THE CLINICAL APPLICATION OF CARDIAC DOPPLER ULTRASOUND

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CONTENTS

Page No.

LIST OF FIGURES

LIST OF TABLES

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March 1987 Iain A. Simpson

SUMMARY

Two-dimensional echocardiography has revolutionized cardiovascular diagnosis by providing a non-invasive method of visualising cardiac structures in precise detail. It is, however, unable to accurately define the haemodynamic consequences of cardiac disease, often necessary for decisions regarding appropriate patient management and surgical recommendation. As a result, invasive investigation is still required in a substantial number of patients. Doppler ultrasound has the potential to provide this valuable haemodynamic information non-invasively, by measuring the direction and magnitude of intracardiac blood flow velocities. This would enhance non-invasive diagnosis and prove of major clinical importance in the management of patients with adult and congenital heart disease.

The aim of this thesis is to investigate the accuracy of Doppler ultrasound in specific types of cardiac disease and more particularly, to establish its clinical role in cardiovascular diagnosis in conditions where it is likely to confer additional advantage over clinical examination and conventional non-invasive techniques, and thereby have its most major clinical impact.

Chapter 1 provides an introduction to and historical review of Doppler ultrasound. The aim of the thesis is discussed and also the reasons why cardiac Doppler is likely to prove of particular value in the investigation of the clinical problems examined in the subsequent chapters.

The methodology of cardiac Doppler ultrasound is described in Chapter 2. The physical principles of Doppler ultrasound are outlined, and a comparison made between continuous wave, pulsed wave and high pulse repetition frequency Doppler. Doppler ultrasound systems alone and in combination with two-dimensional echocardiographic imaging are described and the reasons for the particular choice of Doppler equipment used in this thesis are also discussed. The principles of the Bernoulli and modified Bernoulli equations and their application and importance in the non-invasive measurement of obstructive gradients have been summarized. Finally, the concept of mitral pressure half-time and its relationship to the degree of mitral obstruction has been introduced.

Chapter 3 describes the application of continuous wave Doppler to 50 normal subjects. This chapter details the appropriate techniques and methods of examination used to obtain satisfactory flow velocity recordings and determines the normal range of valve flow velocities, and mitral pressure half-times.

Aortic stenosis can be difficult to assess non-invasively and even cardiac catheterisation is not always successful in determining its severity. Chapter 4 discusses the application of Doppler ultrasound to patients with aortic stenosis demonstrating its accuracy in estimating valve gradients in these patients. In combination with clinical examination and other non-invasive techniques it can also enhance the diagnostic accuracy of non-invasive assessment and predict the need for surgery in a significant number of these patients. Doppler ultrasound is therefore of clinical value in the subsequent management of patients with aortic stenosis and can further reduce the need for invasive investigation in patients with valvular heart disease.

The clinical and non-invasive assessment of patients with prosthetic valves can often prove difficult using conventional non-invasive techniques, and since many patients are maintained on long term anticoagulant therapy invasive investigation is more hazardous. The validity of using the modified Bernoulli equation to assess the degree of obstruction across bioprosthetic valves is demonstrated in Chapter 5 in a pulsatile flow model with excellent correlation obtained between the Doppler derived pressure gradients and those measured directly in vitro. Chapter 6 then demonstrates that Doppler ultrasound can be applied in vivo and accurately assess prosthetic valve gradients. The assessment of mitral prosthetic regurgitation is discussed and illustrates the accuracy of Doppler ultrasound in identifying the presence of regurgitation but also highlights the problems associated with its quantification.

Doppler ultrasound is used in Chapter 7 to investigate different types of newer bioprosthetic valve replacements and highlight the complex pressure/flow relationships that exist across these bioprostheses in vivo, but which cannot be predicted from in vitro study. In addition, in these patients, the detection of bioprosthetic regurgitation, often clinically unsuspected, emphasizes the value of Doppler ultrasound in assessing suspected bioprosthetic valve dysfunction at an early stage.

The combination of Doppler ultrasound measurement of blood flow velocity with echocardiographic measurement of vessel or orifice area can theoretically allow assessment of volumetric flow or cardiac output. Chapter 8 discusses the methodological assessment of cardiac output, with the Doppler instrumentation used in this thesis, and considers the substantial problems related to application of Doppler ultrasound in this area. The results demonstrate that a suitable methodology for measuring cardiac output can be established but that, because of the considerable problems in accurately estimation vessel area, that the value of the technique is in assessing relative changes in output within an individual.

The haemodynamic consequences of varying intracardiac pacing modalities is gaining considerable interest with the introduction of increasingly sophisticated permanent pacemakers. The Doppler assessment of cardiac output, idealy suited to the assessment of rapidly changing pacing modalities, is discussed in Chapter 9 and highlights the particular advantages of the Doppler cardiac output in these patients. The haemodynamic benefits of both atrial and atrio-ventricular (A-V) sequential pacing in contrast to ventricular pacing are demonstrated and also that variation in the A-V interval can alter cardiac output. However, the particular A-V interval providing the optimal haemodynamic response varies with heart rate and also between individuals and cannot therefore be predicted prior to Doppler examination. This suggests that Doppler ultrasound may be of value in assessing the optimal pacing modality in patients prior to permanent pacemaker insertion.

The application of Doppler ultrasound to congenital heart disease is discussed in Chapter 10, with particular reference to those lesions which, despite two-dimensional echocardiography, continue to require invasive haemodynamic assessment. This relates mainly to lesions where obstructive gradients exist and I have demonstrated that continuous wave Doppler can accurately predict gradients in pulmonary valve and artery stenosis and also in infundibular pulmonary stenosis. However, there are major difficulties associated with Doppler assessment of coarctation of the aorta. The accuracy of the technique in this area is questioned and the results of Doppler ultrasound in coarctation should be interpreted with extreme caution. In ventricular septal defects not only can it be used to identify the presence of such a lesion but by measurement of the gradient across the interventricular septum it is possible to predict, non-invasively, the pulmonary artery pressure essential in the surgical recommendation of these patients.

In conclusion, this thesis concentrates on areas of adult and paediatric cardiology where current non-invasive techniques prove inadequate and cardiac catheterisation and angiography are often required. It demonstrates that Doppler ultrasound provides important haemodynamic information, not previously possible by non-invasive investigation, in a wide variety of cardiological conditions. Currently, the major application of this technique is in the assessment lesions where high velocity jets are to be expected, providing an accurate quantification of obstructive gradients, and a more qualitative assessment of regurgitant lesions. More importantly, it demonstrates the major clinical impact of Doppler ultrasound in the assessment of these patients and that is will establish an increasingly important diagnostic role in cardiological practice.

CHAPTER 1

INTRODUCTION AND HISTORICAL REVIEW

INTRODUCTION

Potential Role of Cardiac Doppler

The development of echocardiography over the last 15 years has revolutionized the investigation of cardiac disorders. Its ability to produce accurate real-time images of the heart and associated structures non-invasively has made it an essential part of the assessment of both adults and children with heart disease. As a result in a number of these patients, echocardiography when combined with clinical assessment and routine non-invasive techniques allows surgical recommendations to be made without the need for cardiac catheterisation and angiography. It is unparalleled as a safe, simple, non-invasive technique for providing structural detail, but is of little value in obtaining the haemodynamic information often necessary for full assessment of cardiac lesions and as a result there is a continuing need for cardiac catheterisation. Although a well established procedure cardiac catheterisation is not entirely free from risk, particularly in many patients with valvular heart disease on long term anticoagulant therapy. In addition the procedure itself is not uniformly successful. Clearly, a non-invasive method of obtaining physiological information would be extremely valuable and complimentary to the structural information obtained by conventional echocardiography.

Initial methods of measuring physiological parameters included phonocardiography, pulse wave recordings and the combination of the two to identify systolic time intervals.[1] Although these early attempts at measuring physiological parameters provided some useful information they were often technically difficult to perform and did not have a major diagnostic impact. As a result they are not widely used in current clinical practice. More recently there has been interest in applying Doppler ultrasound to the field of cardiology. The ability of this non-invasive technique to study intracardiac blood flow patterns and velocities allows the potential to provide accurate haemodynamic information in patients with a variety of cardiac disorders.

Doppler Principle

The principle of Doppler ultrasound is based on the Doppler effect first described in 1842 by Christian Johann Doppler. He described the colour change of a star light source produced by the relative motion between it and an observer. This results from the change in frequency of light waves caused by this relative movement between source and observer. A similar effect is recognized with any wave source, the most apparent being the changing pitch, or frequency, of sound made by a passing train or car. In addition the frequency difference between the transmitted and reflected waves is proportional to the velocity of the relative movement. If the sound source itself is immobile the frequency shift and thereby velocity relates solely to the moving object. This is also applicable to ultrasound and it is hardly surprising that one of the major developing applications of the Doppler effect relates to the study of blood flow.

HISTORICAL REVIEW

Clinical Development of Doppler Ultrasound

The first reports of Doppler ultrasound in this respect described the use of continuous wave Doppler. In this technique two separate ultrasonic piezo-electric crystals are used, one continuously transmitting at a given frequency while the other receives the reflected ultrasound. This was first used by Satomura in the 1950s[2,3] and subsequently by Franklin in 1961.[4] The technique was applied to the measurement of blood pressure by detecting the movement of the artery wall restricted by a sphygmomanometer cuff.[5] In 1968 Stegall[6] used this method combining Doppler ultrasound and cuff sphygmomanometery to compare the non-invasive systolic and diastolic pressures with intra-arterial recordings. Correlation coefficients for systolic and diastolic pressures were 0.99 and 0.98 respectively, and similar results subsequently obtained by Poppers in 1973.[7]

The next step involved detection of the moving blood itself, and led Yao et al[8] to measure blood pressure by replacing the stethoscope with ā Doppler probe, and opened the way for the use of Doppler ultrasound in the investigation of peripheral vascular disease.[9] Yao[10] found that the "pressure index", a ratio of brachial and ankle systolic pressures, was related to the amount of functional disability from lower limb vascular disease and Allan and Terry[11] graded the severity of the arterial diseaese by utilizing Doppler ultrasonic pressure measurements at various points along the arterial system of the affected limb. Consequent upon the detection of blood flow there then developed much interest in the shape of the blood flow waveform. Initially described in a qualitative fashion in occlusion of the profunda femoris artery,[12] measurement of the the change in flow waveform shape, by measuring waveform time delays[13] and pulsatility index[14] has lead to the use of these techniques in the quantification of arterial occlusion. Using pulsatility index, defined as the peak to peak excursion of the Doppler waveform divided by its mean height, Gosling has achieved accurate diagnosis of occlusive arterial disease of the lower limbs. More recently flow pattern analysis by Doppler imaging systems has allowed three dimensional appreciation of the internal structure of peripheral arteries and have allowed Doppler data to be analysed from specific parts of the peripheral arterial system.

The application to cardiology of the early Doppler techniques, initially used to examine the peripheral vasculature, was limited by the sole use of continuous wave Doppler. Since it was not possible in the continuous wave mode to selectively study intracardiac flow recordings from different chambers at various depths, examination was essentially limited to the extracardiac structures. These systems were however suitable for recording from the major extracardiac vessels and with the introduction of directional continuous wave Doppler instrumentation[15] the study of Doppler recordings from the aortic arch, or transcutaneous aortovelography, was developed.[16-18] This was the forerunner of much of the current interest in the study of cardiac function by Doppler ultrasound. These early continuous wave systems incorporated full spectrum analysis, providing a visual display of the whole range of frequency shifts obtained over time. Alternative applications soon became apparent and using such a system Tunstall Pedoe was able to demonstrate excessive reverse flow in recordings from the subclavian artery in over 80% of patients with known aortic incompetence.[19]

The introduction of pulsed wave Doppler systems by Peronneau[20] and Baker[21] paved the way for the investigation of depth selected velocity recordings. These early systems used high ultrasonic frequencies, greater than 4 MHz, and as a result tissue absorption made the investigation of deeper structures difficult. In addition pulsed wave systems are unable to measure high velocities accurately and the initial methods used to provide directional velocity[20] further limited the magnitude of the velocities that could be recorded by these systems. The development of a pulsed Doppler velocimeter by Angelson and Brubakk[22] overcame many of these problems by using a lower ultrasound frequency (2 MHz) and a superior method of determining directional velocity, and reflected similar advances in the development of pulsed Doppler systems by other workers.[23-25]

The currently available "stand alone" Doppler systems such as that used for the majority of work in this thesis (Vingmed, Norway) confer many advantages over the above systems by combining both pulsed and continuous wave facilities. They are also interfaced to more sophisticated spectrum analysis instrumentation providing more accurate real time analysis of the Doppler signals. These systems require a substantial degree of skill in manipulation of the Doppler transducer as the Doppler signal is the only aid to obtaining the optimal velocity profile from the appropriate area of interest.

Development of Duplex Systems

There has therefore been much interest in the development of Doppler systems combined with echocardiographic imaging, known as "duplex" systems, to provide a method of guiding the

Doppler beam within the intracardiac image. It should be noted that optimizing a Doppler system has different requirements than that of an echocardiographic imaging system and the combination of the two will, to a degree, compromise the sensitivity of the Doppler equipment. "Stand alone" systems will therefore have some advantages over their "duplex" couterparts. The M-Mode echocardiogram was initially used in an attempt to guide the Doppler ultrasound beam[26] and lead to the introduction of the term "Doppler echocardiography". However the optimal M-Mode echo transducer position is at right angles to the structure of interest in order to provide maximum ultrasound reflection whereas the optimal Doppler transducer position is in the direct line of blood flow in order to maximize the Doppler frequency shift. Clearly the M-Mode echocardiogram is far from ideal in aiding the position of the Doppler beam. This is not so with the combination of Doppler and two-dimensional echocardiographic imaging. Two-dimensional imaging from the apical and suprasternal positions in addition to the parasternal views allows real time appreciation of the intracardiac structures and has the potential to aligne the Doppler beam in direct line of blood flow. It is now possible to obtain simultaneous real time echocardiographic imaging without reducing the maximum velocity that can be measured by pulsed Doppler.[27] With these particular systems it is also possible to perform continuous wave examination with simultaneous echo imaging. This type of system is likely to be of particular value where complex intracardiac anatomy exists as in complex congenital heart disease.

Application of Cardiac Doppler

With the apparent potential of Doppler ultrasound to study cardiac blood flow a number of initial studies have described the use of the technique in a variety of cardiac disorders.

Valvular Heart Disease

In adults with valvular heart disease, Doppler ultrasound was first successfully applied to mitral stenosis by Holen et al in 1976[28] who demonstrated, using continuous wave Doppler, that the pressure drop in mitral stenosis could be calculated from the Doppler measurement of mitral flow velocity. The use of Doppler to assess mitral valve gradients has been confirmed by a number of subsequent studies comparing the Doppler derived pressure drop with that obtained at catheterisation.[29,30] It was Hatle et al[29] who adopted a modification of the Bernoulli formula to calculate the pressure drop across an obstruction from the measured maximum velocity and is becoming a widely accepted method of calculating valve gradients with Doppler ultrasound. A further advance in the Doppler assessment of mitral stenosis occurred when Hatle et al[31] introduced the concept of the mitral "pressure half-time", the time interval taken for the maximum diastolic flow to fall to the equivalent of half its initial pressure derived using a modification of the Bernoulli formula. This provided an estimation of the degree of mitral valve obstruction which was independent of cardiac output and could therefore be related to the mitral valve area itself. In addition to the continuous wave technique, pulsed wave Doppler has also been used to assess mitral stenosis[32,33] but is a less satisfactory method for providing a quantitative assessment, because of its inability to measure high flow velocities. This important aspect of pulsed Doppler will be discussed more fully in Chapter 2.

However pulsed Doppler does have potential advantages in the assessment of mitral regurgitation. Systolic turbulent flow patterns can be detected with the Doppler sample volume positioned within the left atrial cavity and high sensitivity and specificity has been reported in combination both with M-Mode[34-36] and two-dimensional[37,38] echocardiography. In addition to detecting the presence of mitral regurgitation by mapping the extent of turbulent flow within the left atrial cavity, pulsed Doppler has been used to estimate the severity of regurgitation and has compared favourably with left ventricular angiography.[39,40]

Initial reports of assessing aortic stenosis by Doppler ultrasound utilized the continuous wave technique and the application of the modified Bernoulli formula.[41] In measuring valve gradients excellent results were obtained in patients under the age of 50 and superior correlation obtained when children and younger adults were examined.[42] However the technique used was not as successful in patients over the age of fifty. With the introduction of spectral analysis in combination with continuous wave Doppler improved results have been reported in both adults and children with satisfactory application of the technique even in the older patient population.[43-46]

Doppler ultrasound has been reported to be a highly sensitive and specific method of identifying aortic regurgitation even in the absence of clinical findings.[47] In addition estimation of the extent of regurgitation has been made by mapping the extent of the regurgitant jet within the left ventricular cavity[48] or utilizing a forward to reverse flow ratio in patients with pure regurgitation.[49]

There has been little information available relating to the use of Doppler ultrasound in the assessment of right heart lesions although a few reports have used pulsed[50,51] or continuous wave[52-54] Doppler to measure pressure gradients both in pulmonary valve and infundibular stenosis in infants and children and similar results have been reported to those obtained for aortic stenosis. The diagnosis of tricuspid stenosis and regurgitation by Doppler ultrasound has also been reported.[55,56]

Prosthetic Valve Function

In addition to the study of native valve disease several reports have described the application of the Doppler technique to small numbers of patients with either mechanical[57,58] or porcine valve prostheses.[59-61]

Volumetric Flow Analysis

It has been suggested that by combining the Doppler assessment of aortic flow velocity with aortic dimensions a volumetric analysis of flow can be obtained and the potential exists to non-invasively measure stroke volume and cardiac output. Recent studies have shown good results comparing the Doppler assessment with invasive measurement of cardiac output.[62-65] Other workers have validated cardiac output measurements in vitro[66] and in vivo[67,68] using mitral rather than aortic flow in an attempt to overcome potential problems in accurately measuring aortic root dimensions. Doppler ultrasound has also been used to measure aortic flow velocity curves without the combination of echocardiography. Without the measurement of aortic dimension absolute values of stroke volume and cardiac output are not possible but relative changes in these parameters can theoretically be assessed. This has been successfully demonstrated using continuous wave Doppler ultrasound,[69,70] by transcutaneous aortovelography, and also using pulsed wave systems.[71,72]

Despite extensive work in validating the non-invasive measurement of cardiac output by Doppler ultrasound an established methodology has not emerged. The methods using aortic blood flow velocity have been most extensively investigated and tend to be more practical in many intensive care or laboratory situations. It has been suggested that, at present, it is preferable to combine the measurement of aortic flow velocity with aortic root dimension to provide a volumetric assessment of cardiac output[73] though if only relative change in cardiac output is required this can acceptable be measured by Doppler ultrasound alone. However in the studies utilizing aortic blood flow velocity and echocardiographic estimation of aortic root dimension there is considerable variation in the exact methodology used.

If an accurate methodology could be established the technique has many potential applications and reports have already been suggested that it may be of value in the intensive care setting,[62,63,74] and in assessing the haemodynamic response to vasodilator therapy in patients with heart failure.[75] The technique has particular advantage in that it can provide multiple serial measurements without the need for repeated intervention ideal for monitoring cardiac function in critically ill patients, and also of potential value in more healthy individuals where there is often reluctance to subject them to the relatively small risks associated with invasive haemodynamic monitoring.[76,77]

Congenital Heart Disease

In paediatric cardiology echocardiography can now provide information on the intracardiac and great artery anatomy with considerable detail. However decisions regarding the need for surgery require knowledge not only of the presence and structure of a lesion but also of its haemodynamic consequences. If Doppler ultrasound was able to provide such haemodynamic information non-invasively it would clearly have major potential in the assessment of congenital heart disease.

Initial studies of Doppler ultrasound in paediatric cardiology have related mainly to two areas; the detection and quantitation of obstructive lesions, and the assessment of shunt lesions.

The few available reports using Doppler ultrasound to measure pressure gradients in right ventricular outflow obstruction were mentioned earlier. Doppler ultrasound has also been applied to aortic coarctation in a small number of cases[78] but currently little data exists as to the validity of the technique in this area.

In assessing lesions associated with cardiac shunting

Doppler studies have involved two approaches. Either an assessment of the presence and/or magnitude of the shunt has been determined or its haemodynamic consequences measured by the non-invasive assessment of the pulmonary to systemic flow ratio. The measurement of pulmonary to systemic flow ratio by the Doppler technique essentially involves assessing cardiac output from both the right and left heart. Several studies comparing this with invasive methods have reported good correlation between the two techniques.[79-83] In the diagnosis of individual congenital lesions, the use of Doppler ultrasound has been reported in atrial septal defects,[84-86] ventricular septal defects[87-89] and in patent ductus arteriosus.[90]

The use of Doppler ultrasound has been reported in the assessment of complex forms of congenital heart disease[91,92] where, because of the presence of more complex structural abnormalities, the use of an integrated echo and Doppler system is undoubtedly preferable.

AIM OF THESIS

Although these initial reports have suggested a developing potential for the use of Doppler ultrasound in a variety of cardiac disorders the clinical role of the technique remains to be established.

The aim of this thesis was to investigate the areas of cardiovascular medicine where Doppler ultrasound has potentially major clinical application and is most likely to have a significant impact as a diagnostic technique.

THESIS OUTLINE

Chapter 2 will discuss the physical principles of Doppler ultrasound, the methodology used in this thesis and its theoretical basis. I will also deal with the particular Doppler instrumentation and analysis used and the rationale for such a choice.

In applying a new technique to any disease state it is clearly important to first determine what constitutes normality. Chapter 3 will report the normal range of valve flow velocities obtained by Doppler ultraosund and the methods of examination in a series of healthy individuals.

Two-dimensional echocardiography is a well established non-invasive method of assessing the severity of valvar stenoses. In adult patients it is of particular value in the assessment of mitral stenosis,[93] but difficulties have been reported in accurately assessing patients with aortic stenosis.[94,95] Chapter 4, will therefore discuss the clinical value of Doppler ultrasound in assessing the severity of aortic stenosis in adults.

Chapters 5,6, and 7 relate to the study of prosthetic valve function. I will report the validation of Doppler ultrasound both in vitro and in vivo and the application of the technique to the study of 155 investigational bioprosthetic valves.

The non-invasive assessment of cardiac function constitutes a major potential application of Doppler ultrasound. Chapter 8 will concentrate on the methodology of cardiac output assessment in order to establish that most appropriate for the Doppler instrumentation used in this thesis. There is growing interest in the haemodynamic consequences of pacemaker function and the application of non-invasive techniques to its assessment. Having established the appropriate methodology for the non-invasive assessment of cardiac output Chapter 9 will discuss the results obtained in applying this to the haemodynamic investigation of varying pacemaker modalities during electrophysiological study.

Finally, Chapter 10 will deal with the value of Doppler ultrasound in the assessment of congenital heart disease.

Continuing technological advancement in the field of cardiac Doppler ultrasound makes an assessment of its clinical applications subject to continual review. Clearly Doppler ultrasound has the potential to provide functional rather than structural information, complimentary to conventional echocardiography and can therefore have a certain application to most cardiac lesions. However it is my attempt is this thesis to focus on the areas of major impact in both adult and paediatric cardiology and to place the role of Doppler ultrasound in perspective to currently established non-invasive diagnosis.

CHAPTER 2

METHODOLGY

INTRODUCTION

This thesis will investigate and evaluate the major clinical applications of cardiac Doppler ultrasound. It is important to first understand the principles and basic physics of the Doppler technique and the relative merits and limitations of the varying types of Doppler instrumentation. This chapter will consider some of the basic physical principles of Doppler ultrasound with particular emphasis on the techniques used in the subsequent studies, describe the equipment chosen at the inception of these studies and the reasons for such a choice, and also highlight the clinical application of the physical principles of Doppler ultrasound that confers the major potential of this technique as a valuable noninvasive clinical investigation.

BASIC DOPPLER PHYSICS

The Doppler Effect

The Doppler effect first described by Christian Johann Doppler in 1842, related the colour change of star light caused by relative movement between the light source and observer. Although first described for light waves the Doppler effect is relevant to any wave source. The change in the pitch of sound caused by a passing car or train is therefore a result of the Doppler effect. The Doppler effect is also appplicable to ultrasound and as illustrated in Fig. 1 demonstrates the change in frequency of the reflected ultrasound caused by the relative movement between object and sound source. If the object is moving in the direction of the sound source the reflected ultrasound frequency will be higher than the transmitted frequency. Similarly, if the object is moving in the opposite direction then the reflected ultrasound frequency will be lower than the transmitted frequency. It is immediately clear therefore that Doppler ultrasound provides directional information of the object studied. In addition however, the change in the ultrasound frequency caused by the moving object is directly proportional to its velocity as defined by the Doppler equation:-

$$V = \frac{fd.c}{2f.\cos\theta}$$

where V = velocity of blood flow, fd is the Doppler shift in frequency, c = velocity of sound, f = emitted ultrasound frequency and θ = the angle between the direction of blood flow and the ultrasound beam.

For example, the velocity of sound in biological tissue (c) is known at 1560 m/s, for a 2 MHz transducer the emitted ultrasound frequency (f) is 2,000,000 Hz. If the ultrasound beam is in the direct line of blood flow then $\cos\theta$ will be 1. Therefore, if the Doppler frequency shift is, for example,

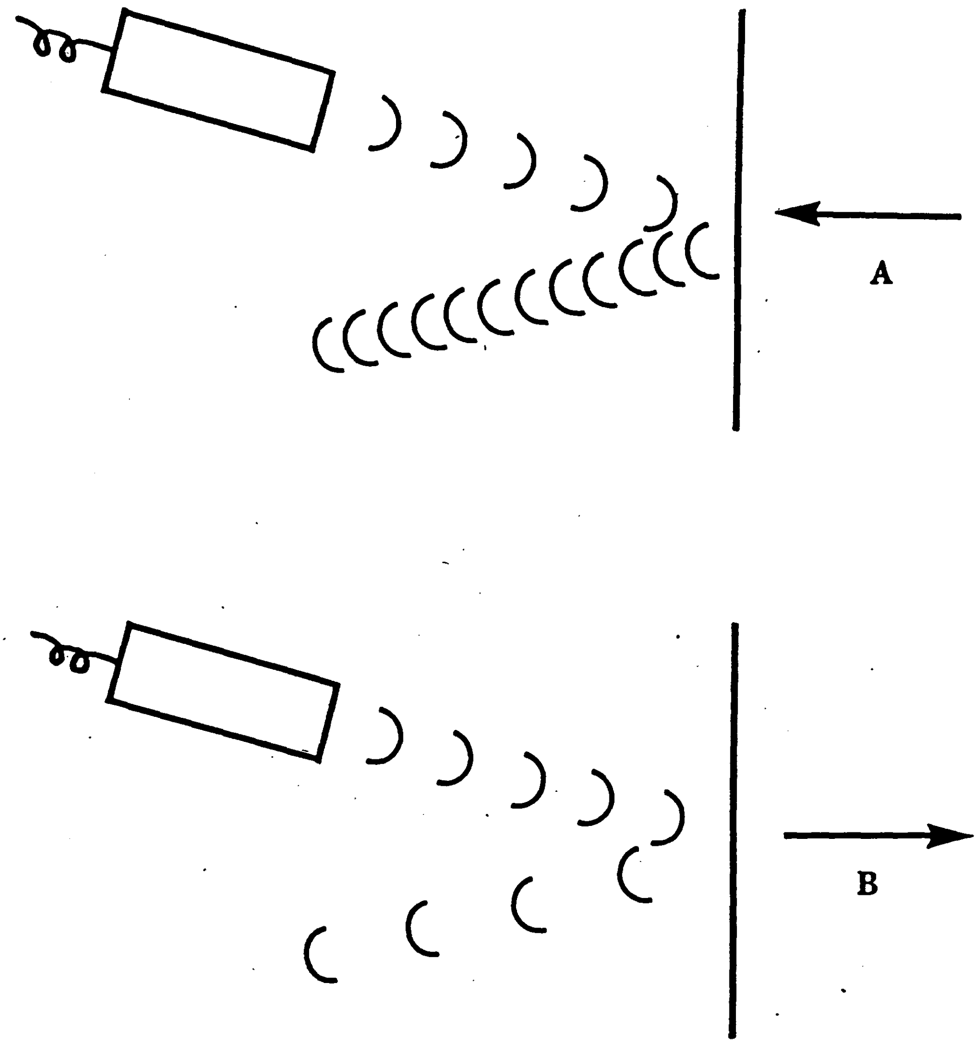


Figure 1: The Doppler effect. An object moving towards a sound source (A) produces an increase in the frequency of reflected ultrasound, and an object moving away from a sound source (B) produces a decrease in reflected ultrasound. In addition the change in the emitted frequency is proportional to the velocity of the moving object.

2560Hz then:-

$$V = \frac{2560 \text{ X } 1560}{4000000 \text{ X } 1}$$

$$= 1 \text{ m/s}$$

Potentially therefore, it is possible not only to obtain te direction of blood flow by Doppler ultrasound, but also its velocity. If the frequency of the Doppler ultrasound transducer (f) is increased, then for a given flow velocity, and a similar intercept angle, the Doppler frequency shift obtained would be higher. Alternately, for an equivalent Doppler frequency shift using a higher frequency Doppler transducer, then the estimated velocity would be less. Therefore in the above equation if a 5 MHz transducer, rather than a 2 MHz transducer had been used, a Doppler frequency shift of 2560 Hz would be equivalent to a velocity of 0.4 m/s.

Since the velocity of ultrasound in biological tissue is constant and all Doppler studies in this thesis were performed using a 2 MHz Doppler transducer, the measured velocity of blood flow is related solely to the Doppler frequency shift and the angle between the Doppler ultrasound beam and blood flow. Ideally the Doppler ultrasound beam should be aligned in the direction of blood flow where $\cos\theta$ will be 1 and the velocity will be accurately reflected by the measured Doppler frequency shift. Since the actual velocity of blood will remain unchanged it can be seen from the Doppler equation that if the intercept angle between the Doppler ultrasound beam and blood flow is greater than zero, cosθ will become less than 1, and the Doppler frequency shift will be lowered, causing an underestimation of the velocity of flow. If the intercept angle is 90 degrees then cosθ will be 0 and since there will then be no change in the transmitted frequency, i.e. no Doppler shift, since flow is neither moving towards or away from the sound source, the detected velocity will also be 0. It would clearly be valuable to measure the intercept angle in combination with the Doppler frequency shift in order to provide an accurate estimation of flow velocity. However, although echocardiography can provide structural detail and it is possible to incorporate Doppler ultrasound with an echocardiographic image, assessment of the intercept angle could only be accurately obtained in two dimensions whereas the actual angle between the Doppler beam and the direction of flow will be related in three dimensions. More important, perhaps, is the fact that the directly of blood flow may be unpredictable, particularly with respect to jet lesions associated with valvular disease, and the direction of flow predicted on an anatomical basis may bear little relationship to the true value. Using this method there is clearly potential to significantly overestimate the intercept angle and cause discrepant overestimation of the true velocity of flow. Fortunately, if the intercept angle is 20 degrees or less, velocity will be underestimated by a maximum magnitude of only 6% which would probably be acceptable for clinical purposes. With the availability of multiple praecordial position for ultrasound transducers it should be possible in the vast majority of cases to angle the Doppler ultrasound beam close to the direction of blood flow, indicated by the position providing the largest Doppler shift for a particular flow velocity. It would then be possible to effectively ignore the intercept angle from the Doppler equation and flow velocity would be related solely to the measured Doppler frequency shift.

With cardiac Doppler the moving objects are mainly the red blood corpusles so that multiple frequency shifts will be obtained from a single Doppler beam sample since this will contain a large number of red blood cells. If all the blood cells are travelling along regular lines at a similar velocity, then blood flow is termed laminar, and a narrow band of Doppler frequency shifts will be obtained. However, if blood flow is turbulent, then within the Doppler sample there will be blood cells travelling at many different individual velocities and directions and will be reflected by the wide range of frequency shifts obtained.

Continuous and Pulsed Wave Techniques

Two basic cardiac Doppler ultrasound techniques are available, continuous and pulsed wave modes. In the continuous wave mode two separate piezo-electric cyrstals are required, mounted side by side. One continuously emits ultrasound at a given frequency while the other receives the reflected ultrasound. Continuous wave Doppler will detect the velocity of blood flow along the entire path of the emitted ultrasound beam and as a result cannot provide any resolution of the depth of sampling. Since the different blood elements along the Doppler beam will have different velocities, a spectrum of Doppler frequency shifts will be received, but as we will see, with spectrum analysis it is possible to distinguish characteristic flow velocities from certain regions along the path of the Doppler ultrasound beam. This is illustrated in Figure 2 where a spectral display of a continuous wave Doppler signal is shown. Although flow velocities are identified along the whole of the Doppler ultrasound beam, the maximum flow velocity signal is clearly a result of flow through the mitral valve when compared with the pulsed Doppler spectral display of mitral flow velocity (Fig. 3). The major advantage of the continuous wave technique however is that, unlike the pulsed wave mode, there is essentially no limitation to the maximum velocity that can be measured. This is an extremely important advantage in the assessment of obstructive lesions where maximum velocities will extend well outwith the range of pulsed Doppler examination.

With the pulsed wave technique a single transducer acts both as a transmitter and a receiver, and ultrasound transmitted in a short burst is received by the transducer after an appropriate time delay. Once the transmitted signal has been received a further burst of ultrasound can be transmitted and

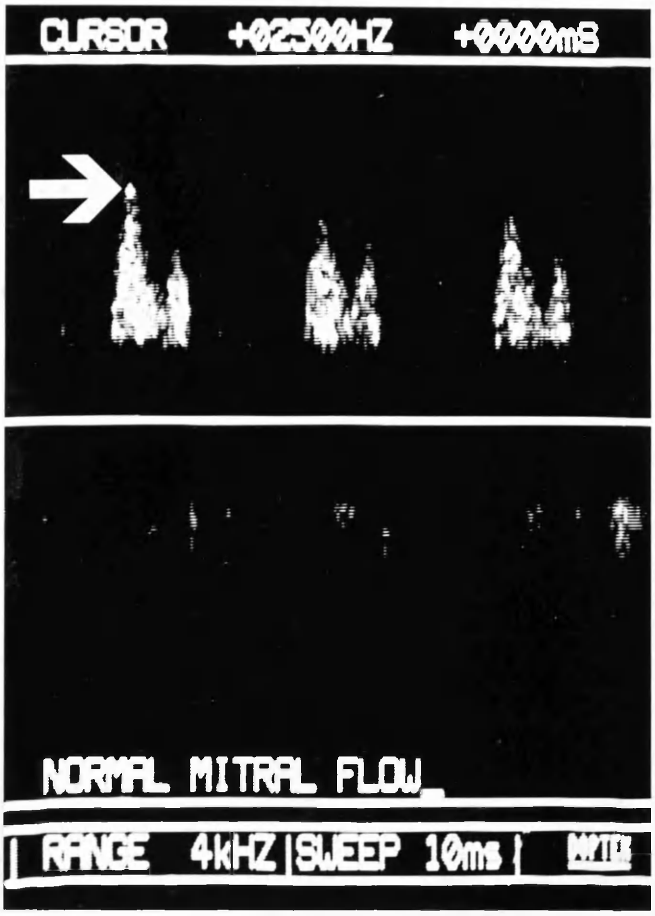


Figure 2: Continuous wave spectral display of normal mitral flow. Since all velocities along the length of the Doppler beam are included the spectral display is "filled in" under the maximum velocity recording. The cursor (arrowed) placed at the peak diastolic signal displays the maximum frequency shift (2,500Hz) equivalent to a velocity of 1 msec^{-1}.

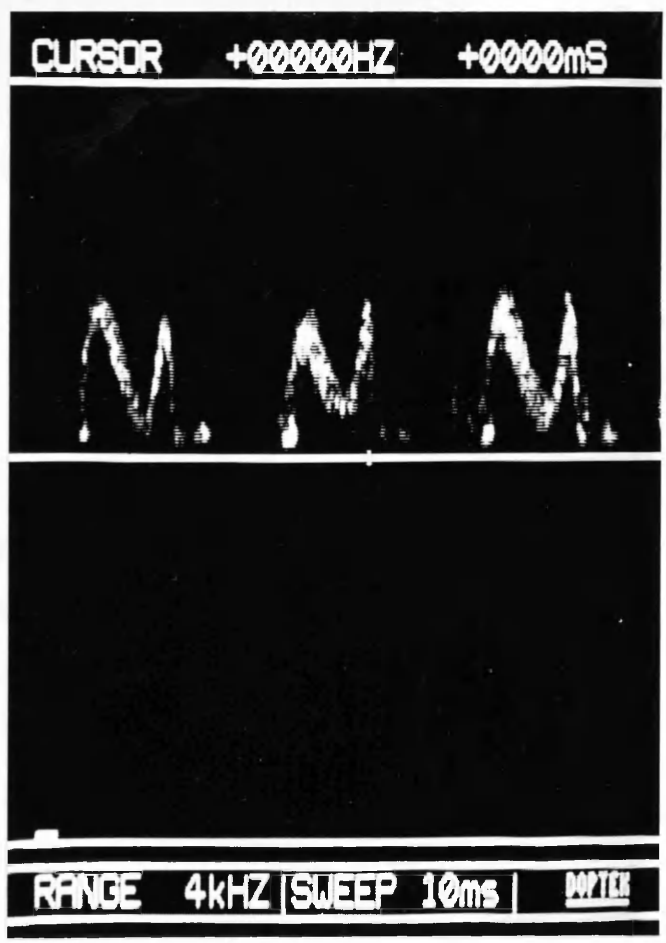


Figure 3: Pulsed wave spectral display of normal mitral flow from the apical position. Since, in the pulsed mode, only one portion of the velocity jet is sampled the signals obtained are of similar magnitude with a narrow band of velocities and the low frequency signals excluded.

the cycle repeated. Since the velocity of ultrasound in biological tissue is constant at around 1560 m/s, the time delay between transmission and reception allows measurement of the depth of the structure reflecting the ultrasound, identical to the principle of conventional echocardiography. By analysing signals occurring after a certain time delay a sample volume can be produced which can be varied to at any depth along the Doppler beam. The length of this sample can also be varied by altering the length of the transmitted pulse. This ability to provide depth resolution of Doppler sampling in conjunction with simultaneous echocardiographic imaging is the major advantage of the pulsed mode over continuous wave examination and allows the site of a particular Doppler signal to be determined in relation to the structural information obtained by echocardiography.

Frequency Aliasing

The disadvantage of the pulsed wave mode results from a phenomenon known as frequency aliasing, which limits the maximum frequency that can be measured at a given depth. The frequency with which a pulsed system transmits ultrasound pulses is known as the pulse repetition frequency. This is limited by the fact that having transmitted a pulse of ultrasound, in order to avoid ambiguity of depth, it has to wait till the ultrasound pulse has been received before a further pulse is transmitted. Since the velocity of ultrasound in biological tissue is constant then it will take longer for an ultrasound pulse to be reflected from a deeper structure, further from the ultrasound transducer, and the pulse repetition frequency will have to be lowered. If a further pulse is transmitted before the previous one has been received it will not be possible to detemine whether a received signal has been reflected from the first ultrasound pulse by a deep structure, or from the second pulse by a structure close to the ultrasound transducer. Since the major advantage of pulsed Doppler is its ability to provide depth resolution, in order to maintain this the pulse repetition frequency will be limited. The effect of pulsed Doppler is similar to that of a stroboscope or movie picture. Here the movement of a spinning object, equivalent to the Doppler frequency, will be accurately defined providing it does not spin faster than half of the time between samples, i.e. half the pulse repetition frequency. When it exceeds this, as with a stagecoach wheel in a Western movie, it will appear to spin as rapidly in the opposite direction. This in effect is frequency aliasing. Using pulsed Doppler therefore the maximum frequency shift, and therefore velocity, measurable will equal one half of the pulse repetition frequency of the system. This limitation to the maximum measured frequency is known as the Nyquist limit. The further from the transducer that the pulsed Doppler sample volume is located then the lower the pulse repetition frequency will be and therefore the lower the Nyquist limit. If a frequency shift higher than half the pulse repetition frequency is produced then frequency aliasing occurs, and the top of the Doppler spectrum appears "cut off" and is located at the extreme limit of the opposite frequency channel, the equivalent to spinning in the opposite direction, as demonstrated in Fig. 4 from a patient with mitral stenosis. In this example, with knowledge of the effect of frequency aliasing, the maximum frequency is still apparent and it would be possible to replace this on top of the positive Doppler frequency spectrum and obtain a true velocity recording. However, it will be apparent that when the maximum frequency shift increases even further, to a level of twice the Nyquist limit, equivalent to the pulse repetetion frequency, then the maximum frequency shift and hence velocity will become lost within the Doppler signal, and a "wrap around" phenomenon occurs. This is demonstrated in Fig. 5 from a patient with mitral regurgitation, where the very high peak velocity, or frequency, associated with this lesion is lost.

High Pulse Repetition Frequency Doppler

A potential solution to frequency aliasing would be to increase the pulse repetition frequency which would increase the maximum velocity that could be measured. However, as discussed this would necessitate transmitting one or more further pulses before the first had been received and this would then cause depth ambiguity, in that the Doppler signal would be a composite of the received signals from each transmitted pulse of ultrasound at different depths along the line of the Doppler beam. The origin of a high velocity recorded in the Doppler signal could be from one of several different depths. The

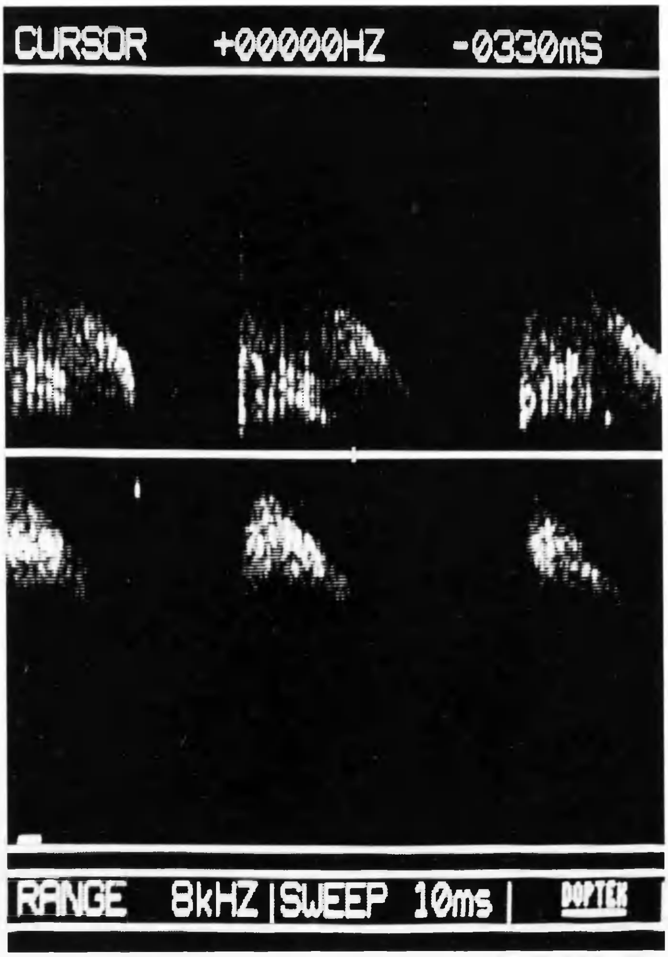


Figure 4: Frequency aliasing with pulsed Doppler in a patient with mitral stenosis. With flow directed towards the transducer (upper channel) the top of the signal is "cut off" and appears in the lower channel.

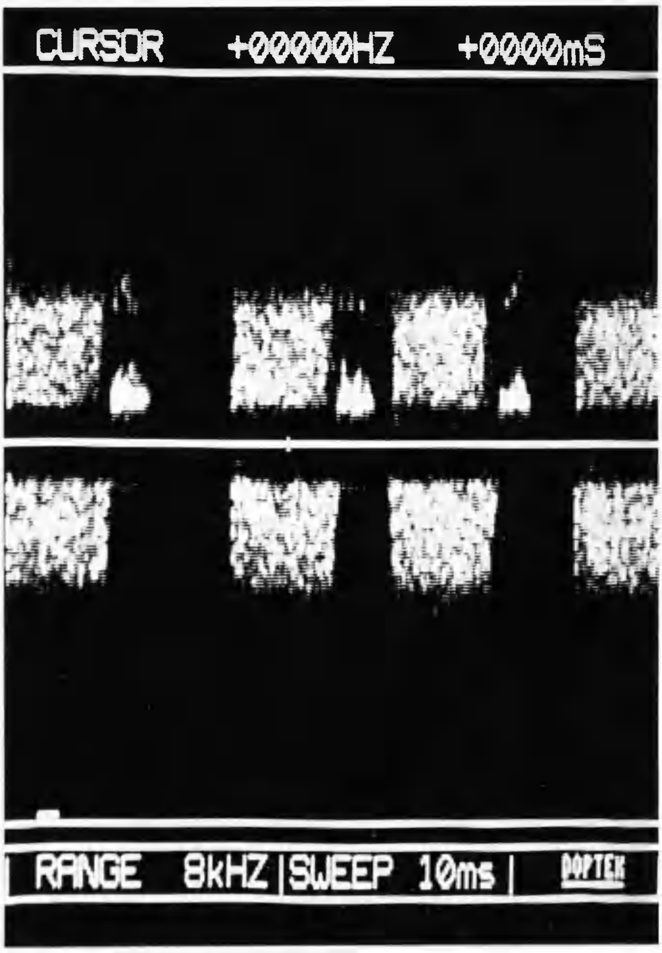


Figure 5: Frequency aliasing with pulsed Doppler in a patient with mitral regurgitation. A "wrap around" phenomenon of the high velocity jet directed away from the transducer gives the appearance of bidirectional flow.

attraction of high pulse repetition frequency (HPRF) Doppler however, is that like pulsed Doppler, it can be incorporated into a real-time two-dimensional echocardiographic image. With HPRF Doppler if the pulse repetition frequency is doubled in order to measure a higher velocity at a particular depth then two Doppler pulse samples will appear within the echocardiographic image. Similarly if it is trebled then three pulse samples will appear. The depth ambiguity caused by HPRF Doppler is only relative however. For example, if one of the three pulse samples is immediately distal to a stenosed aortic valve, while the other two are within myocardium and chest wall echos on the two-dimensional image, then clearly the high velocity jet must be a result of the Doppler shift of ultrasound from the sample distal to the aortic valve, since this is the only sample area where blood flow will be occurring. However, although it may be possible to identify the site of origin of the maximum Doppler frequency shift by careful positioning of the pulsed sample volumes, this requires considerable skill, and complete abolition of depth ambiguity may not be possible. In addition, unlike continuous wave Doppler, since velocity recordings are only obtained from a number of small sample areas, there is considerable potential for missing the presence of a high velocity jet with HPRF Doppler. This could partly be overcome by increasing the length of the pulse sample or by increasing the number of sample gates. Although this would increase the likelihood of identifiying a high velocity jet and increase the maximum recordable velocity, it will also considerably increase the risk of depth ambiguity. In fact continuous wave Doppler could be regarded as an infinite HPRF Doppler, where there are infinite sample gates and no limit to the maximum velocity that can be measured, but in addition there is no depth resolution of the velocity recording.

HPRF Doppler though theoretically attractive is potentially very difficult to use and may confer little benefit over the combination of continuous and pulsed wave Doppler.

The optimal Doppler system therefore is likely to be one that combines both continuous and pulsed wave modes with or without the facility for HPRF Doppler and will therefore allow measurement of high velocities and also providing accurate depth resolution in conjunction with the anatomical data provided by echocardiography.

Signal Analysis

A single blood cell passing through the region of a Doppler beam will cause the reflected ultrasound to oscillate at a single frequency, the so called zero-crossing frequency, for the short period of time which it is within the Doppler beam, assuming that the blood cell is travelling at a constant velocity through the ultrasound field. In reality however, the Doppler signal from moving blood is a composite of multiple zero-crossing frequencies, or harmonic oscillations, from multiple blood cells travelling at varying velocities, for varying times, within the Doppler sample.

Although ultrasound is transmitted at high frequency, the Doppler frequency shifts, or changes in frequency of the reflected ultrasound, are within the audio range. The simplest method of signal analysis therefore is an audio representation of the Doppler frequency shift, and indeed all the information of the Doppler signal will be contained within the audio signal. This also allows the Doppler signal to be recorded on audio tape cassette for data storage and subsequent analysis. Although the audio signal may be of considerable qualitative value, it is clearly unable in itself to provide accurate quantitative information, or display the complex detailed structure of the Doppler signal.

It is possible to calculate an instantaneous zero-crossing frequency from adjacent pairs of zero-crossings within the composite signal and display as a function of time a scatter gram of the instantaneous frequency distribution known as the time interval histogram.[26] Many of the initial cardiac Doppler units displayed the Doppler frequency information in this manner. Using this method of signal analysis, calculation of the mean velocity and an estimation of the width of velocity distribution is possible. However, it does not provide detail of the form of the velocity distribution nor is it able to estimate the maximum velocity,[96] both extremely important aspects of cardiac Doppler examination. As a result the use of time interval histography imposes considerable limitations on the use of cardiac Doppler and with the introduction of spectral analysis rapidly became obsolete.

Spectral Analysis

Spectral analysis has now superseded all other forms of signal analysis. As the name suggests it provides a method of analysing the whole range or spectrum of frequency shifts, and therefore velocities, of which the received Doppler signal is composed. There are essentially two electronic methods of analysing the velocity spectrum; Fast Fourier Transform (FFT) analysis and Chirp-z transform analysis. The former utilizes digital techniques whereas the latter uses a range of analogue frequency "buckets" or "bins". However, the effect of these two methods of spectral analysis is similar. They are capable of separating the composite Doppler signal into its individual frequencies, similar to identifying the individual notes of a musical chord. In addition the number of individual signals of a particular frequency are identified and therefore the intensity or "loudness" of a single frequency within the Doppler signal can be displayed. These electronic computations can be performed very rapidly and updated as quickly as every 5 msec. This allows the whole range of frequency shifts, or equivalent velocities, within the Doppler signal over a very short time period, and their respective amplitudes or intensities, to be displayed visually in real time. From this, judgement of the quality of the Doppler signal, exclusion of electonic noise from visual velocity display by gain adjustment, and identification of the true maximum velocity are more easily obtained. Examples of the display of spectral analysis is shown in Figures 2,3,4 & 5. In this form of display each dot or pixel represents a particular frequency shift, or velocity, within a 10 msec time period and displays the whole range of frequency shifts repeatedly updated every 10 msec. If blood flow is directed towards the transducer then an increase in frequency is produced and is displayed above the zero velocity line, whereas blood flow away from the transducer will cause a decrease in the transmitted frequency and will be displayed as a Doppler frequency shift below the zero velocity line. In addition, the intensity or amplitude of each dot or pixel represents the volume of blood cells within the Doppler beam sample travelling at a particular velocity within the 10 msec time period. Measurement of the maximum Doppler frequency shift is performed from the frozen image by a movable cursor dot, with the maximum signal being assessed visually and the cursor then positioned at the point of maximum frequency as shown in Figure 2. The spectrum analyser will then give a digital readout of the frequency shift related to the cursor, shown at the top of Figure 2 as +2,500 Hz, indicating that flow is towards the transducer and producing a maximum frequency shift of 2,500 Hz. Using the Doppler equation, discussed earlier, the velocity can then be calculated:-

$$\text{Velocity} = \frac{2500\text{Hz} \times 1560\text{m/s}}{4000000\text{Hz}}$$

$$= 1 \text{ m/s}$$

Note from Figures 4 and 5 that the spectral display has no effect on frequency aliasing. It is merely an electronic method of displaying the information within the composite Doppler signal and will have no effect on the ultrasound properties of pulsed and continuous wave Doppler ultrasound. The application of spectral analysis is clearly advantageous in the study of cardiac Doppler and is the major factor which has potentiated considerable advances in the clinical application of the technique.

DOPPLER INSTRUMENTATION

Initial Experience

My initial Doppler experience was with the use of an early pulsed system which displayed the Doppler data as a time interval histogram but was able to provide simultaneous two-dimensional echocardiographic imaging (Diasonics V3400R). Being able to position the Doppler sample gate within the simultaneously displayed echocardiographic image enhanced the initial learning of the Doppler technique and allowed identification of the Doppler recordings from a variety of intracardiac sites. However, major limitations of this system were apparent mainly because of the use of time interval histography,[26] which did not allow assessment of the maximum flow velocity. This would have been inadequete for the proposed studies of this thesis. Since it was able to identify the presence of flow by this signal analysis it was used successfully to detect the presence of mitral regurgitation in a number of the patients with mitral valve replacements studied in chapter 6 where early in the learning curve of the Doppler technique the guided positioning of the Doppler sample volume by echocardiographic imaging was valuable. However, when subsequent improved Doppler equipment became available, which did not provide echocardiographic imaging, - it became clear, not only that improved signal analysis was important but also that the use of simultaneous imaging could significantly compromise the quality of the recorded Doppler signal.

Potential Problems

When proposing further investigation into cardiac Doppler in 1983 there were two very distinct types of Doppler ultrasound equipment. "Stand alone" Doppler was available in the form of a dedicated Doppler velocimeter (Vingmed, Norway) which had no echocardiographic imaging and a number of duplex Doppler systems, combining echo and Doppler facilities had been introduced with inbuilt spectral analysis of the Doppler signal. Despite the apparent advantage of the addition of echocardiographic imaging there were a number of potential concerns regarding duplex systems. The ultrasound transducers available with these systems tended to be large and unsuitable for adequate imaging from the suprasternal notch. Since, by the nature of the Doppler technique, it is important to obtain Doppler signals in the line of blood flow, the suprasternal notch is likely to be an important praecordial position for Doppler recordings. In subsequent investigation of patients with aortic stenosis it became clear that a number of other praecordial positions unsuitable for large imaging transducers were also important, such as the right parasternal and supraclavicular approaches. These duplex systems suffered from a lack of versatility in that they had no method of extracting the raw Doppler data and inflexible calculation packages. This was a potential problem as it was unclear at such a preliminary stage what subsequent calculations or further analysis of the Doppler signal may be required. In addition the importance of compromising Doppler sensitivity by simultaneous two-dimensional imaging had already been raised. More importantly however, was the fact that the duplex systems did not have the facility for continuous wave Doppler which would significantly limit there application, a problem not shared by the "stand alone" counterpart.

Doppler Velocimeter

For the above reasons I felt the most appropriate Doppler instrumentation was the Vingmed Alfred Doppler velocimeter (Vingmed, Norway). This "stand alone" system allowed both pulsed and continuous wave Doppler with a 2MHz transducer which was small, with an angulated head (Fig. 6) and ideal for examination from the suprasternal notch. Indeed all duplex systems have now incorporated either the Vingmed system or provide a separate continuous wave Doppler facilty as part of the echo/Doppler system with a similar separate Doppler transducer. The Vingmed Alfred velocimeter provides an audio Doppler signal in real time and had the facility for recording on a standard strip chart recorder an analogue signal of the mean and maximum velocities estimated by a velocity estimator within the Doppler velocimeter. However, it can also be interfaced to a separate spectrum analyser for full spectral analysis.

Spectrum Analyser

Spectral analysis of the Doppler signal can provide a visual display of the whole range of Doppler frequency shifts and their relative intensities in real time, and as a result is valuable in guaging the quality of the Doppler recording in combination with the audio signal. In the

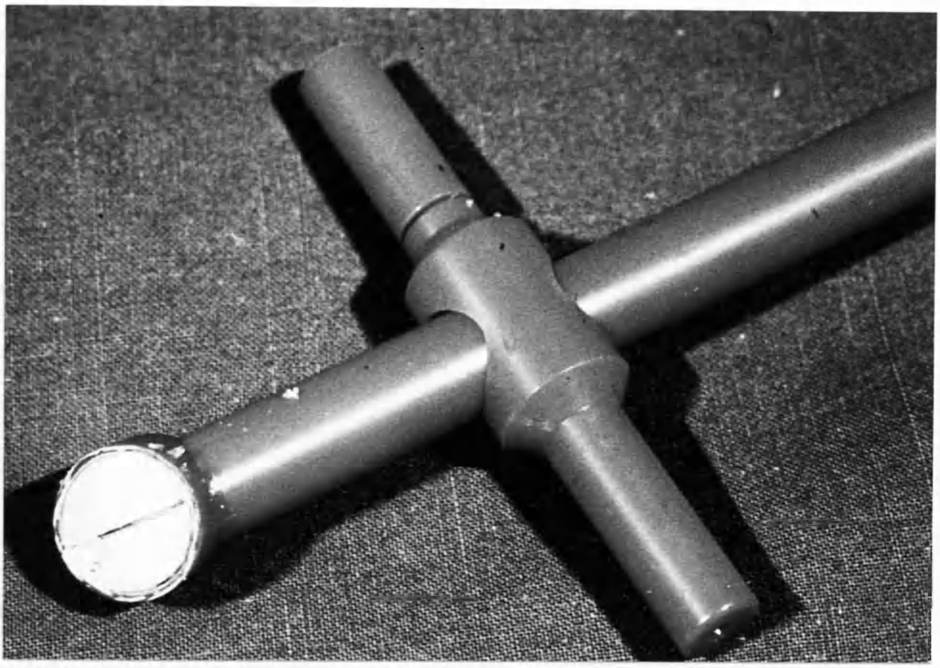


Figure 6: Vingmed continuous and pulsed wave Doppler transducer (2 Mega Hertz). The split piezo-electric crystal allows one half to transmit and the other to receive ultrasound simultaneously during continuous wave operation and the small angulated head and crossbar facilitate positioning of the transducer, particularly in the suprasternal notch and right parasternal regions.

continuous wave mode where no range resolution is possible, blood flow, identified at different points along the Doppler beam, often travels at different velocities and though impossible to separate using the analogue estimator, characteristic flow patterns can often be identified using spectral analysis. It can also prove valuable in some patients, particularly in the elderly, where ultrasound penetration may be difficult and a high velocity jet may be of very low amplitude or intensity particularly at the higher frequency shifts and whereas the few high frequency but low amplitude signals will be apparent on spectral analysis the would almost certainly be missed by a maximum velocity estimator,[97] causing underestimation of the maximum velocity. This is of potential importance in predicting the severity of aortic stenosis in elderly patients where clinical signs may be difficult to assess.

Spectrum analysers have only recently been specifically developed for cardiac work and initially an Angioscan vascular analyser was used in conjunction with the Alfred velocimeter for the first patients studied with aortic stenosis. This provided a satisfactory visual display of the velocity spectrum and proved adequate for measuring the peak Doppler frequency of high velocity jets in the aorta, but there was no facility to display directional velocity and the gain control allowed only four possible settings excluding any finer adjustments.

All spectral analysis for the studies in this thesis was performed using a Doptek spectrum analyser integrated with the Vingmed Alfred velocimeter. This recently developed analyser provided a visual display of the velocity spectrum and allowed appreciation of directional flow. In addition it had a graduated gain control and a ten second storable memory. When a satisfactory image was obtained, a freeze facility allowed the current image to be displayed or any from the previous ten seconds. The peak frequency shift was guaged visually and a movable cursor placed at the appropriate point on the Doppler signal, producing a digital display of the Doppler frequency shift. The equivalent velocity could then be calculated using the Doppler equation. Latterly, in liason with Doptek a movable real time cursor was incorporated which was operator dependent and allowed an appreciation of the frequency shift in real time which allowed easy comparison of signals obtained from a variety of praecordial positions without the need for freezing the image. In addition, since the completion of these studies the frequency shifts obtained by positioning of the cursor have also been displayed as a velocity, assuming the angle with blood flow to be zero, and obviating the need for calculation of the Doppler equation. A facility for computer dumping was available but its use limited by the current lack of suitable computer analysis programmes. The analyser itself also incorporates a calculation package with median and maximum frequency followers. These identify the median and maximum frequency of the Doppler signal at each 10 msec interval and can average either of these over a cardiac cycle or any given time period. They are of particular value when time averaged velocity over a cardiac cycle is required, as in the assessment of cardiac output.

DOPPLER EXAMINATION

The audio signal and the visual display of the velocity spectrum were utilized in combination when performing the Doppler examination to obtain a satisfactory Doppler signal. In addition the Doppler signal was recorded on audio tape and could be replayed through the spectrum analyser at a later time for further analysis. During the examination care was taken to obtain the most satisfactory spectral signal by varying the probe position and the gain control adjusted to reject obvious interference. A satisfactory signal was guaged both by the quality of the audio signal and by the presence of a clearly demarcated spectral display. The addition of the movable cursor line simplified the comparison of different velocities obtained with transducer manipulation and from various praecordial positions.

While providing a versatile system with both pulsed and continuous wave modes and avoiding any compromise of Doppler sensitivity the obvious disadvantage of this system is the lack of positioning of the pulsed wave sample gate by simultaneous echocadiographic imaging. All patients studied had two-dimensional echocardiography performed, where possible at the same time as the Doppler examination. When positioning of the pulsed sample gate was critical, as in the assessment of mitral prosthetic regurgitation, Doppler examination was always performed with the separate two-dimensional echocardiographic facilities available. If required, by alternating the Doppler and echocardiographic transducers an adequate appreciation of the position of the sample gate could then be obtained.

APPLIED DOPPLER PHYSICS

The two major applications of physical theory to the Doppler examination relate to the measurement of pressure gradients and volumetric flow analysis. The theory applied to the measurement of pressure gradients is discussed in this chapter since it is relevant to the majority of studies in this thesis. Volumetric flow analysis is however considered as an intergral part of the methodological assessment of cardiac output discussed in Chapter 8.

Bernoulli Equation

In fluid dynamics, a narrowing in a tube will cause flow passing through it to accelerate from one velocity at a point proximal to the narrowing or obstruction, to an increased velocity at a point within the obstruction. This relationship between the velocity and the pressure drop across an obstruction (p1 - p2) is given by the Bernoulli equation:-

$$p1 - p2 = \underbrace{1/2p(v2^2 - v1^2)}_{1} + \underbrace{p\int_1^2 d\vec{v}/dt\ d\vec{s}}_{2} + \underbrace{R(\vec{v})}_{3}$$

This equation can be applied to the study of blood flow across an obstruction such as found in valve stenosis. Part 1 of the equation relates to the convective acceleration of blood. This acceleration of blood through an obstruction is caused by its convection from one velocity at a point proximal to the obstruction to another velocity at the point of maximum obstruction, hence the term convective acceleration. The driving force to this velocity change is the pressure drop or gradient across the obstruction and the change in velocity is proportional to the obstructive gradient as shown in the Bernoulli equation. The distal velocity is usually high and, as is true in most cases of intracardiac flow recordings the velocity proximal to the obstruction low, usually less than 1 $msec^{-1}$. When these velocities are squared then subtraction of the proximal from the distal velocity makes little difference to the calculated gradient. The proximal velocity can then effectively be ignored and the obstructive gradient relates solely to the maximum velocity measured distal to the obstruction. This assumption should always be borne in mind however, as it may not necessarily be valid in all situations. For example, an increase in cardiac output will cause an increase in the velocity of blood flow proximal to an obstruction, as will the presence of significant valvular regurgitation producing as a result an increase in forward flow.

The second part of the equation involves flow acceleration which relates to the inertial forces encountered with the acceleration and deceleration of flow and will therefore be apparent both at the onset and at the termination of flow, which applies only during valve opening and closure, whereas the maximum pressure gradient will occur at some point in between. These forces are minimal and do not therefore effect the measurement of the obstructive gradient, their main effect being the production of a slight time delay between the calculated and measured pressure curves. Again therefore for clinical purposes flow acceleration forces can be ignored.

The final part of the equation is concerned with forces due to viscous friction, energy changes related to the interaction between blood cells and their interaction with the surface of the cardiac valves. Since the velocity profile of an obstructive jet is flat, little interaction occurs between blood cells at this point and if velocity measurements are made within the jet then energy losses due to interaction with the valves are also avoided. The component of the Bernoulli equation relating to viscous friction is of minimal importance and can, for practical purposes, be ignored.

Application of the above considerations results in the modified form of the Bernoulli equation:-

$$p1 - p2 = 4V^2$$

where V = the maximum velocity recorded distal to the obstruction.

For example therefore if a maximum velocity of 4 m/s was recorded distal to a valve stenosis by Doppler ultrasound the calculated valve gradient, assuming that the velocity proximal to the obstruction was negligible, would be:-

$$4 \times 4^2 = 64 \text{ mmHg}$$

If the velocity proximal to the obstruction was 2 m/s this would have to be taken into account in calculation of the gradient and therefore:-

$$p1 - p2 = 4(V2^2 - V1^2)$$

$$= 4(4^2 - 2^2)$$

$$= 48 \text{ mmHg}$$

This modified formula has become generally accepted as the most applicable in the clinical setting and has previously proved successful in calculating valve gradients from Doppler velocity measurements.[29,41] At this point it should be remembered that measurement of pressure gradients by Doppler ultrasound is dependent on the accurate measurement of the maximum velocity which is related to the intercept angle between the ultrasound beam and blood flow. As with the potential to underestimate velocity of blood flow by a large intercept angle, since gradient measurements are derived from this value, the potential alos exists to significantly underestimate valve gradient if this intercept angle is large. An angle of the Doppler ultrasound beam of 20 degrees to blood flow will only underestimate the pressure gradient by 12%, which would probably be acceptable for the majority of clinical purposes. However, an angle of 40 degrees will cause an underestimation of greater than 40% which is likely to produce clinically unacceptable results. It is therefore of considerable importance to search for the maximum Doppler signal indicative of the smallest intercept angle when attempting to measure valve gradients from the maximum velocity by Doppler ultrasound. With the use of a duplex system where simultaneous echocardographic imaging is available it is theorectically possible to introduce an angle correction factor, and many of the duplex systems will provide this facility. However, blood flow has three rather than two dimensional characteristics and in diseased states the actual direction of the blood velocity jet may different significantly from that predicted from the echocardiographic image and, as a result, the possibility of significantly overestimating maximum velocity and hence pressure gradient exists.

It should be stressed that in certain situations such as found with the combination of valvar and sub-valvar aortic stenosis it is likely that this equation will estimate the total gradient across the left ventricular outflow and if only the transvalvar gradient is desired then the proximal velocity, i.e. that distal to the sub-valvar obstruction, may have to be taken into account.

Mean Valve Gradients

Pressure gradients can be calculated by applying the modified Bernoulli equation to the maximum velocity recorded by Doppler ultrasound. It is standard practice from pressure tracings obtained at cardiac catheterisation to express the gradient across the mitral valve as a mean gradient rather than a maximum gradient or an instantaneous gradient at one point in the cardiac cycle. It is possible to obtain a mean mitral valve gradient by Doppler ultrasound and the modified Bernoulli equation. In order to do so it is necessary to apply the modified Bernoulli equation to the maximum mitral flow velocity at a number of intervals throughout diastole in order to obtain a series of pressure gradients which can then be averaged to provide a mean valve gradient. The larger the number of samples obtained throughout diastole then the more accurate the assessment of the mean valve gradient is likely to be. Since the spectrum analyser will provide updated Doppler frequency/velocity information at 10 msec intervals, for the most accurate assessment of mean mitral gradient the modified Bernoulli equation should be applied at each 10 msec interval throughout diastole and the calculated pressure gradients then averaged.

It should be emphasized that the measurement of mean mitral valve gradient by Doppler ultrasound in no way involves mean velocity, but is a reflection of the average value of a series of pressure gradients related to the maximum mitral flow velocity. In addition because of the squared relationship of maximum velocity and pressure gradient it is essential to assess the pressure gradient from each instantaneous maximum velocity and it is not valid to average the maximum mitral velocity and then apply the modified Bernoulli equation.

The importance of the modified Bernoulli equation to cardiac Doppler ultrasund cannot be over emphasized. Indeed, with respect to this thesis, its clinical value spans not only the investigation of valvular heart disease and ventricular outlet obstruction but also the assessment of prosthetic valve function and the prediction of right ventricular and pulmonary artery pressures in patients with ventricular septal defects.

Pressure Half-Time

In mitral stenosis using Doppler ultrasound from the apical position, it is possible to measure pressure gradients noninvasively from the maximum mitral flow velocity by application of the modified Bernoulli equation.[29] However, the accuracy of assessing the actual degree of stenosis from the pressure gradient will be affected by heart rate, cardiac output and the presence of mitral regurgitation. This is not unique to Doppler ultrasound and the same effect will occur with pressure gradients measured at cardiac catheterisation.

Hatle et al.[31] have suggested a measurement of mitral "pressure half-time" as a method of assessing the degree of mitral obstruction which is independent of variation in mitral valve flow, and therefore related to mitral valve area. Mitral "pressure half-time" is a measurement of the time in msec taken for the pressure drop to fall to half of its initial value. Since pressure gradient can be calculated from the maximum mitral velocity, and there is a linear fall in the mitral velocity from its initial peak, then it should be possible to measure "pressure half-time" from Doppler recording of mitral flow velocity. If the modified Bernoulli equation is applied to the peak mitral flow velocity, a peak mitral gradient can be calculated and the "pressure half-time" is then the time taken for the maximum velocity to fall to a value equivalent to half of the peak pressure gradient.

From the modified Bernoulli equation the peak pressure drop will be $4V^2$ and the "pressure half-time" will be the time taken to reach half this initial value, or $1/2\ 4V^2$. The "pressure half-time" can therefore be expressed in terms of velocity and will be the time taken for the velocity to fall to to a value equivalent to the peak velocity divided by the square root of 2 (1.4). Pressure half-time can therefore be measured directly from the Doppler velocity recording.

Although the peak mitral flow velocity will vary with changing flow through the mitral valve, the rate at which the flow velocity decreases should not, and therefore will provide an assessment of the actual degree of obstruction independent of the calculated pressure gradient. Hatle et al.[31] studied 40 normal subjects, 32 patients with mitral stenosis, 17 patients with mitral regurgitation and 12 patients with combined lesions. In normal subjects, mitral pressure half-times ranged from 20-60 msec, in patients with isolated mitral regurgitation from 35-80 msec, and in patients with mitral stenosis from 90-380 msec. No significant change in pressure half-time occurred with exercise whereas significant increase in pressure gradients were noted, and no change occurred on repeated estimations. In addition, in patients undergoing cardiac catheterisation mitral pressure half-time related closely with invasive estimation of mitral valve area, with increasing pressure half-times occurring with decreasing mitral valve areas.

In order to accurately assess pressure gradients by Doppler, the ultrasound beam must be directed in line of through valve flow, and a significant intercept angle will cause peak velocity and hence pressure gradient to be underestimated. However, Hatle et al. found that although the peak velocity decreased with an increasing intercept angle, measurement of the mitral pressure half-time remained unchanged. This is dependent of the ultrasound beam intercepting the velocity jet albeit at a considerable angle, whereas if the Doppler beam is not directed at the central part of the velocity jet, pressure drop may be underestimated and pressure half-time prolonged. This is a result of Doppler signals being obtained only during part of diastole due to movement of the heart. It is very important, therefore, that careful Doppler examination is performed in order to obtain the centreline velocities, if accurate measurement of mitral pressure half-time is to be made.

By combining the noninvasive measurement of pressure gradient and mitral pressure half-time an improved assessment of mitral valve obstruction is possible than by pressure gradient measurement alone, since pressure half-time will provide an assessment of the actual degree of mitral obstruction, whereas pressure gradient will reflect the amount of flow through a mitral orifice of a particular area. It is possible to assess the degree of stenosis in patients with combined mitral stenosis and regurgitation, where a high pressure gradient in the presence of a normal or only slightly prolonged pressure half-time would indicate predominant regurgitation in the absence of significant stenosis. In addition, by assessing a patient with mitral stenosis on a serial basis, an increase in the pressure half-time will indicate worsening stenosis, whereas increase in the pressure gradient alone will indicate only increased mitral flow.

If the use of mitral pressure half-time could be extrapolated to prosthetic mitral valves, where an intrinsic dergree of obstruction exists, even in normally functioning prostheses, and where clinical assessment is less reliable, then Doppler ultrasound will have considerable clinical potential in the assessment of these patients. In chapters 6 and 7 this thesis will deal with the application and clinical value of mitral pressure half-time in patients will mitral valve replacement.

CHAPTER 3

NORMAL DOPPLER EXAMINATION

INTRODUCTION

Continuous and Pulsed Wave Doppler

In order to successfully apply Doppler ultrasound to the assessment of various cardiac abnormalities it is important firstly to examine normal subjects with this technique and establish the normal range for the various intracardiac blood flow velocities and mitral pressure half-time. For ease of examination, particularly where simultaneous imaging is not available, it is useful to employ continuous wave Doppler to identify the flow pattern of interest. Continuous wave Doppler with identify all velocities encoutered along the Doppler beam including the low velocity signals outwith the main velocity jet (see Fig. 2, chapter 2). Pulsed wave Doppler will display only the velocities present at a specified depth of sampling which, if positioned within the velocity jet, will exclude the low velocity signals emerging from the surrounding blood flow (see Fig. 3, chapter 2).

Velocity recordings in normal subjects will tend to be within the the range of pulsed Doppler, and with duplex systems, simultaneous imaging can be used to position the Doppler beam sample in the area of the velocity jet of interest. Identifying the flow velocity through a particular valve will be more difficult without simultaneous imaging, and the broad Doppler beam of continuous wave Doppler displaying velocity information along its whole length, will simplify examination of normal subjects using "stand alone" Doppler. The use of continuous wave Doppler in normals will not affect the measurement of maximum velocity, the ranges of which are important to establish in order to progress to measuring peak velocity in patients with cardiac abnormalities. In accurately assessing maximum velocity it is essential that ultrasound reflection is obtained from the centreline blood flow velocities, without a significant intercept angle, a situation which will more readily be achieved with non-imaging Doppler using continuous wave examination.

Reported Normal Values

Hatle[98] has reported normal values for maximum velocity measurements in 30 children and 40 adults (Table 1), though the exact methodology used was not clearly detailed. Another study has reported the maximum velocities in the ascending aorta and main pulmonary artery in 20 normal adults.[99] In this study pulsed Doppler recordings were obtained with the aid of simultaneous two-dimensional echocardiographic imaging. Main pulmonary artery velocity was obtained from the parasternal short axis view and aortic flow velocity from the suprasternal notch. Doppler signals were analysed using spectrum analysis. Pulmonary artery velocities ranged from 0.44 to 0.78 m/s, mean 0.63 m/s. Significantly higher aortic velocities were obtained, with a range of 0.72 to

TABLE 1

	Children	Adults
Mitral Flow	0.8 - 1.3	0.6 - 1.3
Tricuspid Flow	0.5 - 0.8	0.3 - 0.7
Pulmonary Flow	0.7 - 1.1	0.6 - 0.9
Aortic Flow	1.2 - 1.8	1.0 - 1.7

Range of maximum velocity ($msec^{-1}$) for valve flow in normals. (Hatle)

1.20 m/s, mean 0.92 m/s. The reported results were highly reproducible with variability less than 10%.

Similar results both for velocity measurements in the ascending aorta and for their reproducibility had previously been reported with a "stand alone" pulsed Doppler velocimeter as used in this thesis but peak velocity was obtained using a maximum frequency estimator rather than spectral analysis.[100]

The largest reported series of normal values for peak velocity measurements through all four valves was reported in one hundred and ten adults and children.[101] Ascending aortic recordings were obtained from the suprasternal notch, pulmonary artery recordings from the parasternal short axis and mitral and tricuspid recordings from the apical position. Peak velocities in the pulsed mode were measured directly from the spectral display and the results shown in Table 2. In this study it was also noted that there was an inverse relationship between the peak velocity and both age and body surface area for mitral, tricuspid and pulmonary flow but not for aortic flow. It was also noted that the acceleration time, or time to peak velocity, in both the pulmonary artery and aorta, increased significantly with age.

In an attempt to provide a more accurate and objective analysis of aortic flow recordings in normal individuals,

TABLE 2

	Range	Mean
Mitral Flow	0.44 - 1.28	0.77
Tricuspid Flow	0.33 - 0.81	0.53
Pulmonary Flow	0.52 - 1.31	0.81
Aortic Flow	0.76 - 1.55	1.04

Peak velocities in $msec^{-1}$ for valve flow in 110 normals. (Wilson et al.)

computer analysis of the Doppler signal has recently been reported[102,103] and has identified a linear increase in the velocity of flow in early ejection, present over a constant time period, unrelated to either age or weight and which is transmitted after an appropriate delay to the peripheral arteries. Unlike the former study mentioned these worker found no significant difference in the time to peak velocity in the aortic flow with varying age. In addition they found a significant reduction in the peak aortic velocity with age and also found a significant inverse relationship between age and acceleration of aortic flow.

Aim of Study

The studies in this thesis relate to distinct cardiac disorders where the application of Doppler ultrasound is likely to prove valuable. In the majority of these lesions high blood flow velocities are likely to be present and therefore only accurately assessed with the use of the continuous wave mode. Where there is severe obstruction, abnormally high velocities will be encountered and it is extremely unlikely that any confusion would arise between normal and abnormal flow. The reference ranges previously reported and described above would probably prove adequate for comparison in the majority of cases. However these studies all used pulsed Doppler instrumentation and it therefore seemed appropriate to first study normal individuals with continuous wave Doppler not only to establish my own range of valve flow velocities but also to identify the optimal praecordial positions for successful examination using this particular "stand alone" Doppler system.

SUBJECTS

50 patients, 28 males and 22 females, age range 5-76 years, mean 31 years were studied. All were asymptomatic and had a normal cardiovascular examination. ECG, chest x-ray and two-dimensional echocardiography were normal and individuals were not selected because of their suitability for ultrasonic examination. Indeed poor quality echocardiograms were obtained in 3 patients included in the study.

METHODS

All recordings were obtained in the resting state immediately following two-dimensional echocardiography. Doppler examination was performed in the continuous wave mode and pulsed wave examination performed only to check that no significant discrepency was obtained between the two maximum flow recordings. Following detection of a satisfactory Doppler signal, as described in the previous chapter, the maximum velocity was calculated using the Doppler equation from the maximum measured frequency shift on a frozen spectral display or, latterly, directly from the spectrum analyser using the movable cursor which displays both frequency shift and velocity in real time. The transducer positions described provided only an initial guide to the detection of the valve flow profile and the optimal Doppler signal was obtained by careful transducer manipulation guided by both the audio and spectral signals.

Transducer Position

Mitral Flow

The patient was positioned semi-supine in the left lateral position and the transducer placed at the cardiac apex and directed towards the mitral valve identified by the previous two-dimensional echocardogram. If flow relating to the left ventricular outflow was apparent, identified by low velocity systolic flow away from the transducer, the transducer was adjusted slighty posterior and lateral in order to exclude this.
In addition to the maximum velocity the mitral pressure half-time was also measured from the spectral display of mitral valve flow as described in the previous chapter.

Aortic Flow

Examination was performed from a variety of praecordial positions and the measurement of maximum velocity obtained from the optimal aortic flow recording in the ascending aorta. With the patient in the semi supine position the examination was performed from the suprasternal notch, the subxiphoid and supraclavicular positions with the transducer directed towards the aortic valve. In the left lateral position aortic flow was identified by positioning the transducer at the apex and in a direction anterior and medial to the mitral flow velocity signal. Finally the patient was placed in the right lateral decubitus position and the transducer positioned in the right parasternal region in either the first, second or third intercostal space. The pulsed wave mode was used only in the apical position to confirm that aortic flow was being obtained rather than flow solely from the left ventricular outflow tract by obtaining a pulsed signals distal to the aortic valve cusps, though in the absence of aortic stenosis little difference in the maximum velocity would be expected between the left ventricular outflow and the ascending aorta.

Tricuspid Flow

This was obtained with the patient in the left lateral position either from the apex with the transducer angled to the right of the mitral flow, or from the left parasternal region directed substernally towards the right.

Pulmonary Flow

With the patient still in the left lateral position pulmonary flow was examined from the left parasternal region, in the first to fourth intercostal spaces, superiorly to that used to detect tricuspid flow.

TABLE 3

Peak Velocities

	Mean	Range
Mitral Flow	0.88	0.40-1.11
Aortic Flow	1.29	0.74-1.79
Tricuspid Flow	0.57	0.30-0.85
Pulmonary Flow	1.19	0.80-1.56
Mitral Pressure Half-time	54msec	30-80msec

Peak velocities in m/s and mitral pressure half-times in msec (continuous wave mode) in 50 normal individuals.

RESULTS

The ranges obtained for peak flow velocities through the four cardiac valves and mitral pressure half-times are shown in Table 3.

Mitral Flow (Fig. 7)

Satisfactory mitral flow signals were obtained from the apical position in the continuous wave mode in all cases. Since all patients were in sinus rhythm the typical biphasic flow velocity pattern towards the transducer was obtained with initial mitral diastolic flow followed by a further increase in flow velocity resulting from atrial systole. Mitral pressure half-times in these patients ranged from 30 - 80 msec, mean 54 msec.

Aortic Flow (Fig. 8)

The most successful praecordial position for obtaining the highest aortic flow velocity within an individual patient was the suprasternal notch, with a single peak flow velocity signal obtained during systolic ejection with flow identified towards the transducer. This provided the optimal Doppler signal in 44 of the 50 patients (88%). In the other 6 patients (12%) the apical position provided the best Doppler signal within an individual, with systolic ejection flow velocity

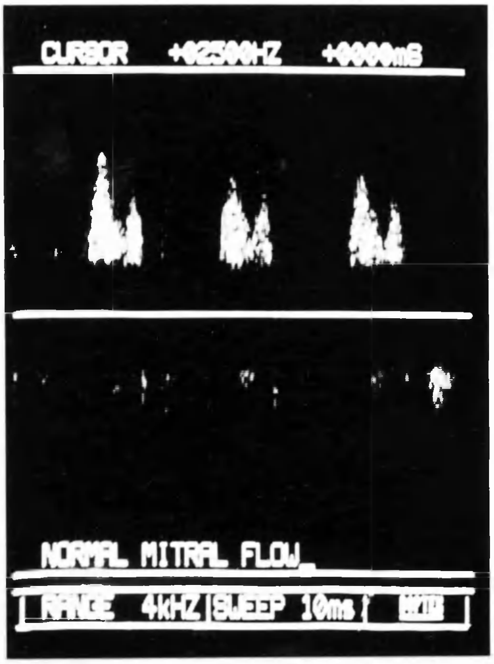


Figure 7: Continuous wave Doppler spectral display of normal mitral flow from the apical position.

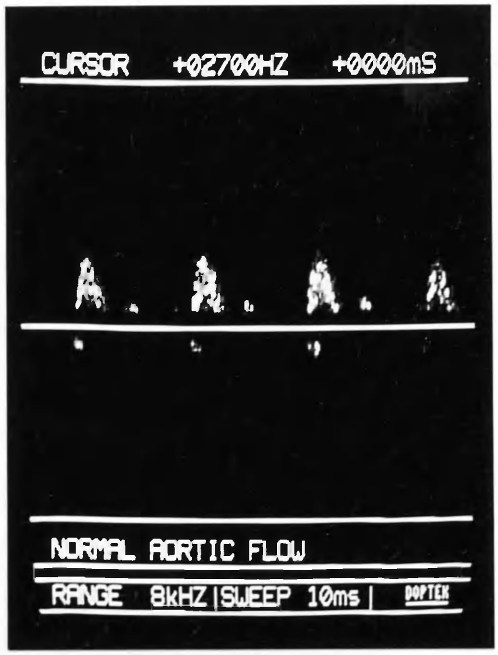


Figure 8: Continuous wave Doppler spectral display of normal aortic flow form the suprasternal notch.

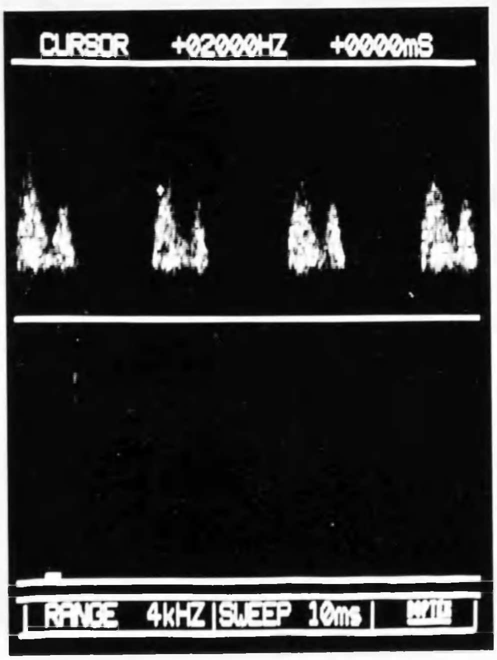


Figure 9: Continuous wave Doppler spectral display of normal tricuspid flow from the left parasternal position.

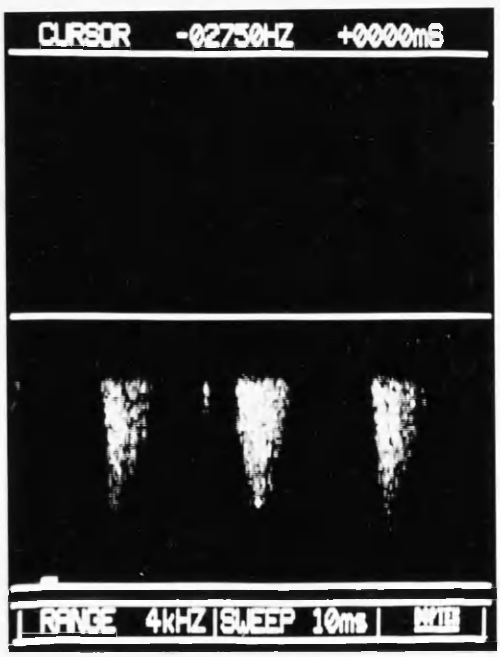


Figure 10: Continuous wave Doppler spectral display of normal pulmonary flow from the upper left parasternal position.

detected away from the transducer. Despite the fact that the suprasternal and apical positions provided the optimal flow in all cases aortic flow could be obtained from several different praecordial positions in all patients.

Tricuspid Flow (Fig. 9)

This was best obtained in all cases from the apical position with biphasic diastolic flow velocity signals, similar to those of mitral valve flow, detected towards the transducer. The parasternal position was also successful in 43 of the 50 patients (86%).

Pulmonary Flow (Fig. 10)

Satisfactory pulmonary flow recordings were obtained in all cases from the upper left parasternal position with systolic ejection flow velocity signals identified away from the transducer.

DISCUSSION

The flow velocities obtained in this series using the continuous wave mode are of similar range and magnitude to those previously reported for pulsed Doppler. In normal individuals the use of continuous wave Doppler examination does not therefore seem to significantly effect the recorded maximum velocity. There was a tendency for the maximum flow velocity to decrease with age, again similar to the previous reports mentioned, though this did not reach statistical significance for any of the valve flows.

Some previous studies have utilized simultaneous two-dimensional echocardiographic imaging in order to position the pulsed Doppler sample gate and it might be suspected that this would prove advantageous in optimizing the flow signal. Certainly, the use of the separate echocardiogram in this study did identify the position of the ultrasonic window which and aided the initial positioning of the Doppler probe particularly at the cardiac apex. However, manipulation of the Doppler transducer was still crucial to identify the optimal signal and this is also the case with duplex Doppler systems. The use of continuous wave rather than pulsed wave Doppler, by recording velocities along the whole of the Doppler beam, made it considerably easier to identify the appropriate flow pattern. However, having done so, switching to the pulsed wave mode will allow identification of flow velocity signals at any single position along the Doppler beam but is not necessary for the measurement of the maximum flow velocity through a particular valve (see Figs. 2 & 3, chapter 2). In addition since the direction of the Doppler transducer at the various praecordial positions was quite distinct for each valve flow there was no potential for confusion of the flow velocity through different valves using the continuous wave mode. The fact that the small Doppler transducer enabled a satisfactory recording in all 3 patients where satisfactory echocardiographic images could not be obtained poses the question that in certain circumstances a "stand alone" system may prove superior to a "duplex" system. This may be so particularly in elderly patients.[104]

Finally although this study has demonstrated the optimal positioning of the Doppler probe to obtain through valve flow in normal individuals, it will subsequently become apparent in this thesis that, in an individual patient, these positions may not necessarily be the most appropriate for studying particular flow velocities in the presence of cardiac disease.

CHAPTER 4

CLINICAL VALUE OF CONTINUOUS WAVE DOPPLER ULTRASOUND IN THE ASSESSMENT OF ADULTS WITH AORTIC STENOSIS

INTRODUCTION

Non-invasive Assessment of Valvular Heart Disease

Conventional echocardiography has been able to provide such detailed information in many patients with valvular heart disease that it has been suggested patients can safely undergo valve replacement without the need for prior cardiac catheterisation.[105-107] Although many of these studies have been criticised for their design,[108] Hall et al[109] have more recently demonstrated, in an elegant prospective study, where cardiac catheterisation was performed in all patients subsequent to non-invasive assessment, that in the majority of patients with valvular heart disease, surgical recommendation can safely be predicted on the basis of a complete non-invasive assessment with clinical examination, ECG, chest X-ray and echocardiography. Aortic stenosis was the one lesion where this non-invasive assessment proved unreliable, particularly in calcific aortic stenosis, and it is in this area that Doppler ultrasound has particular potential to enhance the non-invasive assessment of valve disease.

Pulsed wave Doppler ultrasound has been used to investigate turbulence patterns in aortic stenosis[110] but, as we have seen, it is unable to accurately measure the high velocities present in these patients. Continuous wave

Doppler technique has been used successfully in vitro in a pulsatile flow model to quantitate simulated aortic stenosis[111] and recent reports have suggested that in patients with aortic stenosis there is a good correlation between the Doppler derived gradient and that obtained at catheterisation.[41,44,45] However, the potential clinical application of the technique has yet to be fully established.

Aim of Study

This study was therefore undertaken in patients with clinically suspected aortic stenosis not only to confirm the accuracy of continuous wave Doppler ultrasound in predicting valve gradients but also with the particular aim of assessing its clinical value and possible role in the subsequent management of these patients.

PATIENTS AND METHODS

The study group comprised 54 adults, age range 15-74 years, mean 51 years, undergoing cardiac catheterisation all with clinically suspected aortic stenosis either alone or in combination with other valve lesions. Initially, all patients had a clinical examination performed by two experienced cardiologists. In addition a 12 lead electrocardiogram, chest radiograph, and cross-sectional echocardiogram were performed in all patients before cardiac catheterisation.

Doppler Echocardiography

In all cases Doppler examination was performed prior to cardiac catheterisation using the continuous wave mode. Spectrum analysis was used in all patients since the maximum frequency estimator of the velocimeter is both gain and threshold dependent and there is therefore a tendency for it to underestimate peak velocity and hence valve gradient.[41] Doppler examination was performed in the resting state from a variety of praecordial positions in order to obtain the Doppler signal showing the maximum systolic blood flow velocity in the ascending aorta. In obtaining this Doppler signal, the audio signal was a very important addition to spectrum analysis for indicating the presence of high frequency laminar flow. This permitted the maximum systolic frequency shift to be obtained from a clearly demarcated spectral signal without obvious interference (Fig. 11). In an attempt to minimise the risk of falsely low recordings all possible praecordial positions were examined including suprasternal, apical, subcostal, supraclavicular, and right parasternal in the right lateral decubitus position. Where Doppler examination proved successful from more than one position the highest value obtained from a well demarcated Doppler signal was used to calculate the peak valve gradient. The maximum systolic velocity obtained was then used to calculate the transvalvar gradient using the modified

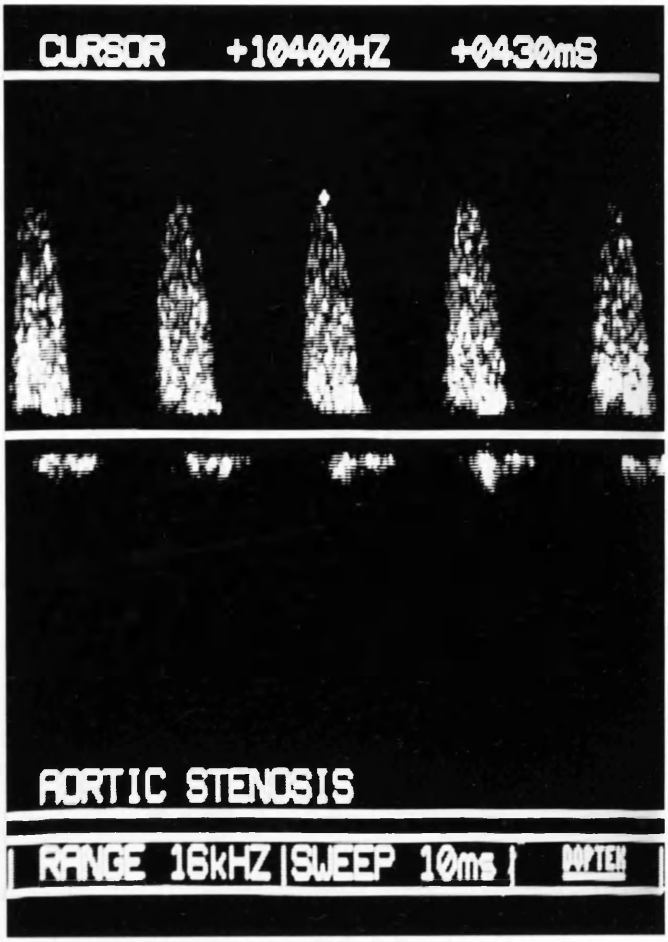


Figure 11: Continuous wave Doppler spectral display from a patient with severe aortic stenosis. High velocity flow in the ascending aorta is detected from the suprasternal notch during each systolic contraction. The maximum systolic frequency shift of 10,400 Hz, indicated by the cursor, is equivalent to a velocity of 4 $msec^{-1}$. Application of the modified Bernoulli equation estimates a peak aortic valve gradient of 64 mmHg.

Bernoulli formula. For example, in Fig. 11 the maximum Doppler frequency shift obtained form the suprasternal notch was 10,400 Hz, equivalent to a peak velocity of 4 m/s from the Doppler equation. The modified Bernoulli equation states that the pressure drop across an obstruction is equal to $4V^2$, so that the calculated peak gradient will be 64 mmHg in this case.

Before cardiac catheterisation an assessment of the severity of aortic obstruction was made by the attending physician on the basis of clinical examination, electrocardiogram, chest radiograph, and cross-sectional echocardiogram. The valve lesion was then graded as either non-significant, surgically significant, or severity in doubt from non-invasive information. The result of the Doppler examination was then added and any appropriate modification of the assessment of severity made prior to cardiac catheterisation.

Cardiac Catheterisation

All patients underwent cardiac catheterisation, using the percutaneous femoral technique and, where possible, peak to peak systolic gradients (in mmHg) obtained by withdrawal of a fluid filled multihole catheter across the aortic valve. In addition, two patients underwent trans-septal catheterisation using the Brockenbrough technique in one and via a patent foramen ovale in another. All patients were prescribed 10mg diazepam orally as a premedication 30 minutes before catheterisation. This may have the effect of lowering cardiac output and transvalvar gradient. In an attempt to assess the effects of sedation on the aortic valve gradient 31 of the 42 patients also had a Doppler examination performed during cardiac catheterisation immediately after withdrawal of the catheter across the aortic valve.

Peak to Peak vs Peak Instantaneous Gradients

The maximum Doppler velocity curve in a patient with aortic stenosis will be a reflection of the pressure difference between the left ventricle and the aorta throughout systole, and the peak systolic velocity will occur at one point in time when the pressure difference between the two is greatest, the peak instantaneous valve gradient. This is different from the gradient measured at cardiac catheterisation by withdrawal of the catheter across the stenotic aortic valve, where the peak systolic pressure of the aortic tracing is substracted from the peak systolic pressure of the left ventricular pressure tracing, the so-called peak to peak valve gradient (Fig. 12). Potentially, significant variation could occur between the peak to peak and peak instantaneous valve gradients, particularly where there is a considerable difference in the systolic timing of the peak aortic and peak left ventricular pressures. Ideally, comparison of the Doppler derived pressure gradient should be made with simultaneous measurement of aortic and left

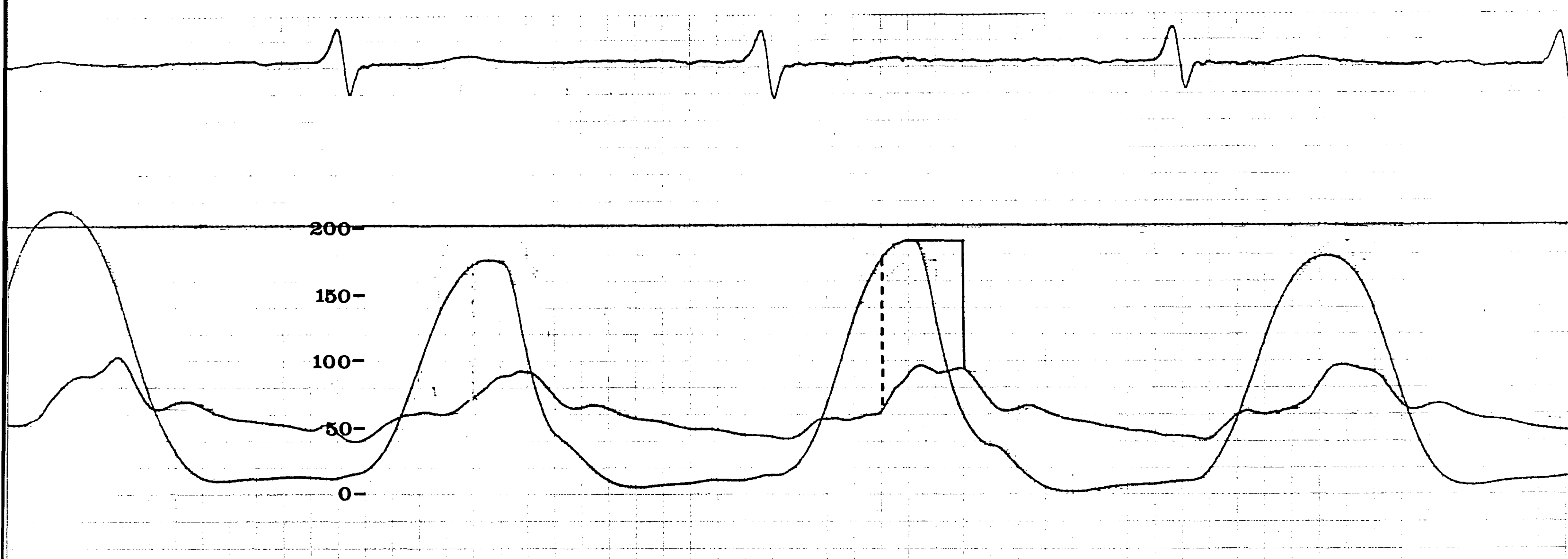


Figure 12: Difference in the peak-to-peak and peak instantaneous pressure gradients caused by delay in the peak aortic pressure compared with the peak left ventricular pressure at catheterisation. The peak instantaneous gradient (broken line) is 120 mmHg and the peak-to-peak gradient (solid line) is 96 mmHg.

ventricular pressures using two catheters, with the pressure tracings superimposed.

Although simultaneous pressures are normally obtained for measurement of mitral valve gradient at catheterisation, from pulmonary capillary wedge and left ventricular pressures, this is not the case for aortic stenosis. This would require trans-septal catheterisation using the Brockenbrough technique, which is more risky, and not routinely performed in our laboratory, and simultaneous recordings were only obtained in two of the patients in this study. It is possible to superimpose aortic and left ventricular pressure tracings which are not obtained simultaneously but, slight variation in heart rate could potentially cause a substantial difference in the peak instantaneous gradient, and unless high fidelity transducer tipped catheters are used, similar problems can arise from slight distortions of the pressure waveforms when fluid filled catheters are used for pressure measurement.

Although it is important to establish that Doppler ultrasound can accurately predict pressure gradients in aortic stenosis, the clinical value of Doppler ultrasound in predicting the severity of stenosis and subsequent patient management that is of paramount importance, and since clinical decisions are curretly based on results obtained at cardiac catheterisation it seems appropriate, in these patients, to compare the results of the peak instantaneous gradients obtained by Doppler ultrasound, with the more established peak to peak value measured at catheterisation in assessing the clinical value of the technique in these patients.

Assessment of Clinical Value

The decision regarding subsequent patient management was made by the attending physician on the basis of all clinical and non-invasive data, including the results of the Doppler examination, in addition to the results of cardiac catheterisation, and a comparison could then be made with the decision reached by non-invasive techniques alone, with and without Doppler examination.

RESULTS

Satisfactory Doppler signals were obtained in all patients. Although the suprasternal notch was the most successful position for obtaining the maximum velocity Doppler signal (34 of 54 patients) it was not possible to predict the most satisfactory praecordial examination position even when separate cross-sectional echocardiography was used to guide transducer positioning. Indeed, although several positions usually provided satisfactory Doppler signals within an individual patient, the right parasternal position provided the highest velocity recording in 13, the subcostal in 5, and the apical in one, and in one patient the only satisfactory view was obtained from the right supraclavicular position.

Comparison with Invasive Investigation

In 12 of the 54 patients undergoing cardiac catheterisation it was not possible to cross the aortic valve retrogradely. Trans septal catheterisation was not undertaken at the discretion of the attending physician and therefore no gradients were obtained in these patients.

In the remaining 42 patients the gradients measured at catheterisation ranged from 0 to 120 mmHg with a mean of 44 mmHg and the Doppler derived gradients in these patients ranged from 8 to 157 mmHg with a mean of 49 mmHg. Figure 13 shows the correlation between the catheter gradients and those obtained by Doppler ultrasound prior to cardiac catheterisation in all 42 patients. In addition, the correlation between the Doppler derived gradients obtained during catheterisation and the catheter gradients is shown in Fig. 14. An improved correlation (r=0.97) was obtained by this method, presumably because both investigations were performed under the effects of sedation. This is suggested by the fact that in the majority (70%) Doppler gradients obtained simultaneously at catheterisation were lower than those obtained prior to catheterisation outwith the effects of sedation.

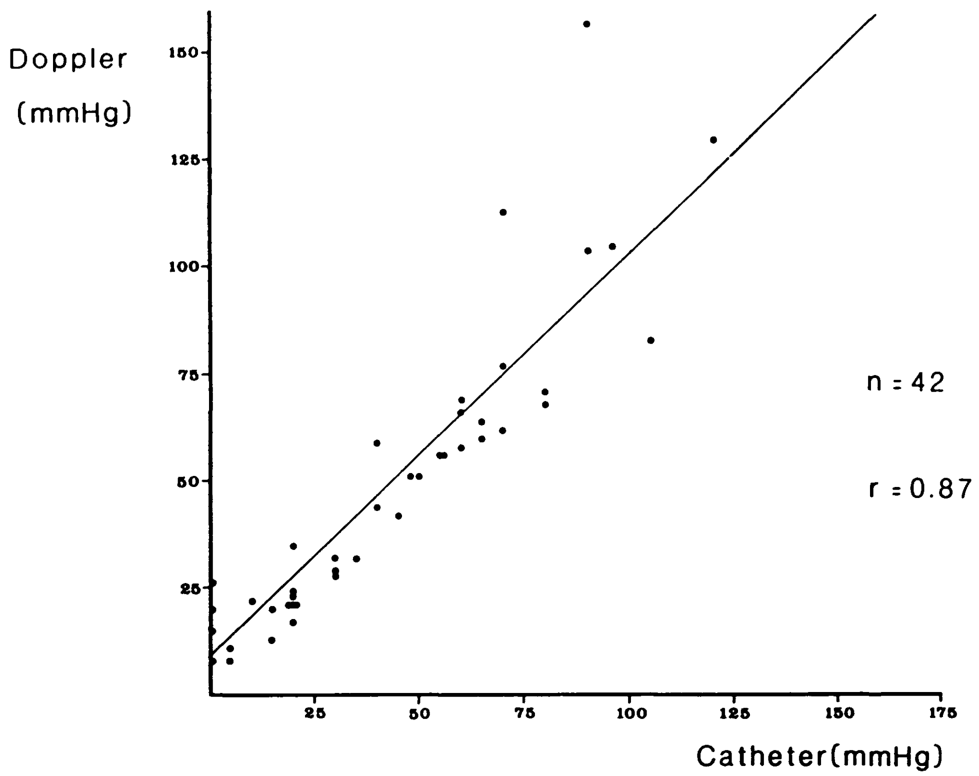


Figure 13: Comparison of the pressure gradients derived from Doppler ultrasound examination with those measured at cardiac cathĕterisation, in all patients with aortic stenosis in whom invasive valve gradients were obtained. Note particularly the patient with a Doppler derived gradient of 157 mmHg prior to catheterisation and a gradient of 90 mmHg by invasive measurement which was performed under general anaesthesia.

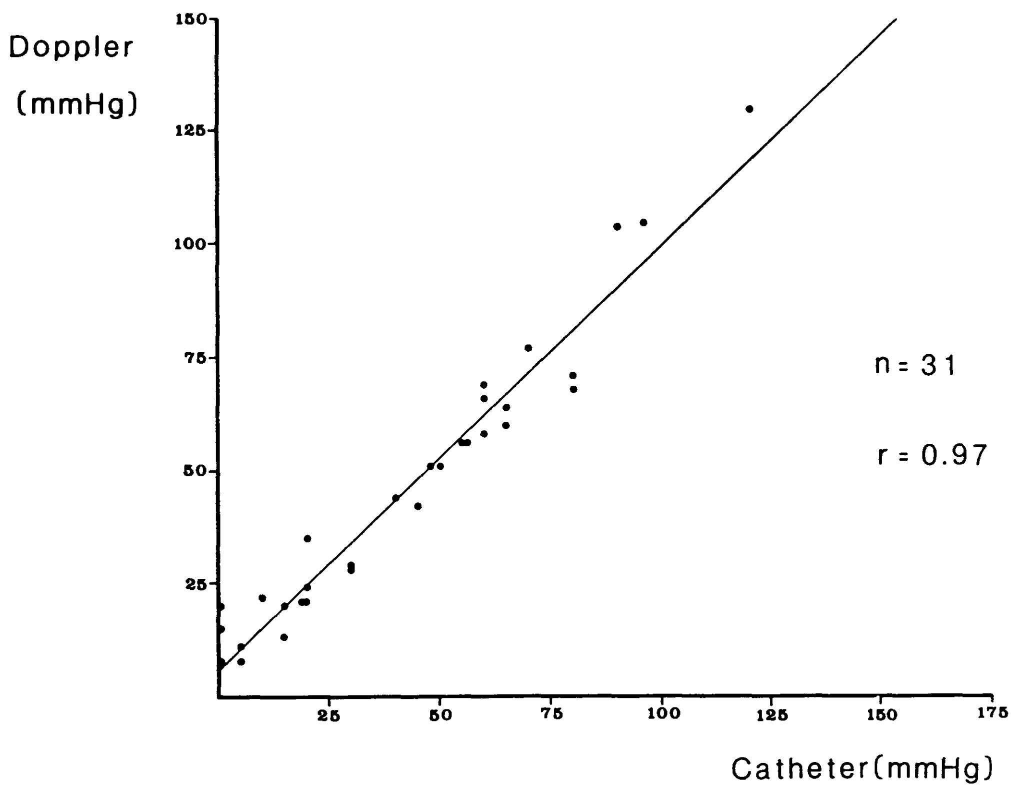


Figure 14: Comparison of pressure gradients from Doppler ultrasound examination performed simultaneously during cardiac catheterisation, with invasively measured valve gradients, in patients with aortic stenosis.

Clinical Value

In the 42 patients in whom valve gradients were obtained at catheterisation subsequent to Doppler study, the clinical and non-invasive assessments of surgical severity, with and without Doppler measurements, were compared with the subsequent surgical decision from the complete data including that obtained at catheterisation. Though in general terms a peak aortic gradient of > 50mmHg was taken as surgically significant in one patient the gradient at Doppler examination was 42 mmHg and 45 mmHg at catheterisation. However, the patient was regarded as having a surgically significant leison by the attending physician despite the valve gradient being below 50 mmHg. Since the Doppler derived gradient was almost identical to that subsequently obtained at catheterisation the decision, based on the non-invasive assessment with Doppler, was for surgical intervention, and the subsequent outcome was unchanged by cardiac catheterisation.

On the basis of the clinical and non-invasive assessment prior to Doppler examination or cardiac catheterisation, 16 of the 42 patients in whom gradients were subsequently obtained at catheterisation, were graded as having aortic stenosis which was unequivocally of a severity requiring surgical intervention. Fourteen were graded as having non-surgical aortic stenosis and in the remaining 12 patients there was doubt as to the severity of stenosis on the basis of clinical and established non-invasive data alone.

In all 16 of the patients thought clinically to have surgically significant aortic stenosis Doppler examination identified a surgically significant gradient, which was subsequently confirmed by catheterisation.

In 11 of the 14 patients with a clinically non-significant lesions the Doppler findings suggested a non-significant lesion which was subsequently confirmed by catheterisation. In the remaining three patients, however, Doppler examination suggested a surgically significant lesion which was confirmed by catheterisation in all three cases.

The remaining 12 patients, however, had inconclusive evidence on clinical and non-invasive data. In 10 patients Doppler examination identified a non-significant gradient confirmed subsequently at catheterisation. In the other two patients Doppler detected surgically significant lesions which were confirmed by catheterisation.

DISCUSSION

It has been suggested that the non-invasive assessment of valve disease can obviate the need for cardiac catheterisation in many cases.[109] However, patients with aortic stenosis are often the most difficult to assess non-invasively, and cardiac catheterisation is almost always required. In this study, however, in an appreciable number of patients (12 of 54, 22%) it was not possible even at cardiac catheterisation to measure the valve gradient. In comparison satisfactory signals were recorded in all patients investigated by the Doppler technique. It is important to emphasize that in patients with aortic stenosis, difficulty may be encountered in obtaining satisfactory Doppler recordings and considerable experience is required to identify the high velocity jet at a low intercept angle, and more so to exclude the presence of a high velocity jet. Multiple praecordial positions need to be interrogated within an individual patient, some of which are not recognized positions for imaging and there will therefore be a substantial learning curve even for those experienced in echocardiography.

The correlation found between the Doppler derived gradient and that obtained at catheterisation indicates that Doppler ultrasound provides an accurate assessment of the gradient across an aortic obstruction. In this group of patients, the accurate relationship of Doppler derived gradients with invasive pressure measurements did not appear to be appreciably affected by the fact that peak to peak systolic gradients were measured at catheterisation, rather than the peak instantaneous gradient as measured by the Doppler technique.[112] In several cases the sedative used as a premedication for catheterisation affected the Doppler derived gradient, slightly lowering its value compared with previous Doppler examinations. Indeed in one patient in whom cardiac catheterisation was performed under general anaesthesia the valve gradient assessed by Doppler ultrasound was 157 mmHg prior to catheterisation, and though still significant, was appreciably lower during the catheterisation procedure at 90 mmHg (Fig. 13). Previous reports have suggested that this sort of discrepancy was a result of variation between the peak to peak and peak instantaneous gradients[41,45] Although this is certainly of some importance, these studies did not perform Doppler examination during invasive study, under the effects of sedation or anaesthesia, and the improved results of shown in Fig. 14 for studies performed during cardiac catheterisation, in comparison to those done prior to catheterisation in Fig. 13, would suggest that sedation or anaesthesia will have important effects on aortic valve gradients and may account, in part, for some of the less accurate correlations previously reported with the technique.

In a number of patients who had no demonstrable valve gradient at catheterisation, Doppler ultrasound had suggested the presence of a small, though clearly non-significant, transvalvar gradient. It is likely that this resulted from failure of the modified Bernoulli formula to take into account the flow velocity proximal to the valve. Several of these patients had aortic regurgitation and is would be anticipated that the flow through the aortic valve would be increased as a result. This would cause a higher peak velocity to be present and therefore suggest a degree of obstruction from the modified Bernoulli equation. Alternately, a small peak instantaneous gradient may have been present, unidentified by the peak to peak measurement performed at catheterisation. However, although there was a discrepancy in some of the patients with mild aortic stenosis this in no way affected the clinical value of the technique in predicting the need for surgical intervention, but one should have reservations about the accuracy of predicting aortic gradients in mild valvular obstruction. In these patients it is sensible to measure the flow velocity in the left ventricular outflow tract, proximal to the obstruction, and if an abnormally high velocity is present it is worthwhile including this proximal velocity in the Bernoulli equation for more accurate estimation of the valve gradient.

The shape of the Doppler velocity recording may also be valuable in assessing the severity of aortic obstruction. In normal aortic flow (see chapter 3), or in mild aortic obstruction, the peak velocity occurs early in systole, whereas in severe obstruction, as in Fig. 11, the peak velocity occurs later, in mid systole. Although this is somewhat subjective, it may be important in the situation of critical aortic stenosis and severe left ventricular dysfunction, where as a result of poor cardiac output, the aortic valve gradient may be relatively low, whereas the shape of the Doppler velocity recording will conform to that found in severe aortic stenosis.

The potential for obtaining falsely low pressure gradients by the Doppler technique is an important consideration, and will be relate not only to the suitability of the patient for ultrasound study but also to the expertize of the investigator. In this study no falsely low recordings were obtained and may be due in part to the care taken in performing Doppler examinations from all available precordial positions in all patients. It is unlikely that Doppler ultrasound will significantly overestimate pressure gradients in patients with aortic stenosis, particularly if account is taken of the velocity proximal to the obstruction, so that it should be possible to comment that the actual pressure gradient is at least as high as that derived from Doppler examination. Nevertheless, it can be argued that by attempting to measure a very small high velocity jet at an unknown angle, the possibility of false low recordings by the Doppler technique must exist. Therefore extreme care should be taken in interpreting the result of a Doppler examination that suggests a less than significant obstruction where this is at variance with either the clinical or routine non-invasive examinations.

More important than the accurate correlation of valve gradients with catheterisation data is the ability of the Doppler technique to help determine the appropriate clinical management of the patient with aortic stenosis when integrated as part of a complete non-invasive assessment. Indeed in this study no patient with a surgically significant lesion would have been missed by complete non-invasive assessment including Doppler examination, and in no patient was there an appreciable overestimation of the severity of obstruction. Where doubt existed as to the severity of a lesion by other non-invasive techniques alone, Doppler examination was able to correctly clarify the degree of obstruction in all cases. Possibly more important is the fact that the Doppler examination identified three patients with surgically significant lesions that would otherwise have been missed by routine clinical and non-invasive assessment.

It can be argued that cardiac catheterisation may be indicated for valve lesions other than aortic stenosis, but, as previously reported, the vast majority of these can be accurately assessed by standard non-invasive techniques.[109] Where the possibility of ischaemic heart disease coexists coronary angiography may well be indicated, but this is a much less hazardous and time consuming procedure than full right and left heart catheterisation. Indeed in an appreciable number of patients undergoing catheterisation for valvar disease coronary angiography is not performed.[109]

Continuous wave Doppler ultrasound has therefore added a new dimension to the assessment of patients with aortic stenosis. When combined with clinical examination and other routine non-invasive techniques it can accurately determine the subsequent clinical management of these patients, and it would therefore seem safe and appropriate to recommend surgery in an appreciable number of patients with aortic stenosis without the need for prior cardiac catheterisation. It is imperative however, that if clinical decisions are to be based on the information obtained by Doppler ultrasound, that examination is performed by someone with considerable experience in Doppler ultrasound, in the full knowledge of the problems and pitfalls of the technique, with particular regard for the very real potential to significantly underestimate the aortic valve gradient in a patient with severe aortic stenosis.

CHAPTER 5

COMPARISON OF DOPPLER ULTRASOUND VELOCITY MEASUREMENTS WITH PRESSURE DIFFERENCES ACROSS BIOPROSTHETIC VALVES IN A PULSATILE FLOW MODEL

INTRODUCTION

There has been much interest in assessment of bioprosthetic valve function in vitro, in determining flow profiles and pressure gradients across valve prostheses in order to assess forward flow characteristics and the degree of mechanical obstruction.[113] The valuable information gained from these studies is limited since they cannot easily be extrapolated to the clinical situation and little in vivo haemodynamic data is currently available.

Doppler ultrasound has been used to accurately measure blood flow velocities both in vivo and in vitro[22] and its ability to measure pressure gradients across normal and diseased mitral valves has been clearly demonstrated.[29] It therefore has the potential to measure the velocity of flow across prosthetic valves and assess the degree of valve obstruction. Presently, this has been used in the clinical situation in only a small number of patients to assess prosthetic valve gradients[57-59] compared with results obtained at cardiac catheterisation. However, no in vitro data is currently available to support the correlation of derived pressure gradients from the Doppler flow velocity with pressure differences across these prostheses. Significant differences in valve function and design exist between the traditional porcine bioprostheses and the newer pericardial bioprostheses.[114]

The porcine valve prostheses have much more prominent struts in comparison to their pericardial counterparts and produce significantly higher transvalvar pressure gradients for a similar valve flow. It is therefore of considerable importance to establish the validity of the Doppler technique and the application of the Bernoulli formula for different bioprosthetic valves under a variety of pulsatile flow conditions.

METHODS

Pulsatile Flow Model

A pulsatile flow apparatus was designed to assess the forward flow pressure drops through prosthetic valves in the mitral position. The layout of the test rig is shown in Fig. 15. Pulsatile flow is produced by a purpose built servo controlled piston pump (Superpump Cardiac Development Laboratory, Victoria, Canada). The pressure difference across the valve is measured with a differential transducer (Gaeltec 3CT Special, Dunvegan, Scotland) with the upstream pressure tapping 25 mm from the valve and the downstream pressure tapping 50mm from the valve mounting ring. The flow through the valve is measured with an electromagnetic flowmeter (Gould S P 2201) with a 24mm probe. The pressure and flow signals are digitized and stored on an Apple microcomputer for subsequent analysis. Data is collected over a period of twenty cycles and an average waveform

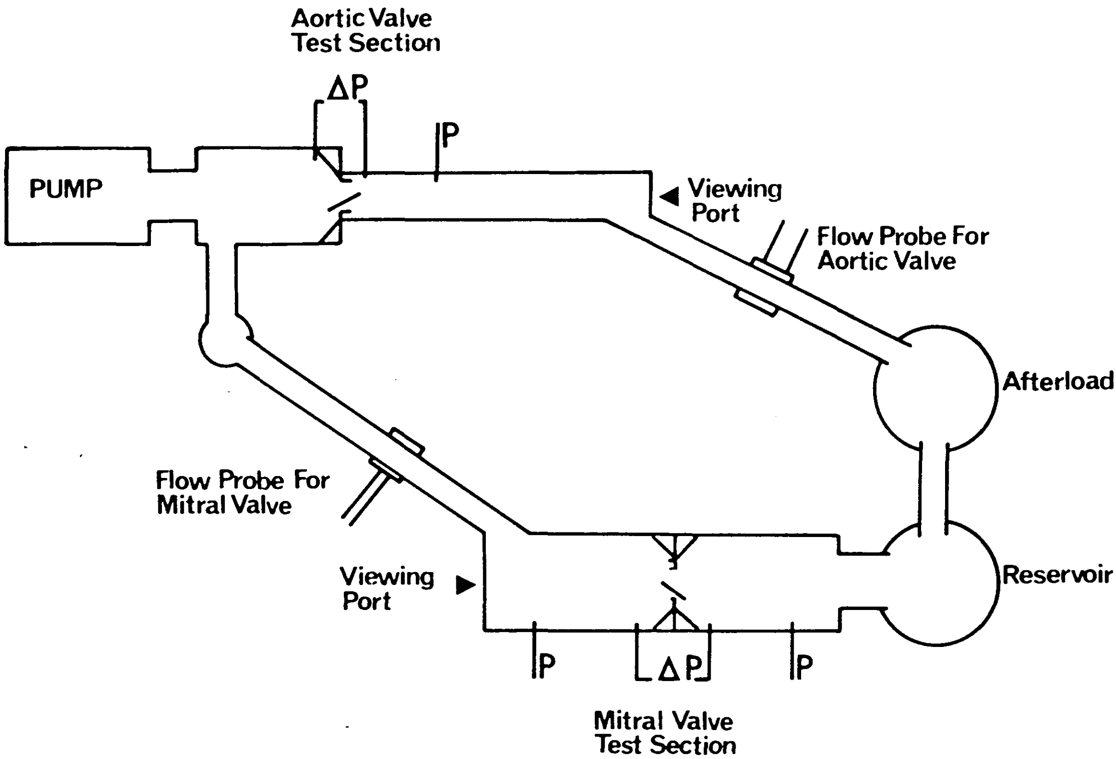


Figure 15: Layout of the pulsatile flow test apparatus, showing th position of the differential pressure transducer (ΔP) and the flow probe.

calculated for each signal.

In this study the valves were tested under four different flow conditions (Fig. 16) corresponding to cardiac outputs of between 4.5 and 9 l/min. The peak flow and peak pressure difference was measured for all four waveforms and in addition the end diastolic flow and pressure were measured for waveforms A and B.

Doppler Ultrasound

The Doppler ultrasound transducer was positioned in a perspex plate aligned along the axis of the test section parallel to the through valve flow and the transducer sealed in position throughout the study (Fig. 17). The valves were tested in 0.9% saline repeatedly aerated during the study in order to provide satisfactory ultrasound reflection for the Doppler recordings.

From the measured peak flow velocity the pressure difference across the prosthetic valve was then calculated using the modified Bernoulli equation[29,115] with the constant 3.75 used in place of 4 to allow for the lower mass density of 0.9% saline (1.00×10^3 kg/m^3) compared to blood (1.06×10^3 kg/m^3).

The results of the Doppler derived pressure gradients

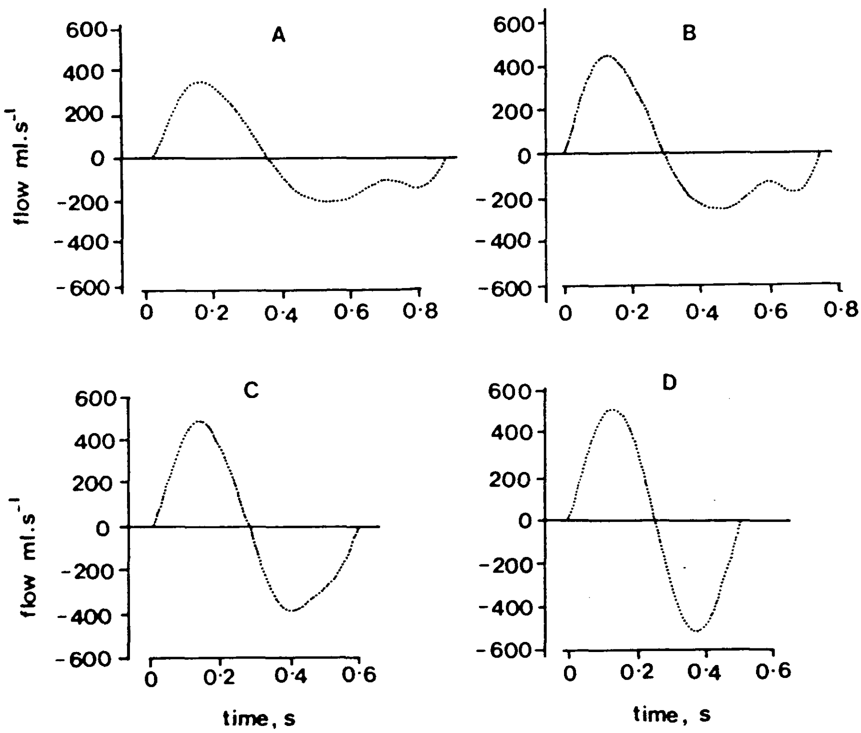


Figure 16: Flow waveforms in the test apparatus. Negative flow indicates the flow through the mitral valve.

Waveform A - Heart Rate (HR) 70 bpm,
Stroke Volume (SV) 70 ml.

Waveform B - HR 88 bpm, SV 80 ml.

Waveform C - HR 100 bpm, SV 80 ml.

Waveform D - HR 120 bpm, SV 80 ml.

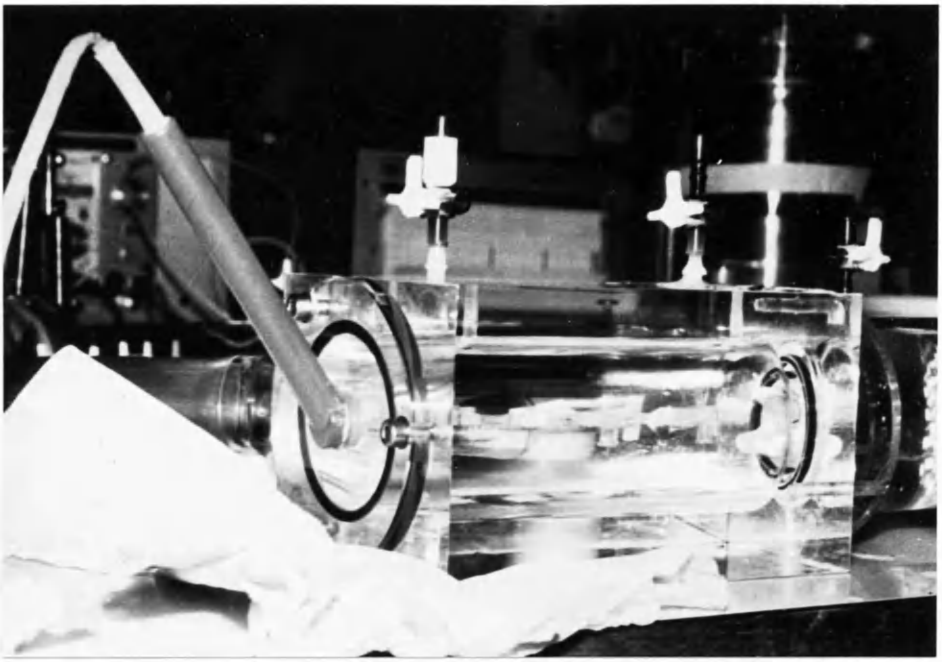


Figure 17: Doppler transducer sealed in perspex end plate of test apparatus in direct line of through valve flow.

Figure 18: A pulsatile flow experiment in progress.

were then compared with those obtained from direct pressure measurement within the pulsatile flow model.

Bioprosthetic Valves

Four bioprosthetic valves (size 29mm) were available for study in the test apparatus (Fig. 18). They included two new pericardial bioprostheses, the Hancock pericardial and Low Profile Ionescu Shiley, and two porcine bioprostheses, the new Wessex Medical bioprosthesis and the more traditional Carpentier Edwards valve. Since the Doppler ultrasound probe was fixed in a position with the beam directed towards the centreline flow, it was not possible to study mechanical valve prostheses where there will be more than one velocity jet through the prosthesis and the velocity jets will be directed at an angle through the valve and therefore, unlike the bioprosthetic valves, it would not be possible to align the ultrasound probe in the direction of through valve flow.

RESULTS

Satisfactory Doppler signals were obtained from all 4 valve prostheses and the Doppler recording (Fig. 19) produced similar flow waveforms to those obtained from the electromagnetic flow meter (Fig. 20). Measured Doppler velocities ranged from 0.76 m/s to 2.64 m/s with a mean of 1.52

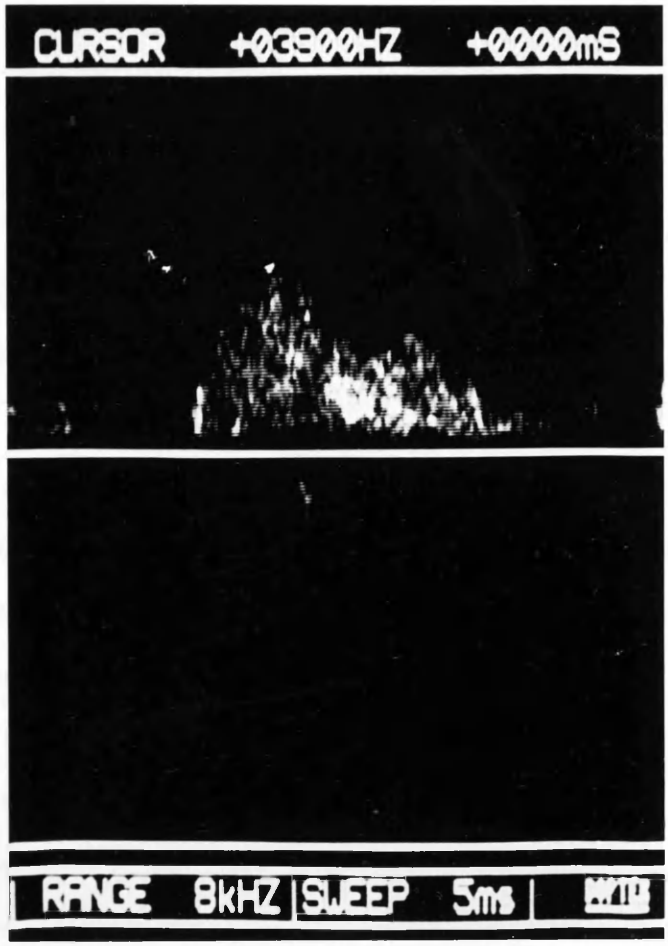


Figure 19: Doppler spectral signal of flow waveform A.

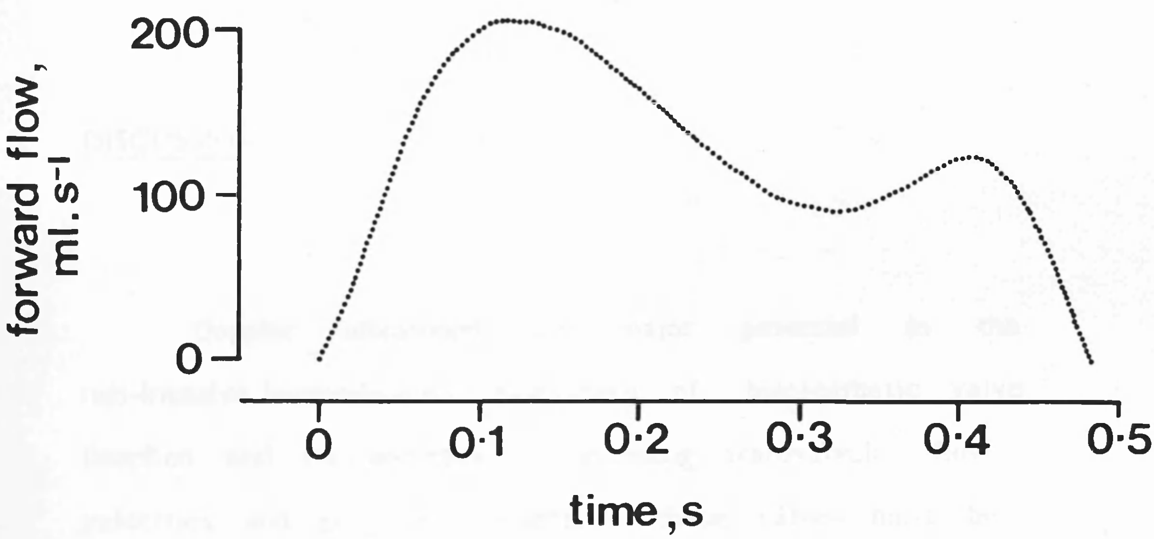


Figure 20: Flow waveform A measured by electromagnetic flow probe displaying similar pattern to Doppler signal.

m/s for the porcine bioprostheses and from 0.50 m/s to 1.84 m/s with a mean of 1.05 m/s for the pericardial bioprostheses. These correspond to the measured pressure differences of 2.5 mmHg to 27 mmHg, mean 10.4 mmHg for the porcine bioprostheses and 1.0 mmHg to 11.3 mmHg, mean 4.15 mmHg for the pericardial bioprostheses. Using both Doppler and direct in vitro measurements significantly higher velocities and pressure differences were obtained with the porcine bioprostheses than with the pericardial prostheses as would be expected from the known in vitro haemodynamic profiles of these types of bioprosthetic valves.[113] The relationship between the measured pressure difference and that derived from the Doppler flow velocity for all valves is shown in Fig 21. The correlation obtained between the two methodologies was 0.98 with a gradient close to unity.

DISCUSSION

Doppler ultrasound has major potential in the non-invasive haemodynamic assessment of bioprosthetic valve function and its accuracy in assessing transvalvular flow velocities and pressure gradients in these valves must be clearly established.

In order to derive the pressure difference from the

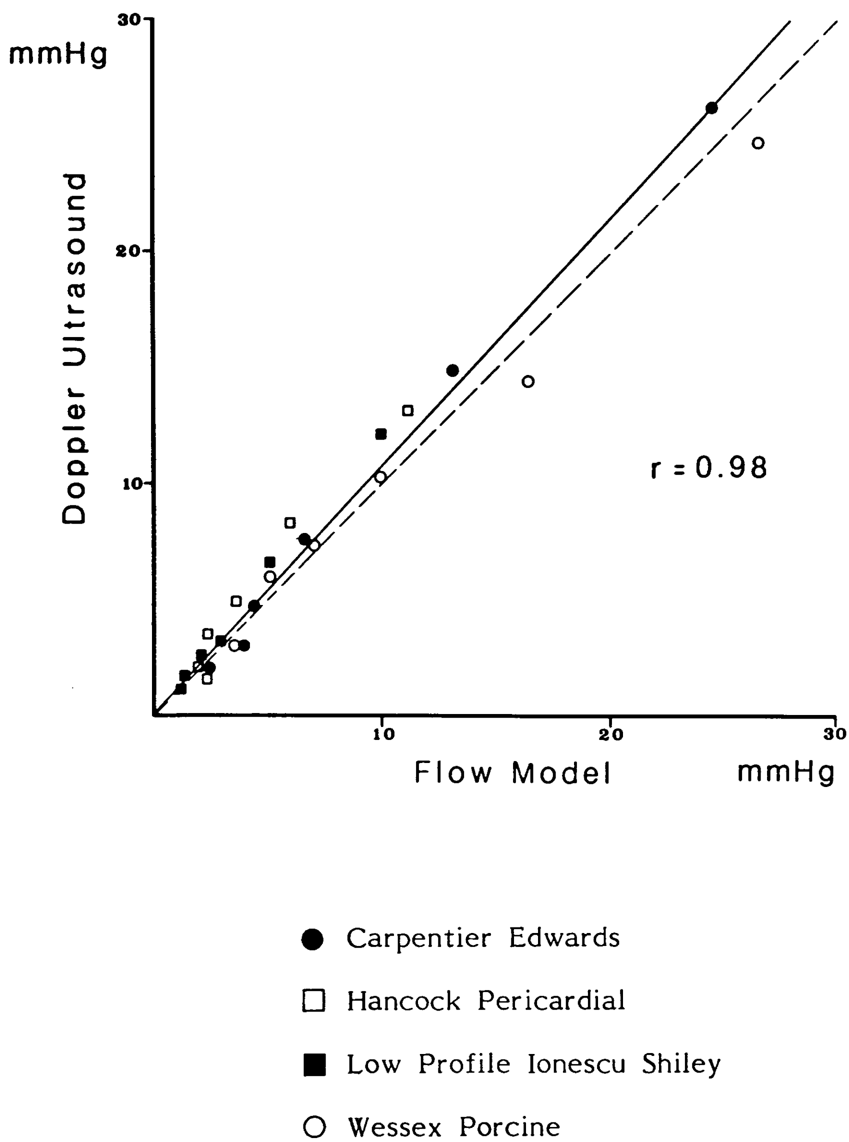


Figure 21: Comparison of the pressure differences at each flow waveform measured by Doppler ultrasound and directly in the flow model.

Doppler flow velocity using the modified Bernoulli equation a number of assumptions have to be made. The equation fails to account for viscous losses due to friction, non streamlined valve flow, losses due to turbulence, contraction of the velocity jet and velocity of fluid proximal to the valve. However despite these assumptions the results were within 3 mmHg of the measured pressure difference in all cases.

Doppler ultrasound tended to slightly overestimate the measured pressure difference in 3 of the valves studied which may be explained by the velocity profile of the jet.[114] This was not found with the Wessex Medical bioprosthesis which has a prominent muscle shelf and may slightly affect the orientation or velocity profile of the jet.

Although having shown a good correlation in vitro the potential for greater variation exists in vivo particularly with the orientation of the ultrasound beam in the direction of maximum through valve flow. However, the few reported studies using Doppler ultrasound to assess valve function in vivo have shown a reasonably good correlation with results obtained at cardiac catheterisation and would therefore suggest that this may not present a significant problem in practical terms.[57-59]

This study has demonstrated the validity of using Doppler ultrasound and the modified Bernoulli equation to measure pressure differences across bioprosthetic valves in vitro. The potential therefore exists to provide a non-invasive haemodynamic assessment of bioprosthetic valve function in vivo. The application of the modified Bernoulli equation remains questionable. It has not been possible to study these prostheses in vitro, and clearly there are considerable differences from the bioprosthetic valves. The presence of a pyrolite disc or steel ball may interfere with the quality of the ultrasound recordings, and not only are there two or more velocity jets resulting from multiple orifices, but also the direction of the velocity jet or jets through a mechanical valve prosthesis will be less predictable. However, since the velocity of flow through any orifice will be dependent and related to the pressure drop across the valve prosthesis, if the velocity jet can be identified in vivo with a small intercept angle it seems reasonable to assume that the modified Bernoulli equation may well be valid for mechanical prostheses also.

CHAPTER 6

IN VIVO HAEMODYNAMIC ASSESSMENT OF MITRAL PROSTHETIC FUNCTION

INTRODUCTION

Assessment of Prosthetic Valve Function

The clinical assessment of a patient with a mitral valve prosthesis can often prove unreliable and where prosthetic dysfunction is suspected cardiac catheterisation is almost always required. This is not, however, a uniformly successful procedure particularly if both mitral and aortic replacements coexist. In addition in patients on oral anticoagulant therapy cardiac catheterisation potentially carries greater risk. Not only can this invasive investigation be unsuccessful but it can also potentiate incorrect haemodynamic information by the invasive nature of the technique. For instance, the induction of ventricular ectopics or tachycardia by the presence of a catheter in the left ventricle can falsely produce mitral regurgitation during left ventricular angiography and cause difficulty in assessing a periprosthetic leak.

In a patient with an isolated mitral valve replacement, clinical examination will be a sensitive method of assessing prosthetic valve dysfunction. Where there is aortic stenosis or an aortic valve replacement in addition, clinical examination may be difficult and further investigations will be necessary to assess prosthetic valve function. Two-dimensional echocardiography has provided a non-invasive method of obtaining structural information on prosthetic valves but it is unable to provide an accurate haemodynamic assessment. Echocardiographic abnormalities tend to be highly specific for prosthetic valve dysfunction, and although some inferences can be made regarding prosthetic valve function from this structural detail, echocardiography suffers from poor sensitivity in defining prosthetic valve dysfunction.[116,117] Cardiac screening will have some role to play if there is a mechanical mitral valve replacement, by assessing any rocking of the valve apparatus and by the extent of movement of the pyrolite disc or steel ball. However, this requires the valve to be adequately visualised in profile, which may not always be possible. In addition occlusion of the valve lumen with thrombus may not be apparent, as valve movement will not necessarily be restricted.

Potential Role of Doppler Ultrasound

A non-invasive method such as Doppler ultrasound which can provide important haemodynamic information has many advantages over conventional echocardiographic imaging and therefore a potentially greater role in the assessment of mitral prosthetic function.

Since the majority of cases of mitral prosthetic dysfunction result from valve regurgitation rather than obstruction, if Doppler ultrasound is to have a significant impact on the assessement of these patients it must be able to identify accurately the presence of mitral prosthetic regurgitation and if possible provide a degree of quantitative assessment.

Doppler ultrasound has already been applied to a small number of patients with mitral valve prostheses[118-120] but reports of its accuracy in predicting valve gradients in these patients, compared with gradients at catheterisation, is limited to 9 patients with mechanical[57] and 8 patients with tissue[59] mitral valve prostheses.

Pulsed wave Doppler has been used successfully to identify mitral regurgitation in native mitral valve disease.[37,38] In addition it has been reported to be of value as a quantiative method by assessing the degree of regurgitation by mapping the extent of turbulent flow within the left atrial cavity.[39,40,121,122] There is considerable variation in the methodology used in these studies with respect to the number of praecordial views and the relative importance and summation of the information they provide and not all reports have shown this technique successful.[123] The simplest method of assessing the degree of mitral regurgitation was that applied by Abbasi et al.[39] who used pulsed Doppler from the apical view to relate the extent of systolic flow detected within the left atrial cavity behind the mitral valve to the severity of mitral regurgitation, with the further that the systolic flow extended into the atrium indicating increasing severity of regurgitation. A modification of this method has been employed in the quantitative assessement of mitral prosthetic regurgitation in this chapter.

Aim of Study

Having established the validity of Doppler ultrasound and the modified Bernoulli formula in predicting bioprosthetic valve gradients in vitro, the aim of this chapter was to examine both bioprosthetic and mechanical mitral valve replacements in vivo, and to assess the ability of Doppler ultrasound to predict mitral prosthetic gradients in normally functioning prostheses and those with prosthetic valve dysfunction. In addition an assessment of the ability to identify the presence of mitral prosthetic regurgitaiton and provide some quantitation of its the severity in these patients.

SUBJECTS AND METHODS

43 patients who had undergone mitral valve replacement were studied. Forty were undergoing cardiac catheterisation either for haemodynamic assessment of investigational bioprostheses or because the presence of significant mitral prosthetic dysfunction was suspected clinically. Three further patients were included, all had obstructed mechanical prostheses and were undergoing surgery on the basis of non-invasive

investigation alone. Their ages ranged from 34 to 73 years with a mean age of 55 years. Thirty patients had a tissue prosthesis, low profile Ionescu Shiley in 11, Hancock pericardial in 9, Wessex porcine in 6, Carpentier Edwards in 4, and 13 patients had a mechanical valve prosthesis, a Bjork Shiley in all cases.

Doppler Examination

Doppler examination was performed in all cases prior to cardiac catheterisation. This was performed from the apical position in order to align the Doppler beam with the mitral valve flow. Mitral valve gradients were obtained by continuous wave Doppler, calculated from the maximum mitral flow velocity curves using the modified Bernoulli equation. Since the valve gradient measurement can vary with cardiac output and the presence of mitral regurgitation the mitral pressure half-time was also measured. Mitral regurgitation was identified by continuous wave Doppler from the apical position by high velocity flow away from the transducer into the left atrium and further investigated using the pulsed wave mode where the presence of flow detected during systole, at various sample depths within the left atrium, used to provide an estimate of the severity of mitral regurgitation as mild, moderate or severe.

In the initial 11 patients Doppler examination was performed using a Diasonics V3400R pulsed wave Doppler with simultaneous 2 dimensional echo imaging, allowing only measurement of the presence and extent of mitral regurgitation. The remaining 29 patients undergoing cardiac catheterisation were studied using a Vingmed Alfred continuous and pulsed wave Doppler Velocimeter. The severity of mitral regurgitation was graded as mild if systolic flow could be detected only up to 1.5 cm behind the mitral prosthesis, moderate if systolic flow was detected between 1.5 - 2.5 cm, and severe if the systolic flow extended further than 2.5 cm into the left atrium. Using the Diasonics V3400R this was performed with simultaneous imaging from the apical position. With the Vingmed Alfred, since simultaneous imaging was not available, the mitral regurgitant jet was first identified using continuous wave Doppler and pulsed wave Doppler used to detect the depth of the valve clicks. Pulsed Doppler was then used to map the extent of the velocity jet into the left atrial cavity. Pulsed wave Doppler was repeatedly interchanged with the continuous wave mode to ensure that the Doppler beam remained aligned with the direction of the regurgitant jet throughout the mapping procedure.

Cardiac Catheterisation

Cardiac catheterisation was performed in 40 of the 43 patients. Mitral valve gradients were measured in the 29 patients in whom simultaneous pulmonary capillary wedge and left ventricular diastolic pressures were obtained and the results analysed independently from the Doppler examination. All patients were in atrial fibrillation and equivalent diastolic cycle lengths were chosen for comparison of the Doppler and invasive valve gradients. Biplane left ventricular angiography, performed in all 40 patients, provided a visual assessment of the presence and extent of prosthetic regurgitation which was graded as either mild, moderate or severe. In all cases results obtained at cardiac catheterisation were analysed by an independent observer. The results obtained by the Doppler examination and those obtained at cardiac catheterisation were then compared.

RESULTS

Satisfactory Doppler recordings were obtained from the apical position in all 43 patients. The spectral display from a patient with a normally functioning mitral prosthesis is illustrated in Fig. 22. There is a slight increase in the maximum mitral frequency shift, 3,800 Hz, equivalent to a peak velocity of 1.48 m/s, but there is a rapid decrease in velocity from the initial peak indicating a relatively short mitral pressure half-time. In comparison, in Fig. 23 from a patient with severe mitral prosthetic obstruction, although the maximum frequency shift is very similar, 4,200 Hz or 1.64 m/s, there is a very slow rate of decrease of the flow velocity, indicating a very prolonged mitral pressure half-time, >400 msec, signifying

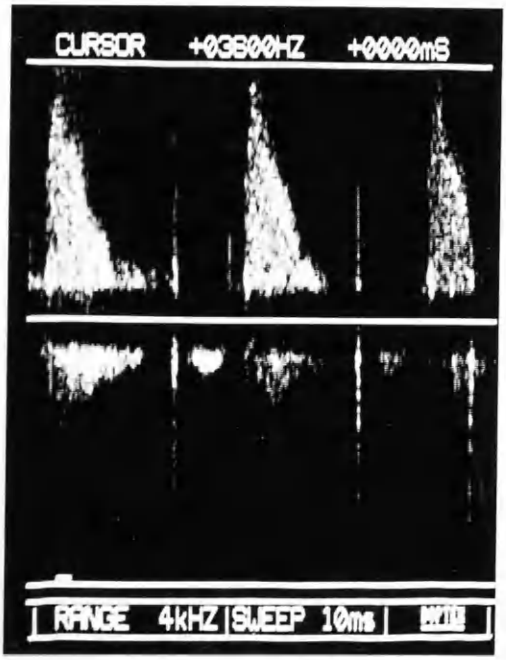


Figure 22: Continuous wave Doppler spectral signal of normal mitral prosthetic flow in atrial fibrillation.

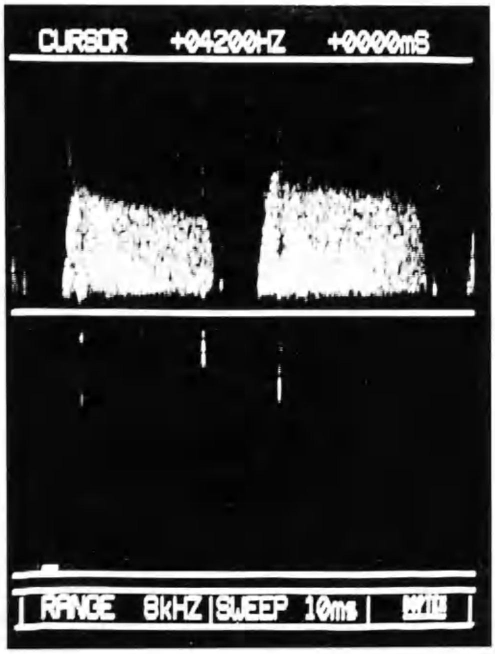


Figure 23: Continuous wave Doppler spectral signal of mitral prosthetic obstruction in atrial fibrillation.

Figure 24: Continuous wave Doppler spectral signal of mitral prosthetic regurgitation demonstrating a high velocity systolic jet.

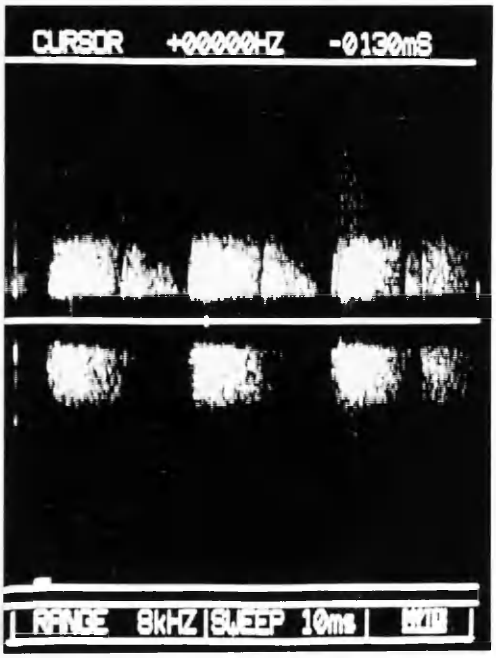


Figure 25: Pulsed wave Doppler spectral signal of mitral prosthetic regurgitation from left atrium of the same patient as Fig. 23.

severe mitral obstruction. Clearly, although the peak velocity is similar in this case to that in a normally functioning prosthesis, if the modified Bernoulli equation is applied at each 10 msec throughout diastole in order to calculate a mean valve gradient, then the calculated mean gradient will be significantly higher in the patient with mitral prosthetic obstruction.

Figures 24 and 25 illustrate the spectral displays in the continuous and pulsed wave modes from a patient with mitral prosthetic regurgitation. In the continuous wave mode a high velocity jet is identified, away from the transducer, into the left atrium, during each systolic contraction, indicating the presence of regurgitation. Switching to the pulsed mode at a particular depth within the left atrium from the apex, a "wrap around" effect has occurred as a result of frequency aliasing, and although the height of the velocity jet is not seen, the presence of systolic flow velocity is still identified, at the particular depth setting of the velocimeter.

Mitral Prosthetic Obstruction

In the 29 patients in whom valve gradients were obtained at catheterisation, mean mitral prosthetic gradients obtained by the Doppler examination ranged from 0 to 15 mmHg with a mean of 5.52 mmHg and those obtained at cardiac catheterisation from 0 to 18 mmHg with a mean of 5.58 mmHg, providing an overall correlation between the two techniques of 0.85 (Fig. 26).

Three patients with bioprosthetic valves had significant mitral prosthetic obstruction requiring reoperation. The mean valve gradients were 15, 15 and 18 mmHg at cardiac catheterisation and 15, 15 and 12 mmHg on the Doppler examination. By measuring the mean mitral gradients it was difficult to obtain a clear separation from some patients with an apparently normally functioning mitral prosthesis. In particular, when mitral regurgitation was present, the mean mitral valve gradient tended to be higher, a result of increased flow through the mitral prosthesis. The mitral pressure half-time (Fig. 27) was however increased in all patients with significant prosthetic obstruction, including the 3 further patients with severe mechanical valve obstruction subsequently confirmed at the time of surgery. The mitral pressure half-time was unaffected by the presence of mitral regurgitation and remained normal in these patients allowing clear separation of the patients with significant prosthetic valve obstruction.

In all patients with a normally functioning prosthesis the mitral pressure-half time was less than 200 msec in comparison to more than 400 msec in all but one patient with an obstructed prosthesis. In this patient with significant though not severe prosthetic valve obstruction the mitral pressure half-time was 240 msec, significantly longer than the normally functioning prostheses. By excluding the patients with

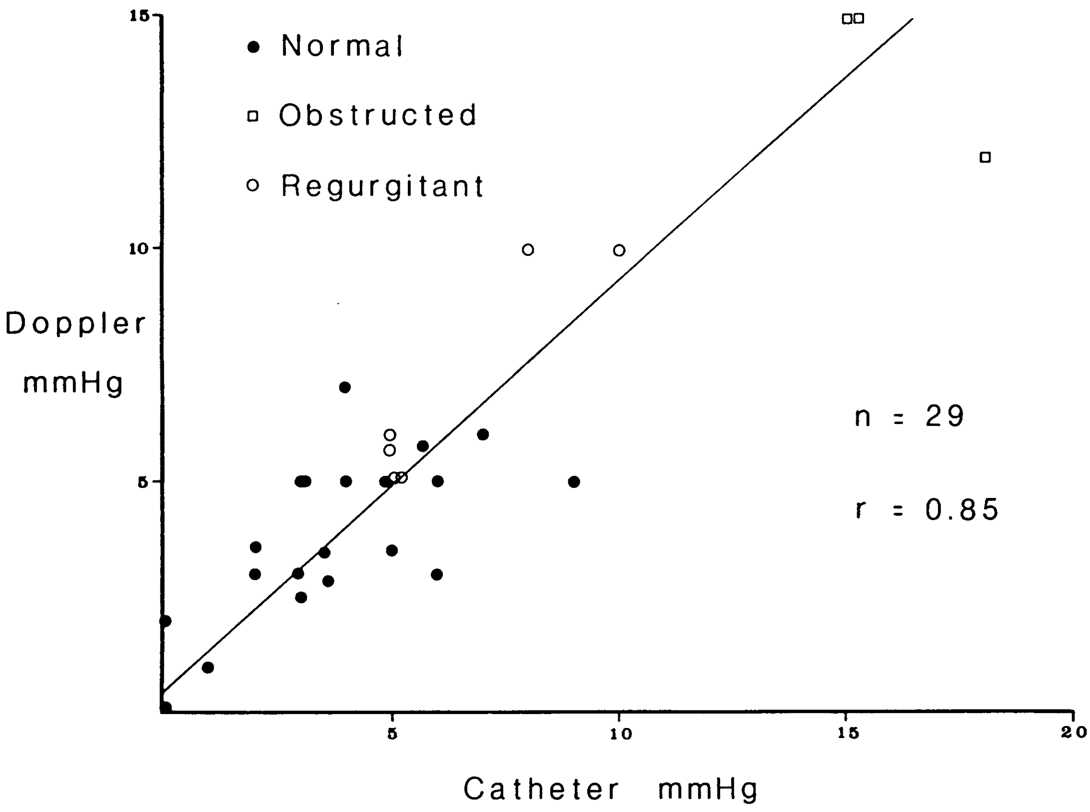


Figure 26: Comparison of mean mitral prosthetic gradients measured by Doppler ultrasound with those obtained by cardiac catheterisation across normal, regurgitant and obstructed mitral prostheses.

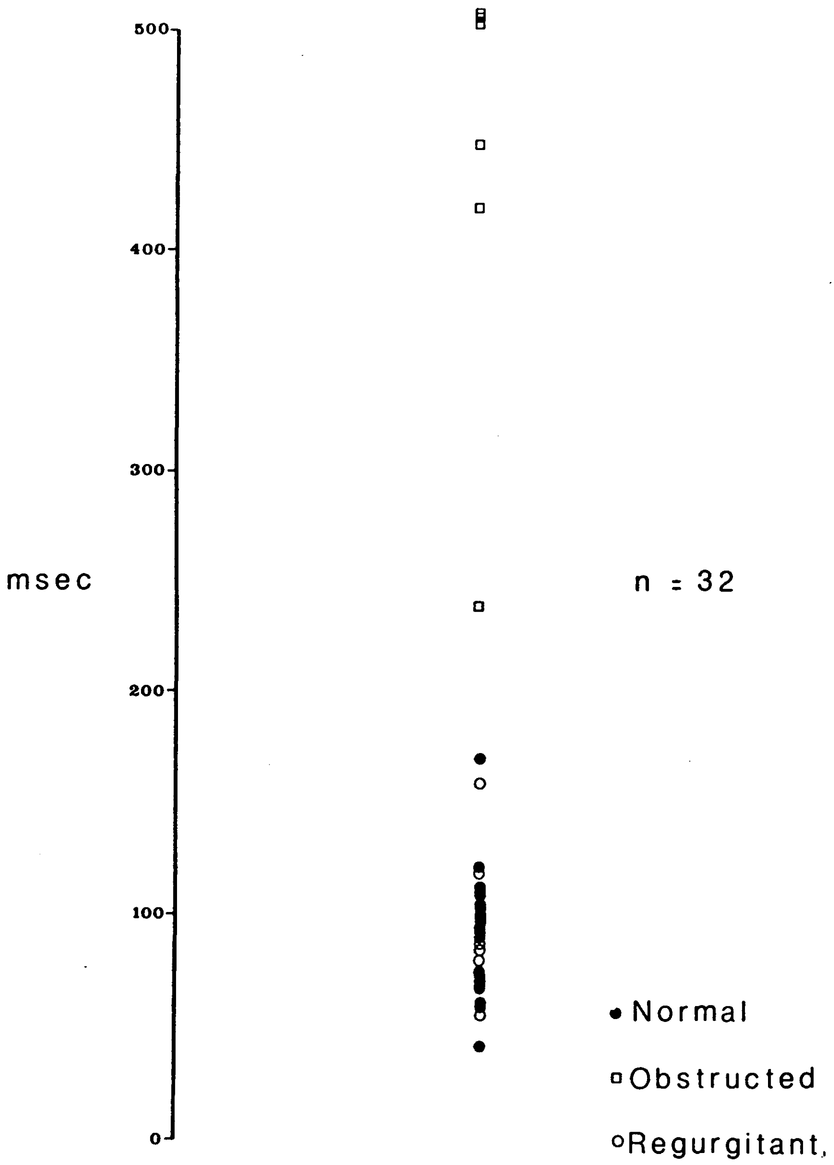


Figure 27: Mitral pressure half-times across normal, regurgitant and obstructed mitral prostheses.

prosthetic obstruction the normal range for mean valve gradients for non-obstructed prostheses by the Doppler examination in this series ranged from 0 to 10 mmHg with a mean value of 5.13 mmHg and more importantly the normal range for mitral pressure half-time from 40 to 170 msec, mean of 91.9 msec. In addition the type of valve prosthesis studied did not appear to alter either the mean valve gradient or the mitral pressure half-time.

Mitral Prosthetic Regurgitation

The comparative results of the Doppler technique and cardiac catheterisation in detecting the presence and extent of mitral regurgitation are shown in Table 4. No false positive results were obtained using the Doppler examination. It failed to detect the presence of mitral regurgitation in one patient who, at cardiac catheterisation, had a very mild degree of peri-prosthetic valve regurgitation. In addition the degree of regurgitation assessed by the Doppler examination correlated well with that found by left ventricular angiography (r=0.97).

DISCUSSION

The haemodynamic information gained by cardiac catheterisation is often vital to the accurate assessment of

TABLE 4

MITRAL PROSTHETIC REGURGITATION

	Doppler	Catheterisation
None	23	22
Mild	3	4
Moderate	3	3
Severe	11	11

Comparison of the presence and severity of mitral prosthetic regurgitation in 40 patients.

prosthetic valve dysfunction and the decision regarding reoperation. The small risk involved in undertaking such an investigation is far outweighed by the information it can potentially provide. However, any investigation which can reduce or even abolish such a risk without compromising necessary information must prove advantageous. In addition, if it can provide such information in situations where cardiac catheterisation is either undesirable or indeed unsuccessful it can,in some respects, prove superior to the invasive investigation. Two-dimensional echocardiography has fulfilled this role only in part, and though often highly specific in detecting prosthetic valve dysfunction it lacks sensitivity and provides qualitative rather than quantitative information.[116,117]

This study has investigated the role of Doppler echocardiography in providing an haemodynamic assessment of mitral prosthetic valve function in vivo. Satisfactory Doppler signals of the diastolic flow velocity can be obtained in virtually all patients with a mitral valve prosthesis, and it is essential to obtain high quality recordings in order to assess prosthetic valve gradients and mitral pressure half-times. All mitral prostheses will have a mild degree of obstruction when functioning normally and slightly higher peak velocities are to be expected, with prolongation of the mitral pressure half-time compared to normal subjects. A reasonably good correlation between Doppler derived mean valve gradients and those measured at cardiac catheterisation has been demonstrated. The gradient across a mitral prosthesis is dependent on valve flow, influenced by cardiac output and the presence and severity of regurgitation. It is clear form this study that a more accurate assessment of the degree of obstruction is obtained by measurement of the mitral pressure half-time, which would appear to be independent of changes in the prosthetic valve flow including the presence of regurgitation.

There are potential problems associated with Doppler examination of mechanical valve prostheses. Signals of very high amplitude occur with opening and closure of a mechanical valve. These valve "clicks", seen in Fig. 22, can mask a velocity signal of lower intensity, requiring appropriate adjustment of the gain settings. This is of particular importance in examining an obstructed or "stuck" mechanical prosthesis. In this case, the velocity of flow through the valve may be very high but will be of a low intensity, and if gain settings are too high, related to the valve "clicks" if still present, then the high velocity, and more importantly, the very prolonged mitral pressure half-time may be missed. Also, since the peak mitral flow velocity will occur almost immediately following mitral valve opening the high amplitude "click" associated with valve opening can cause the impression of a falsely high peak velocity, and invalidate the measurement of mitral pressure half-time. It is usually possible to separate the true peak velocity by close examination of the spectral signal, but it is important to be aware of this problem when examining mechanical valves. One potential advantage, however is that the valve "clicks" define very accurately the timing of mitral flow, and will resolve any doubt as to the origin of the flow velocity signal, separating signal of mitral stenosis from aortic regurgitation, or aortic stenosis and mitral regurgitation, which have similar velocities and directions and can potentially cause confusion from the apical position using continuous wave Doppler where there is no depth resolution. The direction of through valve flow is also less predictable with mechanical valve replacements than with their bioprosthetic counterparts. In particular, the flow direction of a tilting disc valve will be dependent on its orientation, and as a result the praecordial position providing the highest velocity recording will be more variable. Careful searching with the Doppler transducer should be made not only at the apical position, but also more laterally towards the axilla and more medially towards, or even at the sternal edge in order to obtain the most satisfactory Doppler recording. Since all mechanical valves studied were Bjork Shiley disc valve, it is unclear whether the Doppler technique is equally applicable to other mechanical valves, in particular ball valves. Theoretically, the modified Bernoulli equation should still be valid, but the turbulence produced by flow through these valves may make Doppler ultrasound impracticable and accurate peak velocities may not be obtained.

Continuous wave Doppler can provide an accurate method of assessing the presence of mitral prosthetic regurgitation as illustrated by the fact that no false positive results were found in this study and the presence of mild regurgitation was only missed in one patient. However, there are a number of difficulties associated with Doppler examination in these patients and relates mainly to the detection of regurgitation in mechanical prostheses. In bioprosthetic valves, if regurgitation is through the valve, its presence will usually be detected fairly easily from the apical position if a satisfactory mitral diastolic flow velocity recording is obtained, since the Doppler ultrasound beam should be close to the origin of the regurgitant jet. This will not be the case where regurgitation is a result of a periprosthetic leak, as will always occur with a mechanical valve replacement. Here, the origin and direction of the velocity jet will be unpredictable and will not necessarily be detected from exactly the same position as the diastolic flow velocity. Meticulous examination from numerous praecordial positions may be required to identify a regurgitant jet and excluding its presence of a mild degree of regurgitation may be impossible. The problem is further compounded with mechanical valves, where poor ultrasound transmission through a pyrolite disc or steel ball may mask the presence of a regurgitant jet immediately behind the prosthesis. This would explain why regurgitation was not detected in normally functioning Bjork Shiley valves in this study which, by their design as with any mechanical valve, will always have a minor degree of regurgitation around the edge of the pyrolite disc. Despite these limitations, careful Doppler examination by an experienced operator using the continuous wave mode will identify the vast majority of patients with mitral prosthetic regurgitation.

It is considerably more difficult to assess the severity of mitral prosthetic regurgitation by Doppler ultrasound that to detect its presence. Since the volume of blood traversing the Doppler ultrasound beam will be reflected by the intensity of the spectral signal, then some assessment of the severity of regurgitation can be gained from the continuous wave examination. The more intense the Doppler signal then the greater the volume of regurgitation. Clearly, this is a very subjective assessment and is dependent on which portion of the regurgitant jet the Doppler ultrasound beam traverses and also on the gain settings of the spectrum analyser. However,in this study the Doppler spectral signal was of low intensity in patients with trivial regurgitation at angiography, whereas the signal intensity was unpredictable in patients with anything more than a trivial degree of regurgitation. Mapping of the extent of the regurgitant jet using pulsed Doppler ultrasound did provide a semi-quantitative assessment of the severity of regurgitation. In particular, it was able to accurately identify those patients with severe regurgitation. It is important to emphasize that any form of pulsed Doppler mapping of mitral regurgitation is an extremely laborious and time consuming technique that requires considerable experience to perform, and even then is subject to very major limitations. Again, mechanical prostheses will produce an ultrasonic hole behind the valve disc where mapping is not possible. In addition, pulsed Doppler may detect the presence of turbulent flow outwith the main velocity jet and falsely accentuate the extent of systolic flow and hence the degree of regurgitation. Alternately, failure to align the Doppler beam in the direction of the velocity jet will tend to falsely underestimate the severity of regurgitation, though the ability to switch repeatedly between pulsed and continuous wave Doppler and maintain alignment with the velocity jet may reduce some of these problems.

It may not be possible to obtain a precise quantitation of mitral prosthetic regurgitation by this method but it does seem possible to identify those patients with severe regurgitant lesions, and patients with only trivial regurgitation if a velocity jet has been identified by continuous wave examination. However, there is a large grey area in between and, as satisfactory mapping of regurgitant jets will only be possible by operators with substantial Doppler experience, and may take as long as one hour to complete, this technique will be impractical for the majority of clinical studies in patients with suspected mitral prosthetic regurgitation.

Although Doppler ultrasound has been used to assess mitral prosthetic function, this has not been demonstrated for aortic valve replacements since valve gradients are not usually obtained for aortic prostheses during cardiac catheterisation. In retrogradely crossing a mechanical disc valve the aortic regurgitation produced would make a transvalvular gradient meaningless and the risk of wedging the valve open with the catheter makes the risks of such a procedure unacceptable. Although it is possible to retrogradely cross a bioprosthesis this has not been the standard practise in our centre and trans-septal catheterisation is not generally performed. Therefore it has not been possible to obtain a comparison of valve gradients across aortic prostheses. However, having established the validity of Doppler ultrasound in measuring valve gradients across bioprosthetic valves in vitro and demonstrated its ability to accurately predict valve gradients in patients with aortic stenosis and in mitral prostheses it would seem reasonable to assume that it can successfully be applied to aortic prostheses at least of the bioprosthetic type.

Doppler ultrasound, as a non-invasive technique, has considerable potential for the haemodynamic assessement of patients with mitral valve replacement. Continuous wave Doppler can provide an accurate estimation of mitral valve gradients, and accurately assess the degree of prosthetic valve obstruction, particularly using measurement of the mitral pressure half-time. With due care and attention to the potential problems associated with mitral prostheses, continuous wave Doppler can provide important information as to the presence of mitral regurgitation, and with meticulous examination the combination of pulsed and continuous wave Doppler may allow some assessment of its severity.

CHAPTER 7

DOPPLER ASSESSMENT OF 155 PATIENTS WITH BIOPROSTHETIC VALVES: A COMPARISON OF THE WESSEX PORCINE, LOW PROFILE IONESCU SHILEY AND HANCOCK PERICARDIAL BIOPROSTHESES

INTRODUCTION

Haemodynamic Assessment of New Bioprostheses

The recent introduction of a variety of newer bioprosthetic valves has lead to considerable interest in the haemodynamic assessment of these prostheses, as it is important to be able to assess the performance of these valves in patients. Although some in vitro haemodynamic information is available,[124] this is not easily extrapolated into the clinical situation. In vivo assessment of valve prostheses has usually been obtained intraoperatively,[125,126] and only rarely at cardiac catheterisation[127] and there is currently no in vivo haemodynamic data relating to the bioprostheses in this study. Haemodynamic assessment is of considerable importance in the continuing clinical assessment of new or investigational bioprostheses, but the use of repeated invasive investigations in otherwise healthy individuals has major ethical implications. Doppler ultrasound has, therefore, considerable potential to provide a repeatable haemodynamic assessment of bioprosthetic valve function non-invasively.

Aim of Study

Three new bioprosthetic valves, Wessex Medical porcine prosthesis, low profile Ionescu Shiley pericardial prosthesis and the Hancock pericardial prosthesis were under continuing clinical assessment in our institution. Having established the validity of Doppler ultrasound to measure valve gradients across bioprosthetic valves in vitro, and the accuracy of the technique in assessing mitral prosthetic obstruction and the presence and extent of mitral regurgitation in vivo, this study was undertaken to determine the value of Doppler ultrasound in the haemodynamic assessment of patients with these new types of bioprosthetic valves. Not only would this demonstrate application of the Doppler technique to a large series of patients, but would also allow comparison of the haemodynamic profile of these bioprostheses in vivo, and assess the potential for the detection of prosthetic valve dysfunction at an early stage.

SUBJECTS AND METHODS

155 patients with 167 bioprostheses were studied, age range 33 to 76 years, mean 55.8 years. This group comprised 68 with Wessex porcine bioprostheses, (47 mitral, 21 aortic), 54 Hancock pericardial bioprostheses, (27 mitral, 27 aortic), and 45 low profile Ionescu Shiley pericardial valves (29 mitral, 16 aortic). Valve sizes ranged from 29mm to 35mm for the mitral bioprostheses and from 19mm to 27mm for aortic bioprostheses.

Echocardiography

Prior to Doppler ultrasound examination all patients underwent two-dimensional echocardiography to assess any evidence of structural abnormality to suggest prosthetic valve dysfunction. Measurements were made of left ventricular, right ventricular and left atrial dimensions, and left ventricular wall thickness. A visual assessment of prosthetic valve function was made on the basis of leaflet separation and apposition and on the structure and motion of the valve ring.

Doppler Assessment

As in chapter 6, Doppler examination was performed in both the continuous and pulsed wave modes with the patient in the resting state immediately following echocardiographic examination.

Mitral bioprostheses were examined from the apical position, as in the previous chapter, and measurements made of the mean mitral gradient and the mitral pressure half-time from the continuous wave recording as shown in Fig. 28 in a patient with a normally functioning Wessex porcine mitral valve replacement. Here, the maximum mitral frequency shift is 4,000 Hz, equivalent to a velocity of 1.56 m/s. The mitral pressure half-time is the time taken from this peak velocity, for the velocity recording to reach the peak velocity divided by 1.4. In this example, it is the time taken to reach a velocity of 1.1 m/s which was 60 msec, indicating, as expected, no evidence of mitral prosthetic obstruction. The presence of mitral regurgitation was determined from the continuous wave Doppler recording and where present graded on the basis of combined continuous and pulsed wave Doppler as described in the previous chapter (see Figs. 24 & 25).

Aortic prosthetic flow (Fig. 29) was measured in the continuous wave mode from a variety of praecordial positions, as in patients with aortic stenosis, the suprasternal notch, apex, subcostal, supraclavicular, and right parasternal positions. Measurement was made of the peak instantaneous aortic gradient from the maximum systolic velocity using the modified Bernoulli equation. The presence of aortic regurgitation, as illustrated in Fig. 30, was determined by continuous wave Doppler examination from the apical and subcostal positions, and identified by a high velocity jet towards the transducer throughout the diastolic time period.

Tricuspid regurgitation (Fig. 31) was assessed from either the apical or left parasternal positions using continuous wave Doppler, identified as a high velocity jet away from the transducer when this is directed towards the tricuspid valve and right atrium. The signal is similar in timing to that of mitral regurgitation, being pansystolic, but the peak velocity is less, reflecting the lower pressures on the right

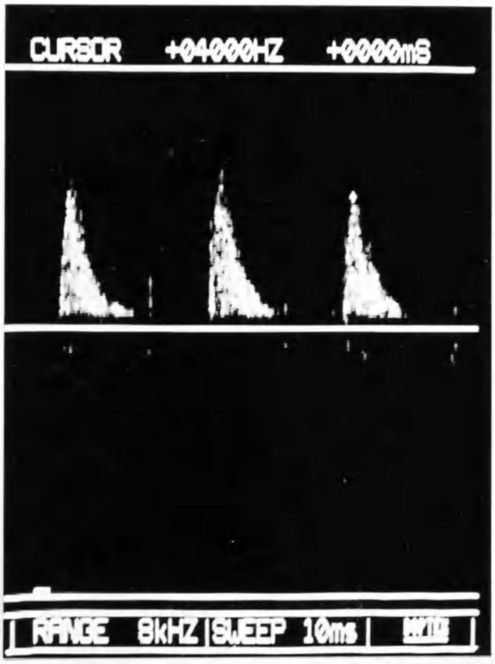


Figure 28: Spectral display of normal mitral flow across Wessex porcine bioprosthesis.

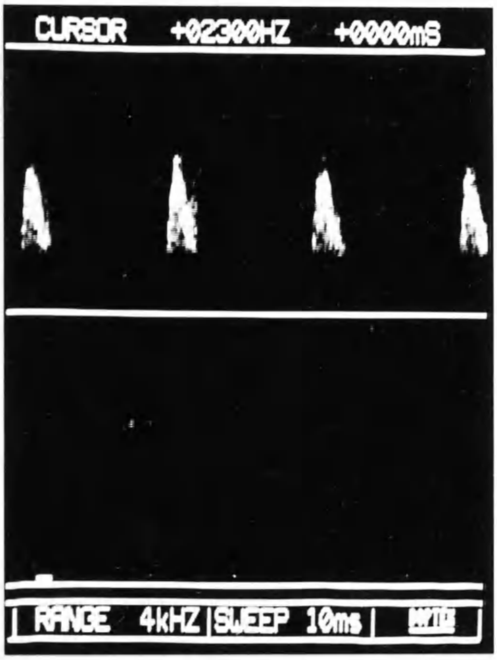


Figure 29: Spectral display of normal aortic flow across an Ionescu Shiley bioprosthesis.

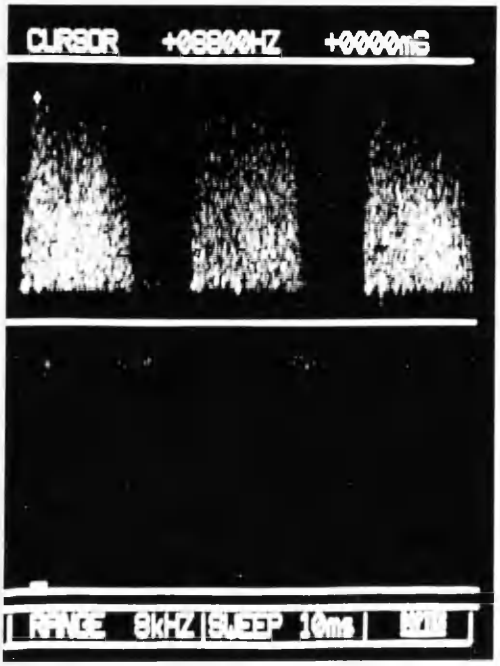


Figure 30: Spectral display of aortic regurgitation in a leaking aortic bioprosthesis indicated by high velocity pandiastolic flow from apical position.

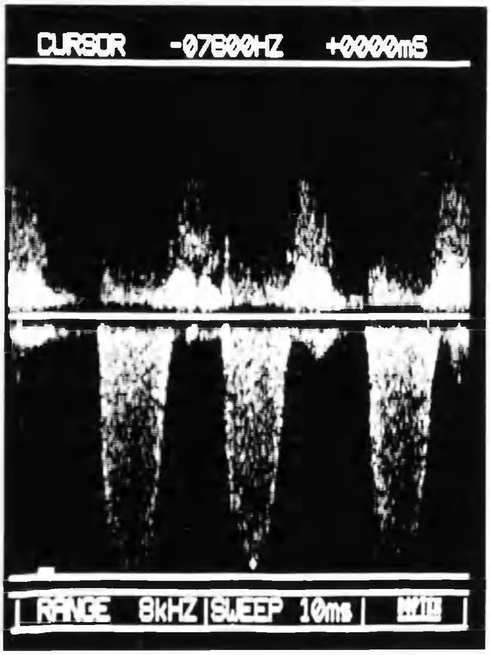


Figure 31: Spectral display of tricuspid regurgitation from left parasternal position in a patient with a mitral bioprosthesis.

side of the heart. Where present, tricuspid regurgitation can be used to estimate right ventricular and pulmonary artery systolic pressure. This is possible since the peak velocity is a reflection of the gradient across the tricuspid valve during systole, the difference between the right ventricular and right atrial systolic pressures. The right atrial pressure can be estimated clinically from the jugular venous pulse, and will be negligable in the absence of significant tricuspid regurgitation or right heart failure. The right ventricular systolic pressure can then be calculated from the pressure gradient across the tricuspid valve using the modified Bernoulli equation, with the addition of the estimated right atrial systolic pressure. For example, therefore, the maximum systolic frequency shift across the tricuspid valve in Fig. 31 is 7,800 Hz, or 3.0 m/s. Using the modified Bernoulli equation, the peak systolic gradient will be 36 mmHg. If the jugular venous pulse is not visible clinically, then the right ventricular systolic pressure will be between 36 and 40 mmHg. In addition, providing there is no right ventricular outflow obstruction, which can also be assessed by Doppler ultrasound, the estimated right ventricular systolic pressure will be equivalent to the pulmonary artery systolic pressure.[128]

Statistical Analysis

Significance values in this study were determined using an unpaired t-test.

RESULTS

Satisfactory two-dimensional echocardiograms were obtained in 133 patients (86%) but failed to reveal any structural abnormality to suggest prosthetic valve dysfunction.

Doppler examination provided satisfactory recordings in all 103 mitral prostheses and in 59 of the 64 (92%) aortic prostheses studied.

There was no significant difference in resting heart rate between the 3 groups of patients (Wessex porcine 84 $\pm$ 7 bpm, Hancock pericardial 78 $\pm$ 5 bpm, low profile Ionescu Shiley 82 $\pm$ 9 bpm).

Mitral Bioprosthetic Gradients

A comparison of the mean mitral valve gradients measured by Doppler ultrasound across the different types of valve prostheses is shown in Fig. 32. The presence of significant mitral regurgitation will cause an increase in the mitral diastolic flow velocity and therefore an increase in the measured valve gradient. Although this would produce an increased gradient even at catheterisation, in order to obtain a direct comparison between the three types of valve prostheses

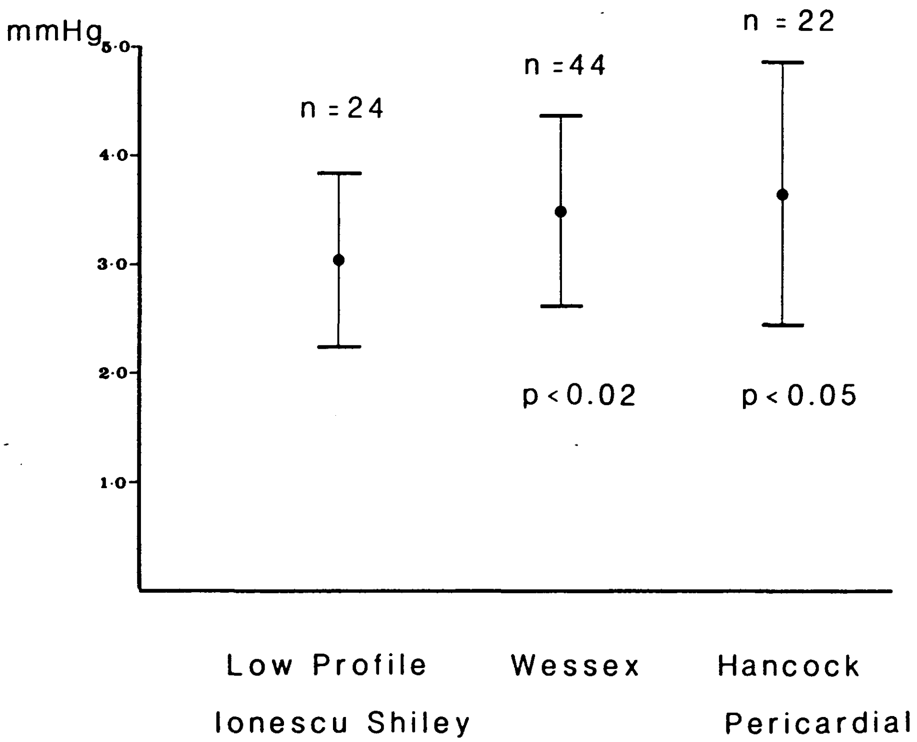


Figure 32: Comparison of mean mitral valve gradients measured by Doppler ultrasound across the three groups of mitral bioprosthetic valves. Results displayed as mean values $\pm$ standard deviation.

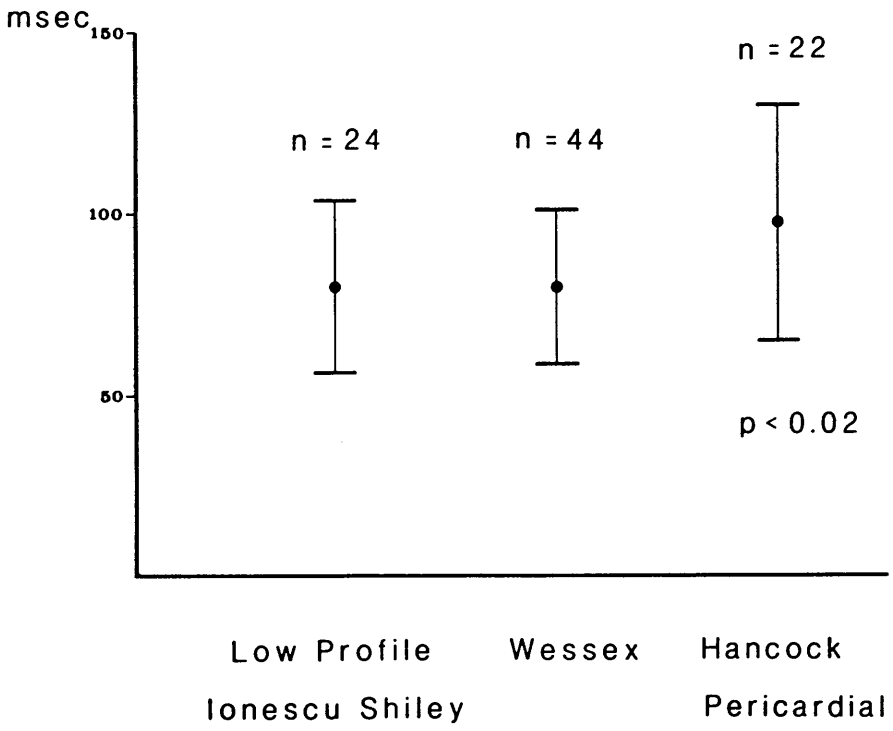


Figure 33: Comparison of the mitral pressure half-times across the three groups of mitral bioprosthetic valves. Results displayed as mean values ± standard deviation.

the mean mitral gradient was not included for those valves demonstrating mitral regurgitation on the Doppler examination. There was a narrow range of valve gradients for each type of bioprosthesis despite the variation in valve size, though significantly lower gradients were found with the Ionescu Shiley low profile valve as compared to either the Wessex porcine bioprosthesis ($p<0.02$) or the Hancock pericardial valve ($p<0.05$).

Mitral Pressure Half-Time

Mitral pressure half-time (Fig. 33) was however significantly longer with the Hancock pericardial bioprosthesis as compared to either the Wessex porcine bioprosthesis ($p<0.02$) or the low profile Ionescu Shiley valve ($p<0.05$) with no significant difference in pressure half-time noted between the Wessex porcine and low profile Ionescu Shiley valves.

Aortic Bioprosthetic Gradients

There was no significant difference in the peak aortic gradients across the three types of bioprostheses, as illustrated in Fig. 34.

Effect of Bioprosthetic Valve Size

A comparison of the varying sizes of all mitral

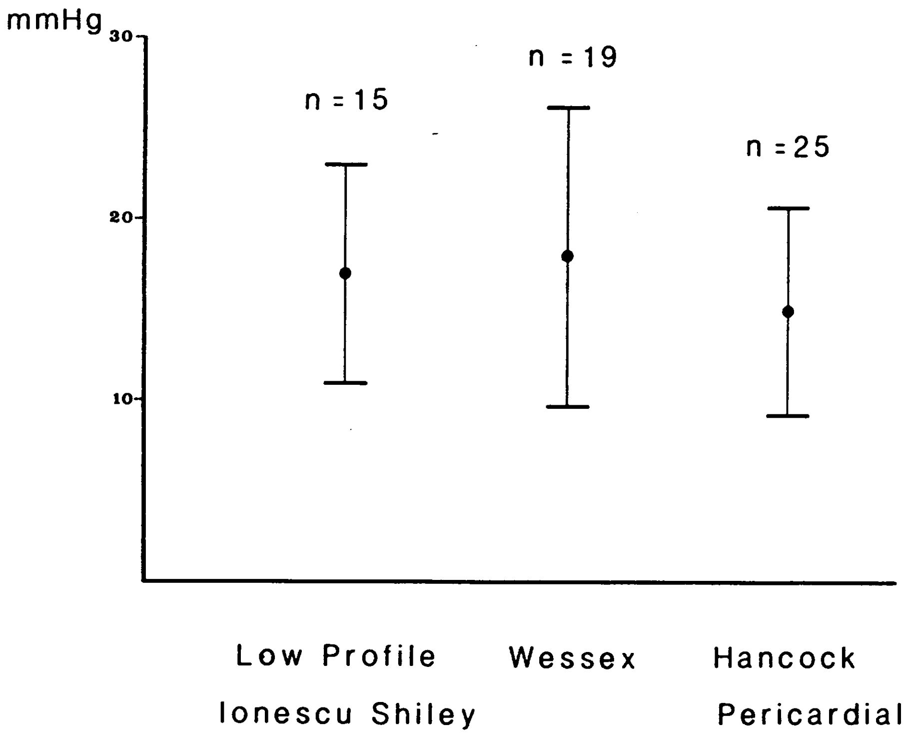


Figure 34: Comparison of peak aortic valve gradients measured by Doppler ultrasound across the three groups of aortic bioprosthetic valves. Results displayed as mean values ± standard deviation.

prostheses is shown in Table 5. Only 2 patients had a 35mm mitral bioprosthesis, Wessex porcine valves in both, and these were therefore excluded from the comparison of valve sizes. The 29mm mitral bioprosthesis had a significantly longer pressure half-time when compared with either the 31mm or 33mm sizes. However there was no difference in either the peak mitral flow velocity or mean mitral valve gradient between the 3 valve sizes. The results of comparing the 3 different bioprostheses of similar sizes is shown in Table 6. There was a significantly higher peak mitral flow velocity demonstrated with the 29mm Wessex porcine valve when compared with the other 2 bioprostheses, though this was not found with the 31mm valves. For a similar size of aortic bioprosthesis (23mm) a significantly higher gradient was demonstrated across the Wessex porcine valve compared to the pericardial bioprostheses (Table 7).

Bioprosthetic Regurgitation

Mitral regurgitation was detected in 13 of 103 (12.6%) mitral bioprostheses, (3 of 47 Wessex porcine, 5 of 29 low profile Ionescu Shiley and 5 of 27 Hancock pericardial) having been suspected clinically in 12 of the 13 patients. The severity of mitral regurgitation as graded by the extent of left atrial systolic flow is shown in Table 8. Three patients were graded as having severe mitral regurgitation, all subsequently required reoperation. Additional evidence of significant bioprosthetic

TABLE 5

VALVE SIZE	29mm	31mm	33mm
No.	n=36	n=40	n=13
Peak Mitral Flow ($cmsec^{-1}$)	145.7 ± 22.7	141.1 ± 23.4	146.5 ± 26.2
Mean Mitral Gradient (mmHg)	3.52 ± 1.07	3.22 ± 0.82	3.51 ± 1.38
Mitral Pressure Half-time (msec)	90.6 ± 32	80.0 ± 20*	74.6 ± 19**

*$p<0.05$ **$p<0.02$

Comparison of valve sizes for all mitral bioprostheses with mean and standard deviation shown. The 2 patients with 35mm bioprostheses are not included in analysis.

TABLE 6

VALVE	29mm			31mm		
	Wessex	Hancock Pericardial	Low Profile Ionescu Shiley	Wessex	Hancock Pericardial	Low Profile Ionescu Shiley
No.	n=9	n=14	n=13	n=22	n=8	n=10
Peak Mitral Flow Velocity ($cmsec^{-1}$)	166.4 ± 17.1	141.7 ± 14.4***	135.7 ± 25.3***	141.1 ± 24.9	151.0 ± 26.9	133.2 ± 14.2
Mean Mitral Gradient (mmHg)	3.69 ± 0.61	3.61 ± 1.39	3.31 ± 0.96	3.31 ± 0.83	3.57 ± 1.02	2.74 ± 0.37**
Mitral Pressure Half-time (msec)	83.3 ± 19.4	105 ± 36.3*	80 ± 30.3	80 ± 21.4	81.2 ± 23.0	79 ± 15.2

*$p < 0.05$ **$p < 0.01$ ***$p < 0.005$

Comparison of different mitral bioprostheses of same size with mean values and standard deviation shown.

TABLE 7

	23mm		
VALVE	Wessex	Hancock Pericardial	Low Profile Ionescu Shiley
No.	n=8	n=13	n=7
Peak Aortic Gradient (mmHg)	21.4±9.8*	15.1±5.6	15.6±4.4

*$p<0.05$

Comparison of valve gradients across different aortic bioprostheses of similar size with mean value ± standard deviation shown.

regurgitation was obtained in the 2 patients with a low profile Ionescu Shiley bioprosthesis who, in the presence of a normal pressure half-time, had peak mitral diastolic flow velocities of 240 and 232 $cmsec^{-1}$, well outwith the range for the competent prostheses (Table 9). The peak mitral velocity in the remaining patient with severe mitral regurgitation, an Hancock pericardial bioprosthesis, and the peak mitral velocities associated with either mild or moderate regurgitation all fell within the range of the competent valve prostheses.

Aortic regurgitation was detected in 11 of 59 (18.6%) bioprostheses, (5 of 19 Wessex porcine, 3 of 15 low profile Ionescu Shiley and 3 of 25 Hancock pericardial) though this was not suspected clinically in 5 of the 11 patients.

Tricuspid regurgitation was detected by Doppler ultrasound in 30 of the 103 (29%) of the mitral bioprostheses but was not found in any patient with single aortic valve replacement. Although the presence of tricuspid regurgitation was identified in 30 patients a clearly demarcated spectral signal from which the peak velocity could be measured was obtained in only 24 of the 30 patients. The estimated pulmonary systolic pressure ranged from 15-33mmHg, mean 21.9mmHg in the 21 patients with a competent bioprosthesis, and was 22mmHg, 33mmHg and 57mmHg in the remaining 3 patients with mitral regurgitation.

TABLE 8

	MILD	MODERATE	SEVERE
Wessex (n=3)	3	-	-
Low Profile Ionescu Shiley (n=5)	3	-	2
Hancock Pericardial (n=5)	1	3	1

Severity of mitral regurgitation in patients with a mitral bioprosthesis graded by extent of left atrial systolic flow.

TABLE 9

	RANGE	MEAN
Wessex (n=44)	0.92 - 2.00	1.49
Low Profile Ionescu Shiley (n=24)	0.88 - 1.80	1.34
Hancock Pericardial (n=22)	1.16 - 2.04	1.43

Peak mitral diastolic flow velocities in $msec^{-1}$ for the competent bioprostheses.

DISCUSSION

Doppler ultrasound has major potential as a non-invasive method of assessing bioprosthetic valve function. Although in vitro studies can provide data regarding the haemodynamic profile of various bioprostheses it is difficult to extrapolate these results to the clinical situation.

It was demonstrated in chapter 5 that the newer pericardial bioprostheses present less obstruction to flow than the porcine bioprostheses in vitro and this has also been shown intraoperatively[126] though it is not certain whether this is of any clinical relevance.

The range of mean valve gradients for bioprostheses in the mitral position was relatively narrow, with acceptably low gradients obtained in all competent prostheses. The lower valve gradients observed with the low profile Ionescu Shiley pericardial valve compared to the Wessex porcine bioprosthesis may have been expected from the results in the pulsatile flow model, though it may not have been expected that they would be significantly lower than the Hancock pericardial valve. Similarly the longer mitral pressure half-time observed with the Hancock pericardial prosthesis would suggest that the obstructive characteristics of this valve in vivo differ from those previously established in vitro.

When comparing the three types of bioprostheses of similar size it is interesting to note that the mean mitral valve gradient was significantly lower for the low profile Ionescu Shiley valve only at the larger 31mm size and not at the 29mm size. However the prolonged pressure half-time noted with the Hancock pericardial valve occurred only at the 29mm and not at the 31mm size. Since the pressure half-time relates more to the initial phase of diastole and the mean mitral gradient to the whole diastolic time period the difference in pressure half-time noted with the Hancock pericardial valve could be explained by an increased restriction to flow during the first part of diastole possibly as a result of less rapid leaflet opening and which may only be of revelance at the smaller valve size. Similarly the low profile Ionescu Shiley pericardial valve may have less obstructive characteristics throughout diastole with a significantly lower mean valve gradient seen with the 31mm valve compared to a similar size of Wessex or Hancock valve, and a lower mean gradient, though non significantly, with the 29mm size. These differences in mean valve gradient and mitral pressure half-time, unexpected from in vitro studies, serve to indicate the complex pressure/flow relationship that exists in vivo across the mitral valve during diastole.

The slight reduction in the mitral pressure half-time noted with the larger bioprostheses when all valves of a similar size were compared indicates a tendency to increased obstruction with smaller bioprostheses, although, since no difference was observed in the mean mitral valve gradients this may only be true, at rest, in the early diastolic period when greater valve flow is encountered.

Although no difference was observed between the 3 types of aortic bioprostheses when all the patients were compared, the Wessex porcine valve did produced significantly higher peak aortic gradients when compared to different valve types of a similar size.

The ability of Doppler ultrasound to identify the presence of bioprosthetic valvular regurgitation has major potential in the assessment of prosthetic valve dysfunction. In this study not only were 3 patients with severe mitral regurgitation, who subsequently required reoperation identified, but mitral bioprosthetic regurgitation was detected in 10 further patients who were symptomatically well. Although there are major difficulties in using pulsed Doppler to quantitate mitral regurgitation from the extent of left atrial systolic flow, it can be possible to identify those with severe regurgitation, particularly where increased mitral diastolic flow velocity is present in addition. Valvular regurgitation in patients with bioprostheses can result from the development of leaflet tears and Doppler ultrasound may identify those at risk patients at an early stage. Using a "stand alone" Doppler system it is not possible to distinguish between a periprosthetic and through valve leak. The use of Doppler ultrasound in combination with simultaneous two dimensional echocardiographic imaging or more particularly the use of real time colour coded Doppler,[129] which allows flow velocity information to be displayed in two dimensions superimposed on structural detail provided by standard two-dimensional echocardiography, will undoubtedly prove superior in this respect.

Whether the patients demonstrated to have less significant mitral regurgitation on Doppler examination will subsequently develop major leaflet tears will only be resolved through careful patient follow-up and findings at reoperation, but Doppler ultrasound may identify this group as at greater risk and who should be followed up more carefully or considered for invasive haemodynamic assessment.

The presence of aortic regurgitation was identified in 11 aortic bioprostheses one of which required replacement as a result of leaflet tear. It was not possible to quantify the severity of aortic regurgitation using "stand alone" Doppler ultrasound, although identification of its presence is important in patients with aortic valve replacements, and in conjunction with clinical and other non-invasive assessment, there is the potential to predict the development of significant aortic prosthetic dysfunction at an early stage.

The estimation of right ventricular and therefore pulmonary artery systolic pressure in patients in whom tricuspid regurgitation is detected by Doppler ultrasound, is a very useful adjunct to the assessment of bioprosthetic valve function. It is becoming increasingly recognized that tricuspid regurgitation is a common finding using Doppler ultrasound, particularly where there is right ventricular dilatation, as for example associated with previous mitral valve disease in patients with a mitral valve replacement, and that the rate of detection is related to how carefully one searches for the tricuspid regurgitant jet. In this study, all patients with a competent mitral bioprosthesis in whom tricuspid regurgitation was detected, the calculated pulmonary systolic pressure at rest was satisfactory, but was significantly elevated in one patient with severe mitral regurgitation.

This study has demonstrated the successful application of Doppler ultrasound techniques to a large series of patients with bioprosthetic valve replacements. Doppler ultrasound would appear to be uniformly successful in providing satisfactory recordings of through valve flow from mitral bioprostheses and the vast majority of aortic bioprostheses. It has allowed a comparison of the haemodynamic profile of different bioprosthetic valves in vivo in a manner which is both non-invasive and easily reproducible. As a result, Doppler ultrasound is likely to have a major impact on the continuing assessment of the newer types of bioprostheses, and their performance in clinical practice. In addition, the ability to identify the presence of bioprosthetic regurgitation in these patients and to provide a semi-quantitative assessment of its severity in patients with mitral bioprostheses confers, a potential for the early detection of developing bioprosthetic dysfunction.

The implications of using Doppler ultrasound to assess prosthetic valve function on a routine basis, outwith the investigation of new prostheses, are far reaching. A major cardiac centre, for instance, may have as many as 1,000 patients with valve replacements. Routine assessment of these patients every 6 months or even every year, which would probably be required to identify developing prosthetic dysfunction, would place a considerable workload on the ultrasound service and may not be cost effective. The role of Doppler ultrasound in patients with prosthetic valves is more likely to be in assessing prosthetic valve function post-operatively as a baseline investigation, with repeated examinations being performed only where there is a clinical indication.

CHAPTER 8

A METHODOLOGICAL ASSESSMENT OF CARDIAC OUTPUT BY DOPPLER ECHOCARDIOGRAPHY

INTRODUCTION

The assessment of cardiac output plays an important role in the clinical management of critically ill patients, particularly after acute myocardial infarction.[130,131] As a result, the measurement of cardiac output by thermodilution[132] has become an establish procedure. This is not entirely free from risk however[133,134] and because of possible complications can only be utilized for a few days at a time. A repeatable non-invasive method of accurately assessing cardiac output would have considerable value, not only in critically ill patients who require careful haemodynamic monitoring, but also in the assessment of cardiac output in relatively healthy patients or in volunteer studies where the small risk associated with right heart catheterisation may prove unacceptable. Doppler ultrasound has the potiential to provide a volumetric assessment of blood flow by combining the Doppler velocity measurement with the vessel cross-sectional area, measured by echocardiography. Theoretically therefore, it should be possible to measure absolute cardiac output by this technique.

Theory of Volumetric Flow Analysis

The theoretical basis for calculating volumetric flow by Doppler echocardiography is to multiply flow velocity in cm/sec with measurement of the area in cm^2 across which this flow velocity occurs, the cross-sectional area. This provides an estimate of volumetric flow in ml/sec which when multiplied by 60 and divided by 1000 provides cardiac output in l/min. The velocity used to assess cardiac output should not be the peak velocity or the systolic velocity, but the average velocity occurring over the caridac cycle, the so-called time averaged velocity. Since there will be a spectrum of velocities throughout the cardiac cycle, both the maximum and mean instantaneous velocities can potentially be averaged, and the appropriate measurement, either the time averaged mean or time averaged maximum velocity, will depend, as we shall see, on the velocity profile of flow within the vessel studied. Although this formula appears simple there are many potential problems associated with such analysis.

In order to make an accurate assessment of the flow velocity it is necessary to know the average velocity across the whole of the orifice area, the so-called space averaged velocity. This could be obtained if the width of the Doppler sample beam encompassed the whole of the orifice area where all the velocities across the vessel area could then be identified.
In attempting to measure the flow through a relatively large orifice, such as the mitral valve or the aorta, this would not be possible clinically because of the restrictive size of such a transducer. The Doppler beam from the small transducer used in this thesis, though allowing satisfactory access and

transducer manipulation, will identify velocities only from a small region within the area of flow.

If the velocity profile across the flow area is flat, that is the blood is moving at the same velocity across the whole of the orifice area, then the velocities identified in the region of the Doppler beam should be representative of the space averaged velocity and, if the flow area of the vessel is known, provide an accurate estimate of volumetric flow and hence absolute cardiac output.

However, if the velocity profile is not flat, but parabolic, then sampling from a region near the centre of the vessel, where the velocities would be higher than near the vessel wall, would tend to overestimate the space averaged velocity. Similarly, if the velocity profile is skewed, then higher velocities will be present at one side of the vessel compared to the other, and if the Doppler sample beam is directed at the higher velocities, overestimation of the space averaged velocity, and hence the cardiac output, will occur.

Although accurate estimation of the space averaged velocity is important in the assessment of cardiac output by Doppler ultrasound, measurement of the cross-sectional area is critical, particularly if this is derived from a radius on diameter measurement of the blood vessel. Any slight error in measurement by echoccardiography will be accentuated when the radius is squared in the calculation of cross-sectional area. Problems encountered with resolution of echocardiographic images, and whether leading edge-to-leading edge or trailing edge-to-leading edge echos should be used, may make considerable difference to the calculation of cardiac output by this technique. In addition since neither vessel nor orifice areas within the heart or great vessels are constant throughout the cardiac cycle, temporal changes in these values will compound the difficulties in accurate measurement of cross-sectional area.

Assessment of Cardiac Function - Velocity Measurement Alone

Since measurement of the orifice or vessel area across through which flow is occurring, is subject to substantial potential error, there has been much interest in the assessment of cardiac function by Doppler ultrasound measurement of flow velocity alone. Although this will be unable to provide an estimate of absolute flow, since the flow area is unknown, it will eliminate a major source of error, and allow comparison of the relative changes in cardiac output within an individual.

The continuous wave Doppler instrumentation used for transcutaneous aortovelography,[16-18] where flow velocity is sampled across the aortic arch, has been used to demonstrate that the area under the systolic velocity curve is proportional to stroke volume. However, major discrepancies become apparent when an attempt is made to calculated absolute flow by combination of this with invasively determined aortic diameter.[69] More recently it has been suggested that the use of transcutaneous aortovelography to calculate stroke distance, the area under the systolic velocity curve, and minute distance, stroke distance multiplied by heart rate, is a valid method of assessing cardiac output without determining the aortic size[70] though this has been treated with some scepticism,[73] and it is generally accepted at present that measurement of orifice or vessel area is required in order to assess volumetric flow. The use of transcutaneous aortovelography may however be a valid method of accurately assessing changes in cardiac output within an individual but again established evidence for this is lacking. In addition since continuous wave Doppler has no depth resolution capabilities and the velocity profile in the aortic arch is complex[135,136] and potentially altered by change in cardiac output, it is not possible to guarantee that the highest measured velocity will emerge from the same position within the aortic arch when measured on separate occasions.

For these reasons there have also been reports of assessing cardiac function by the use of pulsed wave Doppler ultrasound alone. Avoiding problems relating to the velocity profile within the aortic arch these studies have measured flow velocity within the ascending aorta and have demonstrated the accuracy of the technique in assessing relative changes in stroke volume in vitro[72] and in vivo.[71] In addition it has been shown that measurement of peak aortic velocity and the aortic flow velocity integral by pulsed wave Doppler in the ascending aorta can discriminate between patients with dilated cardiomyopathy and those with normal cardiac function.[137] Although able to clearly separate groups of patients at these extremes of cardiac function, it is likely to be of less value in comparing patients with lesser degrees of cardiac dysfunction. The majority of interest has therefore been concentrated on attempting to assess absolute cardiac output by Doppler echocardiography.

Assessment of Cardiac Function - Measurement of Cardiac Output

Despite the problems discussed above a number of reports have demonstrated that cardiac output can indeed be measured accurately by Doppler echocardiography, and the majority of reports have utilized the measurement of aortic flow velocity in combination with vessel diameter.[62-65,138-140] However, although these studies have shown good correlation between Doppler echocardiography and invasive estimation of cardiac output, with correlation coefficients ranging from 0.78 to 0.96, there is considerable variation in the methodology used. In some reports the pulsed wave mode was used to measure aortic velocity,[62,64,138] but in only one of these studies was full power spectral analysis of the Doppler signal used[62] whereas the other studies used analogue estimated velocity recordings. In addition there were differences in the positioning of the Doppler transducer, one study using the parasternal[138] rather than suprasternal approach, and methods of measuring aortic root dimension also varied. In those studies in which Doppler was performed in the continuous wave mode[63,65,139] differences in methodology were again apparent. Although similar methodology with respect to velocity measurement was used, only one employed spectral analysis of the Doppler signal[63] and another study used M-mode estimation of the aortic diameter[139] as opposed to A-mode used in the other two. Other studies have not only investigated aortic or left sided output but have combined this with an assessment of right sided cardiac output obtained from pulmonary artery flow velocity and vessel diameter. These studies have used this to estimate the pulmonary to systemic flow ratio for the assessment of shunt size in infants and children.[62,79,81-83]

All of these studies have used duplex Doppler systems with pulsed mode recordings of aortic and pulmonary velocities. They have all used spectral analysis of the Doppler signal and two-dimensional echocardiography, with one exception,[82] to measure aortic vessel and pulmonary artery diameter.

The accuracy of estimating left sided cardiac output from the aortic flow velocity and aortic diameter would appear to be reasonably well established for duplex Doppler systems but considerable doubt remains as to the most appropriate methodology to apply to the stand alone Doppler systems.

Ihlen et al[140] have however cast some light on this subject. This study reported the use of an Alfred Doppler velocimeter, similar to used in this thesis, to estimate cardiac output. An analogue recording of maximum velocity was obtained from the suprasternal notch using either the continuous wave mode or the pulsed mode at two different positions within the ascending aorta. Aortic diameter was measured using two-dimensional echocardiography at four different positions from the parasternal long axis image and used to calculate the vessel area. The results of cardiac output estimation obtained by Doppler examination were compared with both thermodilution and dye dilution estimates. Overestimation of cardiac output occurred when the aortic root was measured from the two-dimensional image or when the continuous wave mode was employed. The most satisfactory results were obtained when cardiac output was estimated using the pulsed wave mode and two-dimensional estimation of the aortic orifice diameter.

It was suggested that the overestimation of cardiac output by the non-invasive method was a result of the "plug" formed flow out of the left ventricle, resulting in flow in the aorta of equivalent diameter to that at the aortic orifice. Although it has been shown experimentally that the velocity profile within the aorta is fairly flat[135] there is an alternative reason why overestimation of cardiac output may have occurred non-invasively. If the velocity profile in man is more parabolic the use of the maximum velocity integral would significantly overestimate the space averaged velocity and therefore cardiac output. In this case integration of the mean velocity, or time averaged mean velocity, may prove a more accurate estimate of cardiac output in combination with aortic root diameter measurement. In this study spectral analysis was not used in addition to the analogue recording of maximum velocity. This may be the reason why the continuous wave mode was less accurate than reported by other workers.[63] It may be suspected that with a stand alone Doppler system, difficulties would arise in positioning the pulsed sample gate. However variation in the position of sampling in this study did not significatly affect the measurement of cardiac output, confirming what had been suspected from animal experimentation.[141]

Although a possible methodology for cardiac output estimation using a stand alone Doppler system has been suggested, as discussed above, it is clearly important to assess, within an individual laboratory, the appropriate method of estimating vessel area, the relative merits of continuous and pulsed wave Doppler, and the use of the time averaged maximum or mean velocity recordings, in an attempt to determine if it is possible to assess cardiac output non-invasively, and which methodology provides the most accurate results, for a particular Doppler system.

METHODS

Patients

20 patients undergoing cardiac catheterisation were studied. All had either coronary artery disease or isolated mitral valve disease, patients being excluded if they had aortic valve disease or cardiac shunting which would invalidate the methodology. Doppler examination and invasive measurement of cardiac output were performed at the same time in all patients.

Doppler Cardiac Output Assessment

Echocardiography was performed in all cases prior to the Doppler examination in order to make an assessment of the aortic cross-sectional area. Seven separate measurements of the aortic dimensions were made in each patient. Measurements were taken from leading echo edge to leading echo edge from the end systolic echocardiogrphic image and the following measurements made in each patient:-

M-Mode at level of valve cusps (cm)

Aortic root dimension

Aortic cusp separation

2-D parasternal long axis (cm)

Aortic cusp separation

Aortic root at base of valve

Aortic root at tip of valve cusps

Aortic root 2cm above valve cusps

2-D parasternal short axis (cm^2)

Aortic root area at level of valve

In all but the last, the aorta was assumed to be circular at the level of measurement, and the cross-sectional area estimated from the diameter measurement:-

$$CSA\ (cm^2) = \pi D/2$$

where D is the aortic diameter in cm.

Doppler examination was performed with the transducer in the suprasternal notch. Measurements were made with both continuous and pulsed wave modes using both spectral analysis and analogue signal recordings. When spectral analysis was used the pulsed wave examination was guided by the optimal signal initially obtained from the continuous wave mode and recordings made above the aortic valve, 0.5cm apart, where satisfactory pulsed wave signals could be recorded. A variable number of pulsed recordings were therefore obtained from individual patients when spectral analysis of the Doppler signal was employed. Spectral signals were analysed by obtaining the time averaged mean velocity and two separate time averaged maximum velocities (7/8th maximum and 15/16th maximum) over the cardiac cycle using a dedicated frequency follower (Fig. 35). The time averaged frequency obtained from the spectral display was converted into a time averaged velocity in cm/sec. In addition the analogue signal of mean and maximum velocities (Fig. 36), and an estimated time averaged velocity directly from the velocimeter, were recorded on a standard strip chart recorded. The mean and maximum analogue signals using both continuous and pulsed wave modes were time averaged over the cardiac cycle by digitization. All measurements were made over 5 consecutive cardiac cycles in all cases and the averaged value taken for subsequent analysis.

The time averaged aortic blood flow velocity in cm/sec was then multiplied by the measured aortic area in cm^2 to obtain volumetric flow in ml/sec. Cardiac output in l/min was then obtained by the multiplcation by 60 and division by 1000.

For example, therefore, in Figure 35 the time averaged frequency shift is 500 Hz, equivalent to a velocity of 0.195 m/s or 19.5 cm/s. If the aortic cross-sectional area measured by

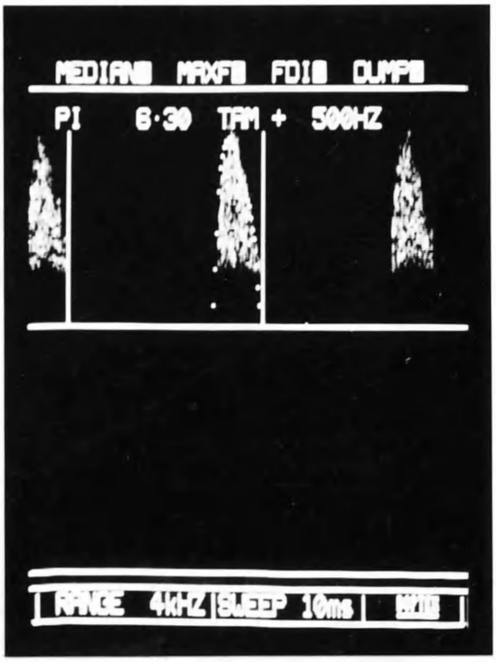


Figure 35: Continuous wave Doppler spectral display of aortic flow velocity. A frequency follower, identified by dotted line, is applied over a cardiac cycle and provides a measurement of the average frequency shift (TAM) over this time period. The time averaged frequency of 500 Hz relates, in this case using a 2 MHz transducer, to a velocity of 19.5 cmsec^{-1} which can then be used, in combibnation with aortic area, to calculate cardiac output.

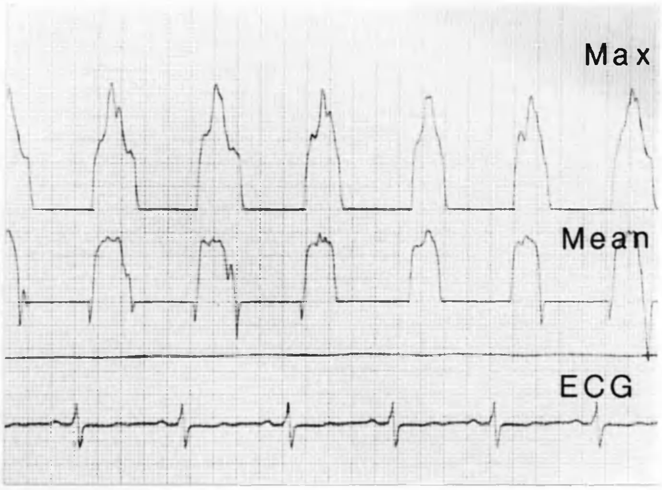


Figure 36 : Analogue display of maximum and mean aortic flow velocities recorded directly from the Doppler velocimeter.

direct planimetry from the two-dimensional echo image is 5.0 cm^2 then cardiac output will be:-

$$19.5 \times 5.0 \times \frac{60}{1000}$$

$$= 5.85 \text{ l/min}$$

Invasive Cardiac Output Assessment

A Swan Ganz catheter was inserted via the femoral vein and manipulated into the right pulmonary artery. Cardiac output was then obtained by thermodilution using an IL 720 cardiac output computer. All measurements were made in triplicate and a mean value taken.

RESULTS

Satisfactory Doppler signals were obtained in all patients and satisfactory echocardiograms in 19 of the 20 patients. In total 36 separate thermodilution cardiac outputs were measured. It was not always possible to apply all 84 methodologies to all patients, though 2,030 Doppler echocardiographic estimates of cardiac output were obtained for comparison with the results of thermodilution.

The comparative results of thermodilution cardiac output with the various methodologies of Doppler derived output are shown in Tables 10 to 21. An accurate estimate of cardiac output was obtained only when the aortic area was measured directly from the two-dimensional image or derived from the aortic diameter measured above the level of the aortic valve. A more accurate estimation of cardiac output was obtained when the time averaged mean velocity rather than the time averaged maximum velocity was used. For example, with spectral analysis of the continuous wave recording in combination with 2-D aortic area, a correlation of 0.82 with a regression line close to unity was obtained using the time averaged mean velocity in comparison to a correlation of 0.74 with a less satisfactory regression line when either of the time averaged maximum recordings were used. When continuous wave Doppler was used to measure the time averaged mean velocity an improved correlation was obtained (0.82) in comparison to the use of pulsed wave Doppler (0.78) though a superior regression line was obtained using pulsed Doppler. Although reasonable correlation could be obtained by the analogue signal recording using either pulsed or continuous wave Doppler the regression line was superior, and therefore a more accurate estimate of cardiac output obtained, when spectral analysis was employed.

Where satisfactory correlation was obtained using pulsed wave Doppler and spectral analysis, a further comparison was made using only the pulsed Doppler signal of highest velocity to estimate cardiac output (Table 22), rather than all

TABLE 10

CARDIAC OUTPUT METHODOLOGY

CONTINUOUS WAVE DOPPLER - SPECTRAL ANALYSIS - MAXIMUM VELOCITY (7/8th Maximum Frequency Follower) n=14

Aortic Dimension Method	Thermodilution Output Mean $\pm$ SD (l/min)	Doppler Output Mean $\pm$ SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	3.8 $\pm$ 0.91	6.96 $\pm$ 2.06	0.27	-
M-Mode Cusp Separation	3.8 $\pm$ 0.91	4.22 $\pm$ 1.72	0.14	-
2-D Aortic Root at Base	3.8 $\pm$ 0.91	5.60 $\pm$ 2.49	0.26	-
2-D Aortic Root at Valve	3.8 $\pm$ 0.91	6.31 $\pm$ 2.48	-0.36	-
2-D Aortic Root above Valve	3.8 $\pm$ 0.91	5.49 $\pm$ 1.13	0.64	Y = 2.49+0.79X
2-D Cusp Separation	3.8 $\pm$ 0.91	3.85 $\pm$ 1.33	0.20	-
2-D Aortic Area	3.8 $\pm$ 0.91	5.83 $\pm$ 1.55	0.74	Y = 1.09+1.25X

TABLE 11

CARDIAC OUTPUT METHODOLOGY

CONTINUOUS WAVE DOPPLER - SPECTRAL ANALYSIS - MAXIMUM VELOCITY (15/16th Maximum Frequency Follower) n=14

Aortic Dimension Method	Thermodilution Output Mean $\pm$ SD (l/min)	Doppler Output Mean $\pm$ SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	3.8 ± 0.91	7.86 ± 2.37	0.32	-
M-Mode Cusp Separation	3.8 ± 0.91	4.75 ± 1.90	-0.13	-
2-D Aortic Root at Base	3.8 ± 0.91	6.30 ± 2.75	-0.25	-
2-D Aortic Root at Valve	3.8 ± 0.91	7.11 ± 2.75	-0.36	-
2-D Aortic Root above Valve	3.8 ± 0.91	6.23 ± 1.35	0.66	$Y = 2.52+0.98X$
2-D Cusp Separation	3.8 ± 0.91	4.34 ± 1.48	0.24	-
2-D Aortic Area	3.8 ± 0.91	6.61 ± 1.87	0.74	$Y = 0.86+1.51X$

TABLE 12

CARDIAC OUTPUT METHODOLOGY

CONTINUOUS WAVE DOPPLER - SPECTRAL ANALYSIS - MEAN VELOCITY (Mean Frequency Follower) n=14

Aortic Dimension Method	Thermodilution Output Mean ± SD (l/min)	Doppler Output Mean ± SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	3.8 ± 0.91	4.77 ± 1.22	0.30	-
M-Mode Cusp Separation	3.8 ± 0.91	3.01 ± 1.12	0.10	-
2-D Aortic Root at Base	3.8 ± 0.91	3.83 ± 1.50	-0.28	-
2-D Aortic Root at Valve	3.8 ± 0.91	4.34 ± 1.50	-0.40	-
2-D Aortic Root above Valve	3.8 ± 0.91	3.78 ± 0.66	0.72	Y = 1.80+0.52X
2-D Cusp Separation	3.8 ± 0.91	2.66 ± 0.87	0.21	-
2-D Aortic Area	3.8 ± 0.91	4.00 ± 0.90	0.82	Y = 0.93+0.81X

TABLE 13

CARDIAC OUTPUT METHODOLOGY

CONTINUOUS WAVE DOPPLER - ANALOGUE RECORDING - MAXIMUM VELOCITY n = 20

Aortic Dimension Method	Thermodilution Output Mean $\pm$ SD (l/min)	Doppler Output Mean $\pm$ SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	5.57 $\pm$ 1.27	12.53 $\pm$ 5.59	0.69	Y =-4.34+3.03X
M-Mode Cusp Separation	5.57 $\pm$ 1.27	5.30 $\pm$ 2.36	0.62	Y = 1.12+1.15X
2-D Aortic Root at Base	5.57 $\pm$ 1.27	8.99 $\pm$ 4.66	0.32	-
2-D Aortic Root at Valve	5.57 $\pm$ 1.27	9.90 $\pm$ 4.63	0.35	-
2-D Aortic Root above Valve	5.57 $\pm$ 1.27	10.79 $\pm$ 3.44	0.73	Y =-0.16+1.97X
2-D Cusp Separation	5.57 $\pm$ 1.27	4.48 $\pm$ 1.41	0.47	-
2-D Aortic Area	5.57 $\pm$ 1.27	10.36 $\pm$ 3.08	0.65	Y = 1.49+1.59X

TABLE 14

CARDIAC OUTPUT METHODOLOGY

CONTINUOUS WAVE DOPPLER - ANALOGUE RECORDING - MEAN VELOCITY n=20

Aortic Dimension Method	Thermodilution Output Mean ± SD (l/min)	Doppler Output Mean ± SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	5.57 ± 1.27	7.57 ± 3.20	0.78	Y =-3.35+1.96X
M-Mode Cusp Separation	5.57 ± 1.27	3.17 ± 1.21	0.79	Y = 1.05+0.76X
2-D Aortic Root at Base	5.57 ± 1.27	5.47 ± 2.65	0.36	-
2-D Aortic Root at Valve	5.57 ± 1.27	6.09 ± 2.82	0.39	-
2-D Aortic Root above Valve	5.57 ± 1.27	6.57 ± 1.98	0.84	Y =-0.71+1.31X
2-D Cusp Separation	5.57 ± 1.27	2.69 ± 0.69	0.70	Y = 0.56+0.38X
2-D Aortic Area	5.57 ± 1.27	6.30 ± 1.73	0.78	Y = 0.36+1.07X

TABLE 15

CARDIAC OUTPUT METHODOLOGY

CONTINUOUS WAVE DOPPLER - ANALOGUE RECORDING - VELOCIMETER ESTIMATED MEAN VELOCITY n=20

Aortic Dimension Method	Thermodilution Output Mean ± SD (l/min)	Doppler Output Mean ± SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	5.57 ± 1.27	7.30 ± 3.63	0.73	Y =-4.35+2.09X
M-Mode Cusp Separation	5.57 ± 1.27	3.02 ± 1.32	0.78	Y =-1.51+0.81X
2-D Aortic Root at Base	5.57 ± 1.27	5.34 ± 3.14	0.39	-
2-D Aortic Root at Valve	5.57 ± 1.27	5.97 ± 3.41	0.40	-
2-D Aortic Root above Valve	5.57 ± 1.27	6.30 ± 2.44	0.76	Y =-1.84+1.46X
2-D Cusp Separation	5.57 ± 1.27	2.54 ± 0.82	0.72	Y =-0.04+0.46X
2-D Aortic Area	5.57 ± 1.27	6.04 ± 2.28	0.68	Y =-0.80+1.23X

TABLE 16

CARDIAC OUTPUT METHODOLOGY

PULSED WAVE DOPPLER - SPECTRAL ANALYSIS - MAXIMUM VELOCITY (7/8th Maximum Frequency Follower) n = 38

Aortic Dimension Method	Thermodilution Output Mean $\pm$ SD (l/min)	Doppler Output Mean $\pm$ SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	3.84 $\pm$ 0.90	7.05 $\pm$ 1.76	0.46	-
M-Mode Cusp Separation	3.84 $\pm$ 0.90	4.22 $\pm$ 1.35	-0.21	-
2-D Aortic Root at Base	3.84 $\pm$ 0.90	5.63 $\pm$ 1.94	-0.29	-
2-D Aortic Root at Valve	3.84 $\pm$ 0.90	6.29 $\pm$ 2.00	-0.37	-
2-D Aortic Root above Valve	3.84 $\pm$ 0.90	5.45 $\pm$ 1.28	0.78	$Y = 1.26+1.10X$
2-D Cusp Separation	3.84 $\pm$ 0.90	3.89 $\pm$ 1.09	0.34	-
2-D Aortic Area	3.84 $\pm$ 0.90	5.85 $\pm$ 1.76	0.82	$Y =-0.27+1.60X$

TABLE 17

CARDIAC OUTPUT METHODOLOGY

PULSED WAVE DOPPLER - SPECTRAL ANALYSIS - MAXIMUM VELOCITY (15/16th Maximum Frequency Follower) n = 38

Aortic Dimension Method	Thermodilution Output Mean ± SD (l/min)	Doppler Output Mean ± SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	3.84 ± 0.90	7.60 ± 1.95	0.37	-
M-Mode Cusp Separation	3.84 ± 0.90	4.57 ± 1.54	-0.24	-
2-D Aortic Root at Base	3.84 ± 0.90	6.12 ± 2.21	-0.30	-
2-D Aortic Root at Valve	3.84 ± 0.90	6.82 ± 2.28	-0.38	-
2-D Aortic Root above Valve	3.84 ± 0.90	5.88 ± 1.37	0.71	Y = 1.77+1.07X
2-D Cusp Separation	3.84 ± 0.90	4.23 ± 1.23	0.26	-
2-D Aortic Area	3.84 ± 0.90	6.28 ± 1.81	0.78	Y = 0.28+1.56X

TABLE 18

CARDIAC OUTPUT METHODOLOGY

PULSED WAVE DOPPLER - SPECTRAL ANALYSIS - MEAN VELOCITY (Mean Frequency Follower) n = 38

Aortic Dimension Method	Thermodilution Output Mean ± SD (l/min)	Doppler Output Mean ± SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	3.84 ± 0.90	5.08 ± 1.13	0.38	-
M-Mode Cusp Separation	3.84 ± 0.90	3.02 ± 0.98	-0.26	-
2-D Aortic Root at Base	3.84 ± 0.90	4.07 ± 1.32	-0.35	-
2-D Aortic Root at Valve	3.84 ± 0.90	4.56 ± 1.36	-0.43	-
2-D Aortic Root above Valve	3.84 ± 0.90	3.95 ± 0.84	0.70	Y = 1.44+0.65X
2-D Cusp Separation	3.84 ± 0.90	2.86 ± 0.79	0.28	-
2-D Aortic Area	3.84 ± 0.90	4.22 ± 1.12	0.78	Y = 0.47+0.98X

TABLE 19

CARDIAC OUTPUT METHODOLOGY

PULSED WAVE DOPPLER - ANALOGUE RECORDING - MAXIMUM VELOCITY n = 23

Aortic Dimension Method	Thermodilution Output Mean $\pm$ SD (l/min)	Doppler Output Mean $\pm$ SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	5.31 $\pm$ 0.91	12.70 $\pm$ 5.01	0.65	Y =-6.35+3.59X
M-Mode Cusp Separation	5.31 $\pm$ 0.91	4.15 $\pm$ 1.09	0.28	-
2-D Aortic Root at Base	5.31 $\pm$ 0.91	9.31 $\pm$ 4.73	0.55	-
2-D Aortic Root at Valve	5.31 $\pm$ 0.91	10.63 $\pm$ 5.91	0.57	-
2-D Aortic Root above Valve	5.31 $\pm$ 0.91	10.82 $\pm$ 3.63	0.64	Y =-2.58+2.52X
2-D Cusp Separation	5.31 $\pm$ 0.91	4.10 $\pm$ 0.84	0.04	-
2-D Aortic Area	5.31 $\pm$ 0.91	10.79 $\pm$ 3.03	0.67	Y =-1.05+2.23X

TABLE 20

CARDIAC OUTPUT METHODOLOGY

PULSED WAVE DOPPLER - ANALOGUE RECORDING - MEAN VELOCITY   n = 23

Aortic Dimension Method	Thermodilution Output Mean $\pm$ SD (l/min)	Doppler Output Mean $\pm$ SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	5.31 $\pm$ 0.91	8.10 $\pm$ 2.97	0.77	Y =-5.15+2.50X
M-Mode Cusp Separation	5.31 $\pm$ 0.91	2.64 $\pm$ 0.59	0.51	-
2-D Aortic Root at Base	5.31 $\pm$ 0.91	5.89 $\pm$ 2.84	0.63	Y = 2.98+0.57X
2-D Aortic Root at Valve	5.31 $\pm$ 0.91	6.70 $\pm$ 3.56	0.63	Y =-6.30+2.45X
2-D Aortic Root above Valve	5.31 $\pm$ 0.91	6.92 $\pm$ 2.08	0.78	Y = 1.53+1.04X
2-D Cusp Separation	5.31 $\pm$ 0.91	2.64 $\pm$ 0.58	0.22	-
2-D Aortic Area	5.31 $\pm$ 0.91	6.95 $\pm$ 1.87	0.78	Y =-1.57+1.60X

TABLE 21

CARDIAC OUTPUT METHODOLOGY

PULSED WAVE DOPPLER - ANALOGUE RECORDING - VELOCIMETER ESTIMATED MEAN VELOCITY n = 23

Aortic Dimension Method	Thermodilution Output Mean ± SD (l/min)	Doppler Output Mean ± SD (l/min)	Correlation Coefficient	Regression Line
M-Mode Aortic Root	5.31 ± 0.91	7.61 ± 3.05	0.84	Y =-7.26+2.80X
M-Mode Cusp Separation	5.31 ± 0.91	2.45 ± 0.70	0.70	Y =-0.38+0.53X
2-D Aortic Root at Base	5.31 ± 0.91	5.47 ± 2.72	0.72	Y =-6.02+2.16X
2-D Aortic Root at Valve	5.31 ± 0.91	6.23 ± 3.40	0.71	Y =-7.79+2.64X
2-D Aortic Root above Valve	5.31 ± 0.91	6.50 ± 2.21	0.85	Y =-4.48+2.07X
2-D Cusp Separation	5.31 ± 0.91	2.48 ± 0.83	0.39	-
2-D Aortic Area	5.31 ± 0.91	6.56 ± 2.25	0.78	Y =-3.69+1.93X

TABLE 22

CARDIAC OUTPUT METHODOLOGY

PULSED WAVE DOPPLER - SPECTRAL ANALYSIS - HIGHEST PULSED SIGNAL n = 14

	Thermodilution Output Mean ± SD (l/min)	Doppler Output Mean ± SD (l/min)	Correlation Coefficient	Regression Line
2-D Aortic Root above Valve				
15/16th Maximum Velocity	3.80 ± 0.91	6.26 ± 1.57	0.79	Y = 1.11+1.36X
7/8th Maximum Velocity	3.80 ± 0.91	5.82 ± 1.35	0.86	Y = 0.98+1.27X
Mean Velocity	3.80 ± 0.91	4.29 ± 0.86	0.89	Y = 1.09+0.84X
2-D Aortic Area				
15/16th Maximum Velocity	3.80 ± 0.91	6.66 ± 2.18	0.81	Y =-0.73+1.95X
7/8th Maximum Velocity	3.80 ± 0.91	6.20 ± 1.92	0.86	Y =-0.68+1.81X
Mean Velocity	3.80 ± 0.91	4.64 ± 1.18	0.89	Y =-0.07+1.22X

satisfactory pulsed signals within an individual. The results demonstrate that a more accurate assessment of volumetric cardiac output is obtained using this method and when the time averaged mean velocity is combined with two-dimensional echocardiographic measurement of aortic area or that derived from the aortic diameter measured above the valve, a correlation coefficient of 0.89 is obtained with a regression line very close to unity.

DISCUSSION

This study illustrates the considerable difficulties encountered with the non-invasive assessment of volumetric cardiac output using Doppler ultrasound.

The velocity recordings used are subject to many assumptions, in an attempt to spatially relate the sample velocities tranversing the Doppler beam to the velocity profile across the aorta. Mainly, it is assumed that the flow profile across the aorta is flat, and that the velocity recordings from the Doppler sample will be representative of flow across the aorta. This may be valid at the region of the aortic orifice where the inlet effect of the left ventricular outflow tract will tend to produce a flat profile, but the flow profile within the aorta will also be subject to temporal changes, and will be altered by the complexities of the aorta along which blood is flowing. In addition, it is assumed that the aorta is a rigid tube, devoid of expansile properities, which is not the case, and that flow to the coronary arteries is negligable. This latter assumption is probably valid since flow velocities will be measured during systole, although averaged over the whole cardiac cycle, when coronary artery flow is minimal.

The use of inbuilt frequency followers does allow reproducible values to be obtained for time averaged velocity from a particular Doppler signal. However, it is essential to have a good quality Doppler signal devoid of any apparent electronic interference, as the presence of this will cause inaccurate appreciation of the Doppler frequency curve by the follower, though this will be apparent from the visual display of the follower on the spectrum analyser.

Again, many assumptions are made with regard to measurement of the cross-sectional area, which may not be valid. For example, when a diameter measurement is used to derive cross-sectional area it is assumed that the aorta is circular at the level of measurement, and that this measurement is constant throughout the cardiac cycle. In addition, since echocardiography is used to measure the diameter of the aorta, such a measurement is subject to the resolution of the ultrasound equipment.

The results of this study indicate that using this particular "stand alone" Doppler system the most appropriate methodology for estimating the aortic vessel area is either direct measurement of the aortic root area from the two-dimensional short axis image or measurement of the aortic root diameter above the level of the valve cusps. Other methodologies of aortic area measurement including M-Mode echocardiography did not provide a good correlation with invasive cardiac output measurement when spectral analysis was used, and although good correlation coefficients were obtained in some cases when the analogue recording was used, these still did not allow accurate assessment of volumetric cardiac output when compared to thermodilution. These results confirm recent suggestions to the effect that two-dimensional measurement of aortic root dimension is superior for volumetric cardiac output assessment.[142] Direct planimetry of the aortic cross-sectional area has obvious advantages, in that it does not assume that the aorta is circular, and it obviates any problem in accentuating an measurement error of the aortic radius when this is squared to obtain a circular area. However, two-dimensional echocardiography suffers from problems of lateral resolution, and although this will not affect measurement of the anterior to posterior aortic diameter, the lateral walls will be less distinct, making direct planimetry more difficult. Also, it requires good visualisation of the whole aortic circumference and will therefore, be applicable to less patients than a simple diameter estimation. The results of this study suggest that, where possible, direct planimetry of the cross-sectional area from the short axis echo image is preferable to diameter measurement.

Spectral analysis of the Doppler signal was more accurate than the analogue signal recording in estimating cardiac output. This is not surprising as the analogue signal is highly gain dependent and in addition is less satisfactory than spectral analysis in guaging the quality of the Doppler signal, which is a particularly important consideration when utilizing a stand alone Doppler system. The results of this study did not confirm the validity of using pulsed Doppler and the analogue signal recording of maximum velocity with aortic orifice area, as reported by Ihlen et al.[140] Although good correlation coefficents were often obtained using the analogue signal, the regression equations were superior when spectral analysis was used. This probably highlights the problems in accurately assessing cross-sectional area and the difficulties of using a methodology suggested by other workers without first validating the technique in ones own laboratory. It must also bring into question the reproducibility of absolute cardiac output assessment by the Doppler technique.

The use of the maximum frequency follower, calculating time averaged maximum velocity, resulted in significant overestimation of cardiac output compared with use of the time averaged mean velocity. This occurred both with spectral analysis and analogue signal recordings. This may have been anticipated from the "plug" formed flow theory suggested by Ihlen et al[140] since aortic root measurements were used in this study rather than aortic cusp separation or orifice area as used by Ihlen et al. However, the methodologies used by Ihlen et al. did not provide satisfactory estimation of cardiac output in this study. Alternately, the overestimation of cardiac output by maximum velocity recordings with this system, could result from measuring a velocity profile within the aorta which is parabolic rather than flat. This would also account for the fact that more accurate estimate of cardiac output was obtained when the mean velocity recording was used. Although this is not equivalent to measurement of the space averaged velocity, it will be closer to this value than the maximum velocity where a parabolic rather than flat velocity profile exists.

Continuous wave Doppler was able to estimate volumetric cardiac output accurately, which is of some importance, because of its relative ease of examination using a "stand alone" system compared to pulsed Doppler. However, improved correlation was obtained when the pulsed wave signal with the highest peak velocity was used. This is not surprising since maximum velocity curve will be similar with pulsed and continuous wave if the highest velocity pulsed recording is compared, but since continuous wave Doppler will identify all velocities along the range of the Doppler beam, it will also include the lower velocities detected outwith the main aortic flow. The mean frequency follower used will then calculate a slightly lower time averaged mean velocity with the continuous wave signal than would be expected from pulsed Doppler with these low frequency signals absent.

Despite in vitro data to suggest the position of the pulsed sample gate within the aorta is not important,[141] in this study an improved correlation was obtained when the highest spectral recording obtained with pulsed Doppler was used in the calculation cardiac output. Indeed, the fact that one pulsed signal was higher than another at different depths along the same Doppler beam, in itself suggests the presence of more parabolic flow profile, at this position within the aorta and explains the reason for the superior results using the mean rather than maximum frequency follower. Ihlen et al[140] did not find that position of the pulsed sample gate affected their results but the two positions chosen were anatomically defined, immediately above the valve and 2 cm higher in the aorta, rather than based on the highest recordable velocity signal. When Doppler examination is performed "blind" as with the stand alone Doppler system, it is easier to search for the Doppler signal in the ascending aorta with the highest velocity, rather than the velocity at an anatomically defined position. As the highest velocity will be recorded this is likely to be from the level of the aorta where the velocity profile is least flat, and estimation of the time averaged mean velocity seems most appropriate. This may not be the case with duplex Doppler systems where the pulsed Doppler sample gate can be positioned at a point within the aorta which is anatomically defined. If this is at the level of the aortic orifice it may be more appropriate to use the time averaged maximum velocity in combination with the cross-sectional area at the same level.

Since it is possible to relate the flow velocity and the anatomical area at the same level using a duplex Doppler system, it is likely to be superior to a stand alone system for estimation of absolute cardiac output. Stand alone Doppler systems will have the advantage that the use of the small angulated transducer may provide satisfactory signals, particularly from the suprasternal notch, in a higher proportion of patients than duplex systems and that the quality of the Doppler information will not be compromised by the presence of simultaneous imaging.

An accurate method of assessing cardiac output was identified for the system used in this study, by combining the time averaged mean velocity determined using a mean frequency follower on the spectral display, with the aortic cross-sectional area measured directly from a short axis echo image. However, it is not clear how reproducible this methodology is, and whether it is applicable in situations, such as during exercise, where the velcoity profile within the aorta may change.

Since difficulties can arise in obtaining an adequete ultrasonic window in some patients using, mainly with duplex Doppler transducers, particularly from the supraternal notch, examination from the apical position has also been suggested, estimating cardiac output either through the mitral valve or in the left ventricular outflow tract and aorta.[66-68] Assessment of volumetric flow in the left ventricular outflow tract does have a number of advantages. In particular, in this area it is more reasonable to assume that the velocity profile is flat and measurement will not be affected by the presence of aortic stenosis, which would invalidate any cardiac output assessment in the ascending aorta. However, as with estimation of flow through the mitral valve, considerable difficulties can arise in accurate measurement of the cross-sectional area.

The introduction of real-time colour flow Doppler may resolve some of the problems of Doppler derived cardiac output estimation. This provides a two dimensional pulsed Doppler flow velocity display, colour coded for flow direction superimposed on an echocardiographic image. As a result, it may allow accurate estimation of the cross-sectional area of flow, rather than the anatomical cross-sectional area, and since velocity information is displayed in two dimensions it may provide valuable information on the velocity profile across the flow area of interest.

What emerges from this study is that there are considerable problems with the assessment of volumetric flow using Doppler ultrasound, and that it is likely that the major source of error is in the estimation of the aortic cross-sectional area. Although it is possible to estimate cardiac output with reasonable accuracy with the "stand alone" Doppler system used in this study, its major value is likely to be in the assessment of relative changes in output within an individual, where measurement of cross-sectional area is of little importance.

It is essential for any laboratory wishing to assess cardiac output non-invasively using the Doppler technique to first establish a methodology suitable to their particular equipment and circumstances before applying the technique to clinical situations, and to do so with full awareness of the considerable problems associated with the technique.

CHAPTER 9

ASSESSMENT OF THE HAEMODYNAMIC CONSEQUENCES OF VARYING PACEMAKER MODALITIES BY DOPPLER ULTRASOUND

INTRODUCTION

The previous chapter has illustrated the potential for using Doppler ultrasound to provide an assessment of relative changes in cardiac output within an individual. There are certain clinical situations where this is particularly applicable, none more so than in the assessment of varying pacemaker modalities. There has been considerable interest over recent years in the haemodynamic consequences of differing pacing modes. An increasingly large number of implanted permanent pacemakers are of the dual chamber variety, providing atrio-ventricular (A-V) sequential pacing, but assessment of the potential beneficial effects of A-V sequential pacing over more standard ventricular pacing within an individual is difficult. Also, any investigations performed to assess the haemodynamic consequences of pacemaker function are usually done after the pacing generator has been implanted.

Non-invasive Assessment of Pacemaker Haemodynamic Function

Although it has long been recognised that preservation of the atrial component during pacing is associated with improved ventricular function[143,144] it has been suggested that invasive haemodynamics may be of value in optimizing cardiac performance in pacemaker patients.[145] Radionuclide ventriculography[146] and Doppler ultrasound[147-151] have both been used in this respect to provide a non-invasive assessment of the haemodynamic consequences of pacemaker function. Nanda et al[148] used transcutaneous aortovelography and demonstrated an 18.4% mean reduction in peak aortic velocity when the pacing mode was switched from dual chamber pacing to ventricular only pacing. These results have subsequently been confirmed by other[149,150] using Doppler ultrasound and in addition Stewart et al[149] have also demonstrated an increased benefit of A-V sequential pacing over the ventricular mode in patients demonstrating retrograde V-A conduction during ventricular pacing.

Other workers[151] have suggested that patients with normal left atrial size on echocardiography are most sensitive to loss of A-V synchrony when relative changes in cardiac output were assessed by Doppler echocaridography. Coskey et al,[146] using radionuclide ventriculography, suggested that changes in heat rate did not affect the haemodynamics of A-V pacing but that LV performance was improved by a shorter A-V interval. This particular study suffered from the two minute data acquisition time and, as with all the above studies, from the fact that the range of cycle lengths and A-V intervals are restricted by the implanted programmed generators in the patients studied. As a result the importance of variation in the A-V interval in dual chamber pacing is far from clear though it has been suggested more recently, using a combination invasive cardiac output measurement, systolic time intervals and M-mode echocardiography, that short A-V intervals produce beneficial effects on cardiac output as a result of the delayed onset of ventricular systole.[152] Again the results of this study are limited by prolonged data acquisition time and that although a satisfactory range of A-V intervals was achieved the study was performed at a single heart rate.

Potential of Doppler Ultrasound

There are therefore a number of potential advantages in performing Doppler ultrasound examination during electrophysiological study. With both atrial and ventricular temporary pacing lines in situ rapid alteration in the pacing modality can be achieved. It is therefore possible to perform atrial, ventricular and A-V sequential pacing in rapid succession at varying cycle lengths and A-V intervals without the need for repeated reprogramming of the pacing generator. This also allows comparisons to be made during a shorter time period and therefore under more stable clinical conditions. In addition it is possible to achieve significantly shorter cycle lengths than with implanted systems and thereby examine the haemodynamic effects of pacing at rapid rates, similar to those found during atrial and ventricular arrhythmias.

Since Doppler recordings can be obtained almost instantaneously, examination can be performed even in the short time available during haemodynamically significant arrhythmias or extremely short pacing cycles. It is worth considering that the previous studies mentioned, in patients with implanted generators, assess cardiac function "after the event" whereas Doppler examination in those patients found during electrophysiological study to require permanent pacing allows prediction of the most appropriate programme for the implanted generator prior to pacemaker insertion.

Aim of Study

The aim of this study was to study the application of Doppler ultrasound and assess its value in predicting the haemodynamic consequences of varying pacemaker modalities, over a wide range of heart rates, or pacing cycle lengths, and A-V intervals in patients undergoing invasive investigation.

SUBJECTS AND METHODS

Patients

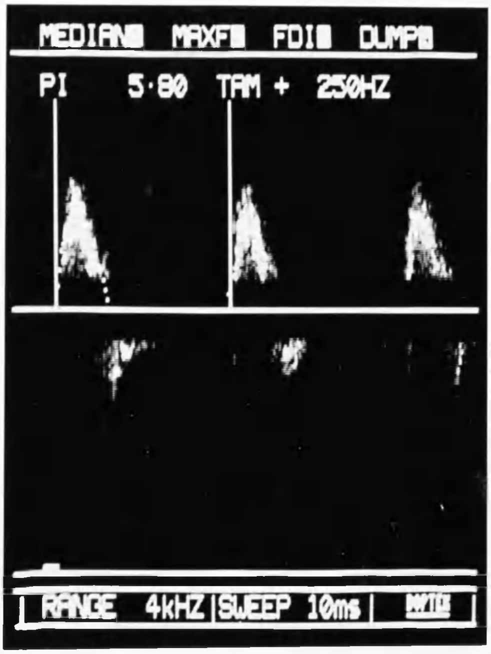
10 patients undergoing cardiac catheterisation and/or electrophysiological investigation were studied. Their ages ranged from 36 to 62 years, mean 52 years. Patients with A-V node disease were excluded as were those with evidence of aortic valve disease which would invalidate the estimation of cardiac output by Doppler ultrasound.

Pacing Protocol

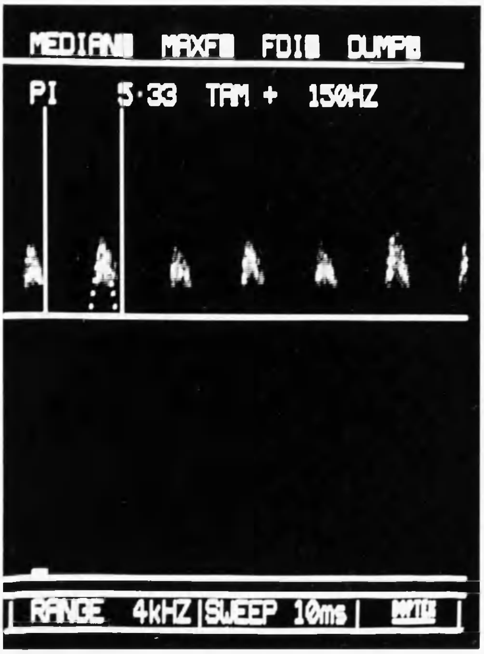
Percutaneous temporary pacing lines were inserted via the femoral vein and positioned in the high right atrium and in the right ventricular apex. Atrial, ventricular and A-V sequential pacing were performed, depending or resting heart rate, at decreasing cycle lengths to 400 msec. A-V sequential pacing was performed at a variety of A-V intervals from 50 msec up to 250 msec. The duration of each pacing sequence was 20 secs performed at 15 sec intervals. Intra-arterial pressure was monitored during each pacing sequence in the 6 patients who underwent arterial cannulation for the purposes of cardiac catheterisation.

Echo/Doppler Study

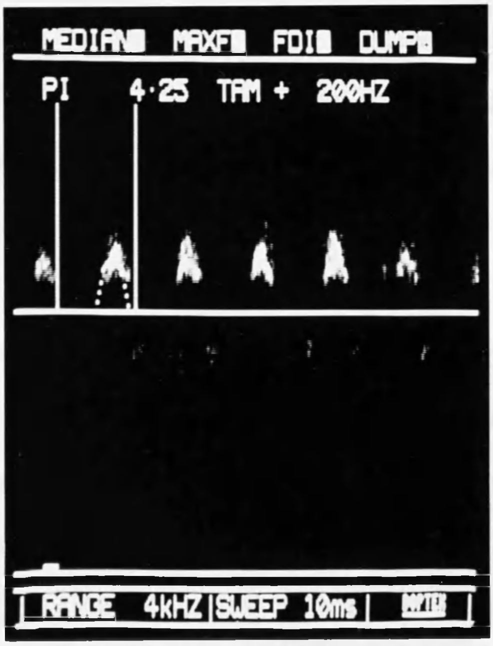
Two-dimensional echocardiography was performed prior to study and Doppler examination was performed from the suprasternal notch with the aortic flow velocity from the ascending aorta recorded continuously during intracardiac pacing. Cardiac output was calculated using the method described in the previous chapter. Although absolute flows were estimated, the results will relate to relative changes in output, since the aortic cross-sectional area is assumed to be constant throughout the study period. Any change in absolute cardiac output measurement therefore will merely reflect the relative change



Aortic flow velocity in sinus rhythm. Time averaged frequency of 250 Hz relates to velocity of 9.8 $cmsec^{-1}$.



Aortic flow velocity during rapid ventricular pacing producing time averaged velocity of 5.8 $cmsec^{-1}$.



Aortic flow velocity during rapid A-V sequential pacing producing time averaged velocity of 7.8 $cmsec^{-1}$.

Figure 37: Effect of varying pacemaker modality on aortic flow velocity recordings in an individual patient.

within an individual.

RESULTS

Satisfactory Doppler recordings were obtained in all 10 patients. The effect on the time averaged velocity recordings of varying the pacemaker modality is illustrated in Figure 37. The relative change in cardiac output is directly reflected by the change in the time averaged velocity. In sinus rhythm, the time averaged velocity is 9.8 cm/s compared with 5.8 cm/s during rapid ventricular pacing. A-V sequential pacing at a similar cycle length, or heart rate, increases the time averaged velocity to 7.8 cm/s.

The results obtained for the group of patients during atrial, ventricular and A-V sequential pacing are illustrated in Figure 38. Cardiac output was significantly lower during ventricular pacing, mean 4.12 ± 1.46 l/min when compared with atrial, mean 5.11 ± 1.46 l/min ($p<0.005$), and A-V sequnetial pacing, mean 5.42 ± 1.61 l/min ($p<0.001$). The profile of cardiac outputs for one individual patient are illustrated in Fig. 39. Cardiac output changed with variation in the A-V interval at each cycle length, the change being more marked at the shorter cycle lengths. Indeed for the group the mean change in cardiac output with A-V interval variation was 12% at a cycle

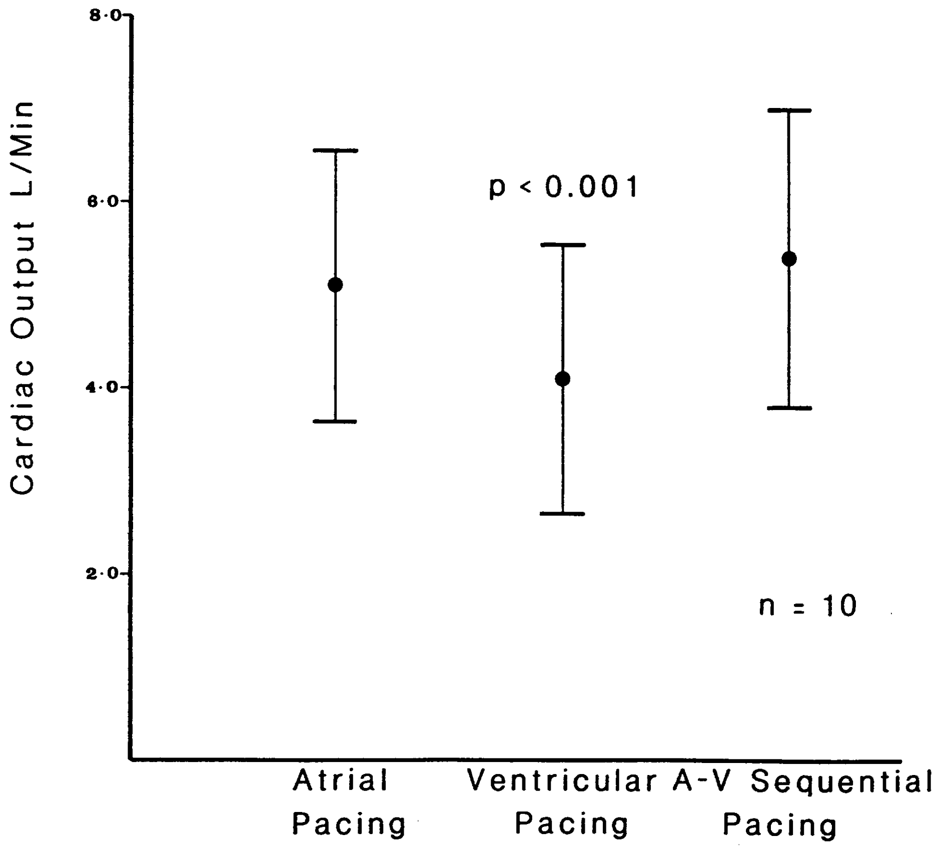


Figure 38: Comparison of Doppler derived cardiac output during atrial, ventricular and A-V sequential pacing. Results displayed as mean value ± standard deviation.

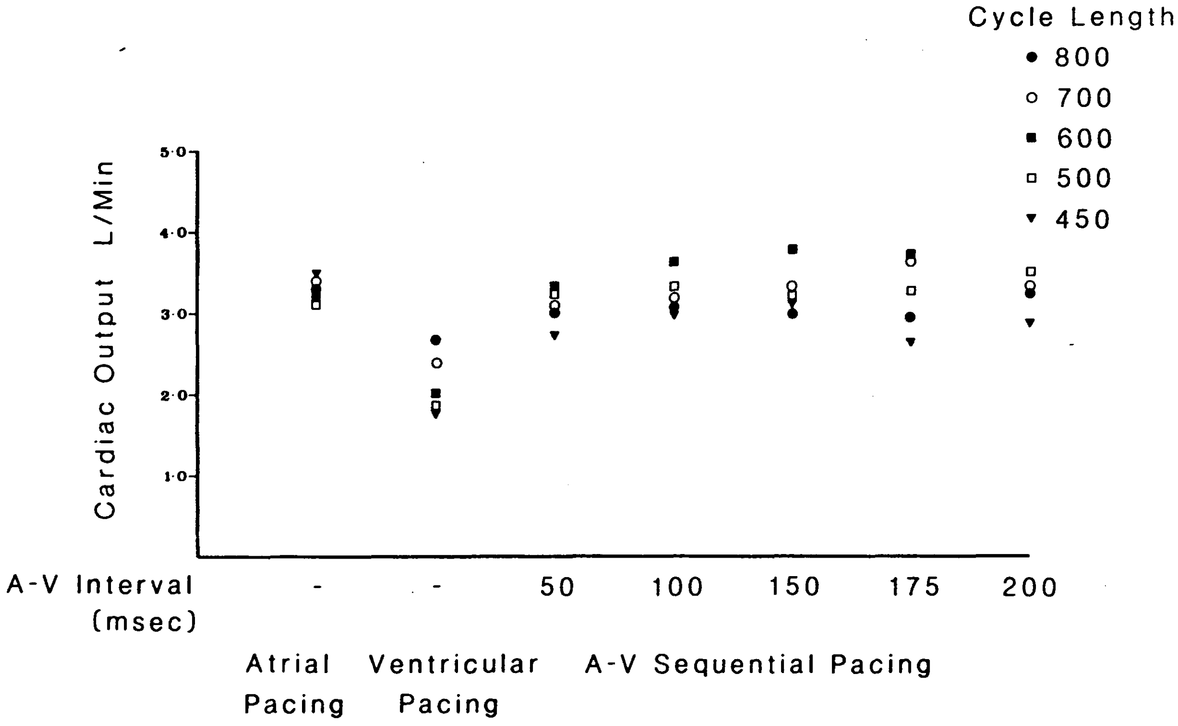


Figure 39: Profile of Doppler derived cardiac outputs in an individual patient resulting from variation in cycle length and pacemaker modality. Note that the A-V interval optimizing cardiac output varies with changes in cycle length.

length of 700 msec and 21.45% at a cycle length of 400 msec ($p<0.001$). In addition the A-V interval which optimized cardiac output varied with cycle length and also varied between individuals at similar cycle lengths. It was impossible therefore to predict the optimal pacing mode for an individual patient prior to Doppler examination.

The profile of intra-arterial pressure recordings in an individual patient is illustrated in Fig. 40. In the patient group there was a reduction in the mean pressure with shortening cycle lengths during ventricular pacing, 94.7 ± 9.4 mmHg at 700msec and 79.7 ± 9.4 mmHg at 400msec ($p<0.005$) and was due almost solely to reduction in systolic pressure. A significant, though less marked, decrease in mean blood pressure occurred during A-V sequential pacing only at the shortest cycle lengths of 400msec and 450msec, for example a mean pressure of 107 ± 11.9 mmHg at 700msec and 91.3 ± 17.7 mmHg at 400msec ($p<0.05$). The reduction in mean blood pressure at the short cycle lengths was dependent on the A-V interval, though that which produced the greatest fall in pressure varied between individuals. No significant change in blood pressure was demonstrated during atrial pacing, the development of Wenckebach usually preventing a rapid ventricular response at the short cycle lengths.

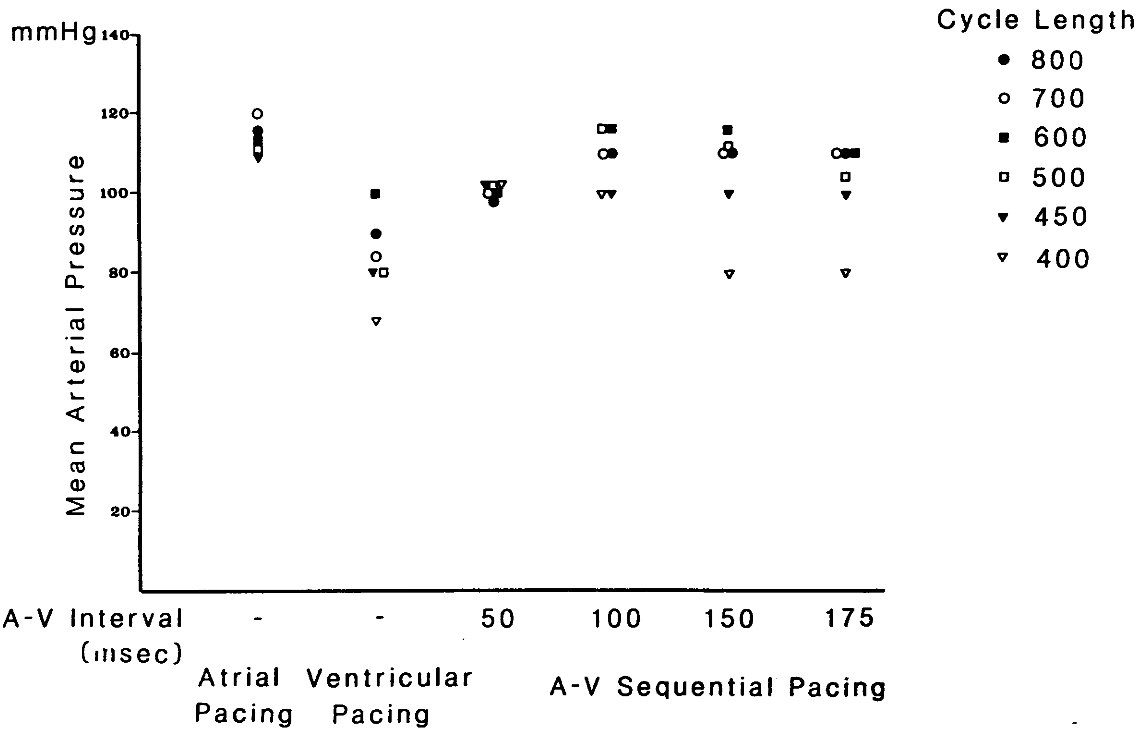


Figure 40: Profile of intra arterial pressure recordings in an individual patient resulting from variation in cycle length and pacemaker modality.

DISCUSSION

This study has demonstrated that Doppler ultrasound can successfully be applied to patients during intracardiac pacing and that valuable information can be gained on the relative change in cardiac output caused by varying pacing modalities within an individual. The increase in cardiac output demonstrated by Doppler echocardiography during atrial and A-V sequential pacing compared to ventricular pacing is of similar magnitude to that found with invasive studies of patients with implanted generators.[149,152] No comment could be made regarding the consequences of left atrial size since this was normal in all patients studied. The variation in cardiac output noted with changes in A-V interval is expected from invasive haemodynamic data.[152] However this study has demonstrated that the A-V interval which optimizes cardiac output varies not only between individuals and but also in a single individual depending on heart rate. The pacing cycle length is also important and the A-V interval optimizing cardiac output would appear to be accentuated at faster heart rates.

Perhaps more important than the actual results obtained in this study is the successful application of Doppler techniques to the assessment of these patients. Here, the relative change in cardiac output is more important than its absolute measurement and the examination of patients during electrophysiological investigation allowed as many as 40 separate pacing modalities to be studied. If thermodilution cardiac output estimation had been used to provide this information this would have necessitated the injection of around 1200 ml of ice cold 0.5% dextrose intravenously over a relatively short period of time, potentially hazardous in patients with compromised ventricular function, the group who are most likely to benefit from A-V sequential pacing, and hence Doppler assessment.

In addition, at the shortest cycle lengths of 400msec and 450msec, particularly during ventricular pacing, haemodynamic decompensation often occurred, as demonstrated by the marked fall in blood pressure during these pacing modalities, and in these circumstances there would have been no time to acquire thermodilution recordings. However, the rapidity of acquiring Doppler recordings allowed haemodynamic information to be gained in these patients during the few seconds available before the termination of pacing was necessary.

Although these rapid heart rates are of little importance for permanent pacemaker implantation they highlight the potential value of Doppler in the assessment of cardiac arrhythmias, an area where echocardiography may also have potential applications.[153,154] Doppler ultrasound may also prove of value during electrophysiological investigation in assessing the consequences of cardiac arrhythmias which produce haemodynamic decompensation where rapid data acquisition is necessary.

The application of Doppler ultrasound within an individual patient resolves many of the problems associated with absolute cardiac output estimation discussed in the previous chapter. Again, however, it is assumed that the velocity profile does not change with variation in absolute flow, and changes in coronary artery blood flow is ignored. Despite this, Doppler ultrasound has the advantage of being non-invasive, having a rapid acquisition time and allowing multiple measurements to be performed, ideal in providing a haemodynamic assessment of pacemaker patients. Doppler ultrasound performed during electrophysiological study may allow a more rational choice of pacing generator and pacing modality prior to permanent pacemaker insertion of allow appropriate setting of an implanted pacemaker to provide the optimal haemodynamic benefit.

CHAPTER 10

THE VALUE OF DOPPLER ULTRASOUND IN THE ASSESSMENT OF CONGENITAL HEART DISEASE

GENERAL INTRODUCTION

Two-dimensional echocardiography now provides so accurate a demonstration of intracardiac anatomy in infants[155] and children[156] with congenital heart disease that surgery can often be undertaken without the need for angiography. However in acyanotic lesions, indications for surgery are often based not simply on the structural abnormality of the lesion, but rather on its haemodynamic effects, such as the severity of obstruction, the pulmonary artery pressure or resistance, or the magnitude of an intracardiac shunt. Some of this vital information can be obtained by echocardiographic assessment of chamber sizes, wall thickness and valve motion but more detailed haemodynamic data is frequently required, making cardiac catheterisation and angiography essential in assessing the need for surgery.

As with two-dimensional echocardiography, infants and children are particularly suitable for Doppler ultrasound examination, since multiple praecordial windows are available, often important in order to align the ultrasound beam in direct line of blood flow and obtain the maximum velocity recording.

Potential Role of Doppler Ultrasound

Doppler ultrasound has potential to provide much of this necessary haemodynamic information non-invasively. The initial reports of Doppler ultrasound assessment of congenital heart disease have related either to the detection and quantification of shunts or to the assessment of obstructive cardiac lesions. Determination of shunt size is based upon the ability of Doppler ultrasound to measure ventricular output from both the left and right heart, and the basis for this was discussed in chapter 8. As we have seen, the problems associated with estimation of cardiac output from the left side of the heart are considerable, but the problems of estimating cardiac output from the right side of the heart are even greater, since accurate estimation of the pulmonary artery cross-sectional area using two-dimensional imaging is extremely difficult. Therefore, although it has been suggested that Doppler echocardiography provides an accurate measurement of shunt size, the clinical value of such a measurement remains very much in doubt. Additionally, in patients with an atrial septal defect, where the majority of shunt estimation by Doppler has been performed, the diagnosis will usually be apparent on clinical examination and by echocardiography, the presence of a dilated right ventricle, paradoxical septal motion, and a hole in the atrial septum will usually allow surgery to be undertaken without the need for cardiac catheterisation.

Although Doppler ultrasound has been successfully used in the detection of patent ductus arteriosus,[157,158] its presence will be determined clinically and visualised by echocardiography in the vast majority of patients. Since closure is recommended because of the risk of infective endarteritis, shunt size in this lesion is not of particular importance and cardiac catheterisation is not usually undertaken.

Doppler ultrasound may prove of some value in the assessment of patients with complex congenital heart disease, or their follow-up post surgery, and some initial studies have reported the application of the technique both preoperatively[91,92] and postoperatively[159,160] in these patients. Doppler ultrasound has even been applied in utero to demonstrate absence of the aortic valve.[161] However, a significant number of patients with complex congenital lesions will still require cardiac catheterisation, but the use of duplex Doppler systems and particularly the introduction of colour flow Doppler, where there is intergration of anatomical and flow relationships, may well expand the role of Doppler examination in the assessment of complex congenital heart lesions.

This chapter will restrict investigation of those congenital heart lesions where an obstructive gradient would be expected and Doppler ultrasound is most likely to be of clinical importance. It will describe the results in patients with acyanotic congenital heart disease undergoing cardiac catheterisation for clinically suspected pulmonary valve stenosis and pulmonary artery bands, pulmonary infundibular stenosis, and coarctation complex. The application of Doppler ultrasound has not been studied specifically in infants and children with aortic stenosis, though it would seem reasonable to expect that the accuracy of the technique discussed in chapter 4 in adults, would also be valid in this group.

This chapter will also include patients with ventricular septal defects where a gradient results from the pressure difference between the left and right ventricles. It may be suspected that Doppler ultrasound has little potential clinical value in these patients since the diagnosis of ventricular septal defect is usually apparent clinically and if surgery is contemplated and left ventricular angiography may be necessary to exclude multiple defects. However, in addition to the diagnosis of a ventricular septal defect, measurement of the gradient across the ventricular septum during systole can potentially predict pulmonary artery systolic pressure, similar to the method used with tricuspid regurgitation in chapter 7. This is of considerable importance for the surgical assessment of these patients and prediction of the pulmonary artery pressure may either identify or obviate the need for cardiac catheterisation in certain patients with a ventricular septal defect.

PULMONARY VALVE OR ARTERY OBSTRUCTION

Introduction

The validity of using continuous wave Doppler and the modified Bernoulli equation for discrete right ventricular outflow obstruction has been demonstrated in an animal model[162] and has also been applied to a small number of patients with pulmonary valve stenosis or pulmonary artery bands.[52,53,163,164] Previous studies have utilized simultaneous echocardiographic imaging and it is therefore appropriate to relate the experience of "stand alone" continuous wave Doppler in the assessment of patients with obstruction to pulmonary arterial flow.

Subjects and Methods

Thirty seven children (age 6 weeks to 15 years, mean 6.4 years) were studied. Patients underwent cardiac catheterisation for suspected pulmonary stenosis in 28, reassessment following pulmonary valvotomy in 6, or pulmonary artery banding in 3. Patients with infundibular pulmonary stenosis are not include here, but are discussed separatley. One patient had combined pulmonary valve and branch stenosis. Six patients had an associated ventricular septal defect, one an atrial septal

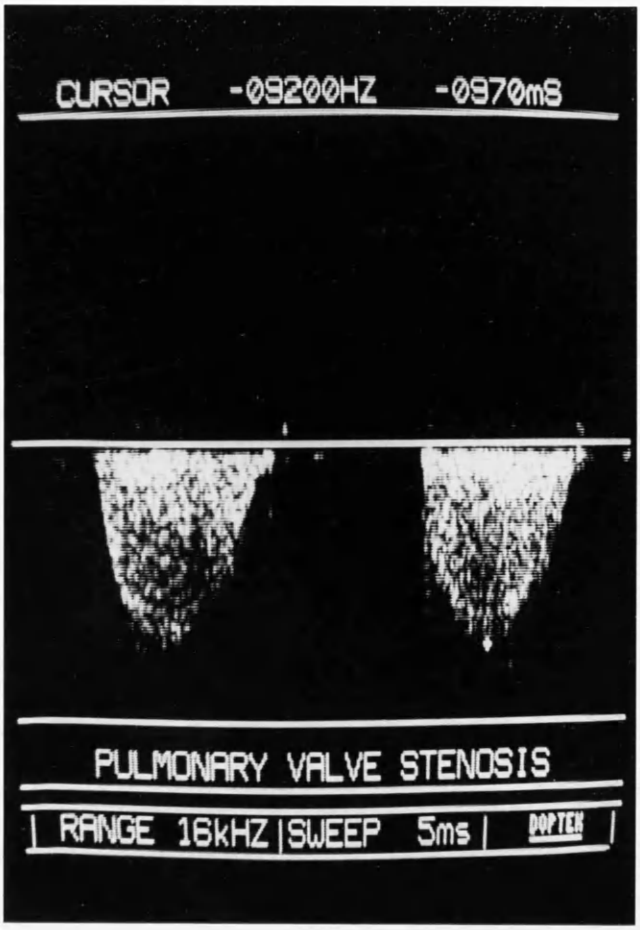


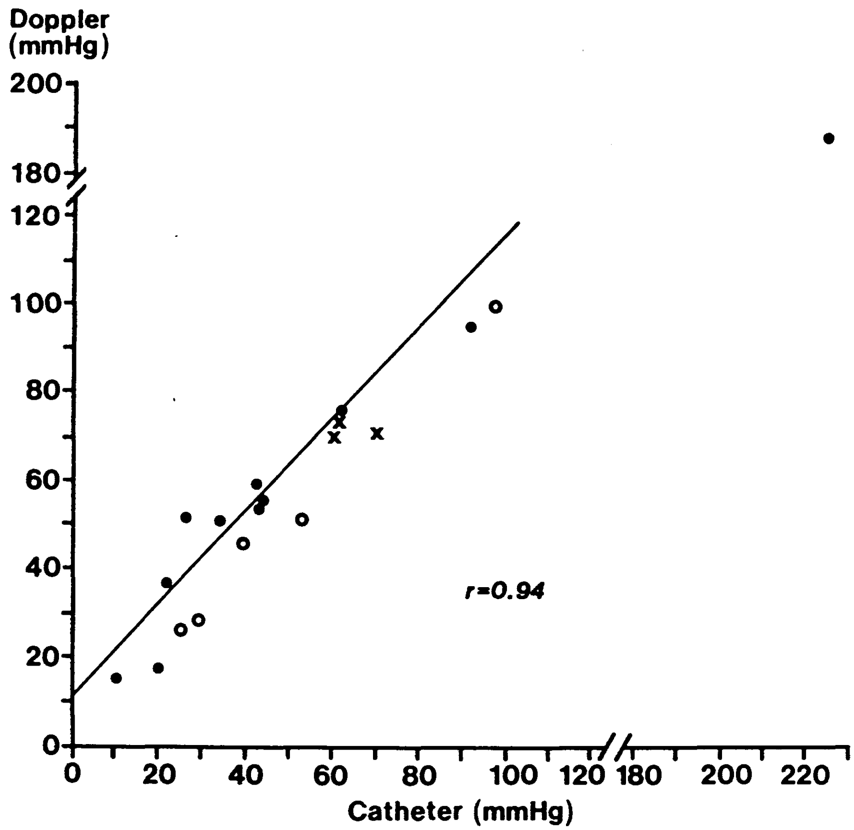
Figure 41: Continuous wave Doppler spectral display from a patient with pulmonary valve stenosis. High velocity flow in the pulmonary artery is detected from the upper left parasternal region, the negative signal representing flow away from the transducer. The maximum systolic frequency shift of 9,200 Hz relates to a velocity of 3.6 $msec^{-1}$ and a calculated valve gradient of 52 mmHg.

defect, and one an absent pulmonary valve with significant stenosis and regurgitation. Cardiac catheterisation was performed under sedation and peak to peak gradients measured from withdrawal tracings by an independent observer. Nineteen patients had Doppler examination performed at cardiac catheterisation, during catheter withdrawal in 7, immediately following withdrawal in 7 and in 5 patients, two catheters were inserted and the simultaneous Doppler examination compared with simultaneously measured right ventricular and pulmonary artery pressures. The remaining 18 patients had Doppler examination performed in the resting state but outwith the effects of sedation.

Two-dimensional echocardiography using an ATL sector scanner was performed in all patients prior to continuous wave Doppler examintion in order to demonstrate the intracardiac anatomy and the appropriate alignment for the Doppler beam, from either the left parasternal or subcostal positions.

Results

Satisfactory Doppler signals were obtained from all patients (Fig. 41). The highest velocity was recorded from the parasternal position in 31 and from the subcostal position in 6. In the patients studied during catheterisation Doppler derived gradients ranged from 15-189 mmHg and peak to peak pressure gradients at catheterisation from 10-226 mmHg. No



O Pressure measured with two catheters.

X Pulmonary artery band.

Figure 42: Comparison of pressure gradients in pulmonary valve and artery stenosis measured at catheterisation with those derived from Doppler examination in the 19 patients studied under sedation in the catheterisation laboratory.

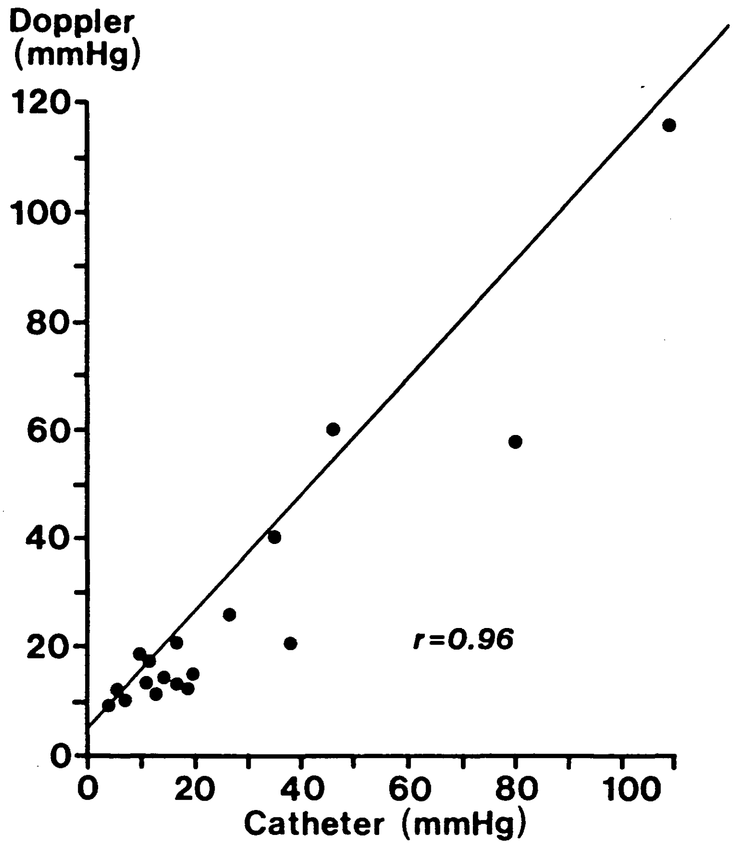


Figure 43: Comparison of pressure gradients in pulmonary valve and artery stenosis measured at catheterisation with those derived from the Doppler examination in the 18 patients studied outwith the catheterisation laboratory.

change in the maximum velocity occurred during catheter withdrawal in the 7 patients in whom Doppler recordings were obtained during this procedure. The results of the comparison of valve gradients in patients studied during catheterisation is shown in Fig. 42. Statistical analysis was performed excluding the patient with a measured gradient of 226 mmHg at catheterisation since this severity of stenosis is uncommon and its inclusion would have produced a marked effect on the regression equation though improving the correlation coefficient from 0.94 to 0.97. Although the Doppler examination underestimated this extremely high gradient it still demonstrated the presence of significant pulmonary stenosis (189 mmHg). The results of those studied at a time separate from catheterisation are illustrated in Fig. 43.

In the 5 patients in whom simultaneous right ventricular and pulmonary artery pressures were measured at catheterisation using two catheters the instantaneous valve gradient was higher than the peak to peak measurement in 4 of the 5 patients (Table 23). Since Doppler ultrasound predicts the instantaneous gradient, as expected, this corresponded better to the instantaneous valve gradient measured at catheterisation, though the differences between the peak-to-peak and peak instantaneous values at catheterisation were minimal and unimportant for clinical purposes.

TABLE 23

VALVE GRADIENTS (mmHg)

	Doppler	Peak-to-peak	Instantaneous
1.	26	25	31
2.	28	29	29
3.	46	39	41
4.	51	53	57
5.	100	97	104

Comparison of Doppler derived gradients with peak to peak and instantaneous maximum pressure gradients at cardiac catheterisation in 5 patients with pulmonary valve or artery stenosis where recordings of simultaneous right ventricular and pulmonary artery pressures were made using two catheters.

Discussion

This study has demonstrated that Doppler ultrasound can accurately predict the pressure gradient across the discrete right ventricular outflow obstruction of pulmonary valve stenosis and pulmonary artery bands.

Doppler derived pressure gradient will reflect the peak instantaneous rather than the peak-to-peak gradient, though in the 5 patients in whom both these measurements were made at cardiac catheterisation, there was little difference between these measurements, and although the numbers are small the differences were not of clinical significance in any of the cases.

Examination of these patients was relatively easy in comparison to adults, reflecting the applicability of Doppler ultrasound to infants and children, and the jet velocity was usually quickly identified from the left parasternal and/or subcostal positions. However, the potential still exists to miss a high velocity jet in a patient with pulmonary stenosis, particularly if this is severe, and careful Doppler examination, to adequately identify flow velocity in the pulmonary artery distal to any potential obstruction, is required to exclude the presence of significant pulmonary valve or artery obstruction.

The patient with an unusually high pressure gradient of 226 mmHg is very interesting. Doppler examination was performed at the time of catheterisation under the effects of sedation, and significantly underestimated the gradient, at 189 mmHg, though clearly still indicated the presence of severe pulmonary stenosis. Simultaneous proximal and distal pressures were not obtained in this patient, but it is unlikely that the discrepancy could be accounted for by differences in the peak-to-peak and peak instantaneous gradients, since, if significantly different, the peak instantaneous gradient, and hence that derived by Doppler, is almost always higher than the peak-to-peak value. It is certainly possible that the Doppler ultrasound beam was at a substantial intercept angle to the direction of flow, but this was not so in any of the other patients studied. However, if the obstruction is very severe, as in this case, energy losses due to viscous friction, normally ignored by the modified Bernoulli equation, can be important[165] and the peak velocity will tend to underestimate the true pressure gradient, which may have resulted in lower Doppler derived pressure drop in this case.

It is worth considering at this point the application of the technique to clinical practice. Surgical treatment of pulmonary valve stenosis is generally undertaken when the gradient across the valve at catheterisation in greater than 40 mmHg. This study would suggest that a Doppler derived gradient of over 50 mmHg indicates the need for surgical intervention. If however the Doppler gradient is less than 30 mmHg the obstruction is not of surgical severity. In patients with pulmonary valve gradients between 30 and 50 mmHg although surgery may be indicated the degree of obstruction is not critical and it may be appropriate in these patients either to procede to cardiac catheterisation or to perform serial Doppler examinations and defer invasive investigation until a later date.

Care should be exercised in interpreting the results of Doppler examination however. In one patient the pulmonary valve gradient on withdrawal was 26 mmHg but 52 mmHg by Doppler, suggesting the patient may have been incorrectly assigned to the surgically significant group. However, there was associated stenosis of the origin of the right pulmonary artery with a total gradient of 50 mmHg from the right pulmonary artery to the right ventricle. The continuous wave Doppler beam was presumably aligned along both these obstructive lesions with a summation effect indicating correctly that the overall obstruction was indeed of surgical significance. This confusion may well have been avoided had pulsed Doppler been used, demonstrating increased velocity at two different sites.

INFUNDIBULAR PULMONARY STENOSIS

Introduction

Comparison of Doppler ultrasound derived pressure gradient across infundibular pulmonary stenosis with gradient measurement at catheterisation has been quoted in only 2 cases.[53] The modified Bernoulli equation has generally been applied to discrete obstructions and ignores energy losses due to friction which may become of importance in elongated or tunnel like obstructions. There may therefore be potential problems on applying the equation to patients with infundibular pulmonary stenosis where the obstruction can be elongated or occur at more than one level. The validity of using the modified Bernoulli equation to assess gradients across irregular, dual and tunnel like obstructions has been demonstrated in vitro[165,166] but in vivo data is currently lacking. The aim of this particular study therefore was to assess the use of the modified Bernoulli equation in providing an estimate of pressure gradient in patients with infundibular pulmonary stenosis.

Subjects and Methods

The study group consisted of 24 infants and children, age 7 days to 16 years, mean 2 years 10 months, with infundibular pulmonary stenosis demonstrated at cardiac catheterisation and angiography. 11 patients had infundibular and possible valve stenosis with a ventricular septal defect and the remaining 13 had tetralogy of Fallot.

At cardiac catheterisation pressures were measured through a fluid filled catheter and the peak to peak gradient across the obstruction recorded not only on catheter withdrawal but also as the catheter was initially advanced into the right ventricle and pulmonary artery. This was possible in only 17 patients, 9 with infundibular pulmonary stenosis and ventricular septal defect and 8 with tetralogy of Fallot. In the others either no attempt was made to pass the catheter into the pulmonary artery because of the severity of the obstruction or the attempt was abandoned when dysrhythmia developed. Peak to peak pressure gradients were measured from the catheter recordings. Simultaneous pressure measurements from the right ventricle and pulmonary artery using two catheters were not performed because of the potential complications related to the infundibular obstruction.

Doppler examination was performed following two-dimensional echocardiography with the patient quiet, sedated

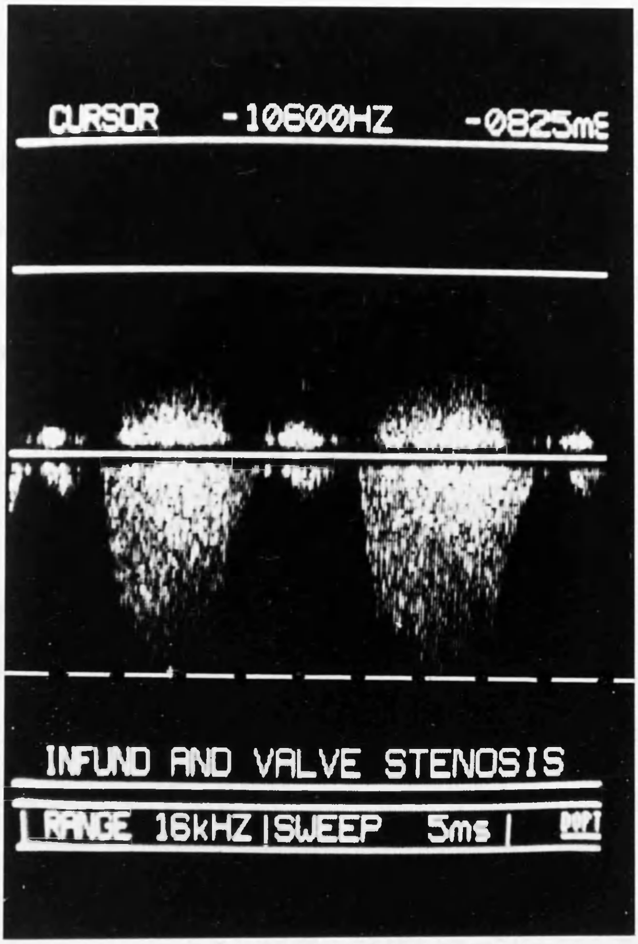


Figure 44: Continuous wave Doppler spectral display from a patient with infundibular pulmonary stenosis. High velocity flow is detected from the upper left parasternal region, the negative signal representing flow away from the transducer. The maximum systolic frequency shift of 10,600 Hz relates to a velocity of 4.2 $msec^{-1}$ and a calculated gradient of 72 mmHg.

or asleep. Of the 17 patients in whom gradients were obtained at catheterisation Doppler examination was performed during sedation for catheterisation in 7, within 24 hours of catheterisation in 3 and during admission for subsequent surgery in the remaining 7. Parasternal, subcostal, suprasternal and supraclavicular positions were explored in all patients to obtain the maximum Doppler velocity from which valve gradient was calculated.

Results

Satisfactory Doppler signals were obtained in all patients (Fig. 44). Maximum blood flow velocities were obtained with almost equal frequency from subcostal and parasternal positions. Comparison of the Doppler derived pressure gradients with gradients obtained at catheterisation are shown, in Fig. 45 on catheter withdrawal and in Fig. 46 on catheter entry.

When comparison is made between the two methods of invasive measurement of pressure gradients, that is at catheter entry and on catheter withdrawal, considerable variation is observed (Fig. 47) with a correlation coefficient of 0.88. The difference was generally related to variation in the right ventricular pressure measurement due to ectopic beats on catheter withdrawal which altered the right ventricualr pressure values, making it difficult to assess the true right ventricular systolic pressure.

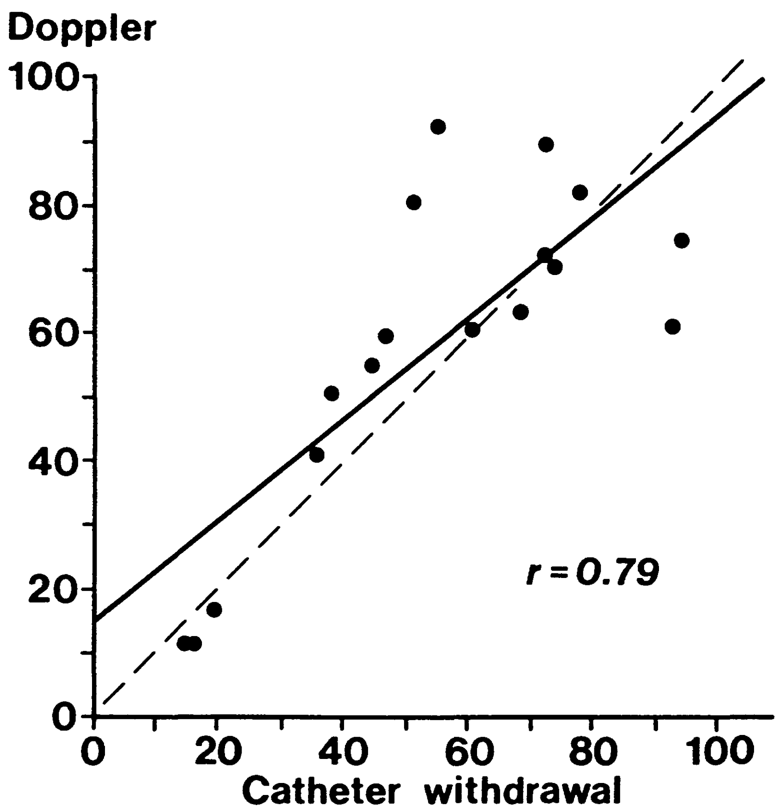


Figure 45: Comparison of pressure gradients derived from Doppler examination with those measured at catheterisation by catheter withdrawal in patients with infundibular pulmonary stenosis.

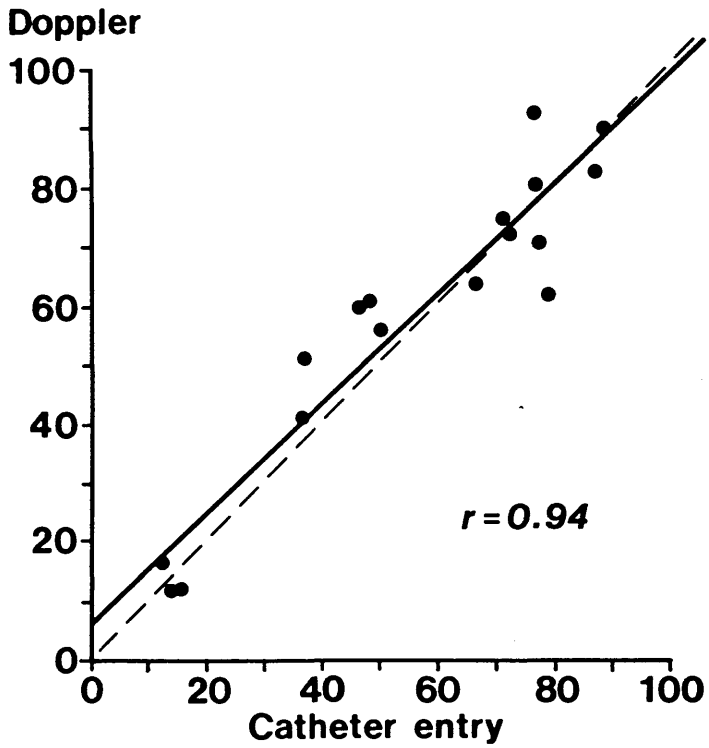


Figure 46: Comparison of pressure gradients derived from Doppler examination with those measured at catheterisation during catheter entry into pulmonary artery in patients with infundibular pulmonary stenosis.

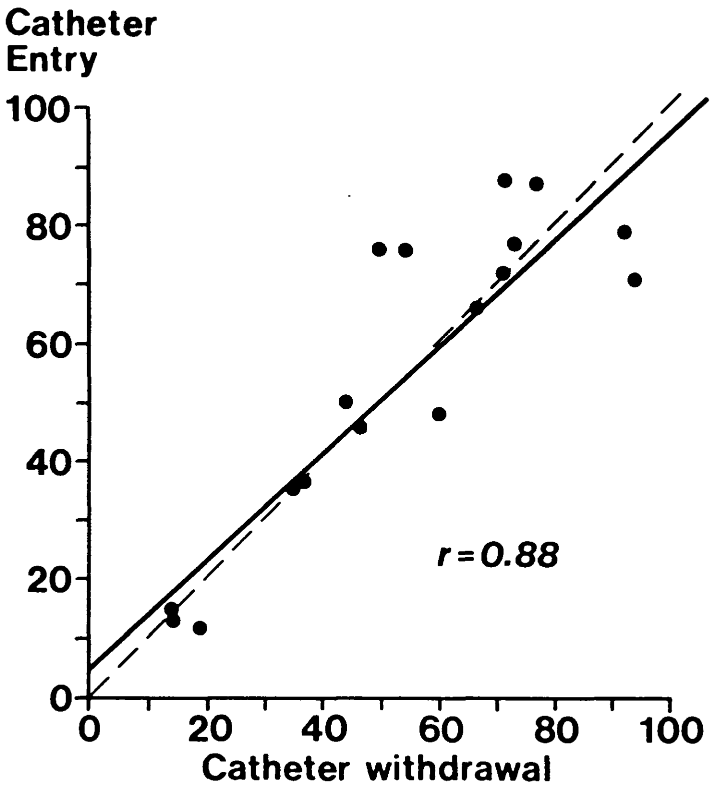


Figure 47: Comparison of invasive pressure gradients measured at catheter entry with those measured by catheter withdrawal in patients with infundibular pulmonary stenosis.

Since the Doppler study was performed with the child in a relatively undisturbed state and not during catheter withdrawal, it would seem more appropriate to compare the Doppler values with those obtained at catheter entry, which resulted in an improved correlation (0.94 compared to 0.79).

Discussion

Despite the potential difficulties the modified Bernoulli equation has been able to accurately assess the total gradient from the right ventricle to the main pulmonary artery in patients with infundibular pulmonary stenosis and infundibular plus discrete valve stenosis.

Persons unfamiliar with the principles of the Bernoulli equation may be surprised that it provides such accurate assessment in patients such as those with tetralogy of Fallot where considerable variation in the severity of infundibular stenosis and blood flow through the right ventricular outflow can occur within an individual patient. However in these patients the pulmonary artery pressure is relatively constant and the right ventricular pressure is at systemic level. Therefore although changes in flow may occur the pressure difference or gradient will remain unchanged and be accurately reflected by the Doppler velocity measurement.

Doppler ultrasound was able to provide an assessment of the pressure gradient where this could not be measured invasively because of the potential hazard of passing a catheter through a severely narrowed outflow tract. In some of these patients clinical examination and echocardiography indicate the need for cardiac catheterisation or surgical intervention. However there are others in whom the degree of infundibular stenosis changes with time and a non-invasive technique able to provide serial measurements is of considerable importance.

Although continuous wave Doppler cannot determine the relative importance of valve and infundibular stenosis the decision with respect to surgery is based on the total rather than individual gradients, and on anatomical information provided by echocardiography or angiography and does not therefore affect the clinical value of the technique.

COARCTATION COMPLEX

Introduction

The diagnosis of coarctation of the aorta is usually based on clinical examination, and further investigations are directed at defining its site and nature in order to permit appropriate surgical intervention. Echocardiography usually provides this information, particularly in neonates and older infants, and allows surgery to be undertaken safely without prior cardiac catheterisation. In older children however, satisfactory echocardiographic images are not always obtained, and a further non-invasive technique in the assessment of patients with coarctation could prove useful. It has been reported that Doppler ultrasound can accurately identify the presence of aortic coarctation and also predict the pressure gradient across the obstruction,[167,168] but there is currently no invasive data to establish the accuracy of Doppler ultrasound in these patients.

Subjects and Methods

53 infants and children, including 15 neonates, with coarctation of the aorta, ages 2 days to 16 years, were studied. Weights ranged from 1.0 Kg to 58 Kg. Cardiac catheterisation was performed in 37 patients and proximal and distal pressures were obtained in 20 patients with significant coarctation. The diagnosis was confirmed in all 53 patients at cardiac catheterisaton and/or surgery.

Continuous wave Doppler examination was performed from the suprasternal and left upper parasternal positions in all patients. The presence of coarctation was suspected when a high velocity jet (defined as greater than 2.2 m/sec) was detected away from the transducer in the descending aorta. Pressure gradients were calculated from the peak velocity using the modified Bernoulli equation. Where a high velocity was present, an attempt was made to localise the depth of the velocity jet using the pulsed wave mode.

In addition, 5 neonates with complete aortic arch interruption was studied in a similar manner.

Results

48 patients had significant coarctation requiring surgical intervention. An increase in the systolic flow velocity was demonstrated in the descending aorta by continuous wave Doppler in 44 of these patients. Of the 20 patients with significant coarctation in whom proximal and distal pressures were measured, an increased Doppler velocity was identified in 17 for comparison of the pressure gradients. Neither the Doppler derived pressure gradient, or that measured at cardiac catheterisation, was predictive of the anatomical severity of the coactation. The overall correlation between the pressure gradients derived from Doppler examination and those at catheterisation was poor, with a correlation coefficient of 0.41 for the peak-to-peak gradient (Y = 0.46X + 26.4) and 0.36 for the peak instantaneous gradient at catheterisation (Y = 0.37X + 27.2). The lack of agreement between the two techniques in better illustrated in Figure 48, where the difference between the Doppler and measured pressure gradients is plotted against their average. The mean $\pm$ 2SD represents the limits of

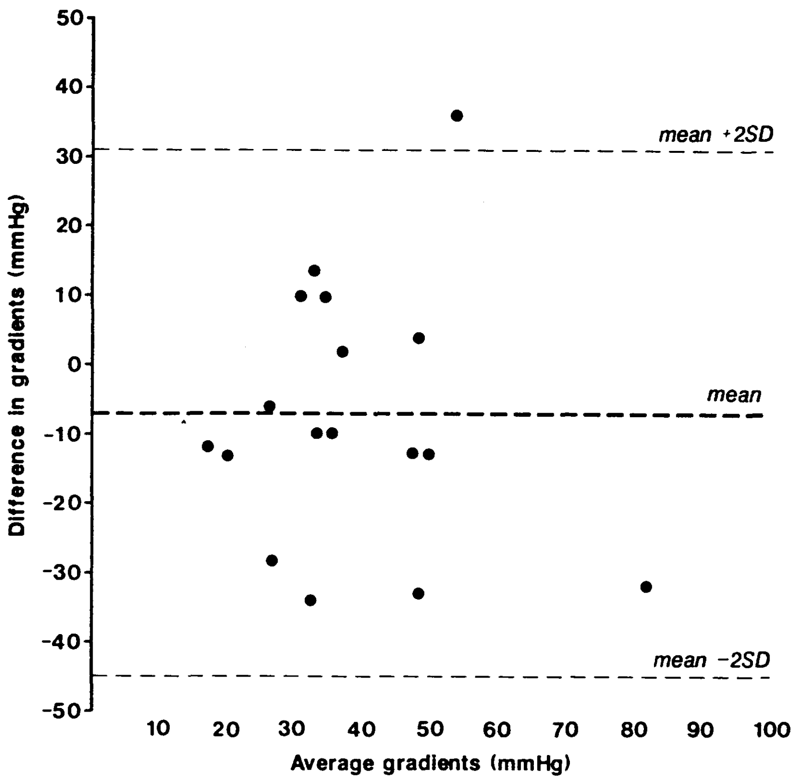


Figure 48: Comparison of the difference between the Doppler and measured pressure gradients with the mean value for each pair of results. The mean $\pm$ 2SD indicating the limits of agreement, show poor agreement between Doppler derived gradients and those measured at catheterisation.

agreement. Therefore, for a gradient at catheterisation, the Doppler derived pressure drop could vary anything between around -35 to +40 mmHg. This is clearly outwith the limits that would be clinically acceptable.

For clinical purposes, it seems appropriate to divide the patients into 2 groups, the neonates with pre- or peri-ductal coarctation, and the older infants and children with mainly post-ductal coarctation.

In older infants and children, Doppler examination failed to detect an increase in the descending aortic velocity in 4 of 33 patients with significant coarctation, 3 of whom had anatomically severe obstruction. In one of these it was possible at cardiac catheterisation to pass a catheter across the coarctation but angiography demonstrated that this completely occluded the lumen. Another was identified at surgery to have a very long segment with a lumen of only 1-2 mm.

In the group of neonates, Doppler ultrasound detected a high velocity jet in the descending aorta in all 15 patients with a significant coarctation. However, a similar high velocity recording during systole was also detected in the descending aorta in 5 patients subsequently demonstrated to have complete aortic arch interruption. Clearly, in these patients, the increased velocity could not have resulted from flow through a coarctation. In one patient, the Doppler derived pressure gradient fell from 33 mmHg to 13 mmHg following infusion of prostaglandins, and in another the velocity signal was abolished by inflating a balloon catheter within the ductus arteriosus, only reappearing after the balloon was deflated.

Discussion

This study has identified major problems with the application of Doppler ultrasound to assessment of coarctation of the aorta, which is at variance with previous reports.[167,168] It is the anatomical severity of the lesion that is important, rather than the pressure gradient across it, which will also be highly dependent of the magnitude of collateral flow. It is not surprising therefore, that neither the Doppler derived pressure gradient or that measured at catheterisation, was predictive of the anatomical severity.

Unlike the assessment of other jet lesions studied in this thesis using Doppler ultrasound, there was a poor correlation between the Doppler derived pressure gradient and that measured at catheterisation, unaffected by the peak-to-peak or peak instantaneous value, with both considerable over and underestimation being apparent. It is not difficult to understand why Doppler ultrasound may underestimate the pressure gradient in these patients. If one is unable to align the Doppler beam in the direction of flow with a suitably small intercept angle, the peak velocity will be underestimated, as will the calculated pressure gradient. In addition it is recognized that in very severe obstructions, energy losses due to viscous friction will cause underestimation of the pressure drop from the peak velocity using the modified Bernoulli equation.[165] Perhaps, it is more difficult to understand why Doppler ultrasound would significantly overestimate the measured pressure gradient. In part, this may be due to the fact that the modified Bernoulli equation does not take into account the velocity of flow proximal to the obstruction, which was up to 2.0 m/s in some of the patients studied. However, this does not account for overestimation of pressure gradients up to 40 mmHg. It is well recognized that there is progressive distortion of the pressure waveform throughout the aorta and into the femoral arteries, and without the use of high fidelity transducer tipped catheters, the apparent overestimation by Doppler ultrasound, may actually be a reflection of the difficulties in accurately measuring pressure gradients at cardiac catheterisation.

In the group of neonates, Doppler ultrasound was able to identify a high velocity jet in all patients with a significant coarctation. However, it was not able to distinguish this from flow into the descending aorta through a restrictive ductus arteriosus in patients with complete arch interruption. The presence of a high velocity systolic jet in the neonatal group will identify the presence of significant aortic obstruction, since high flow velocity through a restrictive ductus will only occur where there is a significant pressure drop between the pulmonary artery and the descending aorta, as in severe coarctation of complete interruption, but it will be unable to distinguish between the two. It might be expected that the use of duplex Doppler systems would separate the two, but since some velocity information will come not only from the well defined Doppler sample gate shown on the echo image, but also from the region around it, in a patient with peri-ductal coarctation the position and direction of the flow velocity jet through the ductus and through the coarctation may be almost identical, and unable to be accurately separated by the use of simultaneous echo imaging.

The results of Doppler ultrasound in neonates should be interpreted with extreme caution and, since high quality two-dimensional echocardiographic images are usually obtained, it may be that Doppler has little to add to the non-invasive assessment of these patients.

In older infants and children, where echocardiography may be less satisfactory, Doppler ultrasound will identify a high velocity recording in the descending aorta in the majority of patients with coarctation. However, it may well miss the presence of a coarctation, particularly if obstruction is severe.

There are, therefore, considerable difficulties with the application of Doppler ultrasound to the assessement of patients with coarctation of the aorta, and any clinical interpretation of the results should only be undertaken in the full knowledge of the associated problems.

VENTRICULAR SEPTAL DEFECT

Introduction

Doppler ultrasound has been successfully used to detect the presence of ventricular septal defects[87-89] and to differentiate them from other causes of systolic murmurs.[34,169,170] Though it may enhance the clinical and non-invasive detection of ventricular septal defects the major potential of Doppler ultrasound is its potential to predict the pulmonary artery pressure in these patients. Doppler estimation of pulmonary artery pressures has been reported by measuring the time interval between pulmonary valve closure and tricuspid valve opening,[171] or, when present, from the peak systolic flow velocity of tricuspid regurgitation,[128] as in chapter 7 for patients with bioprosthetic valves. However, it is also possible to estimate the right ventricular systolic pressure directly from the VSD velocity jet by calculation of the gradient across the septal defect using the modified Bernoulli equation. In the absence of left ventricular outflow obstruction the systolic blood pressure measured by sphygmomanometry will be equivalent to that in the left ventricle and the right ventricular systolic pressure will then be equivalent to the left ventricular systolic pressure minus the trans-septal pressure gradient. As with tricuspid regurgitation, this calculated right ventricular systolic pressure will be identical to the pulmonary artery systolic pressure providing no right vetricular outflow obstruction exists. Even if this is present it should still be possible to estimate the pulmonary pressure by also assessing the Doppler derived gradient across the right ventricular outflow.

Subjects and Methods

21 infants and children, age range 5 weeks to 8 years, were studied. Doppler examination was performed under sedation for catheterisation in 18 patients and in close proximity to the catheterisation procedure in the remaining 3. All possible praecordial sites were examined in an attempt to obtain the maximum velocity signal through the septal defect. If no velocity jet relating to the VSD could be identified this was regarded as indicating a right ventricular pressure at systemic level but only after careful and detailed examination from all praecordial sites. Where a spectral signal with a clear cut peak could not be identified the maximum part of the spectrum was

used for measurement of the trans-septal gradient in the knowledge that this may underestimate the true maximum gradient. Cardiac catheterisation was performed in all patients and non-simultaneous right and left ventricular pressures measured using a single catheter.

Results

Pressure gradients across the ventricular septum ranged from 0 to 98 mmHg by the Doppler technique and 0 to 108 mmHg at cardiac catheterisation. The comparison of gradients is shown in Fig. 49 with an overall correlation coefficient of 0.92. In 2 patients however, the pressure difference across the ventricular septum was considerably underestimated by Doppler ultrasound, thereby overestimating the calculated pulmonary artery systolic pressure.

Discussion

The presence of a significant ventricular septal defect can usually be demonstrated by two-dimensional echocardiography. In infants with heart failure or failure to thrive the need for surgery is often readily apparent. However, in asymptomatic patients it is the presence of pulmonary hypertension suggests the need for early surgical intervention.

This study has demonstrated that Doppler ultrasound

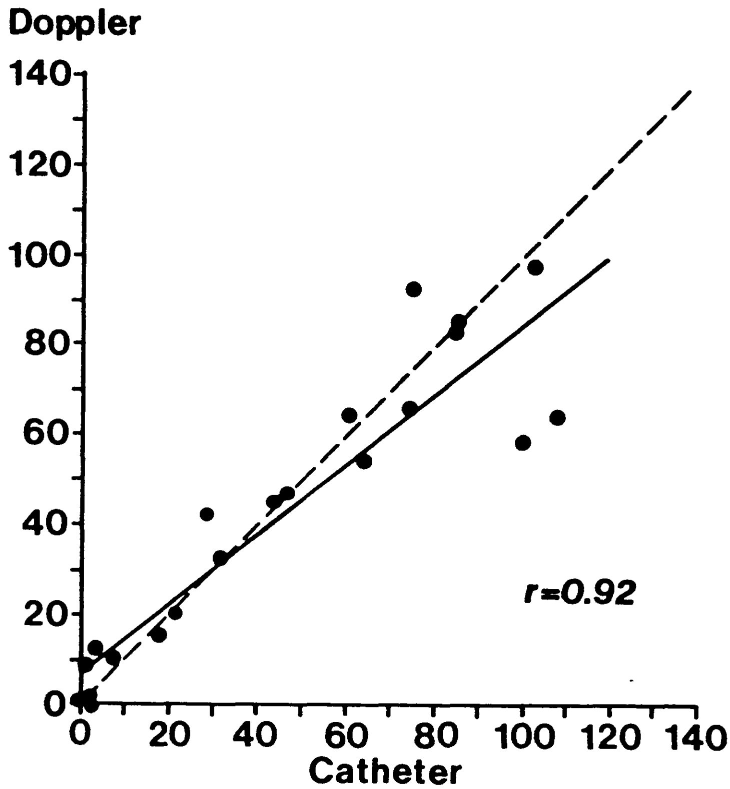


Figure 49: Comparison of Doppler derived pressure gradients across the ventricular septum with those obtained at cardiac catheterisation in patients with ventricular septal defect.

can confirm the presence of a ventricular septal defect and also predict pulmonary artery systolic pressure in patients with ventricular septal defects. As a result it may reduce the need for cardiac catheterisation in these patients. In order to establish the presence of multiple VSD lesions prior to surgery, invasive investigation will still be required in those in whom pulmonary hypertension is demonstrated. However, Doppler examination should reduce the need for catheterisation in those patients in whom the pulmonary systolic pressure is normal on the Doppler examination. A potential source of error exists if the maximum velocity jet is not identified. This will cause underestimation of the pressure gradient across the interventricular septum and therefore tend to overestimate the pulmonary systolic pressure. As a result, some patients with normal pulmonary pressures would therefore still undergo cardiac catheterisation but, more importantly, no patient with significant pulmonary hypertension should be missed or fail to be referred for cardiac catheterisation.

The introduction of real-time colour-flow Doppler[129] may further enhance the non-invasive assessment of these patients by identifying the presence of multiple defects, though, being a pulsed Doppler technique, and therefore subject to frequency aliasing, it would be unable to accurately measure peak velocities associated with VSD jets, or predict pulmonary artery systolic pressure. However, the combination of colour flow and continuous wave Doppler ultrasound may reduce the need for invasive investigation in a significant proportion of patients with ventricular septal defects.

CHAPTER 11

GENERAL DISCUSSION

The development of echocardiography has revolutionized the investigation of cardiac disorders in both adult and paediatric cardiology. In particular, the introduction of two-dimensional imaging has allowed a non-invasive method of precisely detailing structural information from which appropriate surgical recommendations can safely be made in certain patients. However, since it does not provide haemodynamic information, often essential in the assessment of patients with cardiac disorders, the necessity to perform cardiac catheterisation in a substantial proportion of patients still remains.

This thesis has investigated the application of Doppler ultrasound to a variety of cardiac disorders in both adult and paediatric cardiology, where, by the nature of the technique, it had the potential to provide important haemodynamic information and thereby advance the non-invasive assessment of these patients. It has not therefore dealt with many areas of cardiology where Doppler ultrasound could be applied, but where its clinical value is likely to be limited. For example, in mitral valve disease, reports of the use of Doppler ultrasound have demonstrated that accurate estimation of mitral valve gradients can be made, and the actual degree of obstruction assessed by measurement of mitral pressure half-time.[28-31] The assessment of mitral regurgitation will be subject to similar problems discussed earlier, in chapter 6 for mitral valve prostheses, but quantitative assessment has been reported using duplex Doppler.[172] However, the combination of clinical assessment and established non-invasive investigations will provide a very accurate estimate of the severity of mitral stenosis and need for surgical intervention, so that although Doppler ultrasound may well be confirmatory, it is unlikely to substantially change the impact of non-invasive assessment of these patients.

In certain situations, haemodynamic information may be important, but the accuracy of Doppler ultrasound in providing it would be questionable. For instance, in atrial septal defects, the considerable problems of cardiac output estimation necessary for shunt quantification by Doppler have already been discussed, and to confirm the presence of an atrial septal defect, Doppler ultrasound would be required to identify flow across the atrial septum at relatively low velocity. This would almost certainly require the use of pulsed Doppler to exclude other low velocities that may be identified using continuous wave Doppler, and extreme difficulty would be encountered without the facility for simultaneous echocardiographic imaging. In addition, the diagnosis of atrial septal defect will often be suspected clinically and safe surgical recommendation can usually be made on the basis of echocardiography, particularly in infants and children.

In other areas, the resolution of the non-invasive Doppler technique may be inadequate to accurately measure flow velocity, as in coronary arteries. Here, the resolution will be limited by the relatively low frequency transducers required for satisfactory depth penetration, but the use of high frequency transducers intraoperatively or mounted on a catheter tip, may allow flow velocity recordings from coronary vessels to be obtained, and such transducers are currently available. Estimation of coronary flow using this technique however, will remain subject to the considerable difficulties encountered with any form of volumetric flow analysis.

It is not intended to suggest that Doppler ultrasound can not be applied to, or is necessarily unimportant in these areas, merely that its application in clinical practice is likely to be limited in comparison to other areas of cardiovascular diagnosis.

It should be apparent from this thesis that the major application of cardiac Doppler ultrasound is in the assessment of lesions where high velocity jets of blood are to be expected. An accurate quantification of the severity of obstructive gradients can be obtained in the majority of adults and children with stenotic lesions.

In adults, Doppler ultrasound is particularly valuable in the assessment of aortic stenosis, where current clinical and non-invasive investigation can be equivocal, and invasive investigation is not always successful. Here, continuous wave Doppler can accurately estimate the severity of aortic stenosis and allow appropriate surgical recommendation to be made safely in a significant number of patients. It should be emphasized that the information obtained by Doppler ultrasound will not necessarily be identical to the recognized invasive equivalent. For example, in aortic stenosis, Doppler ultrasound will measure the peak instantaneous valve gradient rather than the peak-to-peak value measured at cardiac catheterisation. In addition, Doppler ultrasound will generally be performed outwith the effects of sedation used during catheterisation, so that the Doppler gradient will provide slightly different information,[173] and interpretation of the results of any Doppler study must be made with this in mind.

The modified Bernoulli equation would appear to be valid for prosthetic valves in addition to native valves, and Doppler ultrasound can also provide an accurate assessment of prosthetic valve obstruction non-invasively, over a range of different prostheses. In particular, mitral pressure half-time will accurately reflect the actual degree of obstruction which is independent of through valve flow or the presence of regurgitation.

Obstructive lesions are common in congenital heart disease, particularly right ventricular outflow obstruction, and continuous wave Doppler can assess the pressure drop in patients with, infundibular, valvar or pulmonary artery stenosis.

The value of Doppler ultrasound in the assessment of coarctation of the aorta was disappointing, and possibly rather surprising. As an obstructive lesion, it might be expected that continuous wave Doppler would be very accurate in this area. The considerable problems associated with Doppler assessment of this lesion have already been discussed, but it is worth remembering that the effect of collateral flow and the presence of a restrictive ductus can cause misleading information, potentially dangerous if Doppler examination was performed without sufficient knowledge of these problems. Anatomical rather than functional information is important in assessing the need for surgery in coarctation in infants and children, and emphasizes the fact that Doppler ultrasound will only be of clinical value in lesions where the obstructive gradient is of importance for subsequent patient management, rather than all cases where obstruction exist. It also highlights the importance of obtaining adequate invasive comparisons prior to any acceptance of the technique for clinical purposes.

Although accurate quantification of obstructive lesions can be made, the role of Doppler ultrasound, as used in this thesis, is more qualitative for the assessment of regurgitatant jets. With respect to prosthetic valve regurgitation, continuous wave Doppler is valuable in detecting the presence of regurgitation, but there are considerable difficulties in attempting to assess its severity. This is hardly surprising, since quantification requires an assessment of the volume of blood regurgitating into a particular cardiac chamber, involving three dimensions and a relationship between anatomy and flow. Although the combination of continuous and pulsed Doppler did provide a semi-quantitative assessment of mitral prosthetic regurgitation, and quantification has been reported for both mitral[172] and aortic[174] regurgitation using duplex Doppler systems, the one dimensional information that these systems provide make any such estimation subject to considerable difficulties, and can only be semi-quantitative at best.

The development of real-time colour coded flow Doppler[175-177] will provide a Doppler system which is far more suited to the quantitative assessement of regurgitant lesions. The ability to combine two dimensional structural information from echocardiography with simultaneous two dimensional flow velocity information can only enhance the application of Doppler ultrasound in this area.[178]

Similarly, in the examination of patients with complex congenital heart lesions, where the intergration of structural and functional information is particularly important, colour flow Doppler will potentially have considerable clinical impact.[179]

It may have been anticipated that Doppler ultrasound would be an ideal method of assessing cardiac output non-invasively. However, the results of cardiac output estimation in this thesis would suggest that this is far from the case. Since Doppler ultrasound is measuring flow velocity rather than flow itself, and Doppler velocities are obtained only within the Doppler sample beam and not across the whole blood vessel, major assumptions are required to convert the Doppler information into an assessment of volumetric flow. These assumptions are not necessarily valid, and in order to assess absolute flow, the exact area over which flow is occurring has to be known. This introduces the major source of error in estimation of cardiac output by Doppler ultrasound, the vessel area or diameter measurement by echocardiography. In particular, if diameter measurement is used to calculate the vessel area, any slight error will be accentuated when this value is squared in the calculation of vessel area. For this reason, the role of Doppler ultrasound in the estimation of cardiac output, remains in considerable doubt. However, its current value is likely to relate to reflecting changes in cardiac output within an individual, where measurement of the vessel area is less important, and cardiac output changes will be reflected by changes in the flow velocity alone.

Doppler ultrasound can provide important haemodynamic information in a variety of cardiac lesions in both adult and paediatric cardiology. In order to do so, it is of paramount importance that one is able to obtain good quality Doppler recordings, and this must form the basis of any Doppler examination. It is likely, and sensible, that persons learning cardiac Doppler will do so with an experienced background of two-dimensional echocardiography. Although there are many common factors between the two, Doppler ultrasound requires additional skills, and it would be wrong to assume that valuable information can be obtained without considerable experience. Possibly the major danger with Doppler ultrasound, as with echocardiography, is the tendency to overinterpretation of results, and this is usually related to the quality of the recordings, or images, obtained. However, a solid echocardiography background will be extremely helpful in gaining proficiency in cardiac Doppler ultrasound, and increasingly valuable information will be gained from experience. It is likely that colour flow Doppler will reduce the learning curve by relating flow information and its direction to cardiac structures and praecordial imaging positions.

The major advantage that Doppler ultrasound confers over invasive haemodynamic investigations is that this information can be obtained non-invasively and repeated as often as necessary. Cardiac catheterisation provides haemodynamic information only at one point in time and there is justified reluctance to subject patients to repeated invasive procedures. The ability to follow up patients with a repeated non-invasive haemodynamic assessment has considerable implications for the clinical management of patients with valvular and congenital heart disease, particularly those with only mild or moderate lesions at presentation. Here, it may be possible to separate patients with a developing haemodynamic problem from those who remain static and make appropriate recommendation regarding surgery or the need for invasive investigation. In addition, haemodynamic information may be obtained in situations where invasive investigation is undesirable or unjustified, as with the serial haemodynamic assessment of new types of bioprosthetic valves.

The advancing application of cardiac Doppler ultrasound may change the role of the practicing cardiologist. If the need for cardiac catheterisation is reduced, then it is reasonable to assume that full cardiological assessment may be obtained in a substantial number of patients without the need for invasive facilities. Potentially therefore, surgical recommendations directly from the District General Hospital may be possible in some patients, providing appropriate non-invasive facilities and expertise are available.

In conclusion, Doppler ultrasound has been shown to provide accurate haemodynamic information, of considerable clinical value, in a wide range of cardiac disorders. With adequate training and expertise, and in the knowledge of the problems and pitfalls of the technique, cardiac Doppler ultrasound can provide a valuable clinical diagnostic tool. It is important to emphasize that the technique should not be regarded in isolation. The strength of cardiac Doppler ultrasound lies in its combination with clinical examination, electrocardiography, x-ray, and conventional echocardiography. Cardiac Doppler ultrasound has added a new dimension to non-invasive investigation and will have an increasingly major impact on clinical cardiological practice.

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