PULSED DOPPLER ECHOCARDIOGRAPIC EVALUATION OF THE BLOOD STREAM IN CHILDREN WITH MORPHOLOGICAL HEART LESIONS

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List of abbreviations

d-TGV = dextral transposition of the great vessels
LVO(T) = left ventricular outflow (tract)
MR = mitral regurgitation
RGPD = range gated pulsed Doppler
TIH = time interval histogram
VPS = valvular pulmonary stenosis
VSD = ventricular septal defect

Chapter I

I.1. Introduction

Echocardiography is well estabished as a valuable method for detecting specific lesions and is useful for obtaining information which is helpful in the management of many patients with congenital and acquired abnormalities of the heart and great vessels (1-9). However, conventional M-mode and two-dimensional echocardiographic techniques are not always diagnostic since some acquired and congenital cardiac disorders result in nonspecific echocardiographic findings (10-11).

Range gated pulsed Doppler (RGPD) is a diagnostic approach supplementing M-mode echocardiography in identifying blood-flow patterns at well defined intracardiac sampling areas of interest. The sample areas may be selected at any depth from 2 to 15 centimeters along the ultrasonic beam in order to localize information from a specific zone in a known cardiac cavity or from a great vessel. By demonstrating that intracardiac flow is either laminar or non-laminar, conclusions can be made as to what structural abnormality exists.

The purpose of this investigation was to determine the sensitivity and limitations of range gated pulsed Doppler echocardiography as a method to distinguish children with different forms of cardiac malformations. Precautions were taken to be as blind as possible to the diagnosis.

The studies to be presented have in part been published previously (12-18). Their detailed review and interrelation form the basis of this work.

Chapter II

II.1. Doppler theory and application

The combination of echo and Doppler allows study of blood velocity and characteristics of the passing stream of red blood cells at a selected location in a cardiac chamber or vessel (19).

In accordance with Doppler theory, the incident frequency of sound reflected from an object will be altered when it reflects off a moving object. This change of the reflected frequency is known as Doppler shift (20).

The pulsed Doppler device transmits into the blood stream repetitive bursts of sound in the MegaHertz range from a vibrating crystal (23-24). If the ultrasound is scattered by stationary surfaces, the resulting signal will have the same frequency as the transmitted signal.
In contrast, and in accordance with Doppler theory, ultrasound back scattered from moving particles, such as red cells within the blood stream, will shift the reflected frequency in proportion to red cell velocity. The magnitude of Doppler shift is determined from the frequency difference between the transmitted and received signal. This yields information on the velocity of the blood flow with respect to the transducer. Two Doppler techniques exist; a pulsed and a continuous method. The primary advantage of pulsed echo Doppler compared with continuous wave Doppler is that blood flow velocity may be evaluated from selected intracardiac areas (fig. 1) (21). This is accomplished by electronically rejecting all Doppler signals (range gating) except for an area (2x4 mm), which can be selected anywhere along the beam between 2 and 15 centimeters (fig. 1-2).

The transmitter circuit emits ultrasonic bursts of 1 μ second duration at a pulsed repetition frequency that may be varied between 3.500 and 10.000 bursts / second, depending on the depth of penetration.

Two outputs are available from a RGPD. One is an audible signal that represents the frequency shift. This audio signal is in the range of 400 Hertz to 5 KiloHertz and corresponds to the spectrum of Doppler shifts produced by normal or disturbed flow (19).

The audible signal is a frequency modulated output of the instrument based upon the returned Doppler signal and is not a representation of heart sounds heard by the stethoscope. Disturbed and laminar flows have different auditory characteristics that in some ways resemble those heard during auscultation, but it is important to realize that the auditory display of Doppler velocity contains information (frequency shifts) different from that obtained by auscultation.

The second output available is a recordable time interval histogram (TIH) (22). It is formed as a series of samples recorded, in our case at a rate of 4 KiloHertz. The pattern is derived by measuring the time between successive zero crossings of the audible signal waveform. A zero crossing is defined as the point of time when the Doppler shift signal passes through its zero intensity level. A data point is printed on the paper for each zero crossing event such that the distance of a particular point above or below the zero flow velocity baseline is directly proportional to the Doppler shift frequency (fig. 3).

Any point printed above the baseline (positive) represents relative blood velocity towards the transducer and, conversely, any point printed below the baseline (negative) represents flow velocity from the transducer (20).

This Doppler output has an additional important characteristic. Normal or laminar and abnormal or disturbed flows can be separated by evaluating the frequency analysis of the Doppler time interval histogram. Since most red cells in smooth flow at a given location move approximately at the same velocity and in the same direction, a narrow band of points (frequencies) will be inscribed on the TIH. When a flow disturbance exists, the red cells move in different directions and at different velocities creating a disorganized pattern. The examiner's decision must be based on differentiating these two patterns (20). However, some cut-off point between normal and abnormal is necessary (fig. 4). It was determined with ATL instrumentation that a non transient frequency width greater than 1 cm (on the paper) did not occur in the tracings of normal children. So it was decided to classify the TIH with frequency dispersions less than 1 centimeter in width as normal and the

TIH with frequency dispersions greater than 1 centimeter as abnormal (13).

Strip chart records contain simultaneous recordings of:

1. the M-mode display of the received Doppler signal with a superimposed line indicating the location of the sample volume at any particular time;
2. the time interval histogram of the Doppler signal;
3. a standard electrocardiogram for time references and;
4. the signal strength indicator demonstrating that Doppler gain is appropriately adjusted.

This last parameter is of particular importance in a correct Doppler echocardiographic interpretation. To find the best signal in each instance the Doppler gain is set to show peaks and valleys. Peaks indicate the level of the Doppler signal and valleys indicate limited or low noise during other times. For correct application of the zero crossing technique well defined gain setting is required. The Doppler gain is optimally adjusted when peaks reach full amplitude (halfway, between the bottom of the signal strength indicator and the zero amplitude line on the time interval histogram). However, care should be taken to discard a flat topped signal strength indicator (fig. 5).

II.2. Definitions

Range gating:

The method used to place the sample volume in the desired flow cavity is known as range gating. This is accomplished by electronically rejecting all Doppler signals (range gating) except for an area (2x4 mm) which can be selected anywhere along the beam.

Velocity profile:

It will be shown that clinical useful results may be obtained under the assumption that, in non disturbed flow, red blood cells in chambers or vessels move with a relatively flat velocity profile. This means that the velocity of cells across the stream is relatively uniform at any single point in time. However, the velocity at the interface of the blood and the chamber or the vessel wall is slower than the velocity in the central part of the stream.

Velocity direction:

With Doppler ultrasound techniques the velocity vector can only be measured in the sound beam direction. If the Doppler shift is positive, flow is towards the transducer and vice versa, if the Doppler shift is negative, flow is away from the transducer.

Velocity magnitude:

The magnitude of blood velocity, as sensed by Doppler is a function of the cosine of the angle, at which the flow is intercepted by the Doppler beam. For M-mode Doppler, this angle is unknown. Therefore, the magnitude of the blood velocity is not determined in this investigation.

Laminar and disturbed flow:

With ATL instrumentation, it was observed that a non transient frequency width greater than 1 cm (on the paper) did not occur in the tracings of normal children. Accordingly, the TIH with frequency dispersions less than 1 cm in width (amplitude) were classified as corresponding to laminar flow and the TIH with frequency dispersions greater than 1 cm in width (amplitude) as corresponding to disturbed flow (fig. 4). The term "flow disturbance" has been used instead of "turbulence", since turbulence was not measured. The latter term is usually defined as a deviation in the relationship of flow and pressure gradient in a rigid tube. Since turbulence along these lines was not an issue in this study the term "flow disturbance" (16) was preferred.

Series effect:

Once blood flow is non laminar, it will continue as non laminar flow until rheologic factors convert it back to the laminar state or, until the flow stops as the result of the cardiac cycle. Thus, the characterization of a flow pattern resulting from a second serial obstruction may be misleading (17).

The induction effect:

Under a set of conditions, a flow disturbance can be detected in a great vessel even though no obstructive lesion in the vessel is present. This may occur when an obstruction in the right or left heart produces a flow disturbance in its contiguous vessel.

Vortex shed distance:

In some instances, the first recording of a flow disturbance occurs not at the primary site of a defect, but rather downstream at a secondary or tertiary observation site. This effect occurs when the jet created at a restricted orifice does not shed the vortices for some distance, until the jet enters a secondary observation site (17).

Chapter III

III.1. Instrumentation and techniques

The methodology used in this investigation was the same in all studies (13).

Each child as assigned a number and all information regarding that child was collected and analysed under that number. Examiners were unfamiliar with the children and their diagnoses. Children were studied without sedation. Instrumentation consisted of an ATL 500 A* (* Advanced Technology Laboratories, Bellevue, Washington) echocardiograph and a Honeywell 1856 ultraviolet recorder. This instrumentation package included a second generation TIH output. Other outputs were an ECG lead recorded for time reference and a 3 cm wide M-mode recording. The purpose of the M-mode was to locate the Doppler signal. No expanded M-mode trace was performed. All children were studied with a 3 MegaHertz transducer that provided both Doppler and M-mode signal. The range gating feature allowed the operator to sample the Doppler signal at any desired depth. That depth was depicted as a spike on the A-mode and as a line on the compressed M-mode display. Standard M-mode controls allowed usual adjustments for that display. Doppler controls included threshold, signal level (reject) and baseline. Threshold was non-critical and was permanently set to the highest value, eliminating most background noise. Signal level is basically an indicator of Doppler gain control and input voltage level to the TIH analyzer. This input signal to the TIH was presented on the oscilloscope. Doppler gain was set according to this indicator to show peaks. Excessive Doppler gain caused noise without distinct peaks and resulted in uniform widening of the TIH to about 7,5 mm (on the paper). Too low a setting of Doppler gain resulted in absence of peaks, which consequently caused the TIH to become flat. Between these two extremes the exact setting was not critical.
It required frequent checking and adjusting in each new cardiac location.

An additional control, called "baseline" was unrelated to the line level indicator and was permanently set in the uncompressed state.

In many ways the examination performed was similar to that for a standard precordial and suprasternal echocardiogram (25). Principal differences between M-mode and echo-Doppler examination are:

1. The M-mode tracing is optimal when the reflecting structure is perpendicular to the beam. The highest Doppler signal is theoretically measured if the beam is aimed along the blood velocity vector. Accordingly, the examiner is forced to compromise in each case, in order to obtain the most optimal result.

2. For echo-Doppler, the M-mode output is used exclusively to document the location of the Doppler signal.

3. The Doppler signal is sampled from intracardiac locations that are as free as possible of valve leaflets and walls or septa. These locations may not be classical M-mode sites, but are contained in the heart chamber in question.

The M-mode position was used to identify the site from which the Doppler signal was sampled, and this location was designated on each recording as a straight line within the M-mode record.

During echo-Doppler examination an audible signal represented the Doppler frequency shift. In the investigations presented that signal was used exclusively to find a position in the chamber in question which was free of interfering structures and, at times, to locate the best area for recording the TIH.

Audible signal information was not used to classify the TIH since it was not available when the tracings were reviewed. Moreover it would have introduced a subjective element to the study.

Interpretation of numbered tracings was accomplished by classifying the TIH for each location and phase of the cardiac cycle as laminar or disturbed.

In order to be classified as laminar, the amplitude of the frequency dispersion at any location or portion of the cardiac cycle at least have a width less than 1 cm. Transient dispersion of the 1 cm amplitude due to a valve crossing the sample volume was disregarded (13).

Each record was assessed independently by two observers. Results of each observer were recorded with the examination number. The control code was broken by matching the TIH results to the previously established diagnosis.

In some studies, we used the X^2 test for the statistical evaluation of diagnostic accuracy.

III.2. Population

Our study population consisted of children with different forms of congenital and acquired cardiac malformations who had satisfactory echo-Doppler tracings at Sophia Children's Hospital in Rotterdam.

We conducted our investigation by using the time interval histogram (TIH) output of a range gated pulsed Doppler (RGPD) to suggest different forms of cardiac malformations. In each of the following studies the examiners were unfamiliar with the children or their diagnoses. Records were coded with numbers to achieve anonymity.

Study 1

The aim of this study was to determine the accuracy of TIH of RGPD echocardiography for detecting obstruction to the pulmonary outflow tract in children with d-transposition of the great vessels (d-TGV). Twenty one children were selected from those available with d-TGV and were studied by precordial and suprasternal RGPD echocardiography.

Study 2

The primary purpose of this study was to select, by examination of TIH output of RGPD, all children with left to right atrial shunts, from a pool of 57 children with and without left to right shunt. A secondary purpose was to identify associated lesions in those children with atrial septal defects.

Study 3

In this study the accuracy of the TIH of the RGPD as a means to detect cases with pulmonary stenosis from a pool of 66 children was determined.

Controls consisted of normal children and a group of other children with non-cyanotic forms of congenital or aquired cardiac malformations.

Study 4

The primary purpose of this study was to select all children with left ventricular outflow tract obstruction (LVO) from a population of 45 children with various forms of congenital heart disease. A second objective was to localize the site of the obstruction in those children with LVO tract obstruction. The experimental group consisted of 15 children with aortic stenosis and the control group consisted of 7 children with secundum atrial septal defect, 12 with isolated pulmonary stenosis and 11 with ventricular septal defect.

Study 5

Previous studies demonstrated that frequency dispersions found in transverse aortic arch, ascending aorta or right pulmonary artery, which should indicate flow disturbances in those areas, occurred in a set of lesions which did not involve the expected cardiac anatomic abnormalities.

In this study all documented cases were reviewed in which echo-Doppler had been obtained (N=127), in order to select all the lesions which caused aortic flow disturbance. Our purpose was to learn the range of false positive diagnoses obtained by analysing the frequency dispersions of the TIH of RGPD in transverse aortic arch, ascending aorta or right pulmonary artery.

Study 6

To investigate the clinical incidence and significance of the series effect and vortex shed distance, two phenomena detected by echo-Doppler examination in the previous studies, the echo-Doppler records of 47 children with various forms of congenital cardiac disease were studied.

Study 7

In the atrial septal defect study mitral regurgitation could not be detected in some patients with mitral valve prolapse syndrome and endocardial cushion defects. To discern the range of false negative mitral regurgitation diagnosis the sensitivity of RGPD was tested in order to separate children with a variety of causes of proven mitral insufficiency from an additional pool of 49 children who had various other forms of acyanotic heart disease.

Chapter IV Results

IV.1. Study 1

Pulmonary stenosis in patients with d-TGV

Population

Twenty one children comprised the original group. One was excluded because of lack of cooperation. Another was excluded because the status of the outflow tract was uncertain at the time of catheterization. A third child with a Pott's anasomosis was excluded because the origin of an abnormal pulmonary artery TIH could not be determined by the Doppler examination. An adequate examination was possible in each of the remaining eighteen children. Subjects ranged in age from 12 months to 13 years. The two observers classified the selected patterns identically. No finer gradation than the two patterns of flow was attempted: laminar or disturbed flow.

Doppler results

Eleven children had normal pulmonary outflow tracts (table 1). Ten of these were correctly classified by the RGPD technique and criteria that were applied. One child with a normal valve at pre- and post-operative catheterization was misclassified. The reason for this misclassification was not apparent.

Seven of the children had pulmonary stenosis, 4 valvular, 3 subvalvular (table 1). In each instance the presence and site of the first obstruction was correctly identified. One child (no. 4) had more than one level of obstruction. The second level, in the pulmonary artery, could not be differentiated from the first which occurred at the subvalvular level.

Although two patterns of disturbance were identified in this study, (mild and severe) we concluded that it would be more appropriate to classify them merely as abnormal since no data exist to prove that they indicate a different origin. Examples of each pattern are shown in figs. 6 to 8.

IV.2. Study 2

Atrial septal defect detection

Population

Control group: the control group, aged three months to nineteen years, consisted of three normal children, fifteen with isolated pulmonary stenosis, fifteen with ventricular septal defects and ten with mitral insufficiency.

Experimental group: the experimental group consisted of eight children with secundum atrial defects and six with endocardial cushion defects. Of the latter group, four had the primum form and two had the complete form.

Confirmatory data

Control group: thirty of the forty-three control children underwent cardiac catheterization. Three who had not been catheterized were normal, healthy children. Five others with mitral insufficiency had echocardiographic and physical examination, rather than catheterization confirmation, of mitral prolapse. Six remaining controls without catheterization had their diagnoses based on clinical findings alone (two with ventricular septal defects, two with mitral insufficiency and two with valvular pulmonary stenosis). None of the children had evidence of an atrial septal defect.

Experimental group: thirteen of fourteen children had cardiac catheterization and angiographic evidence of left to right shunt at the atrial level. Catheterization data are shown in table 2. One child, no. 10, was not catheterized but had classical clinical, electrocardiographic, and two-dimensional echocardiographic evidence of an endocardial cushion defect (26) with left to right shunt at the atrial level.

The examination

The examination proved only slightly more difficult than a standard pediatric M-mode study. The usual examination time was ten to twenty minutes. The Doppler portion of the examination was displayed in two ways. It was found that the M-mode echocardiogram, as available on the Doppler display, was of non-diagnostic quality because (1) it was compressed into approximately 2 cm of the vertical axis and (2) the oscilloscope intensity had to be increased more than normal to register the TIH display. Thus, this M-mode was of no diagnostic assistance.

A useful Doppler signal could routinely be obtained from all locations except the left atrium as imaged from the suprasternal notch. Occasionally, in this location, the Doppler signal was no greater than the noise level. An acceptable Doppler examination was recorded from each child.

Doppler results

The specific objective in this investigation was to determine the presence of an abnormal TIH for the right atrial outflow area (fig. 9 and 10) and for those children who demonstrated this finding, a second objective was to attempt to identify any associated lesions.

Control group: None of these children showed an abnormal diastolic TIH for the right atrial outflow. In two subjects (1 VSD, 1 Pulmonary stenosis) a systolic disturbance of a magnitude too low to classify as definitely abnormal was found by one examiner. These were the only findings in the control group related to the right atrial outflow.

Experimental group: (table 3) All fourteen subjects with left to right atrial shunts were detected by study of TIH but not by each examiner. One examiner failed to detect the diastolic disturbance of patient no. 7. This child had the smallest calculated left to right atrial shunt of the group (QP:QS=1.5:1) besides which, flow disturbance by Doppler was the least for the group. This case has been regarded as a false negative finding. Systolic right ventricular outflow disturbance was found by both examiners in four of eight children with secundum defects and one of the examiners noted a similar flow disturbance in an additional child. No disturbances were found in the main pulmonary artery in this group, not even in one child who had a 36 mmHg pressure difference across the valve. However, both examiners found a right pulmonary artery disturbance in that child as well as in another child who had a 12 mmHG pressure difference across the pulmonary valve. Two additional children were found by one examiner to have a right pulmonary artery flow disturbance.

Children with endocardial cushion defects showed a much greater tendency to an abnormal TIH. Half of the children had an abnormality in the right ventricular body TIH judged by both examiners. Children no. 9 and no. 13, who had demonstrated pulmonary valve stenosis, had an abnormal main pulmonary artery TIH, but patient no. 13, who had a 13 mmHg pressure difference at catheterization was judged to have a disturbance by only one examiner. More important was the fact that only three of the children were demonstrated to have left atrial flow disturbance, but all five catheterized patients were shown on angiography to have some degree of mitral insufficiency. The most severe regurgitation occurred in patient no. 7. The remainder, nos. 11-14, showed mild regurgitation based on left ventricular contrast injection. These cases have been regarded as false negative findings for mitral insufficiency.

Observer agreement (table 3)

In the control group, presence or absence of a diastolic right atrial outflow disturbance in the TIH was regarded as the only agreement pertinent to this report. No disturbance was found in any control, so exact agreement was present in 43 instances.

For children with left to right atrial shunts, an additional objective was to define any coexisting lesion. Accordingly, the entire echo-Doppler examination was evaluated. This required 308 decisions (11 cardiac areas x 2 phases of the cardiac cycle x 14 patients). Two hundred and ninety-eight decisions were similar and ten were dissimilar resulting in an agreement percentage of 96.75. However, one critical disagreement occurred, the failure of one examiner to detect one instance of right atrial outflow disturbance.

Statistical test

The X^2 test was used to determine the probability that the diagnostic classification was achieved by chance alone. The chance probability value for the results of either independent examiner or the combination of the two was p<0,0001.

IV.3. Study 3
Detection of pulmonary stenosis

Population

Controls: Controls consisted of 3 normal children, 7 children with mitral insufficiency, 8 children with aortic stenosis, 5 children with tricuspid insufficiency due to the Ebstein anomaly, 13 children with atrial septal defect.

Valvular pulmonary stenosis (VPS): The experimental group consisted of 14 children with isolated VPS.

Confirmatory data

Controls: All but one of the children in the control group had no evidence of pulmonary stenosis confirmed by right-heart catheterization. The remaining child with an endocardial cushion defect had two-dimensional echocardiographic evidence of isolated mitral valve prolapse.

Pulmonary stenosis: Thirteen of 14 children with pulmonary stenosis had cardiac catheterization confirmation (table 4). The child without catheterization had classic physical, roentgenographic and echocardiographic evidence of VPS. One child with VPS also had a secundum atrial septal defect.

RGPD examination

An adequate examination was obtained for each control and experimental child, and no child was excluded to obtain this result. It was possible to place the Doppler sample volume in each chamber and great vessel. The use of Doppler frequency assisted in localizing the pulmonary leaflet, for it could be heard and detected on the TIH as it crossed the Doppler beam at a time before the leaflet was imaged. Additionally, by observing the RGPD output, it was possible to be certain that the echo beam remained within the main pulmonary artery, above the leaflets, when the M-mode echocardiogram of this area was less helpful.

RGPD results

The objective of the RGPD evaluation was to confirm or to rule out VPS. A child was judged to have no pulmonary stenosis by Doppler examination if no flow disturbance originated in the pulmonary artery or its right branch. That child was classified as a control. Children with flow disturbances originating in the pulmonary artery or its right branch were classified as having pulmonary stenosis. For the pulmonary stenosis group, a second objective was to determine if other lesions coexisted (figs. 11 a, b, c and d).

Controls: Three false positive cases of VPS were encountered in this group. Two controls with valvular aortic stenosis had disturbed flow in the pulmonary artery. The third was a patient with ventricular septal defect. These false positive cases will be discussed in more detail later. Twenty three controls had right ventricular flow disturbance, and in 16 of the 23 this continued into the main or right pulmonary artery. These were classified as series disturbances, as the disturbance originated proximal to the pulmonary valve and continued into the pulmonary artery. Thus, they did not meet VPS criteria. However, one child had a flow disturbance that appeared to originate in the right pulmonary artery. This case was the third false positive for pulmonary stenosis.

Pulmonary stenosis: In the pulmonary stenosis group (table 5), disturbed flow was found in the main or right pulmonary artery by both examiners in 13 of 14 children. Only one examiner detected disturbed flow for patient 11; this patient represented a false negative for one examiner. Patient 6 had an atrial secundum defect, and this accounted for the diastolic disturbance in right atrial outflow and the minimal but definite systolic disturbance in the right ventricular outflow tract. No transmitted disturbance was found in the main pulmonary artery. However, in the right pulmonary artery, a second and much greater disturbance was found. The second flow disturbance was interpreted as resulting from pulmonary stenosis. Thus, each case of pulmonary stenosis was detected by one or both observers exclusively from examination of the TIH.

Examiner agreement

In the control group one of two examiners indicated pulmonary disturbance in two children with aortic valve disease. These constituted the only examiner disagreements for control subjects.

The problem of examiner agreement was somewhat more complex for patients with disturbances originating in the pulmonary artery or its right branch, since the second objective (defining coexisting malformations) required cataloging data for the complete Doppler study.

For those subjects, 308 decisions were required (11 cardiac areas x 2 phases of cardiac cycle x 14 patients); 305 of these decisions were identical, and 3 decisions differed.

Statistical evaluation of diagnostic accuracy

The X^2 test was used to determine the probability that the diagnostic classification was achieved by chance alone. The chance probability value for the results of either independent examiner or the combination of the two was $p<0{,}0001$.

IV.4. Study 4

Echo-Doppler in aortic stenosis

Population

Controls: The control group, aged two months to fifteen years, consisted of seven children with secundum atrial defect, eleven with ventricular septal defect, and twelve with isolated pulmonary stenosis.

Experimental group: This group consisted of fifteen children. Two different levels of LVOT obstruction were represented. Three had subvalvular aortic stenosis and twelve had valvular aortic stenosis.

Confirmatory data

Controls: The thirty children that served as the control group were previously catheterized. In each instance a positive diagnosis was established. None had LVOT obstruction as evidenced by left heart study.

Experimental group: Eight of fifteen children had cardiac catheterization and cineangiographic evidence of LVOT obstruction. Data are shown in table 6. The seven remaining children were not catheterized but had clinical signs, typical carotid pulse waveform, and two-dimensional echocardiographic evidence of LVOT obstruction. For the latter, the technique of Weyman and co-authors was used (27). Four of the fifteen children with cardiac catheterization showed angiographic evidence of aortic regurgitation. One uncatheterized child had clinical and carotid pulse tracing evidence of aortic insufficiency.

Examination

An adequate RGPD examination was possible in each instance. It was possible to place the sample volume in the desired area in each instance.

Doppler results

The specific objective of this study was to detect the presence of LVOT obstruction, and to locate the site of obstruction in those children who demonstrated this finding (figs. 12 a, b, c and d).

Controls: No control demonstrated evidence of LVOT obstruction by evaluation of the TIH of the RGPD.

Experimental group: Data are summarized in table 7. All fifteen patients with LVOT obstruction were detected by both observers who evaluated the TIH. In two instances (nos. 9 and 10) one observer did not detect aortic root flow disturbance but made the diagnosis from an abnormal pattern in the transverse aortic arch. In five patients LVOT diastolic disturbance of the TIH was found (fig. 13) by both examiners. Four patients (nos. 1, 6, 7 and 9) had evidence of aortic insufficiency as determined by other techniques. Additionally, systolic right ventricular outflow disturbance was found by both examiners in patient no. 2. This specific case will be discussed.

Two additional patients (nos. 3 and 4) were found by one examiner to have systolic flow disturbance in the main pulmonary artery or right pulmonary artery. These cases represented false positive findings of pulmonary stenosis. A systolic flow disturbance was found by both observers in the body of the left atrium of patient no. 5. This child underwent cardiac catheterization and left ventricular angiography, and the diagnosis of mitral regurgitation was confirmed.

Observer agreement (table 7)

No disturbance was found in any control in the LVOT; thus agreement was present in thirty instances. For children with LVOT obstruction 330 decisions were required (11 cardiac areas x 2 phases of cardiac cycle x 15 patients). Three hundred and twenty-two decisions were similar and eight were dissimilar. Agreement percentage was 97.6. No important disagreements were found.

IV.5. Study 5

Detection of aortic flow disturbances and interpretation of the findings

Population

One hundred ninety-six echo-Doppler studies were evaluated and one hundred twenty-seven of these had the correct criteria to enter the present study. Of those rejected, 35 were excluded because neither cardiac catheterization data nor operative confirmation of the diagnosis had been obtained. Twenty-eight additional records were rejected because of improper gain or threshold settings or M-mode tracings that were inadequate to designate the range gate locator position. The additional studies were excluded because one or both of the two areas of interest were not present in the record.

Interpretation of the accepted records

Normals: Sixteen normal individuals were evaluated and results are tabulated in table 8. Three were shown to be normal at cardiac catheterization and the remainder were normal healthy individuals without history or findings of heart disease.

Aortic root: The recorded systolic velocity signal was positive with respect to the transducer. A transient artifact was created by the aortic leaflet crossing the ultrasound beam at the beginning and the end of systole and was always present. During the deceleration phase (peak of the velocity tracing) a minor point dispersion was occasionally observable but this did not exceed 1 cm of vertical distance. In one subject dispersion for a definite short duration (25% of systole) was consistently present.

Transverse aortic arch: Recordings showed a high velocity, positively directed inscription. The amplitude was clearly a function of the transducer/vessel intercept angle. Valve crossing artifacts were absent. Minor point dispersions of less than 1 cm amplitude were usually present during systolic deceleration. None of the children of the control group demonstrated systolic dispersion greater than 1 cm amplitude.

Right pulmonary artery: Systolic velocity was usually positively directed, but with a change in transducer angle, negative velocities could also be recorded. Frequency dispersions greater than 1 cm were not recorded in a normal.

Forms of aortic stenosis

All 16 children with documented left ventricular outflow tract obstruction were detected by flow disturbances in the aorta and or transverse aortic arch (table 9). In one instance (no. 1), the flow disturbance was not found in the aortic root but was noted in the transverse aortic arch. In another, the opposite was true (no. 7). In the remainder, a flow disturbance was found in both ascending aorta and transverse aortic arch. In all instances, except patient no. 11 who had idiopathic hypertrophic subaortic stenosis and patient no. 6 who had a subaortic membrane, the flow, as judged by Doppler technique, was laminar below the aortic valve. However, patient no. 7, who also had a subaortic diaphragm, showed no flow disturbance below the aortic valve (fig. 14).

Patients no. 3 and no. 6 demonstrated a right pulmonary artery flow disturbance but cardiac catheterization failed to demonstrate a pressure gradient or a cineangiographic pulmonary outflow tract abnormality. These cases represented false positives for right ventricular outflow disturbance. Patient no. 11 also had a right ventricular outflow tract, main and right pulmonary artery flow disturbance, but in this child, a 20 mmHg pressure gradient was found at the right ventricular infundibular level as a consequence of the idiopathic hypertrophic subaortic stenosis.

Patent ductus arteriosus (table 10)

Eleven children with confirmed diagnoses were studied. All eleven had a flow disturbance in the right pulmonary artery. Of these eleven, nine also had flow disturbances in the transverse aortic arch and seven of those nine had flow disturbances in the aortic root. The two children who had no flow disturbance in either section of the aorta were not recognizably different from the other members of the group. These children had neither small shunts nor pulmonary vascular obstructive disease.

Ventricular septal defect (table 11)

Seventeen children had adequate records. Seven had a flow disturbance in the right pulmonary artery and two of these had a flow disturbance detected in the aortic root and transverse aortic arch. Cardiac catheterization in these two children failed to demonstrate a defect that was expected to cause a left sided flow disturbance.

Tetralogy of Fallot (table 12)

Of 12 children with tetralogy of Fallot, 4 were operated, 7 had prior Blalock-Taussig shunts, and one had a Waterston anastomosis. In 5 of the 12 children, it was not possible to find and/or record an adequate Doppler signal in the right pulmonary artery. In all of the other 7, a flow disturbance was uniformly found in the right pulmonary artery. Of those with no prior operation, 3 had flow disturbances in the transverse aortic arch and 3 had flow disturbances in the aortic root. However, all 4 had at least 2 of these disturbances noted. Of those with systemic-to-pulmonary artery shunts, all but one had a flow disturbance in the aortic root or transverse aortic arch. An example of flow disturbance in the aortic root is shown in fig. 15.

Pulmonary stenosis (table 13)

Eighteen children with pulmonary stenosis were evaluated. All eighteen had a flow disturbance distal to the pulmonary valve, but in two, it was found in the main pulmonary artery and not in the right pulmonary artery. Four demonstrated flow disturbances in the aorta. Three showed a flow disturbance in the aortic root and a fourth in the transverse aortic arch only. None of these children had cardiac catheterization evidence of any defect that would produce a left sided flow obstruction.

Atrial septal defect (table 14)

Sixteen children with atrial septal defect were included. Seven had a right pulmonary artery flow disturbance and one of these had a flow disturbance in the transverse aortic arch. None of these children had a left cardiac lesion.

Mitral disease (table 15)

None of the 10 children with mitral insufficiency had aortic, transverse aortic arch or right pulmonary artery flow disturbances.

Complex and other cardiac disease (table 16)

Eleven children had multiple defects or other lesions not previously categorized. Five of these had a flow disturbance in the great vessels. Two (nos. 3, 11) had aortic valvular stenosis to account for aortic root and transverse aortic arch abnormalities. Patient no. 3 had a ventricular septal defect which could account for the right pulmonary artery flow disturbance. The flow disturbances found in patients nos. 1, 2 and 4 could be excluded on the basis of the lesions.

Aortic and transverse aortic arch flow disturbances as a function of a right pulmonary artery disturbance

Forty-eight percent (23/48) of children with right pulmonary artery flow disturbances (excluding those with aortic stenosis and complex lesions) had secondary flow disturbances found in the aortic root or transverse aortic arch. The probability of detection of a disturbance in the aortic root or transverse aortic arch was much higher if aortic flow was high as was seen in children with patent ductus arteriosus (82%) or tetralogy of Fallot (89%) as compared to those with isolated pulmonary stenosis (22%) or atrial (7%) or ventricular septal defects (12%). When no right pulmonary artery disturbance was found in patients without left-sided obstructions, aortic root and transverse aortic arch disturbances were virtually absent. The only exception was a single nontypical short disturbance found in an apparently normal individual.

Right pulmonary artery flow disturbance as a function of transverse aortic arch disturbance

Two individuals (13%) with aortic outflow obstruction (one supravalvular and one subvalvular) had classical flow disturbances in the right-sided circulation as found by means of cardiac catheterization. None of the normal children demonstrated disturbed flow in the right pulmonary artery.

IV.6. Study 6

Detection of series effect and vortex shed distance

The flow model construction and its results were previously published (17). It must be stressed that for the purpose of this investigation the series effect and the vortex shed distance were verified by direct visualization in the in vitro plexiglas model.

A total of 47 patients met all criteria to be included into this study. Echo-Doppler results are displayed in fig. 16. Nine patients with ventricular septal defect, 14 with atrial septal defect, 14 with pulmonary stenosis and 10 with aortic stenosis had echo-Doppler examinations that provided acceptable tracings of at least a primary and secondary downstream site in which disturbance, if present, could be detected. Abnormalities, such as mitral insufficiency, could not be evaluated since the secondary M-mode imaging site, i.e. the pulmonary veins was not available. Flow disturbances were found by echo-Doppler examination in all 47 patients who qualified for this examination yielding an echo-Doppler flow disturbance detection rate of 100% (fig. 16). However, in 9 patients, the flow disturbance was not detected in the primary site, that is, the first chamber in which a flow disturbance would be expected. In these 9 patients (7 with pulmonary stenosis, 1 with valvular aortic stenosis and 1 with subvalvular aortic stenosis) the flow disturbance was initially observed distal to the area of the cardiac defect at the secondary site.

The series effect, defined as disturbance of flow detected at a primary and downstream site, was observed in 57% of ventricular septal defect patients, 100% of subvalvular and valvular aortic stenosis patients, 86% of pulmonary stenosis patients, 50% of secundum and 83% of primum atrial septal defects patients. Flow disturbances were detected at the primary site and not at a secondary site in 10 patients (2 with pulmonary stenosis, 3 with ventricular septal defects, 4 with atrial secundum defects, and 1 with a primum defect). Accordingly, it was more common to detect patients who had evidence of a series effect than to detect those with a flow disturbance only at the primary site.

IV.7. Study 7
Detection of mitral regurgitation

Population

Controls: The control group, aged two months to fifteen years, consisted of twelve children with ventricular septal defects, fifteen with pulmonary stenosis, fourteen with aortic stenosis, and eight with secundum atrial defect.

Mitral insufficiency group: This group consisted of seventeen children. Seven had rheumatic mitral regurgitation, four had mitral valve prolapse, and six had endocardial cushion defects.

Diagnositic confirmatory data

Controls: The forty-nine children who served as the control group were previously catheterized. In each instance, a definite diagnosis was established. None had evidence of mitral insufficiency from evaluation of the left heart by cardiac catheterization and angiography.

Mitral insufficiency group: Seven children with rheumatic mitral insufficiency had cineangiographic evidence of mitral regurgitation. In each case, the mitral insufficiency was felt to be primary and not induced by catheter position. All five children with endocardial cushion defects had cineangiographic evidence of mitral insufficiency and left-to-right shunt at the ostium primum level.

The four remaining children were not catheterized but had clinical and echocardiographic evidence (36) of mitral valve prolapse.

Echo-Doppler examination

An adequate range gated pulsed Doppler examination was possible in each instance. In each patient, an adequate M-mode examination for range gate location was possible.

Echo-Doppler results

The specific objective of this investigation was to determine whether or not an abnormal time interval histogram of the left atrium was present as demonstrated by frequency dispersion (fig. 17). Directional flow and attempts at quantification were not considered in this study

Control group: None of the control patients demonstrated a significant time interval histographic frequency dispersion in the left atrium.

Mitral insufficiency group: All seven subjects with rheumatic mitral insufficiency had a significant left atrial dispersion of the time interval histogram. Systolic left atrial inflow disturbance was found by both examiners in two of four children with mitral valve prolapse, but by only one examiner in the other two children. Both observers found a systolic left atrial time interval histographic disturbance in only one of five children with endocardial cushion defects.

Observer agreement

Two left atrial areas were evaluated for each patient, one recorded from the precordium and the other from the suprasternal notch.

Accordingly, 132 decisions were required for the 66 participants. In two cases, a different interpretation was made by the two examiners yielding an agreements percentage of 98%. No important disagreement was found that would alter the correct diagnosis in a control child. However, one of the two observers failed to detect a left atrial systolic flow disturbance in two children with mitral valve prolapse. This finding would have altered the diagnosis on the basis of range gated pulsed Doppler investigation of these two children.

Chapter V Discussion

Pulsed Doppler systems appeared some years after the first blood velocity measurement by Doppler detection of red cells movement (28). Despite the introduction in 1973 of the combination of the range gated pulsed Doppler (RGPD) with M-mode echocardiography (29) most prior clinical studies were performed in peripheral vascular applications (30-32).

In clinical cardiology, RGPD was used to diagnose morphological heart disease but virtually all attention had been focused on the audible output which represents the Doppler frequency shift (33-34).

Pulmonary stenosis in patients with d-TGV

Our first study was performed in order to assess the reliability of the recordable output of RGPD, the time interval histogram (TIH), for seperating children with pulmonary outflow obstruction in d-transposition of the great vessels.

For the purpose of this study the term "pulmonary outflow tract" was used with reference to the area located from the left ventricular outflow tract up to the pulmonary artery and its right branch. Although the different types of LVO obstruction are numerous (35), they can be generally classified as subvalvular, valvular or supravalvular. This classification is functional for purposes of Doppler evaluation, since the individual lesions are recognized only by their location.

The population had been previously studied and their diagnoses were established by pressure recording across the area of interest by means of cardiac catheterization, angiography, and in most cases, results were confirmed by direct observation and examination of the pulmonary outflow tract at operation.

In this study the criteria for flow disturbances were established and tested by classifying the TIH as laminar or disturbed.

Another important outcome of this first study was that independent examiners who were unfamiliar with the children and their diagnoses could ascertain approximately the same information from the Doppler record. This similarity of conclusions established the objectivity of TIH analysis. It was also shown that a frequency dispersion of 1 cm of the TIH was abnormal and smaller dispersions were normal. Since the areas examined in this study produced strong Doppler signals and were among the simplest to classify it was necessary to evaluate other areas of the heart which could prove to be more difficult. For this reason additional studies were performed to assess the reliability of TIH information.

Atrial septal defects

The atrial septal defect study, demonstrated that apart from the ability to detect a specific lesion (i.e. an atrial septal defect) Doppler could also help to diagnose additional heart defects. Thirteen of fourteen children with atrial septal defects had their diagnoses confirmed by detection of right atrial outflow diastolic disturbances. The differential diagnosis of the right atrial diastolic outflow disturbance must be considered. The abnormal echo-Doppler examination indicated only increased flow through the tricuspid valve, so the precise entry site of the left-to right shunt was not detected by this investigation. Entry sites could have included an atrial septal defect, anomalous pulmonary venous connection to the right atrium or any other form of anomalous coronary drainage into the right atrium. A ruptured sinus of Valsalva or a left ventricular - right atrial shunt would probably have produced a systolic disturbance in addition to that in diastole and would have been expected by means of RGPD examination. The Ebstein abnormality has not been confused with atrial septal defects since the principal flow disturbance in Ebstein's abnormality is systolic. True tricuspid stenosis would not have been distinguished from a disturbance due to a left-to-right atrial shunt by Doppler alone. An M-mode examination might separate the two entities (37). In the present study the failure to recognize mitral insufficiency in three patients by means of Doppler is a matter of concern. The child with the greatest insufficiency as found by angiography (patient 9) was recognized by both observers. The other four catheterized patients each had mild mitral insufficiency but only two of them were detected by means of RGPD. The degree of insufficiency of the uncatheterized patient was unconfirmed. Johnson and co-workers have indicated that they detected 28 of 32 instances of confirmed mitral regurgitation (34). However, no indication was present that any of these had insufficiency on the basis of a cleft leaflet. Investigation into detection of disturbance on cleft mitral leaflets was indicated and this was one of the purposes of the later mitral regurgitation study.

This study opened several questions; the two most important were: (1) are flow disturbances found beyond the chamber where they are created and (2) why is mitral insufficiency missed in some patients with mitral clefts? Those questions were answered in studies 5, 6 and 7.

Pulmonary stenosis

This investigation was considered as a validation of the usefulness of RGPD for detecting systolic flow disturbances close to the transducer. Detection of valvular pulmonary stenosis by noninvasive testing is a difficult problem. Previous echocardiographic studies did not solve the problem. Weyman and associates published their experience with M-mode echocardiographic detection and showed that a deep pulmonary "a" wave occurs in patients with VPS (38). However, Goldberg and associates found numerous children with VPS who do not have a deep pulmonary valve "a" wave (39). Moreover, the pulmonary valve may be difficult or impossible to image by M-mode echocardiography in patients with severe pulmonary stenosis or hypoplasia. Feigenbaum reported that doming of the pulmonary valve may be imaged by two-dimensional echocardiography in patients with VPS but the clinical usefulness of this method remains to be confirmed (40). Detection of pulmonary stenosis by RGPD has previously been reported for one patient (29). Baker and associates indicated that a broad-band pattern could be detected on the TIH in pulmonary stenosis, but they presented no data (20). In the present study disturbed flow was found in the main or right pulmonary artery, by both examiners, in 13 out of 14 children. Only one examiner detected disturbed flow in patient 11; this patient represented a false negative finding for one examiner. Patient 6 had an atrial secundum defect, and this accounted for the diastolic disturbance in the right atrial outflow and the minimal but definite systolic disturbance in the right ventricular outflow tract. No transmitted disturbance was found in the main pulmonary artery. However, in the right pulmonary artery, a second and much greater disturbance was found. This second flow disturbance was interpreted as resulting from pulmonary stenosis. For the controls, one of two examiners indicated pulmonary disturbance in two children with aortic valve disease.

Twenty-three controls had right ventricular flow disturbances and in sixteen of the twenty-three this was detected in the main or right pulmonary artery.

Important features were noted from this study. It was proven that independent examiners who were blind to the diagnosis were able, by examining a pool of unordered numbered TIH tracings, to separate patients with pulmonary stenosis from those with other cardiac malformations. The valvular stenosis was mild to moderate in all circumstances and the pressure difference across the obstructed area ranged from 11 to 60 mmHg. Mild instances of VPS frequently present diagnostic problems for other noninvasive techniques but the present data suggest that RGPD accurately detects most cases of mild VPS. Perhaps the most important feature found in this study was the demonstration of the vortex shed distance. In seven cases of pulmonary stenosis, pulmonary disturbance was not detected in the main pulmonary artery but was recognizable in the right pulmonary artery. This fact was of concern and indicated that when blood crosses the stenotic orifice the jet remains laminar until vortices begin to shed. If the vortex shed distance is long enough to reach a secondary site, the primary site may be effectively masked. In this instance, the echo-Doppler frequency analysis will show no disturbance at the primary site and initial disturbance at the secondary site. Although this priniciple is known in hydraulics, it had not been significantly applied to clinical medicine. This observation emphasizes the need to evaluate events occurring at the pulmonary valve via the suprasternal notch approach. It also suggests that supravalvular stenosis will be difficult to separate from valvular stenosis by RGPD.

A major disadvantage of RGPD that evolved from the present study was that in most instances, only the first of two obstructions in a series can be detected. The reason for this finding is that disturbance in flow is not quickly damped. A second obstruction in series that produces further disturbance will probably not be recognized if it is physically close to the first and if the blood remains in motion past both obstructions. The detection of series flow disturbance was encountered in the 16 controls in whom TIH tracings were recorded above and below the pulmonary valve. However, none of these had evidence of pulmonary flow obstruction at catheterization. In one instance (patient 6) a small disturbance was found in the right ventricle, and a major one was found in the right pulmonary artery. Because of the significant differences, the greater disturbance in the right pulmonary artery, was considered to have a different cause from that in the right ventricle. In two instances, controls with aortic stenosis had pulmonary artery TIH tracings that were interpreted as indicating flow disturbances. These instances were false positive findings. It was important to know whether the false positive results represented true disturbances in the pulmonary arteries or could be considered a judgement error. It is well established that pulmonary and aortic stenosis cause palpable thrills in the suprasternal notch (41). Anatomically, the right pulmonary artery and aorta are positioned against each other. In the instance of pulmonary stenosis, the suprasternal notch thrill is transmitted through the aorta in order to be palpable in the suprasternal notch. It remained unknown whether the aortic flow, in this circumstance, was completely laminar or some disturbance was induced by disturbance in the other vessel. The opposite situation, in which a disturbance in the pulmonary artery might be induced by disturbance in the aorta also remained unknown. In order to investigate the possible induction effect raised in the present study and in order to confirm the vortex shed distance and the series effect additional studies were performed: one on patients with outflow obstructions of LVOT, a second on patients with lesions that cause aortic flow disturbances and a final one in order to confirm the dynamics of the series effect and the vortex shed distance.

LVOT obstructions

This study was performed to detect the presence of LVOT obstruction, and for those children who demonstrated that finding to locate the site of obstruction. Our study group contained patients with valvular and subvalvular stenosis. All fifteen patients with LVOT obstructions were detected by both observers who evaluated the TIH. In two instances (nos. 9 and 10) one observer dit not detect aortic root flow disturbance but reached the diagnosis by observing an abnormal pattern in the transverse aortic arch. This was still another example of a vortex shed distance. As a result of the vortex shed distance concept it was only possible to isolate those children with LVOT obstructions, but the exact site of the obstruction could not be correctly determined.

The identification of disturbed flow in the transverse aortic arch showed the series effect once again and emphasized the necessity of including flow patterns from all ultrasonically available cardiac areas in order to avoid misdiagnosis.

To investigate and confirm the presence of an induction effect as suspected in the previous studies an additional investigation was performed concerning flow disturbances in the aortic root.

Aortic flow disturbances

To learn the range of the induction problem all the documented cases in which an echo-Doppler had been obtained were reviewed (N=127). For the purposes of this study only cases that: (1) had satisfactory echo-Doppler tracings recorded at Sophia Children's Hospital in Rotterdam or at University of Arizona Hospital, and (2) had positive confirmation of the status of the left ventricle, the left ventricular outflow tract, aortic valve and aorta by cardiac catheterization, were used. For infants and children with patent ductus arteriosus, confirmation was also permitted by operation, provided that these children demonstrated no positive physical findings of other cardiac lesions. The reason why patients with different morphological forms of heart lesions were included in this study was that a number of children with patent ductus arteriosus and tetralogy of Fallot demonstrated unexplained aortic flow disturbances (42). Following operation, these disturbances disappeared. It seemed possible that the flow disturbance in the aortic root and transverse aortic arch might have resulted from high blood flow secondary to the ductus arteriosus or the right-to-left shunt in tetralogy patients. However, it soon became apparent that this phenomenon also occurred, although less frequently, in situations that were not associated with high aortic blood flows. This finding was proven in the pulmonary valvular stenosis study in which flow disturbances in the aorta did not correspond to anatomic abnormalities detected by cardiac catheterization. The present study demonstrated that all instances of false positive appearances of flow disturbance in the aortic root or transverse aortic arch were detected in patients with flow disturbances in the pulmonary artery. However, only 48% of patients with pulmonary artery flow disturbances showed additional disturbances in the aorta. Additionally, two cases were found in which flow disturbance in the aorta may have induced a secondary disturbance in the pulmonary artery. However, a cause and effect relationship cannot be concluded from these cases. Since echo-Doppler was used as a qualitative tool, it was not possible to determine whether ectopic appearance of the disturbance was a function of the magnitude of the disturbance at its origin or whether it occurred for another reason. The magnitude of dispersion in the pulmonary artery may appear larger or smaller depending upon the intercept angle of the Doppler gain with the flow direction. The closer the flow is to a Doppler intercept angle of 180^{o}, the greater the amplitude of recorded flow and the more apparent a flow disturbance. Since the range gated location was determined from an M-mode rather than a cross-sectional image, the angle was unknown. This lack of angular information makes a relationship between frequency dispersion and magnitude of flow disturbance totally qualitative.

An important feature resulting from the present study is that an aortic flow disturbance cannot be relied upon to indicate an obstruction in the left ventricular outflow tract unless no flow disturbance is found in the pulmonary artery. Although only two cases were available, the reverse phenomenon can also be predicted.

It is concluded that the range gated pulsed Doppler allows relatively reliable detection of flow disturbances created by obstructions in the left ventricular outflow tract. However, false positive findings occur and these are the result of flow disturbances in the right ventricular outflow tract. The disturbance in the right ventricular outflow tract, particularly when accompanied by an increased aortic valve flow, appears to cause a secondary disturbance in the aortic root and transverse aortic arch. Part of this disturbance may be an induction effect. This investigation demonstrates that caution is required in interpretation of range gated pulsed Doppler findings in the aorta. Moreover, the study predicts that quantification of flow by combining Doppler with two-dimensional echocardiography may be more difficult than expected in patients with cardiac disease. Quantification requires laminar flow, and laminar flow may not be present in some individuals as the result of induced disturbances, persistent flow disturbances beyond the site of origin. Artifacts caused by high flows at greater depth will also create errors in quantification. The lower pulse repetition rate required at greater depth does not allow the complete detection of the full Doppler shift when sampling occurs below the Nyquist rate.

Presently, combinations of range gated plus continuous Doppler are introduced to solve this problem.

Series effect and vortex shed distance

The previous investigation demonstrated that, although flow disturbances could be often detected at or near the site of cardiac abnormality, they could also be detected distal to that site. This observation was defined as "series effect", because flow disturbance was found at the primary site of the cardiac abnormality and continuation of that disturbance could also be recorded downstream at secondary or perhaps tertiary locations. In some instances, it was found that the first recording of flow disturbance occurred not at the primary site of a defect, but rather downstream at a secondary or tertiary observation site. This second effect, the vortex shed distance, occurs when the jet, created at a restricted orifice, does not shed the vortices until it enters a secondary observation site. The purpose of this investigation was to confirm the existence of these two observations in patients and in a flow model and to document their clinical evidence and significance in children with congenital cardiac disease.

The existence of the series effect, which was clinically suspected from several prior studies, was confirmed by demonstrating that, in a flow model, the flow disturbance which could be visually detected had significant length. This in vitro evidence correlated with findings from patients who demonstrated a high propensity for detection of flow disturbances only at secondary and tertiary, but not always at primary sites.

The importance of the vortex shed distance was also elucidated for 19% of the patients demonstrating a flow disturbance initially in a secondary area, probably as a result of a long vortex shed distance. Observations of flow characteristics by laser beams or particle injection are not unique but have initially been used for engineering purposes (43, 44). The flow model in the present study allowed correlation of echo-Doppler and visual observation of flow characteristics distal to an obstructive orifice. The combination of results from the two observational techniques suggests that flow disturbances which could be detected visually are sensed by echo-Doppler examination. Conversely, in areas where no flow disturbance was observed, the echo-Doppler result indicated presence of laminar flow. The presence of the series effect requires that interpretation of echo-Doppler results take this phenomenon into account. Additionally, it was proven that the length of the vortex shed distance may result in observation of disturbed flow initiating at a secondary or tertiary site, while laminar flow in the form of a jet persisted at the primary site.

Mitral regurgitation

This study was performed to evaluate the problem of attenuation of signals coming from a distant area, the left atrium. Previous reports of MR detection by echo-Doppler suggested the effectiveness of the technique but a range of causes of MR was not tested in those investigations. Abassi et al classified adult patients as rheumatic and non-rheumatic (45); the etiology of MR in the non-rheumatics is unclear but was indicated as noncongenital. The etiology of mitral regurgitation is unclear in the report of Stevenson et al: 40% were catheterized but no specific etiology was designated and, of the noncatheterized patients, 4 were indicated to have mitral valve prolapse without etiology being attributed to the remainder. In those studies, the investigators indicate that the patient had MR (45) or VSD (33). In contrast, the examiners in this study had no knowledge of the diagnostic mixture and the mitral insufficiency group contained patients with rheumatic mitral insufficiency, mitral valve prolapse and endocardial cushion defects. The results suggest that if the examiner has no reason to suspect that a given pastient has mitral insufficiency, the detection rate may be reduced. Rheumatic mitral insufficiency was relatively easy to detect by RGPD. However, detection of mitral regurgitation in mitral valve prolapse and in endocardial cushion defect appeared to be more difficult. Possibly, in these conditions, the flow disturbance is small or in a localised area of the left atrium that is so distant from the transducer that the echo-Doppler is relatively insensitive for detection. The distance between the disturbance and the transducer is critical because velocity detection decreases with increasing distances of the sample volume from the transducer. This factor reduces the possible frequency dispersion.

Failure to recognize mitral insufficiency in patients with endocardial cushion defects deserves comment. The pattern of mitral regurgitation in a cleft mitral valve is expected to be correlated with the anatomic derangement. The morphology of the ostium primum and the anterior mitral valve leaflet cleft is such that a jet of blood from the left ventricle may enter the right atrium (46). RGPD will detect flow disturbance only at the end of the jet, since the jet is usually laminar. If the jet is long, the flow disturbances might first be detected in the right atrium rather than the left in patients with combined mitral insufficiency and atrial septal defects. The five patients with endocardial cushion defects had left ventricular angiography which showed streaming of blood from the left ventricle into the right atrium. Atlhough a jet may be visible on angiography, it is usually difficult to determine with angiography where disturbed flow begins. Thus, a direct correlation between echo-Doppler and angiography regarding the initial point of a flow disturbance is not possible. In the present investigation flow direction was not evaluated and no attempt was made to gauge the regurgitant volume. Only with marked flow disturbance, an average flow direction could be determined in some patients with mitral regurgitation. Doppler direction is referenced with respect to the transducer, and M-mode transducer placement at the apex, aimed in the direction of the mitral ring, allows general flow direction to be determined. This directional technique is most effective in patients with rheumatic mitral regurgitation and an otherwise normal heart, but in patients with congenital cardiac disease, the spatial plane of the mitral valve is more variable. For this reason, any quantative regurgitation estimate by M-mode Doppler is hazardous.

In conclusion, these results suggest that rheumatic MR is relatively easy to detect by RGPD, because the disturbance is of large magnitude. Detection of MR in mitral valve prolapse syndrome may be difficult because the flow disturbance is small and may be localized in an area of the left atrium very distant from the transducers. The Doppler signal is attenuated by distance. Finally, the difficulty of MR detection in endocardial cushion defect emphasises the problem of the vortex shed distance discussed in the previous study. (The first flow disturbance did not occur in the left atrium.)

Summary and conclusions

With Doppler techniques information can be obtained on blood velocity. The method is noninvasive and well tolerated by the patient.

The principle is based on the determination of the frequency shift of a transmitted ultrasound wave, as it is reflected by red blood cells. The Doppler spectrum can be made audible, but its assessment is to some extent subjective.

This investigation was carried out with a new Doppler method, in which pulsed ultrasound was used and an approximate graphic display of the Doppler spectrum, via a time-interval-histogram, was made available. By using pulsed sound, the depth at which the velocity of the blood flow is measured, is known.

The time-interval-histogram method, based on "zero-crossing" technique, enables the examiner to make a distinction between a zone of laminar flow and a zone of "disturbed" blood flow.

The main feature of this investigation was to prove that independent observers, who were blind to the diagnosis, were able to separate patients with different forms of congenital and acquired cardiac malformations, by examining a pool of unordered numbered TIH tracings.

Patients with transposition of the great vessels with pulmonary stenosis were chosen for the first study. Knowledge of the presence of pulmonary stenosis complicating d-TGV is important in view of its surgical implications (47, 48). Furthermore pulmonary stenosis may develop or increase in severity at any time in the course of the disease (49, 50). M-mode echocardiography was chosen in combination with Doppler as a noninvasive test, which could follow the course of the disease. This was the first published study that demonstrated, under controlled circumstances, that the TIH alone contains the necessary information for detecting flow disturbance due to morphological heart defect. The criteria for flow disturbance were established and it was also demonstrated that two different examiners could get approximately the same information.

To assess the reliability of TIH at other areas of the heart a study of children with atrial septal defect was performed. The objectivity of the technique for detecting a specific lesion was confirmed and it was seen that Doppler could, at the same time, make the diagnosis of some other types of defects. The atrial septal defect study raised two important questions: (1) why were flow disturbances found beyond the chamber where they were created and (2) what caused the inability to detect mitral insufficiency in comparison with other investigations (33, 45). To look for an answer to the first question two investigations were performed: the pulmonary stenosis and the left ventricular outflow tract obstruction studies.

These studies confirmed the objectivity of TIH to detect stenotic areas. However, the site of the stenosis was difficult to find. Three issues were raised from these studies. First, if a flow disturbance was present in the outflow tract of a ventricle the status of the main vessel was difficult to determine by echo-Doppler examination unless the main artery patterns were normal. This finding was called the series effect and other studies were performed to confirm it. Secondly, if a flow disturbance occurred in the aorta, a false positive disturbance could be recorded in the right pulmonary artery. This feature was called the induction effect and the induction effect was confirmed with other studies. Finally, it was demonstrated that detection of the site of a pulmonary stenosis could present a significant problem for echo-Doppler, since a disturbance could be seen first in the right pulmonary artery or as far as the transverse aortic arch, even though it originated at the valve. This demonstrated the importance of the vortex shed distance. Two additional studies were performed, one in patients with flow disturbance in the aorta to investigate and confirm the induction effect and another study to confirm the dynamics of the series effect and vortex shed distance in a model.

Finally, patients with different causes of mitral regurgitation were studied in order to learn the reason for the difficulties found when studying children with atrial septal defects. This last study provided another example of a long vortex shed distance in patients with endocardial cushion defects and demonstrated limitations of Doppler sensitivity at deep sample volume positions. This presentation of studies formed the basis for understanding Doppler interpretation. Doppler was evaluated only as qualitative information. Quantification of the different lesions could not be assessed with the present instrumentation.

Echo-Doppler appears to be a promising technique which has the capability of providing information in the indicated areas as well as in many areas other than those described in this investigation (51-61). Present technical and inherent problems create important limitations, but should not detract from further investigations of its usefulness.

Samenvatting en conclusies

Met Doppler technieken is het mogelijk om gegevens te verzamelen over de bloedstroom snelheid. De methode is niet invasief en voor de patient niet belastend. Het principe berust op meting van de frequentie verschuiving van een uitgezonden en door bloed teruggekaatste ultrageluidsgolf. Het Doppler spectrum kan hoorbaar worden gemaakt. De beoordeling hiervan door de onderzoeker is enigszins subjectief.

Dit onderzoek werd uitgevoerd met een nieuwe Doppler methode waarbij gepulsed geluid wordt gebruikt en een benaderde grafische weergave van het Doppler spectrum via het tijd-interval-histogram ter beschikking was. Door gebruikmaking van gepulsed geluid is de diepte waarop de bloedstroomsnelheid wordt gemeten bekend.

De tijd-interval-histogram methode, die gebaseerd is op "zero-crossing" techniek staat toe onderscheid te maken tussen een zone met laminaire stroom en een zone met "verstoorde" bloedstroomsnelheid.

Het belangrijkste oogmerk van dit onderzoek was het bewijs te leveren, dat twee onafhankelijke onderzoekers, die niet van de diagnose op de hoogte waren, in staat zouden zijn uit een ongeordende verzameling van genummerde tijd-interval-histogrammen, patiënten met verschillende aangeboren en verworven hartafwijkingen van elkaar te onderscheiden.

Kinderen met transpositie van de grote vaten en pulmonaalstenose werden voor de eerste studie bestemd. Informatie omtrent de aanwezigheid van pulmonaalstenose als complicatie van d-TGV werd van belang geacht met het oog op de chirurgische implicaties (47, 48). Bovendien kan pulmonaalstenose vroeg of laat ontstaan of in ernst toenemen bij deze aandoening (49, 50).

M-mode echocardiografie in combinatie met Doppler werd, als niet invasief onderzoek, gekozen om het ziekteverloop te volgen. Dit was de eerste gepubliceerde studie waarin, onder gecontroleerde omstandigheden, kon worden aangetoond, dat het TIH de noodzakelijke informatie bevat om "flow disturbance" ten gevolge van morphologische hartafwijkingen op te sporen. De criteria voor "flow disturbance" werden vastgesteld.

Ter evaluatie van de betrouwbaarheid van het TIH in andere delen van het hart, werd een studie bij kinderen met een atrium septum defect verricht. De objectiviteit van de techniek voor het opsporen van een specifieke laesie werd bevestigd en tevens werd het duidelijk, dat met Doppler de diagnose van enige andere afwijkingen kon worden vastgesteld. De studie van het atrium septum defect wierp twee belangrijke vragen op: (1) waarom werd flow disturbance gevonden op afstand van de plaats waar deze teweeg gebracht werd en (2) waarom was het niet goed mogelijk mitralisinsufficiëntie op te sporen in vergelijking met ander onderzoek (33, 45). Speurend naar een antwoord op de eerste vraag werden twee onderzoeken verricht: de pulmonaalstenose en de linker ventrikel uitstroom obstructie studies. Deze bevestigden de objectiviteit van het TIH bij het aantonen van een vernauwd gebied. Evenwel kon de plaats van de stenose moeilijk worden gelocaliseerd. De volgende drie bevindingen kwamen uit deze studies naar voren: Ten eerste, wanneer een flow disturbance in het uitstroomgebied van een ventrikel aanwezig was, kon de toestand van het hoofdvat moeilijk worden vastgesteld met echo-Doppler onderzoek tenzij de (flow)-patronen uit deze arterie normaal waren. Deze bevinding werd het "series effect" genoemd en andere studies werden ter bevestiging uitgevoerd.

Voorts, wanneer een flow disturbance in de aorta optrad, kon een vals positieve disturbance in de rechter pulmonaalarterie worden aangetroffen. Deze bevinding werd met "induction effect" aangeduid; het mogelijk aanwezig zijn van deze situatie werd in andere studies bevestigd.

Tenslotte werd aangetoond, dat opsporen van de plaats van een pulmonaalstenose met behulp van echo-Doppler moeilijkheden kan opleveren, aangezien een disturbance soms pas blijkt op te treden in de rechter pulmonaal arterie of helemaal in de transversale aortaboog, zelfs wanneer deze afkomstig was van de klep. Het belang van de "vortex shed distance" (afstand tussen oorzaak van verstoring en de werkelijk optredende stroomverstoring) werd hiermede aangetoond. Twee aanvullende studies werden uitgevoerd; één in patienten met flow disturbance in de aorta, om het induction effect nader te onderzoeken en te bevestigen en één studie om de dynamica van het series effect en de vortex shed distance in een model te bestuderen.

Als laatste groep werden patiënten met mitralis insufficiëntie van verschillende herkomst bestudeerd om de oorzaak van de moeilijkheden bij kinderen met een atrium septum defect na te gaan. Deze laatste studie leverde nog een voorbeeld op van een lange vortex shed distance in patiënten met een endocardkussendefect en demonstreert tevens de beperkingen van Doppler gevoeligheid bij meting op groter diepte.

Deze serie van studies legt de basis voor een duidelijker Doppler interpretatie. Doppler werd uitsluitend als kwalitatieve informatie geëvalueerd. Kwantificering van de verschillende afwijkingen was met de huidige instrumentatie niet mogelijk.

Echo-Doppler lijkt een veelbelovende techniek, welke mogelijkheden biedt voor het verkrijgen van informatie op andere gebieden dan in dit onderzoek beschreven (51-61). Huidige techniek en inhaerente problemen leiden tot belangrijke beperkingen, welke echter geen afbreuk moeten doen aan verdere exploratie van zijn bruikbaarheid.

Sumário e conclusões

A investigação que efectuâmos consistiu em separar crianças com diferentes formas de cardiopatias congénitas ou adquiridas utilizando como único critério a análise do registo gráfico fornecido pelo eco-Doppler.

Este registo gráfico é composto pelas mudanças de frequência dos ultrasons emitidos pelo transdutor do eco-Doppler e reflectidos pelas células sanguineas. O registo obtido é um histograma traçado em função do tempo e tem vantagens consideráveis se for comparado com a informação auditiva correspondente às mudanças de frequência entre o feixe emitido e o feixe reflectido de ultrasons.

A principal vantagem do registo gráfico consiste na possibilidade de conservar a informação obtida para que possa ser analisada em qualquer altura. Outra vantagem consiste na objectividade da observação do gráfico em contraste com a subjectividade da análise de uma informação auditiva. Finalmente, a informação obtida pelo histograma permite identificar a direccao do fluxo sanguineo em contraste com a impossibilidade dessa informação pelo sinal auditivo.

O primeiro de uma série de estudos que fizemos nesta investigação consistiu na tentativa de detectar a presença de estenose pulmonar em doentes com transposição completa dos grandes vasos. Neste estudo podémos constatar que o histograma fornecido pelo eco-Doppler contém por si só informação suficiente para detectar perturbações do fluxo sanguineo devidas a doenças cardiacas. Podemos ainda neste estudo estabelecer os critérios para separar fluxos sanguineos normais e fluxos sanguineos anormais e ainda concluir que dois investigadores podiam de uma forma perfeitamente independente chegar a conclusões semelhantes. Os estudos que posteriormente efectuâmos confirmaram a objectividade do método e permitiram concluir que o eco-Doppler pode detectar no mesmo doente mais de que uma forma de malformação cardiaca. Contudo, o estudo efectuado em criancas com comunicação interauricular levantou alguns problemas, sendo o principal saber porque razão era possivel encontrar perturbações sanguineas situadas para além do local onde a malformação cardiaca existia. Fizemos em seguida o estudo pelo eco-Doppler de crianças com estenose pulmonar, estenose aórtica e formas complexas de cardiopatias que tinham em comum fluxos sanguineos aórticos anormais.

Esta série de estudos permitiu concluir que (1) a perturbação do fluxo sanguineo persiste em camaras ou vasos sanguineos até que a circulação possa normalizar, (2) a perturbação da corrente sanguinea pode não ser detectada no local onde existe a malformacao cardiaca, mas sim na camara ou vaso que está em continuidade com a estrutura anormal, (3) o fluxos sanguineo anormal pode propagar-se da artéria pulmonar para a aorta e vice-versa por contiguidade das duas estruturas.

Os três factores assinalados são de verdadeira importância na utilização da técnica do eco-Doppler e, se não forem suficientemente valorizados, podem constituir limitações importantes desta técnica. Por outras palavras, resultados falsos podem ser criados pela utilização deficiente da informação obtida pelo eco-Doppler.

Esta investigação permitiu concluir que o eco-Doppler é uma técnica complementar de ecocardiografia de grande utilidade. É ainda a única técnica de ecocardiografia que estuda o comportamento da corrente sanguinea.

Alguns problemas e limitações técnicas não permitem, neste momento, informações mais pormenorizadas.

No entanto, cremos que com o aperfeiçoamento da tecnologia a eco-Doppler vai ser uma tecnica de grande utilidade para estudo do comportamento da corrente sanguinea em doentes com cardiopatias.

Table 1. COMPARISON OF ECHO-DOPPLER AND ACTUAL DIAGNOSIS

Pt.	Age yrs.	Doppler		True diagnosis of pulmonary outflow tract	Most recent evaluation procedure	Doppler assessment	
		LVOT	Pulm. Art.			right	wrong
1	1	N	N	no obstruction	operation	x	
2	13	N	+	51 mm. pulm. valv. stenosis	catheterization	x	
3	13	N	N	no obstruction	operation	x	
4	9	+	+	subvalv. stenosis and pulm. banding	operation	x	
5	9	N	N	no obstruction	operation	x	
6	7	+	+	40 mm. subvalv. stenosis	catheterization	x	
7	3	+	+	40 mm. subvalv. stenosis	operation	x	
8	9	N	+	84 mm. valv. stenosis	operation	x	
9	5	N	N	no obstruction	operation	x	
10	6	N	N	no obstruction	operation	x	
11	4	N	+	hypoplastic pulm. with obstr. post valvotomy	operation	x	
12	7	N	N	no obstruction	catheterization	x	
13	11	N	N	no obstruction	catheterization	x	
14	1,5	N	N	no obstruction	catheterization	x	
15	9	N	N	no obstruction	operation	x	
16	2	N	N	no obstruction	operation	x	
17	6	+	+	130 mm. gradient subvalv. stenosis not resected	operation	x	
18	8	N	+	no obstruction	catheterization		x

N = no detectable disturbance; + = disturbance detected. No obstruction means no pressure difference across any portion of the outflow tract measured that exceeded 10 mm. Hg at catheterization or no detectable narrowing of the outflow tract at direct operative examination.

Table 2. RESULTS OF CATHETERIZATION

Pt.	Age yrs.	Assoc. lesions	Pressure mm Hg.						Saturation percentage						
			RA	RV	PA	LA	LV	AO	SVC	RA	RV	PA	LA	LV	AO
1	16	none	4	25/4	25/6	4	125/4	126/76	63	87	86	85	88	88	92
2	7	none	4	32/4	32/10	4	110/4*	130/90*	74	90	90	90	99	98	98
3	6	none	4	40/5	33/5	4	-	142/65	79	82	88	86	94	-	97
4	11	none	4	36/4	24/10	4	109/4*	125/71*	80	93	92	92	97	98	98
5	8	none	4	34/4	22/10	5	107/5*	96/76*	75	83	88	88	95	95	95
6	4	VPS	4	62/4	26/9	4	95/4	-	77	82	83	78	98	98	-
7	7	none	3	20/3	18/10	3	106/3	106/67	77	84	82	83	98	98	92
8	6	none	4	33/4	33/11	4	93/4	100/54	83	89	90	-	94	94	92
					Endocardial Cushion Defects										
9	6	complete AV canal, VPS	4	119/4	85/43	7	126/7*	145/71*	73	83	86	84	92	91	92
10	4	complete AV canal		no catheterisation											
11	7	primum	4	39/4	37/23	3	111/8*	131/74*	72	80	83	84	94	94	94
12	3	primum, VPS	3	74/3	89/5	3	92/3	91/49	68	81	85	87	91	92	90
13	14	primum	5	47/6	34/10	5	132/6	-	83	90	90	90	98	98	98
14	2	primum	8	63/9	60/23	9	94/9	-	70	89	89	-	97	95	-

* = not simultaneous; RA = right atrium; RV = right ventricle; PA = pulmonary artery; LA = left atrium; LV = left ventricle; AO = aorta; SVC = superior vena cava; VPS = pulmonary stenosis; AV = atrioventricular.

Table 3. OBSERVER AGREEMENT ON TIH -LEFT-TO-RIGHT ATRIAL SHUNT

Pt.	RA out		RV		RVOT		PA		SSRPA		LAB		SSLA		LA out		LVOT		AO		TAA	
	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D
1	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	x	-	-	-	-	-	-	o	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	x	-	-	o	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
5	-	x	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6	-	x	-	-	x	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
7	-	o	-	-	x	-	-	-	o	-	-	-	-	-	-	-	-	-	-	-	-	-
8	-	x	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
9	-	x	-	-	x	-	x	-	x	-	x	-	o	-	-	-	-	-	-	-	-	-
10	-	x	-	-	o	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
11	-	x	x	-	o	-	-	-	o	-	-	-	-	-	-	-	-	-	-	-	-	-
12	-	x	x	-	-	-	x	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-
13	-	x	x	x	o	-	o	-	x	-	-	-	-	o	-	-	-	-	-	-	-	-
14	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

The 11 evaluated areas of the heart and two phases of the cardiac cycle are listed. A dash indicates that both observers independently indicated a normal TIH for that phase of the cycle and that location. An "x" indicates that both observers found a flow disturbance at the designated area and phase. An "o" indicates that one observer graded an area and cardiac phase as normal and the other indicated a flow disturbance.

RA out = right atrial outflow; RV = right ventricle; RVOT = right ventricular outflow tract; PA = pulmonary artery; SSRPA = suprasternal notch, right pulmonary artery; LAB = left atrial body; SSLA = suprasternal notch, left atrium, LA out = left atrial outflow; LVOT = left ventricular outflow tract; AO = aorta; TAA = transverse aortic arch.

S = systole; D = diastole.

Table 4. CATHETERIZATION DATA IN PULMONARY STENOSIS

Pt.	Pressure mm Hg.						Saturation percentage						
	RA	RV	PA	LA	LV	AO	SVC	RA	RV	PA	LA	LV	AO
1	3	75/3	15/5			115/60	75	76	76	76			97
2	5	65/5	20/12			110/58	72	72	69	71			91
3	4	48/5	15/10			102/54	75	77	74	74			98
4	3	32/3	13/5	7	115/7	112/53	77	78	77	75	96	96	95
5	not catheterized												
6	3	62/3	26/9	7	95/2		77	82	83	83	98	98	
7	3	30/3	19/10			104/64	80	82	82	81			97
8	2	40/3	26/9			104/32	81	81	83	83			99
9	3	40/4	19/10			100/60	77	78	78	77			96
10	2	54/2	19/3			110/68	67	72	67	67			92
11	2	55/2	17/8			122/76		82	80	81			99
12	5	55/5	18/10			140/76	82	81	80	81			99
13	4	65/4	18/8			145/70	81	83	82	82			99
14	2	35/2	15/10		120/5	120/95	82	78	78	77	94	94	94

Cardiac catheterization pressure data are shown in millimeters Hg. RA = right atrium; RV = right ventricle; PA = pulmonary artery; LA = left atrium; LV = left ventricle; AO = aorta; SVC = superior vena cava.

Table 5. OBSERVER AGREEMENT ON TIH

Pt.	RA out		RV		RVOT		PA		SSRPA		LAB		SSLA		LA out		LVOT		AO		TAA	
	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D
1	-	-	-	-	o	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
6	-	x	-	-	x	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
8	-	-	-	-	o	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-	o	-	-	-	-	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	x	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-
14	-	-	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

The 11 evaluated areas of the heart and two phases of the cardiac cycle are listed. A dash indicates that both observers independently indicated a normal TIH for that phase of the cycle and that location. An "x" indicates that both observers found a flow disturbance at the designated area and phase. An "o" indicates that one observer graded an area and cardiac phase as normal and the other indicated a flow disturbance. The TIH from the left and right atrial outflow (RA out and LA out) were recorded with sample volume placed between the leaflets of the respective atrioventricular valves.

RV = right ventricle; RVOT = right ventricular outflow tract; PA = pulmonary artery; SSRPA = suprasternal notch, right pulmonary artery; LAB = left atrial body; SSLA = suprasternal notch, left atrium; AO = aorta, TAA = transverse aortic arch.

S = systole; D = diastole.

Table 6. CATHETERIZATION RESULTS

Pt	Age yrs	Assoc. disease	Pressure mm Hg. RA	RV	PA	LA	LV	LV out	AO	Saturation percentage SVC	RA	RV	PA	LA	LV	AO
1	6	AI	$\bar{3}$	27/5	27/12	$\bar{6}$	130/6		104/74	85	83	82	73	98	98	98
2	10		$\bar{3}$	56/5	30/13		164/7	112/7	106/70	81	82	80	82	97	97	97
3	14		$\bar{3}$	25/4	22/15		137/10	90/6	90/63	75	75	76	78	97	98	98
4	13		$\bar{3}$	32/3	24/11		120/2		98/70	84	81	83	83			98
5	4	MI	$\bar{4}$	70/4	70/30	$\overline{13}$	130/15	80/6	73/47	75	75	79	74		98	98
6	15	AI	$\bar{4}$	22/5	21/10		135/4		104/60	85	83	74	76		100	100
7	7	AI	$\bar{2}$	28/4	24/15	$\overline{13}$	160/14		94/62	79	78	77	77	95	98	
8	7	AI	$\bar{2}$	22/4	17/8		135/13		110/62	78	78	77	76		96	97

AI = aortic insufficiency; MI = mitral insufficiency; $\bar{n}$umber = mean value; Assoc. disease = associated disease; RA = right atrium RV = right ventricle; PA = pulmonary artery; LA = left atrium; LV = left ventricle; LV out = left ventricle outflow; AO = aorta SVC = superior vena cava.

Table 7. OBSERVER AGREEMENT ON TIH AORTIC STENOSIS

Pt.	RA out		RV		RVOT		PA		SSRPA		LAB		SSLA		LA out		LVOT		AO		TAA	
	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D	S	D
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	x	-	x	-
2	-	-	-	-	x	-	-	-	-	-	-	-	-	-	-	-	x	-	x	-	x	-
3	-	-	-	-	-	-	-	-	o	-	-	-	-	-	-	o	x	-	x	-	x	-
4	-	-	-	-	-	-	o	-	-	-	-	-	-	-	-	-	-	-	x	-	x	-
5	-	-	-	-	-	-	-	-	-	-	o	-	x	-	-	-	o	-	x	-	x	-
6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	x	-	x	-
7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	o	x	-	x	-
8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	-	x	x	-	x	-
9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	o	-	x	-
10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	o	-	x	-
11	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-
12	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	x	-
13	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	x	-
14	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	x	-
15	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	x	-	x	-

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RA out = right atrial outflow; RV = right ventricle; RVOT = right ventricular outflow tract; PA = pulmonary artery; SSRPA = suprasternal notch, right pulmonary artery; LAB = left atrial body; SSLA = suprasternal notch, left atrium, LA out = left atrial outflow; LVOT = left ventricular outflow tract; AO = aorta; TAA = transverse aortic arch.

S = systole; D = diastole.

Table 8. NORMALS

Pt.	Confirmation	AOR	TAA	RPA
1	cath.	-	-	-
2	cath.	-	-	-
3	cath.	-	-	-
4	exam.	-	-	-
5	exam.	-	-	-
6	exam.	-	-	-
7	exam.	-	-	-
8	exam.	-	-	-
9	exam.	-	-	-
10	exam.	-	-	-
11	exam.	-	-	-
12	exam.	-	-	-
13	exam.	-	-	-
14	exam.	-	-	-
15	exam.	+*	-	-
16	exam.	-	-	-

The transverse aortic arch or right pulmonary artery is indicated by a "+". Inability to detect a flow disturbance in these locations is indicated by a "-". Symbols are similar in subsequent tables.

* Wide dispersion lasting $<\frac{1}{2}$ of systole. AOR = aortic root

exam. = by physical examination. TAA = transverse aortic arch

cath. = by cardiac catheterization RPA = right pulmonary artery

Table 9. AORTIC STENOSIS

Pt.	Obstruction	AOR	TAA	RPA	Gradient (mm Hg.)
1	valvular	-	+	-	50
2	valvular	+	+	-	35
3	supravalvular	+	+	+	85
4	valvular	+	+	-	100
5	valvular	+	+	-	170
6	diaphragm, SA	+	+	+	50
7	diaphragm, SA	+	-	-	70
8	tunnel, SA	+	+	-	130
9	valvular	+	+	-	26
10	valvular	+	+	-	58
11	IHSS	+	+	+	47*
12	valvular	+	+	-	22
13	valvular	+	+	-	57
14	valvular	+	+	-	31
15	valvular	+	+	-	66
16	valvular	+	+	-	25

* Right ventricular outflow gradient of 20 mm was also present

SA = subaortic

IHSS = idiopathic hypertrophic subaortic stenosis

Table 10 PATENT DUCTUS ARTERIOSUS

Pt.	Confirmation	AOR	TAA	RPA
1	cath.	+	+	+
2	op.	-	+	+
3	op.	-	+	+
4	cath.	+	+	+
5	cath.	-	-	+
6	op.	+	+	+
7	cath.	+	+	+
8	op.	+	+	+
9	cath.	+	+	+
10	op.	+	+	+
11	op.	-	-	+

cath. = cardiac catheterization op. = at operation

Table 11. VENTRICULAR SEPTAL DEFECT

Pt.	AOR	TAA	RPA	QP:QS
1	-	-	-	2.1
2	+	+	+	1.1
3	-	-	+	2.6
4	-	-	-	2.1
5	-	-	-	2.1
6	-	-	-	1.4
7	-	-	-	1.4
8	-	-	+	1.8
9	-	-	-	2.7
10	+	+	+	2.7
11	-	-	-	2.4
12	-	-	-	1.3
13	-	-	+	1.6
14	-	-	+	2.2
15	-	-	-	1.7
16	-	-	+	1.2
17	-	-	-	1.6

QP:QS = ratio of pulmonary to systemic blood flow.

Table 12. TETRALOGY

Pt.	Op. procedure	AOR	TAA	RPA
1	none	+	-	N.E.
2	none	+	+	+
3	none	-	+	N.E.
4	none	+	+	+
5	Blalock	-	+	+
6	Blalock	-	+	N.E.
7	Blalock	-	-	N.E.
8	Blalock	-	+	+
9	Blalock	-	+	+
10	Blalock	-	-	N.E.
11	Blalock	+	+	+
12	Waterston	+	+	+

N.E. = not evaluated

Table 13. PULMONARY STENOSIS

Pt.	AOR	TAA	RPA	Gradient (mm Hg)
1	+	-	+	52
2	-	+	+	78
3	+	-	+	120
4	-	-	+	38
5	-	-	+	60
6	-	-	+	45
7	-	-	+	33
8	-	-	+	19
9	-	-	+	36
10	-	-	+	11
11	-	-	+	20
12	-	-	-*	21
13	-	-	+	35
14	-	-	+	38
15	-	-	+	37
16	-	-	+	47
17	-	-	-*	20
18	+	+	+	70

* = + in main pulmonary artery.

Table 14. ATRIAL SEPTAL DEFECTS

Pt.	Lesion type	AOR	TAA	RPA
1	secundum	-	-	-
2	secundum	-	-	-
3	secundum	-	-	-
4	secundum	-	-	+
5	secundum	-	-	-
6	secundum	-	-	+
7	secundum	-	-	-
8	secundum	-	-	+
9	primum	-	+	+
10	primum	-	-	-
11	primum	-	-	+
12	primum	-	-	-
13	primum	-	-	+
14	primum	-	-	-
15	secundum	-	-	+
16	secundum	-	-	-

Table 15. MITRAL DISEASE

Pt.	Diagnosis	AOR	TAA	RPA
1	MI, AS	-	-	-
2	MI	-	-	-
3	MI	-	-	-
4	MI	-	-	-
5	MI	-	-	-
6	MI	-	-	-
7	MI	-	-	-
8	MI	-	-	-
9	MI	-	-	-
10	MI, MS	-	-	-

MI = mitral insufficiency

MS = mitral stenosis

AS = aortic stenosis

Table 16 COMPLEX AND OTHER DISEASE FORMS

Pt.	Diagnosis	AOR	TAA	RPA
1	ASD, PDA, TAPVD	+	+	+
2	TAPVD	-	-	+
3	COARCT, VSD, AS	+	+	
4	PDA, VSD, INTERR. ARCH	+	+	+
5	Ebstein's	-	-	-
6	Ebstein's	-	-	-
7	Ebstein's	-	-	-
8	Ebstein's	-	-	-
9	Ebstein's	-	-	-
10	Ebstein's	-	-	-
11	MI, AS	+	+	-

ASD = atrial septal defect
PDA = patent ductus arteriosus
TAPVD = total anomalous pulmonary venous drainage
COARCT = coarctation of the aorta
VSD = ventricular septal defect
AS = aortic stenosis
INTERR. ARCH = interrupted aortic arch
MI = mitral insufficiency

POSITION DOPPLER SAMPLE VOLUME

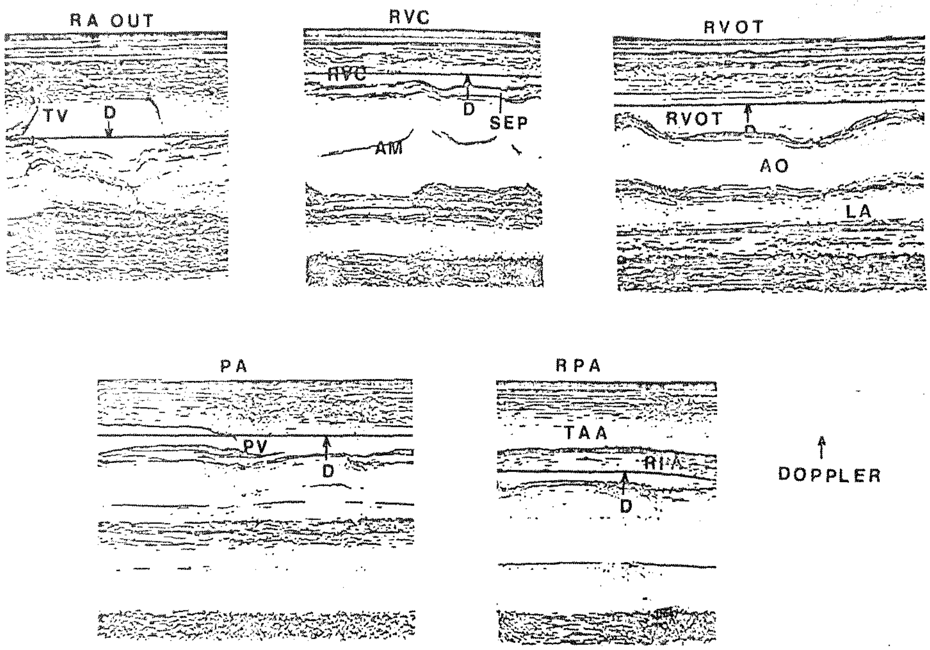


Figure 1. The position of the Doppler sample volume for each cardiac area is indicated by a "D" on the M-mode echocardiogram. Abbreviations: RA = right atrium; RVC = right ventricular cavity; RVOT = right ventricular outflow tract; TV = tricuspid valve; AM = anterior mitral leaflet; PA = pulmonary artery; TAA = transverse aortic arch; RPA = right pulmonary artery; LVOT = left ventricular outflow tract; SSLA = suprasternal notch approach to the left atrium; LA = left atrium; SEPT = septum; Ao = aorta; PV = pulmonary valve leaflet

POSITION DOPPLER SAMPLE VOLUME

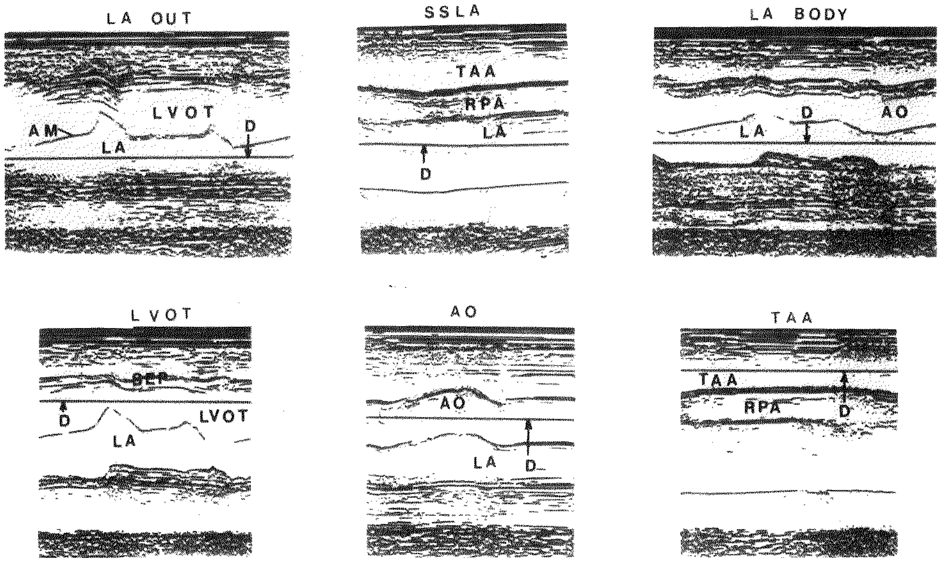


Figure 2. The position of the Doppler sample volume for each cardiac area is indicated by a "D" on the M-mode echocardiogram. Abbreviations: RA = right atrium; RVC = right ventricular cavity; RVOT = right ventricular outflow tract; TV = tricuspid valve; AM = anterior mitral leaflet; PA = pulmonary artery; TAA = transverse aortic arch; RPA = right pulmonary artery; LVOT = left ventricular outflow tract; SSLA = suprasternal notch approach to the left atrium; LA = left atrium; SEPT = septum; Ao = aorta; PV = pulmonary valve leaflet

TIME INTERVAL HISTOGRAM (TIH)

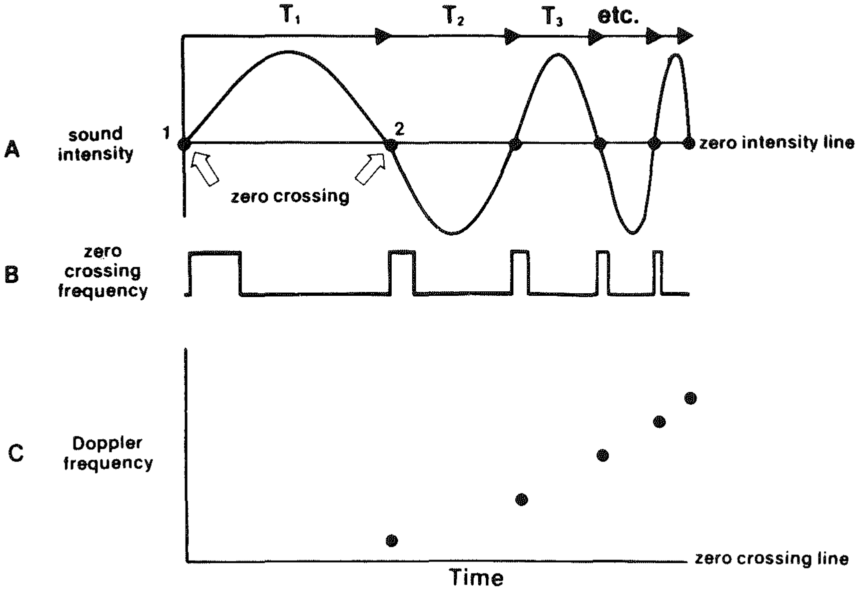


Figure 3. Production of a Time Interval Histogram (TIH)

A. Each time the zero intensity is crossed by the Doppler sound wave signal, the time period to the previous zero crossing is measured.

B. Graph illustrating when the zero crossings occur.

C. The time interval histogram. For each zero crossing event of the Doppler shift frequency signal, the time period (T) to the previous zero crossing is measured and a dot on a "frequency scale" is printed.

(Adapted from Baker et al.: Pulsed Doppler Echocardiography, in Bom, N. (ed.): Echocardiology, The Hague; Martinus Nijhoff Medical Division, 1977, p. 207.)

DOPPLER FLOW CHARACTERISTICS

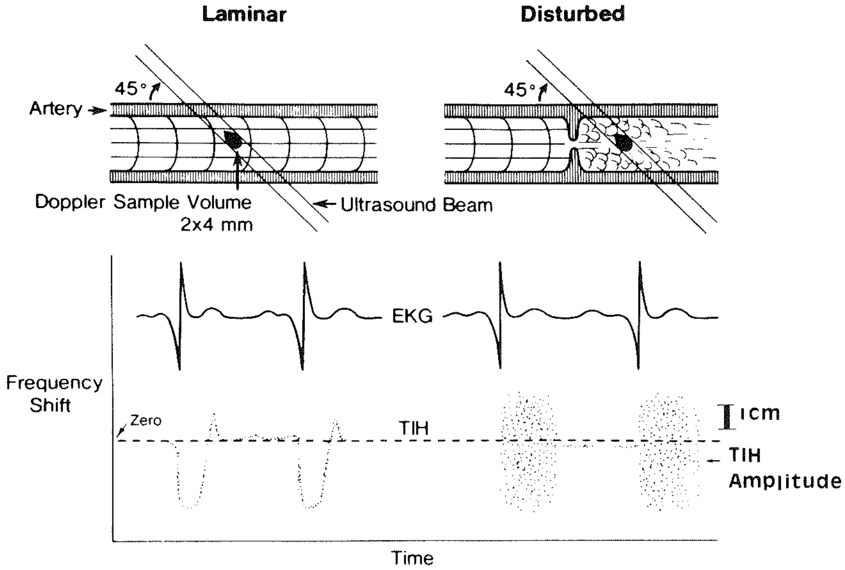


Figure 4. Doppler flow characteristics. The ultrasound beam is intersecting an artery to allow Doppler sampling. In the first panel, flow is laminar and the TIH shows frequency dispersions less than 1cm. in width (amplitude). In the second panel, an obstruction is present in the artery creating a systolic disturbed flow and the TIH has frequent dispersions greater than 1cm. in width (amplitude). Diastolic flow in each instance is laminar.

(Adapted from Allen H, et al.; Ultrasound cardiac Diagnoses, in Symposium on pediatric cardiology, the Pediatric Clinics of North America, November 1978, p. 682.)

ADJUSTMENT OF THE DOPPLER GAIN

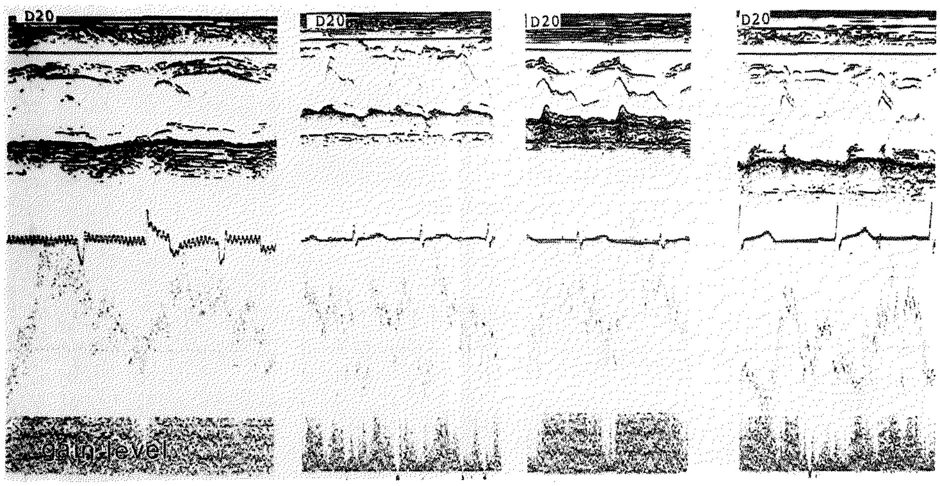


Figure 5. This example demonstrates different adjustments of the Doppler gain. Only the second panel from the left has the Doppler gain appropriately adjusted showing peaks and valleys. The other three panels show a flat topped signal strength, indicating too high Doppler gain.

NORMAL RPA AND NORMAL TAA

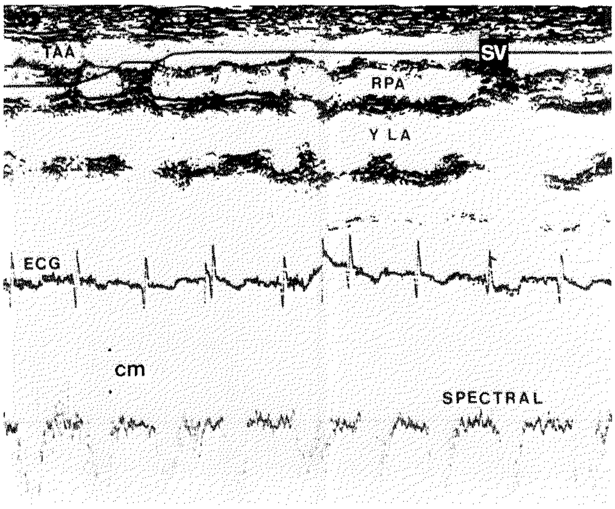


Figure 6. This suprasternal notch study sample was from patient n. 15, who had no obstruction of the pulmonary outflow tract. The example shows time interval histogram (TIH) during a sweep from the right pulmonary artery (RPA) to the transverse aortic arch (TAA). Each dot represents the "average frequency" of reflections during 1/4,000 of a second. Transient RPA disturbance in beat 1 is an artifact and not repeated in beat 2. SV = sample volume; YLA = left atrium viewed in the Yaxis.

MARKED RPA DISTURBANCE

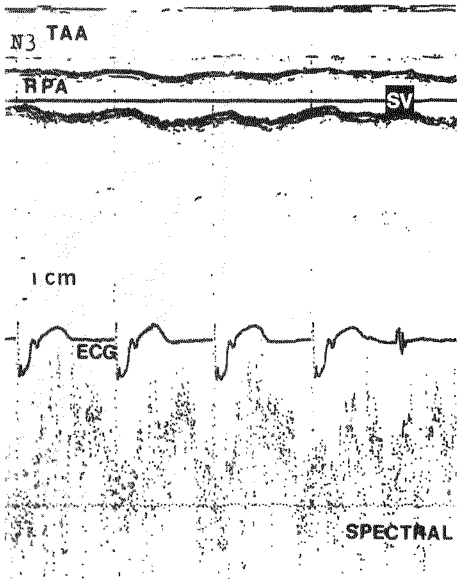


Figure 7. The sample volume (SV) is in the right pulmonary artery (RPA). Systolic TIH dispersion is greater than 1cm. amplitude. TAA = transverse aortic arch.

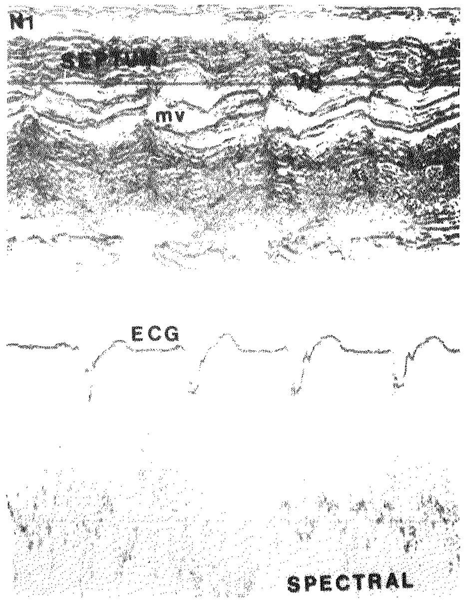


Figure 8. The sample volume is in the left ventricular outflow tract. SV = sample volume; MV = mitral valve; The pattern, although not smooth in diastole is laminar. Frequency dispersion in diastole does not exceed 1cm.

NORMAL RA OUTFLOW (2)

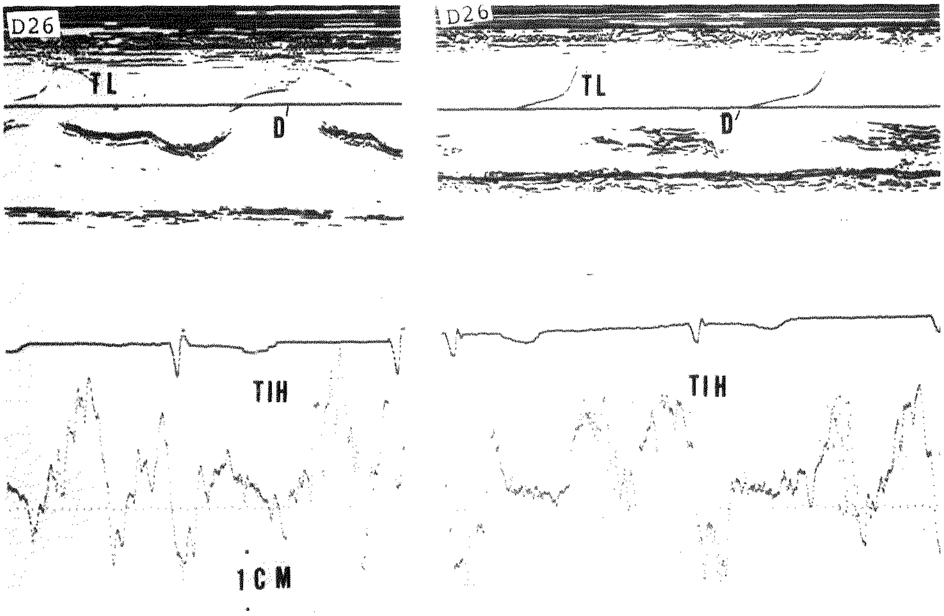


Figure 9. This panel, recorded from the right atrial outflow, demonstrates two Doppler samples recorded from normal children. Both examples demonstrate very limited frequency dispersion and regular patterns. The difference between the two is that the right figure was recorded at a high line level setting and displayed slight dispersion which is not at the 1cm. level. RA = right atrium; TL = tricuspid leaflet; D = Doppler sample site; TIH = time interval histogram; TAA = transverse aortic arch.

RA out ATRIAL SEPTAL DEFECT RPA

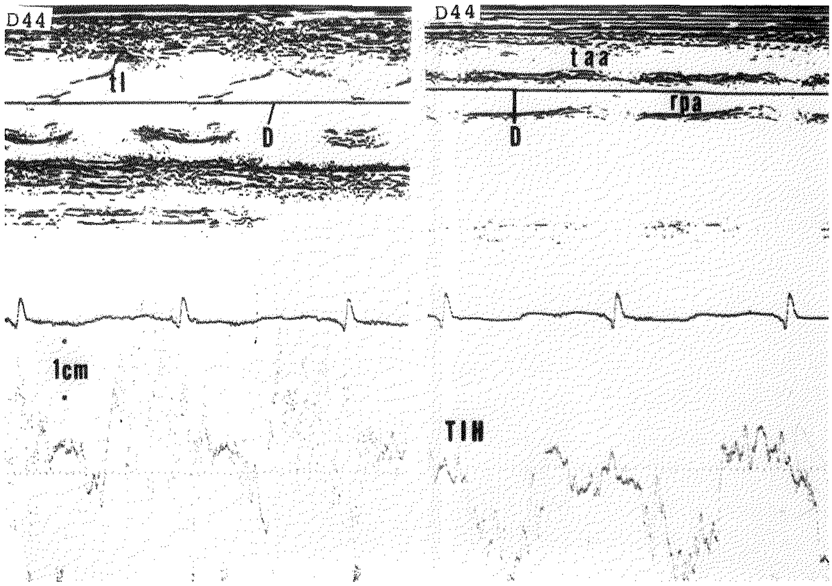


Figure 10. This panel demonstrates the typical result in the right atrial outflow area and right pulmonary artery (RPA in a patient with atrial septal defect. The frequency dispersion measures 2.6 cm. in the right atrial outflow in diastole, but systole, again, shows a laminar pattern. The RPA shows no significant frequency dispersion in this particular patient. Flow disturbance in the RPA was an inconstant feature in atrial septal defect (ASD). RA = right atrium; TL = tricuspid leaflet; D = Doppler sample site; TIH = time interval histogram; TAA = transverse aortic arch.

NORMAL RVOT

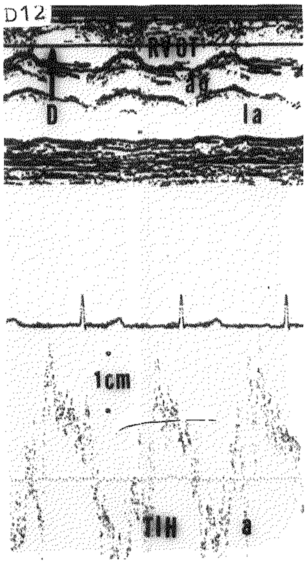
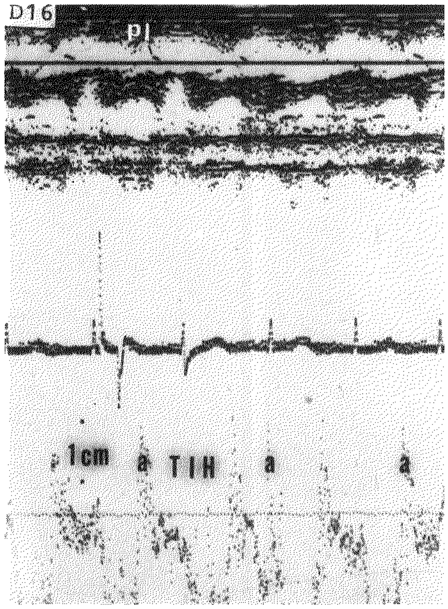


Figure 11. a. b. c. d.

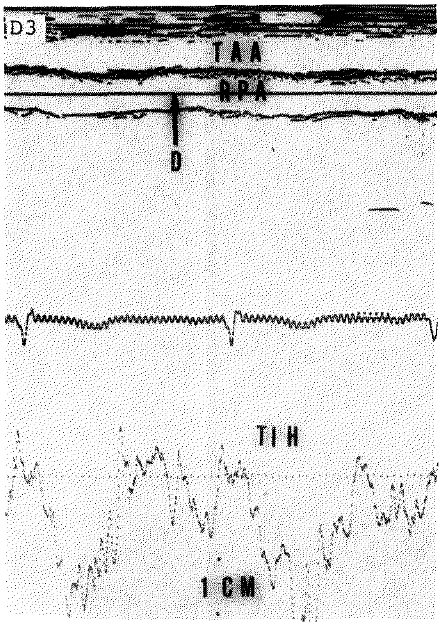
11 a. The Doppler sample volume is in the right ventricular outflow tract (RVOT). TIH shows a laminar pattern, with no dispersion exceeding 1 cm. A transient disturbance occurs in early diastole for each beat and is labeled "a "(artifact). This artifact represents a structure crossing the Doppler sample (D); Ao = aorta; LA = left atrium.

NORMAL POT

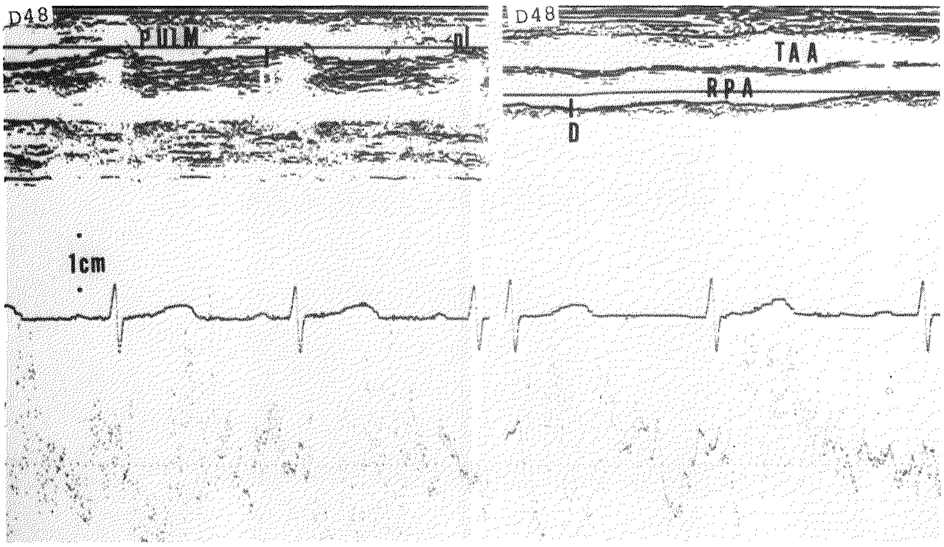


11 b. A pulmonary outflow tract (POT) normal trace is shown. Dot dispersion does not exceed 1cm vertically. The pulmonary leaflet (PL) is visualized and crosses the Doppler sample "a" in early diastole and causes a transient artifact.

NORMAL RPA



11 c. A normal right pulmonary artery (RPA) TIH is shown. The Doppler sample is marked by a D in the right pulmonary artery. TAA = transverse aortic arch.



11 d. Pulmonary stenosis. In the left panel, the Doppler sample D is in the area of the area of the pulmonary valve leaflet. Marked systolic dispersion is shown. The pattern becomes more laminar in diastole. In the right panel, the frequency dispersion in the right pulmonary artery (RPA) is demonstrated. Diastolic pattern is again normal. TAA = transverse aortic arch; D = dispersion; D = Doppler sample volume in the left panel; PL = pulmonary leaflet.

NORMAL LVOT

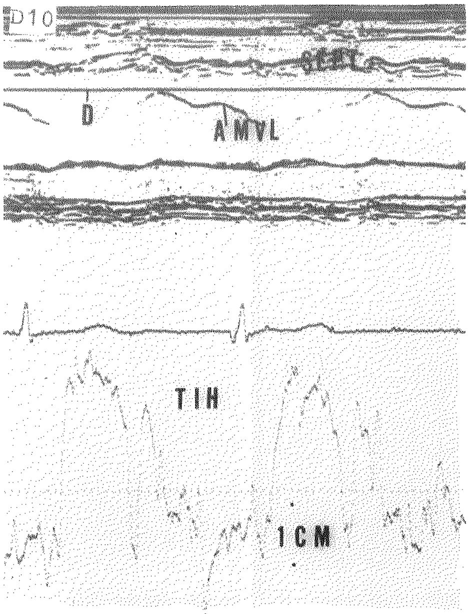
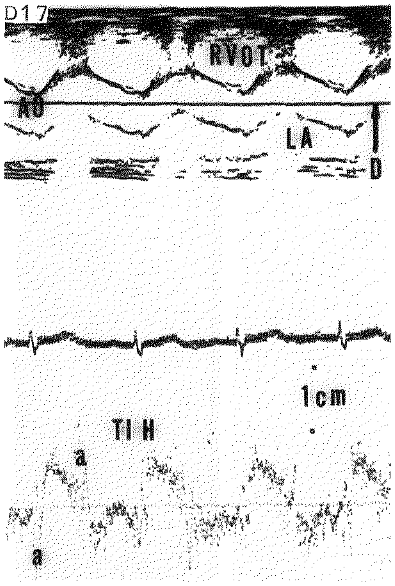


Figure 12. a. b. c. d. Three examples of a normal pattern and one example of aortic stenosis are shown.

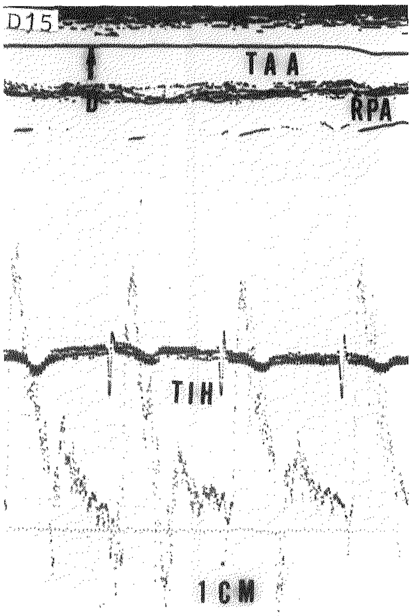
12 a. Demonstrates the result of a normal time interval histogram (TIH) in the left ventricular outflow tract with optimal setting of the Doppler gain.

NORMAL AO

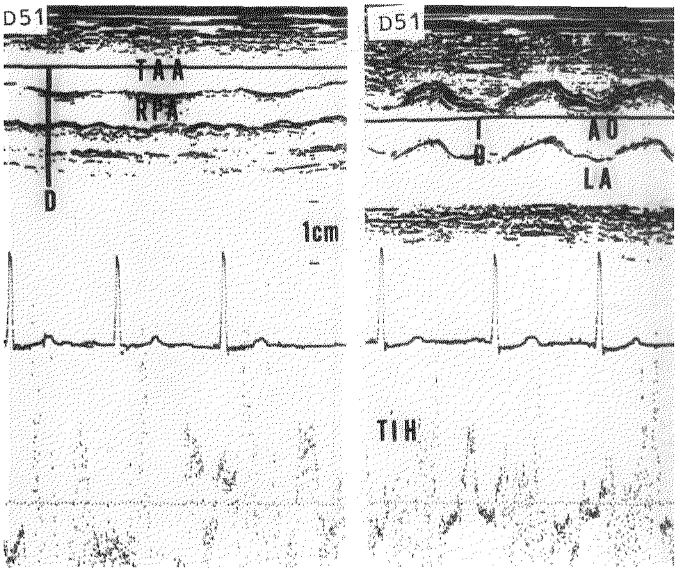


12 b. Demonstrates the TIH of a situation in which the Doppler gain was adjusted quite high. Nonetheless, frequency dispersion is not so great as to exceed 1cm of displacment except at the time the aortic leaflets cross the Doppler beam. These are marked by the "a" as a transient disturbance.

NORMAL TAA



12 c. Demonstrates the TIH of normal transverse aortic arch.



12 d. Demonstrates abvious dispersion of the TIH. The sample volume in the left portion is in the transverse aortic arch and in the right portion of the aorta. Marked frequency dispersion occurs in systole but the normality returns in diastole. This is evidence of aortic stenosis. SEPT = septum; AMVL = anterior mitral valve leaflet; Ao = ascendent aorta; LA = left atrium; RVOT = right ventricular outflow tract; TAA = transverse aortic arch; RPA = right pulmonary artery.

AI BEHIND AMVL

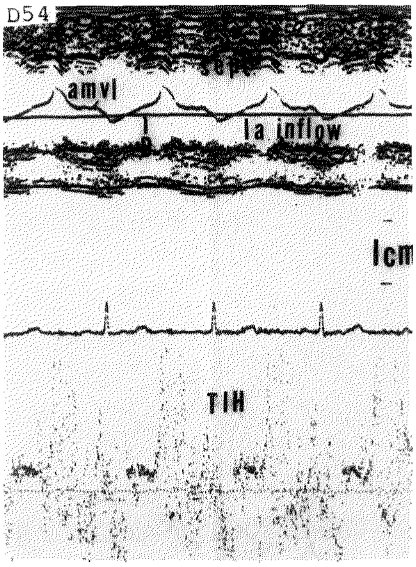


Figure 13. Demonstrates the typical findings of aortic insufficiency. The sample volume is located principally posterior to the anterior mitral valve leaflet in the left atrial outflow. Marked diastolic frequency dispersion is demonstrated as evidence of aortic insufficiency. A normal pattern is present during systole. SEPT = septum; AMVL = anterior mitral valve leaflet; LA inflow = left atrial inflow.

SUB-AORTIC DIAPHRAGM

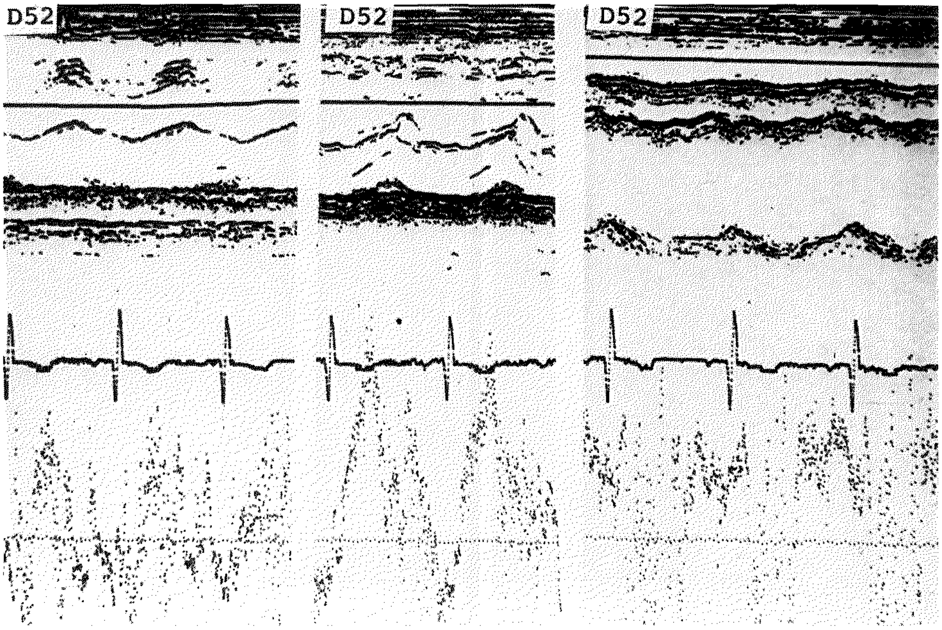


Figure 14. Results of a patient with a subaortic diaphragm. In the left panel, the horizontal range-gated line is seen in the aorta, in the middle panel in the left ventricular outflow tract and in the right panel in the transverse aortic arch. Frequency dispersion is seen in the aorta and transverse aortic arch, but was not found in any level of the left ventricular outflow tract. This would represent a false negative for subaortic diaphragm. The existence of some form of aortic stenosis was shown by the more distal appearance of the frequency dispersion.

TETRALOGY OF FALLOT

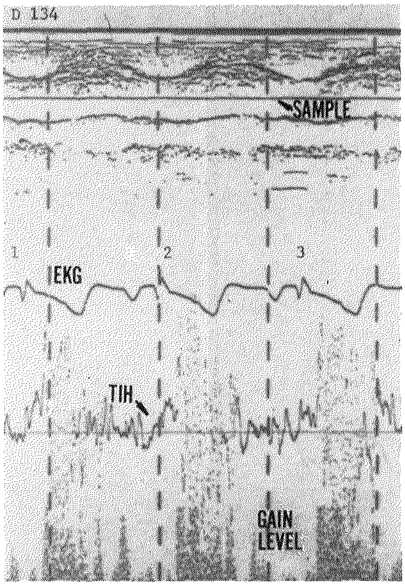


Figure 15. This example shows the aortic root (aorta) and the aortic Doppler tracing of a patient with tetralogy of Fallot and a Blalock anastomosis. The range gate is within the aortic root. The important feature is the obvious frequency dispersion in systole. This patient had no aortic stenosis. This figure illustrates certain technical considerations. Signal strength is best adjusted for the beat after the first QRS from the left. The beat after the third QRS shows "flat topping" of the signal strength indicator and results are unreliable.

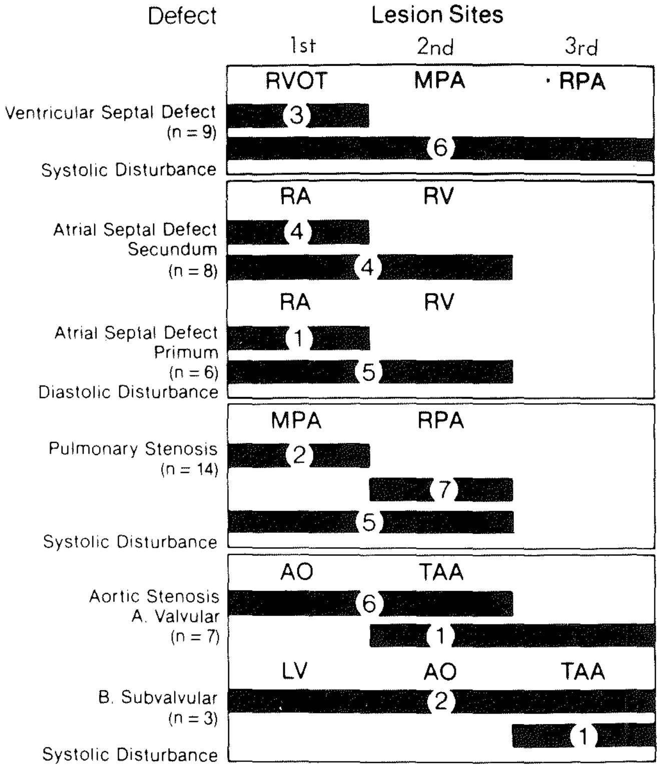


Figure 16. Results of patients primary (1st), secondary (2nd) and tertiary (3rd) echo Doppler sites are listed on the long axis. On the vertical axis are the defects and number of patients with each defect. The black bar indicates the number of patients with each finding. For example, of the nine patients with ventricular septal defects, three had a flow disturbance only in the right ventricular outflow tract (RVOT) and six had a flow disturbance in the RVOT, main pulmonary artery (MPA) and right pulmonary artery (RPA). RA = right atrium; RV = right ventricle; Ao = Aortic root; TAA = transverse aortic arch; LV = left ventricle.

MITRAL REGURGITATION

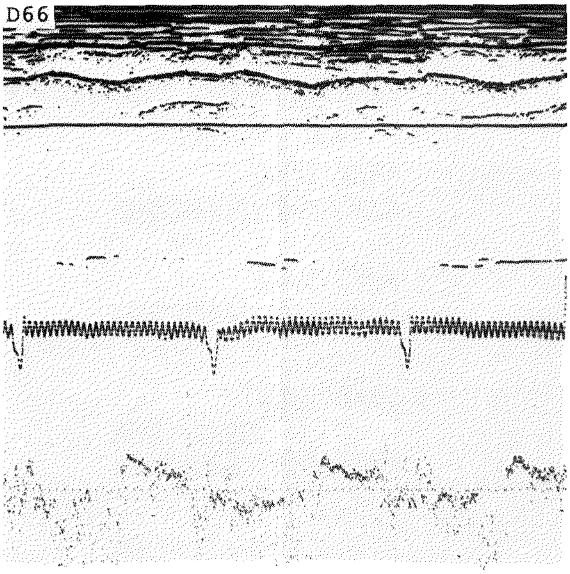


Figure 17. Example of Doppler detection of mitral regurgitation. The range gate is in the left atrium. The time interval histogram shows marked systolic flow disturbance.

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