Use of Tissue Velocity Imaging in the Diagnosis of Fetal Cardiac Arrhythmias

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Background—Precise diagnosis of cardiac arrhythmias in the fetus is crucial for a managed therapeutic approach. However, many technical, positional, and gestational age–related limitations may render conventional methods, such as M-mode and Doppler flow methodologies, or newer techniques, such as fetal electrocardiography or magnetocardiography, difficult to apply, or these techniques may be unsuitable for the diagnosis of fetal arrhythmias.

Methods and Results—In this prospective study, we describe a novel method based on raw scan-line tissue velocity data acquisition and analysis. The raw data are available from high-frame-rate 2D tissue velocity images and allow simultaneous sampling of right and left atrial and ventricular wall velocities to yield precise temporal analysis of atrial and ventricular events. Using this timing data, a ladder diagram-like “fetal kinetocardiogram” was developed to diagram and diagnose arrhythmias and to provide true intervals. This technique was feasible and fast, yielding diagnostic results in all 31 fetuses from 18 to 38 weeks of gestation. Analysis of various supraventricular and ventricular arrhythmias was readily obtained, including arrhythmias that conventional methods fail to diagnose.

Conclusions—The fetal kinetocardiogram opens a new window to aid in the diagnosis and understanding of fetal arrhythmias, and it provides a tool for studying the action of antiarrhythmic drugs and their effects on electrophysiological conduction in the fetal heart. (Circulation. 2002;106:1827-1833.)

Key Words: echocardiography ■ arrhythmia ■ electrophysiology

Most cardiac arrhythmias in the fetus can be diagnosed using conventional M-mode and/or Doppler echocardiography. However, these methods are limited by the orientation of the fetus and by difficulties in adequate alignment of the atria and ventricle with ultrasonic beams. New techniques, such as signal-averaged fetal ECG or magnetocardiography, provide useful information on time intervals in the fetus. Nonetheless, they still carry significant limitations related to ease of use and gestational age range of applicability. The aim of the present study was to assess the use of 2D tissue Doppler in diagnosing simple and complex cardiac arrhythmias in the fetus.

Methods

This prospective study included 31 consecutive fetuses who were referred because of cardiac arrhythmia for echocardiography at the Children’s Hospital in Boston, Mass, at the Oregon Health and Science University Hospital, Portland, Ore, and at the Hadassah-University Hospital, Jerusalem, Israel (Table). The gestational age at first referral was 28±5.8 weeks (range, 18 to 38 weeks). Thirty fetuses had normal cardiac anatomy and function, and one fetus (No. 5) had a complete atrioventricular septal defect. This study was approved for human subjects at all 3 institutions.

Data Acquisition

Tissue velocity imaging (TVI) was performed using the GE Vivid FiVe system after completing conventional fetal echocardiography. TVI images were acquired using the 4-chamber view equivalent with 3.5- to 5-MHz phased-array transducers. We obtained the highest image frame rate by narrowing the angle of TVI interrogation and optimizing the field of view. Depending on the distance of the fetal heart from the transducer, frame rate ranged from 48 to 136 Hz (mean, 72 Hz) when TVI was applied. Three cine loops of TVI raw data, each containing 3 to 10 cardiac cycles (median, 5 cycles), were stored as digital scan-line data for later offline analysis using the integrated EchoPac software, at which time simultaneous TVI curves of segmental motion were obtained by sampling the following 4 regions of interest (3×3 pixels): the posteroseptal wall of the right and left atria and the right and left ventricular free wall insertions at the level of the atrioventricular annulus¹ (Figure 1).

The temporal resolution of these TVI curves is (10 ms+500 ms)/(frame rate [Hz]) (manufacturer data). Thus, for the frame rates used in our study, time resolution ranged from 13.6 to 20.4 ms (mean, 17.3 ms).

Data Analysis

Typical triphasic TVI curves² were obtained at atrial and ventricular levels. They were composed of 2 diastolic waves produced by tissue motion away from the apex during the early diastolic rapid-
Characteristics of the 31 Fetuses Included in the Study

<table>
<thead>
<tr>
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<th>Anatomy</th>
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<tr>
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<tr>
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<tr>
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<td>35</td>
<td>SVT</td>
<td>Normal</td>
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CAVB indicates complete atrioventricular block; CAVSD, complete atrioventricular septal defect.

Using the FKG, data analysis was undertaken for the same cases by 2 authors, who agreed completely on all diagnoses based on FKGs developed by each.

Statistical Analysis of Quantitative Data
All parametric data were expressed as mean±1SD. We compared the atrioventricular time interval during the atrial premature beat and during normal beats using a paired t test because each fetus provided the control normal time interval for reference (normal and abnormal beats in the same fetus). P<0.05 was considered statistically significant.

Results
Feasibility and Time of Acquisition
Digital TVI data in 2D format files were obtained in all 31 fetuses, regardless of fetal gestational age or position.

The time for data acquisition was 2 to 6 minutes for files judged adequate for analysis (median, 4 minutes). Offline analysis required 4 to 15 minutes (median, 8 minutes).

Diagnoses
Twenty-seven fetuses (87%) had a supraventricular arrhythmia, two had ventricular ectopy (6%), one presented with complete atrioventricular block (3%), and one had sinus bradycardia (3%) (Table).

Supraventricular Arrhythmias
Among supraventricular arrhythmias, there were 19 fetuses with atrial premature beats (APBs) and 8 with supraventricular tachycardia.

Atrial Premature Beat
APBs occurred sporadically in 74% of the cases (14 of 19 fetuses) and in atrial bigeminy or trigeminy form in 5 fetuses. In approximately half of the cases (9 of 19 fetuses), the APBs were blocked.

Characterization of APBs by TVI
An APB was easily diagnosed as a premature tissue velocity wave (A’) recorded at the atrial level with a shorter-than-expected atrial cycle length compared with other sinus beats. In general, A’ occurred close to the E wave (Figure 3A), sometimes superimposed or even preceding it. In very early APBs occurring during ventricular systole, the direction of the atrial wall motion of A’ was opposite to regular A wave deflections because of the reversed atrial contraction against the closed atrioventricular valve. Blocked APBs were characterized by an inverted A’ wave, as observed for early conducted APBs during the ventricular S wave, as recorded from ventricular myocardium (Figure 3B).

When plotted on an FKG, the incomplete compensatory pause was readily measured (Figure 4).

Origin of APBs
In 10 fetuses, we could identify the origin of the APB in the right or left atrium (Figure 4) by comparing the time delay between the onset of the APB and the onset of the contralateral atrium from the FKG. An APB originated in the left atrium in 7 of the 10 cases with left atrial contraction preceding the right atrial contraction by 26±4 ms. In 3 fetuses, the right APB preceded the left atrium contraction by

filling phase (E) and during atrial contraction (A). The third wave (S) occurred in the opposite direction during systole and corresponded to the ventricular contraction with ventricular motion toward the apex (Figure 1). The polarity of these 3 waves depended on the position of the apex in relation to the transducer. When the apex was up, close to the transducer, S would be positive and E and A negative.

To assess the time-relationship between atrial and ventricular events, we identified the following time events from the TVI curves: the onset of atrial contraction, which was defined as the point where the TVI curve crosses the baseline, and the onset of ventricular activity, which was defined as the point where the curve returned to the baseline at the end of atrial contraction. This point also represented the onset of the ventricular isovolumic contraction.

These different time events were measured from the beginning of the cineloop and were entered for each cycle in an Excel file (Microsoft), from which a “fetal kinetocardiogram” (FKG) ladder diagram was automatically drawn (Figure 2). This FKG exhibited the onset of right and left atrial contraction, the atrioventricular interval, and the subsequent onset of right and ventricular contraction. When right- and left-sided events were superimposed or were <10 ms apart, the same time was entered. The temporal and spatial location of a premature beat in regard to other beats was assessed
35±19 ms. In the other fetuses, the onset of A’ in the right and left atria were practically superimposed.

Supraventricular Tachycardia
In two fetuses, we readily diagnosed atrial flutter by simultaneously sampling the atrial and ventricular walls (Figure 5A). In both cases, there was a fixed 2:1 atrioventricular conduction with atrial flutter rates of 440 and 475 bpm.

In the third case of supraventricular tachycardia, we documented atrial tachycardia of 227 bpm (Figure 5B), with a 1:1 atrioventricular conduction. The ectopic focus seemed to originate in the right atrium, with a right-to-left atrial delay of 11.2 ms. In the fourth case, we were able to record the end of the atrial ectopic tachycardia (203 bpm), which was apparently of right-sided origin (42 ms right-to-left interatrial delay), and the recovery to sinus rhythm. On the sharp cessation of the tachycardia, we observed a prolonged recovery time (sinus node recovery?) of 450 ms, with gradual acceleration of the sinus rhythm back to a physiological range. The ventricular rates of the remaining cases ranged from 240 to 290 bpm.

Figure 1. Left, Apical 4-chamber view equivalent of the heart. Four regions of interest (3×3 pixels) are selected: left and right ventricular myocardium at the level of the atrioventricular valve annulus and right and left atrial posterior walls. Right, TVI curves obtained simultaneously from 4 regions of interest. Line color corresponds to the color of the regions of interest in left panels. Atrial velocities are much slower, with positive A waves (atrial contraction) in opposite direction to the A wave obtained from ventricular myocardium sampling. The asterisk and arrow indicate onset and termination of the atrial contraction, respectively. E indicates rapid filling of the ventricle; IVC, isovolumic contraction; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; and S, ventricular systole.

Ventricular Arrhythmias
We diagnosed isolated ventricular premature beats (VPBs) in two fetuses. One fetus had a complete atrioventricular septal defect.

Characterization of VPBs Using TVI
The classic features of the VPB were readily detected by inspecting the FKGs (Figure 6). The atrial (sinus) rhythm was regular, whereas the ventricular diagram showed the premature beat originating from the ventricle. The FKG clearly showed the atrioventricular dissociation during the premature beat. The post-extrasystolic pause was almost fully compensatory (variability of ±10 to 19 ms). In the fetus without a structural heart defect, the premature beat clearly originated from the left ventricle, with an 81 ms delay between the VPB and right ventricular contraction (Figure 6A). In the fetus with a complete atrioventricular septal defect, the deflection of VPB on the right side preceded the left by 46 to 55 ms (Figure 6B).
Complete Atrioventricular Block

One fetus exhibited complete atrioventricular block at 24 weeks of gestation. The FKG clearly showed the complete atrioventricular dissociation with a supraventricular (sinus) rate of 133 bpm and a ventricular rate of 77 bpm (Figure 7).

Structural Heart Disease and Other Findings

One fetus had atrioventricular defects diagnosed at the second fetal echocardiogram session. All other fetuses had normal anatomy. None of the 31 fetuses with supraventricular tachycardia (SVT) had effusions, significant atrioventricular valve regurgitation, or other signs of compromised hemodynamics.

Comparison With Other Methods

Standard gray-scale M-mode and/or pulsed Doppler interrogation was performed in 12 of the 31 fetuses. Acquisition time added to the study ranged from 5 to 20 minutes (mean, 13.3±5.2 minutes) and was significantly longer than the 3.1±1.4 minutes it took to store TVI data \((P<0.0001)\).

APBs were correctly diagnosed in 7 of 8 fetuses using M-mode and pulsed Doppler, mainly because of the lack of full compensatory pause. The blocked APBs of fetus 14 were misdiagnosed as drop beats (atrioventricular block), because no atrial signal could be detected by M-mode. Atrial flutter (fetus 10) was diagnosed by M-mode, but it took 12 minutes to get an adequate recording. Although the diagnosis of complete atrioventricular block in fetus 7 (who had bradycardia) was suspected, a clear recording of atrial and ventricular events simultaneously could not be obtained, probably because of fetal position (side-to-side) by M-mode or pulsed Doppler. The VPBs of fetus 5 were misdiagnosed as APBs by M-mode Doppler.

Postnatal Confirmation of the Diagnoses

ECG was available in 9 newborns who were studied prenatally in this series. Five fetuses with APBs had a normal ECG at birth. One fetus with APBs (No. 23) had APBs and runs of SVT on its fourth day of life. Two fetuses with SVT (Nos. 4 and 24) had runs of SVT in the neonatal period that required treatment.

Discussion

The earliest analyses of fetal arrhythmias were first based on M-mode echocardiography, when the cursor would be directed through the atrial wall and the ventricular wall or the atrioventricular valve.4–7 This technique was not only tedious, but was also sometimes unsuccessful because of an inability to align the M-mode cursor through these structures due to the position of the fetus. Dual M-mode echocardiography\(^8\) has been used to overcome some of these difficulties. Simultaneous pulsed Doppler interrogation of the inflow and outflow of the ventricle or of the superior vena cava and aorta\(^9\) is easier to perform and has been suggested as an easier technique to use compared with M-mode echocardiography.\(^10\) However, because blood flow is sampled, there is a resultant inherent inaccuracy related to blood flow inertia.

Atrioventricular block, unless it is in its most serious form (ie, complete atrioventricular dissociation), has not been diagnosed accurately by M-mode or conventional Doppler techniques. Recently, new techniques, such as sophisticated fetal electrocardiograms\(^11,12\) and magnetocardiograms,\(^13–16\) have been developed with the goal of having an accurate and repeatable modality to measure conduction time intervals in the fetus. However, interpretation of the fetal ECG using cross-correlation techniques for suppression of maternal ECG is limited after 28 weeks of gestation due to the distribution of the vernix caseosa, which distorts the ECG in an unintel-
ligible way.\textsuperscript{17} In addition, in a recent study, magnetocardiograms were found to be unsatisfactory for PR interval measurement, which could only be assessed in 50\% of the fetuses younger than 27 weeks of gestation.\textsuperscript{15} Clinical use of the fetal magnetocardiogram has been most limited by the need for a magnetically shielded room. In addition, fetal ECG and magnetocardiography are both augmented signal-averaging methods, making beat-to-beat analysis of random ectopic contractions less routinely successful. Our study showed that direct recording of mechanical activity of atria and ventricles using TVI was feasible in all 31 fetuses, with no limitations regarding the age of gestation (18 to 38 weeks). The time for acquisition (median, 4 minutes; range, 2 to 6 minutes) was much shorter than the usual time spent in acquiring an M-mode of adequate quality, which could typically range from 5 to 30 minutes.

TVI, when stored as scan-line raw data, offers the unique possibility of analyzing the activity in any region of the heart and obtaining multiple (up to 8) tissue velocity curves within the same unique temporal domain.

Atrial Premature Beats
TVI has the major advantage of recording atrial contraction directly from the atrial wall. Therefore, TVI has the significant merit of allowing detection of an early APB, even when it occurs during ventricular contraction. Doppler flow interrogation cannot provide this information because the atrial wave does not reach the ventricular outflow sampling as the atrioventricular valve is closed. In fact, ECG also sometimes does not detect an early APB because the P wave could be incorporated in the QRS or QT segment.

Supraventricular Tachycardia
Atrial tachycardia may cause severe hemodynamic disturbances in the fetus.\textsuperscript{18–20} Early and precise diagnosis of this
type of arrhythmia is paramount for optimal therapy. Reentrant tachycardia is the most prevalent mechanism of these tachycardias, as verified postnatally.\textsuperscript{20} Atrial flutter represents 25\% to 30\% of all fetal SVTs.\textsuperscript{20,21} In our study, we diagnosed atrial flutter in 2 of the 8 fetuses with SVT. The atrial flutter rate was \( \approx 450 \text{ bpm} \), with a 2:1 atrioventricular conduction in both fetuses.\textsuperscript{22,23}

In one fetus with supraventricular arrhythmia, the atrial rate was 227 bpm, with 1:1 atrioventricular conduction. We could not determine if this was sinus tachycardia or SVT with 1:1 conduction. However, the fact that the rest of the fetal echocardiogram showed episodes of frequent APB suggests that the nature of the tachycardia was atrial and not sinus. In the fourth fetus with SVT, evidence of prolonged recovery, which corresponded to a classic prolonged sinus node recovery time, tended to support our assumption that this was indeed a supraventricular and not sinus tachycardia.

**Ventricular Premature Beats**

Although much more rare than atrial premature contraction, VPBs have different causes with different clinical significance. They may be associated with structural heart disease, myocardial disease, and tumors, or they may result from extracardiac or even maternal conditions (such as cocaine ingestion). In one of our 2 fetuses presenting with VPB, a complete atrioventricular septal defect was diagnosed. Typically, a VPB would be diagnosed by M-mode Doppler by detecting a premature motion in the ventricle that was not preceded by an atrial motion. However, the early and faint atrial motion could be missed and a nonconducted APB misdiagnosed as a VPB. TVI directly detects atrial and ventricular motion independently. Furthermore, detecting a ventricular ectopic focus would be the only way to differentiate ventricular from junctional ectopic activity.\textsuperscript{24}

**Atrioventricular Conduction**

TVI analysis of atrioventricular conduction is theoretically feasible whenever reasonable-quality 2D echocardiography is available. We were able to obtain adequate TVI tracings from 18 weeks up to 38 weeks of gestation. We were also able to measure atrioventricular conduction in normal beats and

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**Figure 6.** Typical FKG of VPBs. A, The VPB originates from the left ventricle (fourth cycle) and even precedes the right atrial signal. As expected in a VPB, the sinus rhythm is undisturbed, with evident atrioventricular block in the VPB cycle. B, Two VPBs are displayed (third and sixth cycles) that originate from the right ventricle. Abbreviations as in Figure 2.

**Figure 7.** FKG of a fetus with complete atrioventricular block. The atrial and ventricular signals are clearly dissociated. Abbreviations as in Figure 2.
compare them with atrioventricular conduction in APBs in the same fetus. This method could be useful for assessing the effect of maternally administered drug therapy.

**Limitations of the Method and of Our Study**

**Measurement**

Inaccuracy in this methodology could result from two sources: poor image quality or the timing accuracy of the velocity traces inherent in the system specifications and related to the 2D TVI frame rate, which ranged from 14.2 to 20.4 ms of accuracy (mean, 17.3 ms).

**Verification**

Although the diagnoses of the arrhythmias in the fetuses we studied were clear and reproducible between observers, we could not systematically verify the nature of the arrhythmia after birth. SVT present in 2 fetuses before birth was found in the newborns. However, the fact that the majority of prenatal APBs could not be confirmed after birth does not contradict the prenatal diagnosis, because these arrhythmias may be transient.

**Conclusion**

We describe a new methodology based on TVI to analyze fetal cardiac arrhythmias. This method is extremely easy to implement and it is sensitive, because it allows precise timing of atrial and ventricular events.

**References**

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Circulation. 2002;106:1827-1833; originally published online September 9, 2002;
doi: 10.1161/01.CIR.0000031571.92807.CC
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

The online version of this article, along with updated information and services, is located on the
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