a good correlation between the measured dimension and the actual dimension, indicating the accuracy of measurement of color flow width for the determination of the functional mitral orifice.

We measured the color flow width of mitral inflow at a site just distal to the annulus from the apical long-axis view (anteroposterior diameter) and apical 4-chamber view (mediolateral diameter). The area of the mitral orifice was calculated by assuming the shape of the orifice to be ellipsoid. The calculated cardiac output correlated well with that measured by the thermodilution method \( r = 0.91 \). This correlation was closer than that obtained by other conventional methods (0.84 for the left ventricular outflow method and 0.86 for the mitral annular method), although the standard error of the estimate was similar for all 3 techniques. In addition, the correlation coefficient was higher than that obtained by the conventional method, in which the area of mitral annulus was measured by assuming it to be circular. This suggests that the color Doppler method for estimating cardiac output may be of use in patients who show inadequate 2-dimensional echo images, although in a few cases even this method is not applicable.

**Clinical Implications**

The present color Doppler method may have potential for calculating not only cardiac output but also regurgitant volumes in mitral or aortic valve regurgitation. By comparing transmural inflow determined by the present method with flow volume through the left ventricular outflow tract, the regurgitant fraction could be calculated as the difference between the results of the 2 methods, as described by Rokey et al. Indeed, our preliminary results have shown that measurements of mitral regurgitant volume, determined as the difference between mitral flow volume by color Doppler and left ventricular outflow volume, correlated well with those determined by ultrafast computed tomography, which was applied as a gold standard. Therefore, by applying the present method, noninvasive estimation of the regurgitant volume is possible even in patients in whom measurements cannot be made by conventional echocardiographic methods.

**Limitations**

Several problems are still to be resolved. First, in the present study, we measured the color width of the mitral inflow in early diastole only. Although we assumed that the orifice area where the Doppler sample volume was placed remains substantially unchanged during the diastolic period, there was evidence that the dimension of the human mitral annulus can be changed slightly. Asch et al. reported that, in the experimental model, the annular cross-sectional areas and flow calculations derived from the mid-diastolic dimensions were consistently larger than those obtained in early diastole. Thus, variation in the data obtained by the present method can be explained by these changes in the size of the mitral orifice during the cardiac cycle. Averaging of the color width during the period of mitral inflow may overcome this shortcoming, although we did not determine the actual changes in color width during a cardiac cycle. Also, changes in left ventricular contraction may affect the changes in the size of the mitral orifice area as well as the annulus area. Under these conditions, the calculation error may be augmented in patients in whom a hyperdynamic left ventricle is associated with high-output heart failure. Fortunately, no patients with hyperdynamic heart failure were included in the present study.

Second, a potential issue concerns the velocity of the transmitral jet. Because, in the present Doppler color echocardiographic system, minimum flow velocity must be more than 12 cm/sec to produce clear color flow images, a high-velocity jet might yield a well-defined jet border that is easy to measure. However, in patients who show low cardiac output not associated with such a velocity of transmitral inflow, it may be difficult to determine the actual border of color images. Improvement in the sensitivity of color imaging will be necessary to determine accurately the color width of the transmitral flow in these patients with low cardiac output.

Another limitation is that Doppler color flow assessment is still somewhat instrument dependent. However, one should be able to reproduce the results of the present method using other Doppler color flow equipment. The specific techniques used in this study
to obtain high-quality images, that is increased line density and the use of multiple bursts per line, are available on most commercial equipment. As this was a feasibility study of cardiac output measurement by color Doppler echocardiography, demonstration of intraobserver and interobserver variabilities in all patients might provide further information regarding the accuracy of the data.

Conclusions

We have proposed an enhanced method for determination of cardiac output using Doppler color flow imaging techniques to measure mitral orifice diameter, and validated it in an experimental model and in clinical patients. In addition to the newer Doppler method for cardiac output measurement\(^2\) we suggest that the present technique can be used to enhance the determination of cardiac output, particularly in patients in whom recordings obtained by the conventional method are technically inadequate.

Acknowledgments

Drs Mohibullah and Azizul were supported by a grant for the cardiology training course from Japan International Cooperation Agency (JICA), Tokyo. Dr Majunder was supported by a grant from the Japan Cardiovascular Research Foundation, Suita, Osaka. Dr Yamagishi received the Bayer’s Award in 1996 from the Japan Cardiovascular Research Foundation, Suita, Osaka.

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