Use of Time Interval Histogramic Output from Echo-Doppler to Detect Left-to-Right Atrial Shunts

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SUMMARY The primary purpose of this study was to attempt to select, by examination of the time interval histogram (TIH) output of a range gated pulsed Doppler (RGPD), all children with left-to-right shunt at the atrial level from a pool of 57 children. Fifty-four of the children had various forms of cyanotic cardiac disease.

A secondary purpose was to identify any associated lesions in those children with atrial defects. Examiners were unfamiliar with the children and their diagnoses. Results were interpreted independently by two examiners. Detection of diastolic TIH dispersion was used when studying the right atrial outflow tract to separate children with atrial left-to-right shunts from control children. All controls were judged negative by this technique, and 13 of 14 children with atrial shunts were detected by both examiners; the 14th was detected by one examiner. Of a total of 308 TIH decisions on the atrial shunt group, 298 were made identically by both examiners for a 97.7% agreement, demonstrating the objectivity of the method. This study demonstrated the usefulness of the TIH evaluation, indicating that continued investigation and equipment improvements are warranted.

The use of range gated pulsed Doppler (RGPD), combined with echocardiography, has not grown clinically since its introduction in 1973. Although this could, in part, be due to concentration of investigators and clinicians on M-mode and two-dimensional echocardiography, it is probably more related to the difficulty in learning to use information obtained by RGPD. Until now, virtually all attention has been focused on the audible output which represents the Doppler frequency shift. Recently, a time interval histogram (TIH) output has become available. The TIH provides information which is closely related to results of spectral analysis. The theory underlying the principles and use of the TIH are covered in detail elsewhere.

The red cell velocity, under conditions of laminar flow in the heart or great vessels, is approximately uniform at a given instant of time. The RGPD senses the back scatter from each red cell that intersects the ultrasonic beam and reflects a signal back to the receiver. The receiver and processor electronically convert the information to frequency shift, and that shift is a function of particle velocity. Variance of velocity throughout the cycle causes the frequency to shift in a similar manner. The TIH depicts the frequency shift of reflecting particles as a point on the y axis of the histogram at a sampling rate of 4,000/sec. Thus, the velocity pattern from each heartbeat is represented by a series of points inscribed in a histogramic format. Laminar flow produces a narrow band width of points, since the velocity of the reflecting particles is nearly uniform. Disturbed flow, such as results from an obstruction, produces a wide spectrum of velocities and thus a dispersed series of points on the TIH.

The theory of the TIH is sound in principle, but it has not been tested under rigorous conditions. This study assesses the diagnostic accuracy of the TIH, used under carefully controlled circumstances, to separate children with proven atrial septal defects from those with other cardiac malformations.

Methods

Our study population consisted of a random sample of children with left-to-right atrial shunts selected from the population at Sophia Children's Hospital of Rotterdam. Controls consisted of 43 children with other forms of cyanotic congenital or acquired cardiac malformations. Each child was assigned a number and all information regarding that child was

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Received October 10, 1977; revision accepted February 22, 1978.


2. Chenler E, Beck W, Schrire V: Selective catheterization of pulmonary or bronchial arteries in the preoperative assessment of pseudotruncus arteriosus and truncus arteriosus type IV. Am J Cardiol 26:20, 1970

collected and analyzed under that number. Examiners were unfamiliar with the children or their diagnoses. Children were studied without sedation. Instrumentation consisted of an ATL 500A* echocardiograph and a Honeywell 1856 ultraviolet recorder. This instrument package included a second generation TIH output. Other outputs were an ECG lead recorded for time reference and a 3 cm high M-mode recording, of which only part of the height was usually usable. 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 MHz transducer that provided both Doppler and M-mode signal. The range gating feature allowed the operator to sample the Doppler signal at any desired level. That level 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. Depth was set at 12 cm. Doppler controls included threshold, line level and baseline. Threshold was noncritical and was permanently set fully to the left, eliminating most background noise. Line level is basically a Doppler gain control and alters speaker and TIH level, but does not change the basic characteristics of the TIH output. The input signal to the TIH is presented on the oscilloscope. This indicator of line level was set so that this input signal was represented as peaks off the baseline. Excessive line level caused a uniform thickening of the indicator baseline without distinct peaks and resulted in uniform widening of the TIH to about 7.5 mm. Too low a setting of line level resulted in no peaks off the baseline and caused the TIH to become flat. Between these two extremes, the exact setting was not critical. It required checking and possibly changing in each new cardiac location. An additional control, called “baseline,” was unrelated to the line level indicator and was permanently set in the noncompressed state.

The examination was performed in many ways similar to that for a standard precordial and suprasternal echocardiogram. Principle 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, whereas the opposite is true for the Doppler signal. Accordingly, the examiner is forced to compromise in each instance to display 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 intra-cardiac 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 in the chamber of interest.

The M-mode position was used to identify the site from which Doppler signal was being sampled, and this was recorded on each recording as a straight line. During echo-Doppler examination an audible signal was present which represented the Doppler frequency shift. In the present investigation that signal was used exclusively to find a position in the chamber of interest which was free of interfering structures and, at times, to locate the best area for recording the TIH. The audible signal information was not used to classify the TIH for, by design, it was not available when the tracings were reviewed.

Interpretation of numbered tracings was accomplished by classifying the TIH for each cardiac location and phase of the cardiac cycle as coherent or noncoherent. Examples of each pattern are shown in figure 1. To be classified as noncoherent, the amplitude of dispersion at any location or portion of the cycle was required to have an envelope at least one cm high without regard to the reference line and with controls set as indicated. Transient dispersion of one cm amplitude due to a valve crossing the sample volume was disregarded. If a complex was of an amplitude greater than 3 cm, the dispersion was required to be at least a third of the complex height. These criteria resulted from a pilot investigation which demonstrated that normals did not exceed an envelope amplitude of 7.5 mm. Each record was judged 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.

Results

Population

Control Group

The control group, aged 3 months to 19 years, consisted of three normal children, 15 with isolated pulmonary stenosis, 15 with ventricular septal defects and ten with mitral insufficiency.

*Advanced Technology Laboratories, Bellevue, Washington, USA.

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**Figure 1.** The top 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 1 cm level. The lower panel demonstrates the typical result in the right atrial outflow tract and right pulmonary artery (RPA) in a patient with atrial septal defect. The frequency dispersion measures 2.6 cm in the right atrial outflow tract in diastole, but systole, again, shows coherence. The dot pattern at the bottom of the lower panel demonstrates the output of the line level indicator which shows some peaks off baseline and is thus properly set. 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 RA OUTFLOW (2)

RA OUT

RPA

TL D' TL D'

TIH

TL D'

TIH

1 cm

1 cm

TIH
Atrial Shunt Group

The children with atrial shunts 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 43 control children had undergone cardiac catheterization. Three who had not were normal, healthy children. Five others with mitral insufficiency had echocardiographic rather than catheterization confirmation of mitral prolapse. Five remaining controls without catheterization had diagnosis based on clinical findings alone (two with ventricular septal defects, two with mitral insufficiency and one with valvular pulmonary stenosis), and none had evidence of an atrial septal defect.

Atrial Shunt Group

Thirteen of 14 children had cardiac catheterization and angiographic evidence of left-to-right shunt at the atrial level. Catheterization data are shown in table 1. One child, patient 10, was not catheterized but had classical clinical, electrocardiographic and two-dimensional echocardiographic evidence of an endocardial cushion defect with left-to-right shunt at the atrial level. Confirmation of mitral insufficiency was attained by transatrial left ventricular angiography. In each instance the mitral insufficiency was felt to be primary and not catheter-induced.

The Examination

The examination proved only slightly more difficult than a standard pediatric M-mode study, after which this examination is patterned. The usual examination time was 10–20 minutes. The Doppler portion of the examination was displayed in two ways. A Doppler locator line appeared on the M-mode and A-mode and the TIH was displayed on the bottom one third of the oscilloscopic screen. The M-mode echocardiogram was non-diagnostic because 1) it was compressed into approximately 2 cm of the vertical axis and 2) the oscilloscopic intensity had to be increased more than normal to register the TIH display. However, the M-mode was used exclusively as a locator of the depth of the RGPD and was adequate for that purpose.

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 diastolic TIH for the right atrial outflow area (fig. 1). For those children who demonstrated this finding, a second objective was to attempt to identify any associated lesions.

Control Group

No control demonstrated an abnormal diastolic TIH for right atrial outflow. In two subjects (one with ventricular septal defect, one with pulmonary stenosis), a systolic disturbance too low to classify as definitely abnormal was found by one examiner. These constituted the only findings in the control group related to the right atrial outflow.

Atrial Shunt Group (fig. 2)

All 14 subjects with left-to-right atrial shunts were detected by study of the TIH but not by each examiner. One examiner failed to detect the diastolic

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Table 1. Results of Catheterization

| Pt | Age (yrs) | Assoc. Lesions | 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  | 92  |
| 2  | 7         | none           | 4  | 32/4| 32/10| 4  | 110/4*| 130/90*| 74  | 90  | 90  | 90  | 90  | 98  |
| 3  | 6         | none           | 4  | 40/5| 33/5| 4  | —    | 142/65| 79  | 82  | 88  | 86  | 94  | —   |
| 4  | 11        | none           | 4  | 30/4| 24/10| 4  | 109/4*| 125/71*| 80  | 93  | 92  | 92  | 97  | 98  |
| 5  | 8         | none           | 4  | 34/4| 22/10| 5  | 107/5*| 96/76*| 75  | 83  | 88  | 85  | 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  |
| 8  | 6         | none           | 4  | 33/4| 33/11| 4  | 93/4 | 100/54| 83  | 89  | 90  | —   | 94  | 94  |

| 9  | 6         | complete AV canal, VPS | 4  | 119/4| 85/43| 7  | 126/7*| 145/71*| 73  | 83  | 86  | 84  | 92  | 91  |

Endocardial Cushion Defects

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*Not simultaneous.

Abbreviations: 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.
disturbance of patient 7. This child had the smallest calculated left-to-right shunt of the group (Qp/Qs = 1.5:1), and flow disturbance was the least for the group. This instance is a false negative.

Other Doppler findings were present in the experimental group. 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 another child. No disturbances were found in the main pulmonary artery in this group — not even in one child who had a 36 mm Hg pressure difference across the valve. However, both examiners found a right pulmonary artery disturbance in that child and one other who had a measured 12 mm pressure difference across the pulmonary valve. Two additional children were found by one examiner each to have a right pulmonary artery flow disturbance. These constituted the abnormal findings in children with secundum defects.

Children with endocardial cushion defects showed a much greater tendency to demonstrate an abnormal T1H. Half had an abnormality in the right ventricular body T1H judged by both examiners. Patients 9 and 12, who demonstrated pulmonary valvular stenosis, had an abnormal main pulmonary artery T1H, but patient 13, who had a 13 mm Hg pressure difference at catheterization, was judged to have a disturbance by only one examiner. More importantly, 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 9. The remainder, patients 11-14, showed what was interpreted to be true mild mitral regurgitation based on left ventricular contrast injection from a transatrial approach. Patients 11 and 14 were false negatives for mitral insufficiency.

Observer Agreement (fig. 2)

For controls, the only agreement pertinent to this report regards the presence or absence of a diastolic right atrial outflow disturbance in the T1H. 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 × 2 phases of the cardiac cycle × 14 patients). Two hundred and ninety-eight decisions were similar and 10 were dissimilar, for a 96.75% agreement. However, one critical disagreement occurred — the failure of one examiner to detect an instance of right atrial outflow disturbance.

Statistical Test

The chance probability of detecting all controls and 13 of 14 patients with left-to-right atrial shunts is less than 1/10,000 as determined by the Chi-square test.

Discussion

The unique feature of this investigation is the demonstration that the T1H alone contains the necessary information for detecting flow disturbance due to a left-to-right atrial shunt. T1H information also appears objective, as the similarity of conclusions by two independent observers under controlled circumstances in this study was 96.75%.

The use of diastolic flow disturbance at the level of the tricuspid valve as detected by RGPĐ was first reported by Johnson and coworkers in 1973.1 Among 20 patients they studied, four had atrial septal defects, and these were detected in each instance by the audible method. This flow disturbance is probably related to

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Figure 2. Observer agreement. The 11 evaluated areas of the heart and two phases of the cardiac cycle are listed. A blank indicates that both observers independently indicated a normal T1H 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 "0" indicates 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.
the diastolic murmur which is heard during auscultation at the lower left sternal border in children with left-to-right atrial shunts.\(^6\)

The term "flow disturbance" has been used instead of "turbulence," for we have not measured turbulence. The latter term is usually defined as a deviation in the relationship of flow and pressure gradient in a rigid tube.\(^7\) We did not measure the latter and prefer to use the less specific term, flow disturbance. The problems of defining turbulence in a pulsatile system are even more complex.

Detection of gross disturbances of the TIH is not a problem; however, recognition of minor disturbances may be one. Moreover, it is not yet clear how much importance should be attached to detection of minor disturbances. The TIH is a zero crossing detector and is, therefore, not ideally sensitive or immune from noise. We required that the disturbance be quite obvious and that dots appear in a broad band at least 1 cm in amplitude, or greater if the complex was large. With gain adjusted as described, this procedure was effective in defining disturbances at the tricuspid level in at least 13 of 14 instances. However, the authors cannot be certain that the 1 cm amplitude criterion holds for all instruments. Other investigators are urged to standardize their instruments on normal subjects.

One further point regarding the TIH deserves attention. The pattern is one of dots, but no method exists to determine the number of dots which overlay one another at a particular coordinate point on the TIH (i.e., no density function is provided). Density function information and an electronic means of computing the dispersion would be a major improvement.

A major factor in obtaining a good Doppler signal is line level adjustment. The setting is not critical, but it must be checked in each new cardiac position. A low line level will cause all dispersion to disappear and too high a line level will increase noise which has its own dispersion. The instrument permits observation of the input signal to the TIH, and this appears to be an accurate method for adjusting line level.

Failure to recognize mitral insufficiency in three patients was of concern. The child with the greatest insufficiency by angiography was patient 9, and this was recognized by both observers. The other four catheterized patients each had mild mitral insufficiency, but by RGPD only two were recognized. The degree of insufficiency of the uncatheterized patient is unconfirmed. A recent RGPD communication indicated no difficulty in finding audible characteristics of mitral insufficiency in seven catheterized instances and 10 others with only clinical mitral insufficiency.\(^9\) However, none of these children had mitral regurgitation from a cleft in the anterior mitral leaflet. Johnson and co-workers have indicated that they detected 28 of 32 instances of confirmed mitral regurgitation. No indication is present that any of these had insufficiency on the basis of a cleft leaflet.\(^7\) In the presence of a cleft, the jet may be directed toward a more difficult area to locate than is the case of a jet-directed between the leaflets. Alternatively, the TIH method or our interpretation may be insensitive to small disturbances, but these insufficiencies were not audible by RGPD during the examination. Further investigation into detection of disturbance in cleft mitral leaflets is indicated, but was not the subject of our investigation.

The differential diagnosis of the right atrial diastolic outflow disturbance must be considered. The abnormal echo-Doppler examination detected 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 atrial system or any form of anomalous coronary drainage into the right atrium. Possibly, a similar TIH could be found with only elevated cardiac output, but this was not evaluated. 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 suspected by RGPD examination. The Ebstein abnormality has, in our experience, not been confusing, for the principle flow disturbance is systolic. True tricuspid stenosis would not be distinguished from disturbance due to a left-to-right shunt by Doppler alone. An M-mode examination could separate the two entities.\(^8\)

In summary, the usefulness of evaluating the TIH output of a RGPD was demonstrated by this investigation under controlled circumstances. The method was shown to be effective for separating children with left-to-right atrial shunts from those without that condition. Moreover, the method appears objective as similar results, in most instances, could be obtained independently by two observers. The technique and instrumentation are early in their development, and although the results are encouraging, much further investigation into the potential and problems of the technique is necessary.

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Use of time interval histographic output from echo-Doppler to detect left-to-right atrial shunts.
S J Goldberg, J C Areias, S E Spitaels and V H de Villeneuve

_Circulation_. 1978;58:147-152
doi: 10.1161/01.CIR.58.1.147

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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