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Editorial

# Better Precision in Fetal Arrhythmia Diagnosis and Management: Pre-excitation in Fetus or the Cardiologist?

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Fetal arrhythmias complicate approximately 1%-2% of pregnancies, with specific rhythm disturbances ranging from benign extrasystoles to incessant supraventricular tachycardia (SVT).[1] The most common types of fetal SVT include atrioventricular (AV) re-entry tachycardia and atrial flutter, which are responsible for 70%-90% and 20%-30% of diagnoses, respectively.[2,3] Rarely, untreated sustained SVT is associated with significant mortality and morbidity with the development of hydrops fetalis (up to 50%) and intrauterine demise (9%-17%). Treatments for fetal arrhythmias include transplacental antiarrhythmic therapy or expedited delivery, depending upon gestational age, arrhythmia load, degree of fetal compromise, and local resources. Hence, it is imperative to diagnose fetal arrhythmias as early as possible and to have an established monitoring and treatment plan to ensure an optimal pregnancy outcome.

In the current issue of *CJC Pediatric and Congenital Heart Disease*, Veillette et al.[4] reported the AV conduction intervals measured for 9 fetuses with a postnatal diagnosis of ventricular pre-excitation, selected from 103 fetuses diagnosed with all types of fetal SVT. Data were collected from fetal echocardiograms performed between January 2000 and July 2021 at a single centre. The authors hypothesized that among this group with fetal SVT and postnatal pre-excitation, the fetal AV interval, as measured in sinus rhythm using the superior vena cava (SVC)-Aorta (SVC/Ao) Doppler technique on fetal echocardiography, would be shorter than normal and statistically associated with the presence of pre-excitation on the postnatal electrocardiogram (ECG). Normalcy was defined by $z$-scores $\leq 2$ using prediction equations previously reported by their institution. They reported a median AV interval of 107 ms (interquartile range: 104-116 ms), representing a $z$-score of $-1.27$ ($-2.01$ to $-0.56$). Six fetuses (67%) had repeated AV intervals $\leq -2$ standard deviation on multiple fetal echocardiograms. Three (33%) had Wolf-Parkinson-White (WPW) syndrome on postnatal surface ECG but did not have short AV intervals on fetal echocardiography (false-negative). The AV intervals for fetuses without pre-excitation on the postnatal ECG are not reported for comparison, so false-positive results are unknown. The authors concluded that Doppler echocardiographic AV interval measurements in fetuses with arrhythmias allow identification of prenatal WPW. Based on these findings, the authors suggest that the use of a simple Doppler technique can help clinicians be more precise about the underlying mechanism of SVT in fetuses. Knowing the likely underlying mechanism of SVT, that is, AV re-entry vs automatic vs intra-atrial re-entry (atrial flutter) might help to target with appropriate antiarrhythmic therapy. The authors should be congratulated on pushing the knowledge envelope further to better understand these mechanisms and allow more precision in antenatal counselling of those whose fetuses have SVT. However, like many other studies in the paediatric and congenital cardiac world, the findings from this single-centre study with such a small sample need to be validated using a larger multicentre sample before widespread clinical application should be adopted.

Fetal arrhythmias are assessed for frequency, duration, and type of arrhythmias based on fetal heart rate, the relationship between atrial and ventricular contractions, the relative ratio of AV and ventriculoatrial (VA) intervals, and gestational age at onset. Knowing the underlying mechanism not only helps in diagnosis but also helps in planning appropriate treatment with prognostication. As previously shown by the authors from the same institution,[5] the underlying mechanism of fetal arrhythmia can be estimated based on the relative durations of the AV and VA interval. Different echocardiographic views and techniques are used to measure the mechanical AV interval, and each has its own strengths and limitations.

Cardiac rhythm assessment uses 2-dimensional, M-mode, pulsed Doppler and tissue Doppler modalities. The assessment of fetal rhythm with M-mode echocardiography takes advantage of high temporal resolution for precise timing of atrial and ventricular myocardial contraction simultaneously. The timing of atrial and ventricular contraction can be measured using Doppler echocardiography of simultaneous mitral valve inflow/aortic outflow (in/out), pulmonary vein/branch pulmonary artery (PA/PV), or SVC/Ao.

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Doppler-based time intervals are commonly used because of the ease of obtaining measurements, their reproducibility, and the availability of normal values. However, the accuracy of Doppler-based intervals is dependent upon a well-aligned Doppler cursor with an adequate sample volume. Tissue Doppler can also be used to measure atrial and ventricular myocardial time intervals by interrogation of the lateral mitral or tricuspid valve annulus. This requires good 4 chamber images of the AV valve annuli.[6] Given the variety of options available for measurements, most clinicians rely on a constellation of measurements using different techniques to form a general clinical impression about interval timing.

Over the years, efforts have been made to establish normal values and *z*-scores for all time intervals on fetal echocardiogram, including efforts by those at the authors' own institution. Overall, AV and VA intervals are correlated positively with gestational age and negatively with fetal heart rate. For AV intervals, PA/PV Doppler revealed the longest mean AV and shortest VA time interval, and SVC/Ao Doppler showed the shortest AV interval.[7,8] The SVC/Ao time intervals demonstrated the least variability related to fetal heart rate. For left ventricular in/out, SVC/Ao, and PA/PV, intraobserver and interobserver reliability coefficients showed excellent agreement (all intraclass correlation coefficients $\geq$0.80).[8]

The authors used the SVC/Ao Doppler method to assess AV intervals in the present study, which makes sense as their institution has vast experience in measuring time intervals on fetal echocardiogram using different methods. They have previously reported that AV intervals were significantly longer with M-mode than with Doppler ultrasonography. Reliability coefficients were excellent (at least 0.89) for all intraobserver measurements. Comparisons of AV and VA interval measurements made by 2 observers gave better intraclass correlation coefficients via the Doppler approach.[5] However, making a diagnosis of the shortest AV interval using a technique that reports the shortest AV interval of all available techniques may be expected to potentially result in the overdiagnosis of a short mechanical PR (AV interval), and by extension, using the suggestions of this study, of ventricular pre-excitation. This may be one of the reasons that half of the patients in the present study with a short AV interval on fetal echo had a normal PR interval on postnatal ECG. It might have been more useful with fewer false-positive results if the authors had used an average AV interval from various techniques to measure the antenatal AV interval, rather than relying on a single technique that may intrinsically underestimate the AV intervals for all patients.

There are also several potential reasons for a short PR interval: pre-excitation syndromes such as WPW, Lown-Ganong-Levine syndrome, premature atrial contractions originating from the lower atrial region, glycogen storage disorders such as Pompe's disease, and pseudo short PR interval with AV dissociation. Although the commonest cause is an AV accessary pathway resulting in orthodromic re-entry tachycardia, especially in structurally normal hearts, a shorter AV interval does not always translate to WPW syndrome. Given the potential serious complications associated with WPW and the potential implications of prenatal counselling about potentially life-threatening disorders, caution is necessary before concluding that a short AV interval on fetal echocardiography is translatable to WPW syndrome in the postnatal period.

It is well known that a prenatal diagnosis of fetal arrhythmias not only reduces mortality and morbidity but also helps parents to prepare for frequent monitoring, delivery planning, and postnatal management at a tertiary care centre.[6] However, it is unknown whether a fetal diagnosis of SVT vs WPW-associated SVT makes any difference to parent counselling and perinatal management. Mothers of fetuses with antenatally diagnosed SVT mostly deliver in tertiary care centres where an ECG can be recorded immediately after birth to definitely determine the presence of ventricular pre-excitation. In such cases, the diagnosis of pre-excitation can be explained to parents, in addition to the overall diagnosis of the arrhythmia and its management. The AV interval is dynamic, and it may normalize with advancing gestational age. Therefore, there is a high possibility that a shorter AV interval (presumed WPW) may disappear or may be intermittent by the time of birth and hence is not a reliable parameter for prenatal counselling and follow-up. Given all of this, it is unclear whether the additional assessment of the AV interval warrants further characterization of an arrhythmia as likely related to a pre-excitation syndrome.

Overall, this study reminds readers of how a simple Doppler technique can be helpful in understanding the mechanism of SVT. It has also helped to generate more hypotheses about whether it is possible to be more precise about the likely mechanism of SVT antenatally. At this point, however, the clinical benefits and utility of the AV interval as a predictor of WPW are likely best viewed as uncertain.

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