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The use of Doppler techniques for quantitative evaluation of valvular regurgitation

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A satisfactory method for measuring the severity of valvular regurgitation would provide important information and prove valuable for clinical decision-making in patients with incompetent cardiac valves. Clinical examination, which is non-invasive and readily available, provides only indirect evidence of the results of regurgitation (size and dynamics of cardiac chambers) and is not a quantitative approach. Angiographic methods, described over twenty years ago, have provided the historical standard of reference for quantitating valvular regurgitation, but these techniques are not readily suited for screening purposes or repeated examination. Accordingly, recent attention has focused on a variety of newer, largely non-invasive technologies for quantitating valvular regurgitation.

Several ultrasonic techniques have been applied to the evaluation of valvular regurgitation. Both M-mode and two-dimensional echocardiography, by demonstrating evidence for chamber enlargement and increased stroke volume, provide indirect evidence of valvular regurgitation. However, these findings do not tell specifically which valve is regurgitant, nor do they indicate reliably the degree of regurgitation. Doppler echocardiography, an ultrasonic technique that utilizes changes in ultrasound frequency to measure blood flow velocity, has been used more recently to evaluate valvular regurgitation[1,2]. This non-invasive technique permits direct evaluation of intracardiac haemodynamics, and it allows quantitative assessment of blood flow through each of the cardiac valves. Studies in a number of laboratories have documented that Doppler techniques can be used to establish the presence or absence of valvular regurgitation with a high degree of certainty, using selective cineangiography as a standard of reference[3]. This paper will review several Doppler echocardiographic techniques that permit non-invasive quantitation of valvular regurgitation.

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Fluid dynamics of valvular regurgitation

The ways in which Doppler echocardiography can be used to evaluate valvular regurgitation are best understood in light of the fluid dynamics that characterize this pathophysiologic situation. In a sense, an incompetent valve can be thought of as creating a discrete obstruction to retrograde flow. A normal (competent) cardiac valve prevents blood from flowing out of the higher-pressured chamber located just downstream from the valve, into the lower-pressured chamber located just upstream from the valve. For example, during diastole the closed aortic valve keeps blood in the aortic root from regurgitating into the left ventricle. When valve coaptation is rendered abnormal by a variety of processes (i.e. trauma, infection, degenerative change, congenital abnormality, etc.) so that the valve becomes incompetent, the pressure gradient forces retrograde flow across the regurgitant orifice (in the above example, from the aortic root into the left ventricle). Because regurgitant orifices are typically small, this situation creates a jet of high velocity flow through the regurgitant orifice. Substantial pressure differences exist across the aortic valve in diastole, and across the mitral valve in systole. Thus, when the aortic or mitral valves are incompetent, the peak velocity of retrograde flow (which is directly proportional to the peak pressure gradient) is quite high. The kinetic energy within the high-velocity regurgitant jet is then dissipated as a series of vortices in the chamber that receives the regurgitant flow. These vortices, in which blood cells 'swirl', cause a broad spectrum of simultaneous Doppler frequency shifts because of the multiple directional components within the area of disturbed flow.

To maintain effective forward cardiac output, an increased volume of flow must pass antegrade across the regurgitant valve. Thus, the volume of antegrade flow across the regurgitant valve will exceed net forward flow, and the difference between total and

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net forward flow will represent the magnitude of regurgitant flow. Because of the increased volume of antegrade flow across the regurgitant valve, the velocity of forward flow through this valve may be increased, sometimes substantially. These increased antegrade flow velocities provide an additional marker for valvular regurgitation, and they can be used to help determine the degree of regurgitation.

Finally, the disparities in the volume of blood flowing through different portions of the heart are also useful indicators of the severity of regurgitation. Under normal conditions, the same volume of blood must flow through each of the four cardiac valves. However, if the mitral valve is regurgitant while the aortic valve is normal, the volume of flow passing antegrade through the mitral valve must exceed forward flow across the aortic valve by an amount equivalent to the regurgitant volume. The ability of Doppler to measure flow volumes at different intracardiac sites[4] provides yet another approach to quantitating valvular regurgitation.

Approaches to quantitating valvular regurgitation

DOPPLER FLOW MAPPING

The alterations in fluid dynamics that characterize valvular regurgitation, discussed above, provide a number of means for quantifying the severity of valvular regurgitation. Perhaps the most widely used approach is known as flow mapping. This technique is based upon the hypothesis that regurgitant flow disturbances will be distributed more diffusely with progressive degrees of regurgitation. The spatial distribution of the regurgitant flow signals is mapped by means of range-gated pulsed Doppler, typically in relation to the boundaries of the chamber of interest as viewed tomographically on a frozen-frame two-dimensional echocardiographic image. For example, this method would be used to assess the degree of mitral regurgitation (MR) by examining the left atrial cavity for evidence of a systolic flow disturbance, using pulsed Doppler. By selectively sampling flow in different regions of the left atrium, the examiner would determine if the flow disturbance was localized near the plane of the coapted mitral leaflets, distributed widely throughout the left atrial chamber, or intermediate in distribution. Regurgitant flow mapping is used to grade, semi-quantitatively, the degree of regurgitation, using derivations of the 1+–4+ scale first applied to cineangiography by Sellers *et al.*[5]. The severity of MR has been graded as 1+ when regurgitant signals are recorded only low in the left atrium near the plane of the coapted mitral leaflets, 2+ when regurgitant signals could be tracked no more than one-third of the way from the mitral plane to the left atrial roof, 3+ when regurgitant signals could be tracked over the basal two-thirds of the atrium, and 4+ when regurgitant signals fill the left atrium[6]. Similarly, the severity of aortic regurgitation (AR) has been considered mild (1+) when regurgitant signals are localized to an area high in the left ventricular outflow tract, moderate (2+) when regurgitant flow can be mapped down the outflow tract to (but not beyond) the mitral leaflet tips, and severe (3+ to 4+) when regurgitant flow signals can be mapped down to the level of the chordae tendineae or beyond[7]. A relatively small number of published validation studies have compared the results of pulsed Doppler flow mapping to semi-quantitative angiographic studies, and these studies have generally been encouraging. However, there are a number of difficulties in applying this technique in the clinical setting (Table 1), as discussed below.

Table 1 Cautions in applying Doppler flow mapping

1	Spatial distribution of regurgitation only approximated
2	Jets may be oblique or asymmetric
3	Influence of chamber size probably important
4	Different views available; several should be used
5	System sensitivity limited, especially at great depths
6	Approach is time-consuming

First, it must be recognized that Doppler flow mapping can provide no more than an *approximation* of the spatial distribution of regurgitant flow signals. Since Doppler recordings are not made simultaneous with two-dimensional imaging, one needs to assume that the chamber of interest is 'stationary' while regurgitant flow is mapped over a sequence of beats. One needs also to assume that the degree and direction of regurgitation is consistent from beat to beat. These assumptions may well be violated by arrhythmias or by beat-to-beat alterations in chamber performance.

Second, the technique of flow mapping does not specifically take into account the size of the chamber receiving the regurgitant flow. It seems sensible to suppose that when regurgitant signals fill a small left atrium in a patient with MR, for example, the volume of regurgitation is not as great as when regurgitant flow fills a substantially enlarged left atrium. To take into account these variations in chamber size, some authors have suggested that regurgitant severity be graded on the distance, in centimeters, over which the regurgitant jet can be tracked. Again, however, even this approach does not take into account the breadth as well as the length of the regurgitant jet. The blood that actually regurgitates through an incompetent valve is distributed in three-dimensions within the chamber that receives the regurgitation, while flow mapping (as described above) generally has been used to define only the distance from the incompetent valve over which regurgitation can be detected. Using this approach, a broad jet of mitral regurgitation extending back 4 cm into the left atrium would not be distinguished from a narrow jet of regurgitation that also extended a similar distance, even though the former situation would probably involve a larger volume of regurgitant flow than the latter.

Third, a number of different echocardiographic views can be used to define the distribution of regurgitant flow signals in a given chamber. In theory, since blood cells swirl in vortices in a flow disturbance, the accompanying broad-banded Doppler signals can be recorded from a variety of orientations, and one does not need to align the ultrasound beam with the direction of flow (in fact, this cannot be done because there are *multiple* directions within a flow disturbance). In practice, flow disturbances can indeed be recorded from a variety of ultrasonic windows, some of which orient the ultrasound beam approximately perpendicular to the net direction of flow. This also implies that at least some components of flow do indeed move toward and away from the transducer, even when the examining beam appears to be at right angles to the flow direction. From a clinical standpoint, the availability of multiple ultrasonic examining windows is advantageous in some patients, because of variations in ultrasonic access to a given chamber from different examining windows. In certain patients, for example, ultrasound penetration from the cardiac apex is superior to that from the precordium, so that detection of AR or MR might be most easily accomplished using apical views. In other patients, however, ultrasound penetration from the parasternal windows is superior to that available from other views, making it attractive to map regurgitation from the parasternal approach. In the case of MR, use of the parasternal window often allows positioning of the Doppler sample volume closer to the skin surface than when the apical window is used. Since ultrasonic signal strength decreases as a function of distance from the transducer, it is usually advantageous to examine at the shallowest depth possible, and this may well favor the parasternal over the apical windows, assuming equivalent ultrasound penetration. The multiplicity of potential examining views, and the possibility of disparate findings from view to view (which would be expected if regurgitant jets were not symmetrically distributed throughout the chamber) makes it unrealistic to expect consistent mapping data from view to view. Moreover, because of the above factors, it is possible that the finding of more widespread distribution of regurgitant signals could be due not only to the actual degree of regurgitation, but also a function of the diligence and completeness of the mapping examination.

The detection of regurgitant flow signals may also be limited by system sensitivity. The ability to record the broad-spectrum Doppler frequencies characteristic of a flow disturbance requires that an ultrasound signal of sufficient magnitude interacts with a large enough number of blood cells to generate Doppler signals that can be distinguished from background noise. However, ultrasound signal strength is governed by the interaction of several factors. Ultrasound penetration typically is not identical from different ultrasonic windows in a given patient, and substantial variability also exists from patient to patient. Accordingly, in patients in whom ultrasonic penetration is poor, the ability to detect the abnormal signals of a flow disturbance may be limited, and accurate delineation of the true spatial extent of the flow disturbance may not be possible. The strength of the ultrasonic signal also decreases with increasing depth of examination. This is particularly important when one attempts to map a flow disturbance as it moves away from the transducer. Of particular note is the mapping of MR from the apical window. In many patients, particularly those with substantial left ventricular and left atrial enlargement, the Doppler sample volume at mid-left atrial level may lie 15 cm or more from the transducer. Typically, substantial attenuation of ultrasonic signal strength has already occurred at these depths, so that the sensitivity to flow disturbances may well be inadequate to determine accurately the extent of MR. Finally, clinical experience suggests that not all ultrasonic instruments have equivalent sensitivity to faint flow signals; accordingly, the ability to map fully the extent of a flow disturbance may vary somewhat from instrument to instrument.

The preceding caveats are reminders that the mapping of a flow disturbance using range-gated pulsed Doppler provides only an approximation of the spatial distribution of regurgitant flow. Optimally, one needs to examine from several ultrasonic windows, to attempt to define the breadth as well as the length of a regurgitant jet, and to be cognizant of factors that may limit ultrasound signal strength and hence prevent detection of abnormal flow signals that are present. Notwithstanding these provisos, however, the technique of Doppler flow mapping has proved quite useful in daily clinical practice for assessing the severity of valvular regurgitant lesions. Although this technique does not provide a precise numerical expression of the degree of insufficiency, it does usually permit distinction of mild from moderate from severe regurgitation. In a practical sense, the finding of a localized flow disturbance by pulsed Doppler in a patient with major symptomatic limitations suggests that other causes for the symptoms must be sought. In contrast, the finding of a diffuse flow disturbance (particularly in an enlarged cardiac chamber) lends credence to the hypothesis that the regurgitant lesion is the cause of the symptoms. Finally, the finding of moderate regurgitation (by Doppler or by angiographic techniques) remains problematic in a patient with significant symptomatic limitations; in this situation, the clinician often remains uncertain that the degree of regurgitation is really enough to account for the symptoms, and usually searches for alternative diagnostic possibilities. We do find the ability of pulsed Doppler flow mapping to distinguish mild from severe regurgitation to be quite helpful in clinical patient management.

COMPARISON OF FLOW VOLUMES MEASURED AT DIFFERENT SITES

The mapping of the spatial distribution of flow disturbances is relatively time-consuming and tedious, and it provides only a semi-quantitative expression of the severity of regurgitation. Because of these shortcomings, investigators have been motivated to develop and test several newer, more quantitative approaches for evaluating valvular regurgitation. One such approach capitalizes on the ability of Doppler techniques to measure the volume of blood flow at several different intracardiac sites.

The volume of blood per beat that passes a given intracardiac site (i.e. the stroke volume) can be determined if one knows the distance-per-beat travelled by the average blood cell, and the cross-sectional area through which blood cells pass. In essence, these measures are equivalent to the height and area of a cylinder-shaped volume of blood filled during each beat. The cross-sectional area of flow can be determined by measuring the diameter of the corresponding chamber or valve, and assuming that the area of flow is circular and relatively constant during the period of flow, and that flow fills this cross-sectional area. The distance per beat travelled by an average blood cell can be determined from the profile of forward flow velocity through the chamber or valve. The temporal average velocity during the period of flow, multiplied by the duration of flow, defines how far the average blood cell travels during the period of flow. For example, stroke volume in the ascending aorta would be determined from the aortic diameter and systolic flow velocity curve. The aortic cross-sectional area would be calculated as $\pi(\text{diameter}/2)^2$. The product of average velocity and flow duration would be measured by integrating the area under the systolic velocity curve. The product of area (in cm^2) and velocity integral (in cm) would define the stroke volume (in cm^3 per beat). This has been shown to provide accurate measures of stroke volume in man[8]. Note that this approach is predicated upon the assumption that the profile of flow velocities across the area of flow is 'blunt', so that the velocity of flow actually measured is representative of the average spatial velocity across the chamber or vessel at each point in the cardiac cycle.

These principles can be applied to measure volume flow in a variety of intracardiac locations[4,9,10], so long as the preceding approximations are valid. Hence, normal volume flow can be measured in the ascending aorta, left ventricular outflow tract, mitral valve orifice, and main pulmonary artery. Validation experiments in both experimental animals and patients have shown reasonable agreement between flow volumes, measured in these sites using echo/Doppler techniques, and reference standard measures made using electromagnetic flowmeters or indicator dilution techniques[9–12]. It has been suggested that volume flow measurements can also be made from the tricuspid valve region and right ventricular outflow tract[13]. Under normal conditions, of course, volume flows should be equal at different intracardiac sites. However (as discussed above), when valvular regurgitation is present the total volume of forward flow through the regurgitant valve must be greater than the net forward flow, which potentially can be measured at a second intracardiac location.

To quantify valvular regurgitation, the volume flow technique is applied in the following manner. Total stroke volume is measured at or just beyond the regurgitant valve, from the integral of the forward flow velocity curve times the cross-sectional area through which flow passes. Net forward stroke volume is measured at a second intracardiac site, again using the forward flow velocity integral and the cross-sectional flow area. As an example, let us consider a patient with MR. Total stroke volume would be measured from the mitral diastolic flow velocity integral and the mitral annular diameter,

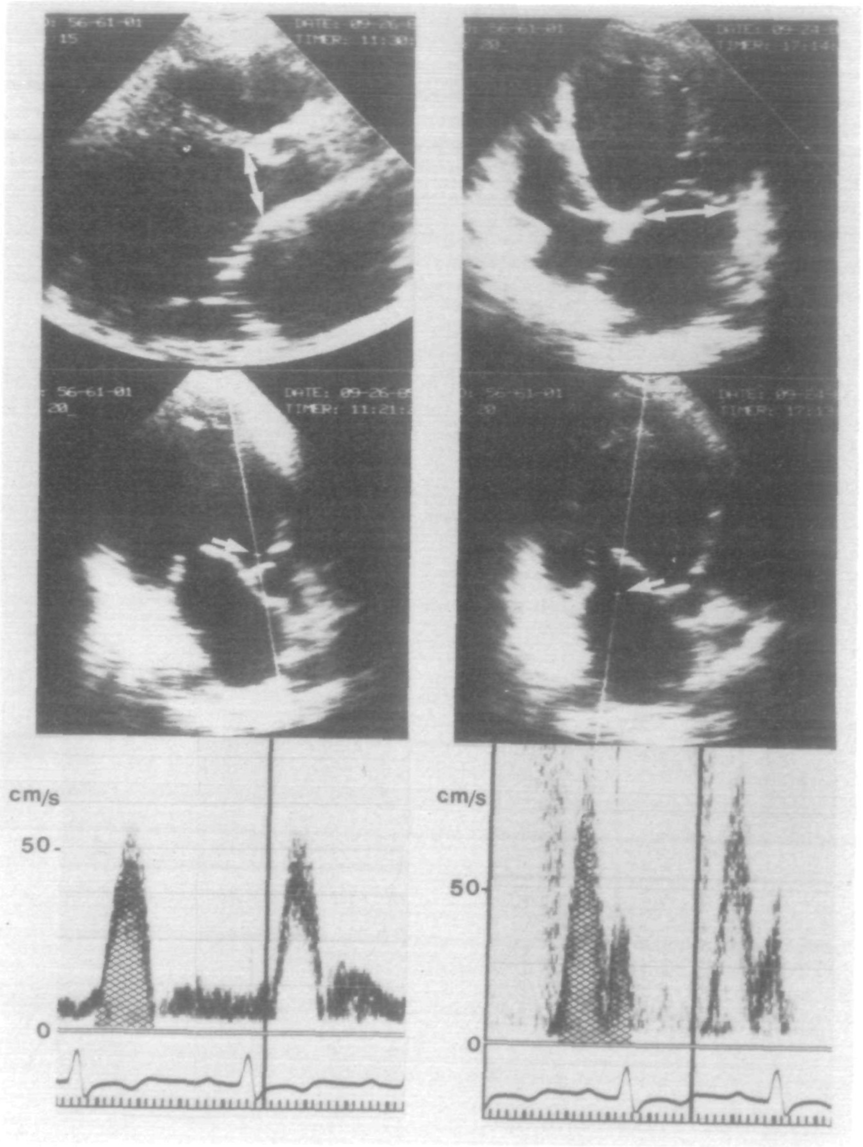

Figure 1 Measurement of volume flows in mitral regurgitation Left panels—determination of forward flow. Left ventricular outflow tract diameter (double-headed arrow, top) is measured from an apical view, and flow velocity is recorded just below the aortic valve (arrowhead, center) using pulsed Doppler. The systolic velocity integral (shaded area, bottom) is planimetered. Right panels—determination of total flow Mitral annular diameter (double-headed arrow, top) is measured from an apical view, and diastolic transmitral flow recorded from the region of the annulus (arrowhead, center) using pulsed Doppler. The diastolic velocity integral (shaded area, bottom) is planimetered. In this example from a patient with severe MR, the Doppler regurgitant fraction was 70%

assuming that the annulus is circular in cross-section and relatively constant during diastole, and that annular cross-sectional area is equivalent to the average area through which mitral flow passes in diastole. Net forward stroke volume could be measured at a variety of intracardiac locations, such as the left ventricular outflow tract, aortic root, or main pulmonary artery, so long as the aortic or pulmonic valve was competent. Using the forward velocity integral and the systolic diameter of the left

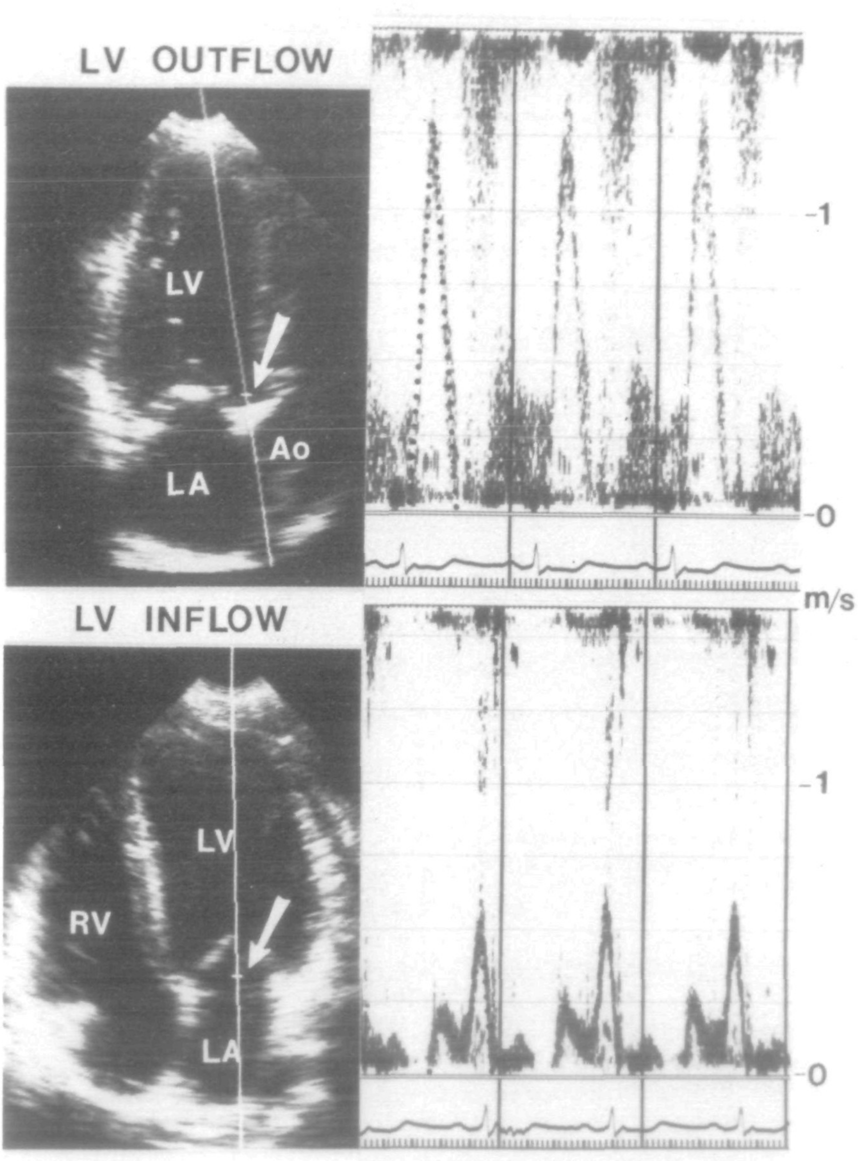

Figure 2 Measurement of volume flows in aortic regurgitation. Top panels—left ventricular (LV) outflow is measured from outflow tract diameter (left) and systolic flow velocity (right) to determine total flow. Bottom panels—LV inflow is measured from mitral annular diameter (left) and diastolic flow velocity (right) to determine net forward flow. In this example from a patient with aortic stenosis and mild aortic regurgitation, the Doppler regurgitant fraction was 32%.

ventricular outflow tract, aortic root, or main pulmonary artery, forward stroke volume would be determined. The difference between total and forward stroke volumes would be regurgitant volume; the ratio of regurgitant to total stroke volume, times 100%, would represent the regurgitant fraction. An example of this approach to quantitating mitral regurgitation is demonstrated in Fig. 1. A similar approach could be used to quantitate aortic regurgitation, by measuring total stroke volume in the left ventricular outflow tract or aortic root, and forward stroke volume through the mitral valve or in the pulmonary artery (Fig. 2). These principles have been used to measure regurgitant volume and regurgitant fraction

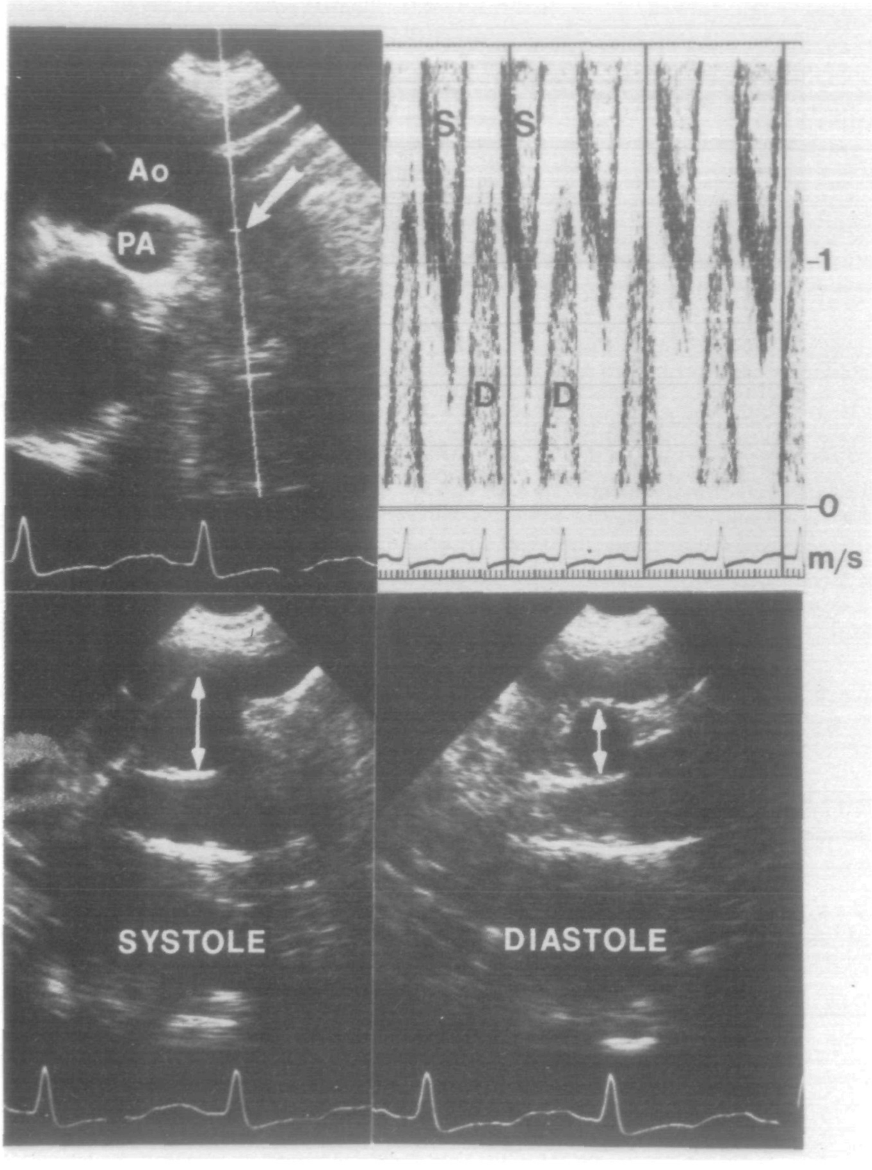

Figure 3 Measurement of forward and reverse flows in aortic regurgitation. Using a suprasternal approach (top left), flow in the proximal descending aorta (Ao) is recorded (arrow). The area under both systolic (S) and diastolic (D) waveforms is planimetered (top right). Vessel cross-sectional area is determined from both systolic and diastolic diameters (bottom panels). Maximum systolic diameter is used to determine systolic cross-sectional area, while diastolic and systolic diameters are *averaged* to determine mean diastolic cross-sectional area. Regurgitant fraction is determined as the ratio of diastolic to systolic velocity integrals, multiplied by the ratio of diastolic to systolic vessel area. In this patient with severe AR, Doppler regurgitant fraction was 63%.

in both experimental animals and small series of patients undergoing cardiac catheterization[12,14–16], with encouraging results. Of course, the same approach applies to the determination of pulmonary: systemic flow ratios in patients with intracardiac shunting, and excellent agreement with invasively measured values has been shown in a number of series of pediatric patients[12,17,18]. These clinical results support the ability of echo/Doppler techniques to measure, accurately, the volume of both normal and abnormal intracardiac flow. Although this approach has not been used to determine the severity of valvular regurgitation in large numbers of patients, it is appealing because of its attractive theoretical nature, its relative computational simplicity, and its fully-quantitative nature.

ANALYSIS OF FORWARD AND REVERSE FLOW IN THE AORTIC ARCH

A related method for determining the severity of valvular incompetence has been developed and applied to AR. In this circumstance, it is possible to measure both forward and reverse flow in the aortic arch (Fig. 3). The volume of flow that passes antegrade through the aortic arch during systole represents the total stroke volume; some of this blood regurgitates back into the left ventricle during diastole, while the rest flows peripherally and represents the net forward stroke volume. The volume of blood that passes retrograde through the aortic root, in diastole, represents the regurgitant volume itself. Several investigators have used Doppler echocardiographic techniques to measure the vessel cross-sectional area and the integral of the flow velocity waveform, and thereby to determine both total and regurgitant stroke volumes in patients with catheterization-proven AR. Boughner[19] first applied this technique using continuous-wave Doppler to record from the proximal descending aorta; he assumed that aortic cross-sectional area did not change substantially between systole and diastole, and thus calculated aortic regurgitant fraction by Doppler as the ratio of the retrograde and antegrade flow velocity integrals. Regurgitant fractions determined by Doppler in 15 patients compared quite closely to those measured by conventional angiographic techniques ($r = 0{\cdot}91$). More recently, Touche *et al*[20], applied a modification of this technique to 30 patients with cath-proved AR. These investigators used pulsed Doppler to record flow in the proximal descending thoracic aorta, and they calculated aortic cross-sectional area during both systole and diastole. Once again, excellent agreement ($r = 0{\cdot}90$) between Doppler and angiographic measures of regurgitant fraction, determined simultaneously, was observed.

To date, this approach has probably received the least clinical attention. On the other hand, it is computationally the simplest approach to determining regurgitant fraction directly, in patients with AR, and so it appears to merit further study. Additionally, the work of Touche *et al.* suggests that this approach provides repeatable measures of regurgitant fraction which may be useful for evaluating the influences of pharmacologic intervention on the severity of AR.

Current clinical role of Doppler techniques in valvular regurgitation

Doppler echocardiographic approaches for quantitating valvular regurgitation have substantial appeal because of their completely non-invasive nature, lack of apparent risk, and relatively wide availability. On the other hand, these techniques are relatively new and, in some cases, additional validation studies may well be desirable. Finally, these techniques always require substantial technical skill and meticulous attention to detail, and some of the applications are rather tedious. The attractive features of Doppler techniques for quantifying valvular regurgitation, and the practical problems in their clinical implementation, pose a dilemma.

At the current time, it would seem prudent to view Doppler techniques for quantifying valvular regurgitation as quite promising, but still in evolution. Based on our daily clinical experience, we believe these techniques are useful in distinguishing mild from severe regurgitation; this distinction, not always made easily on clinical grounds, is helpful in clinical decision-making in individual patients. More sophisticated quantitative techniques, however, are needed to define the severity of valvular regurgitation precisely, in order to study the progression of disease or its response to therapeutic intervention. Further refinement of the promising quantitative techniques described above will be needed to determine the proper methodologies for measuring valvular regurgitation not only accurately, but also repeatably. These studies will need to take into account the influence of heart rate and ventricular loading conditions on the regurgitant volume and regurgitant fraction, and the fact that haemodynamic conditions can change rather rapidly. Optimally, therefore, comparison of Doppler techniques to alternate measurement methods (such as angiography) would best be done simultaneously. Moreover, it must be recognized that other techniques for quantifying valvular regurgitation in the clinical setting also are subject to a number of approximations and shortcomings. Thus, problems with reference standard techniques may make it difficult to determine the true accuracy of Doppler echocardiographic measures. Notwithstanding these challenges, it appears that further studies will be needed to answer such questions as: Which sites are best to use for volume flow measurement? Which measurement conventions are most appropriate to determine flow cross-sectional area? How should flow mapping studies best be carried out and graded? What role does Doppler flow imaging play in quantitating valvular regurgitation?

The recent growth of Doppler echocardiography as a quantitative technique has been explosive, and Doppler echocardiographic measures of cardiac haemodynamics are already being used as a substitute for invasive determinations in some situations (such as pressure gradients across stenotic valves). The promise of the several available techniques for quantitating valvular regurgitation, coupled with widespread interest in their application for this purpose, makes it reasonable to expect that in the near future, quantitative Doppler techniques will play an increasingly important role in patients with valvular regurgitation for determining severity, investigating natural history, and determining the influence and proper use of both medical and surgical therapy.

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Addendum

Since the original submission of this article, several additional Doppler methods for evaluating valvular regurgitation have been described. Failure to explain these methods in the present article is not intended to imply that they are without merit in evaluating valvular regurgitation.