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Professor Special Lecture: 153rd Regular Meeting of the Medical Society of Toho University

Review Article

Assessment of Fetal Cardiac Function and Development of a Novel Technique

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ABSTRACT: Fetal circulatory physiology differs from that of the neonate. A concept of biventricular combined cardiac outputs is necessary to understand and assess the fetal cardiac function. Fetal cardiac function has been estimated using echocardiographic methods such as M-mode, B-mode, color flow mapping, and pulsed wave Doppler. In addition, recent studies have reported the utility of tissue Doppler imaging in fetal echocardiography. However, established parameters for fetal cardiac function remain to be unresolved. Table 1 shows variables which have been reported in the literature and used in clinical studies in these days. Therefore, we developed two novel techniques to assess fetal cardiac function; one is automatic fractional shortening method, the other is E/e' by dual gate Doppler methods. These two techniques are expected to be reliable and useful methods to assess fetal pathological status in various conditions.

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KEYWORDS: fetal cardiac function, dual gate doppler, E/e', AutoFS

1. Fetal Cardiovascular Physiology

Fetal circulatory physiology differs from that of the neonate. The oxygenated blood from the placenta enters directly into the left heart through the ductus venous, providing higher oxygenated blood to the brain and the upper body, whereas rather deoxygenated blood from the inferior and superior vena cavae is delivered to the lower body through the right heart. Blood flow from the right heart largely bypasses the lung via ductus arteriosus because of greater pulmonary vascular resistance than the systemic vascular resistance. The placental circulation, which mainly determines the right ventricular afterload, is maintained to be of low resistance, whereas cerebrovascular resistance, which mainly determines left ventricle afterload, is responsive to hypoxic fetal conditions and regulated automatically. The right ventricle provides greater proportion of cardiac output during the second half of gestation until birth.[1] Systolic pressure is equal in both ventricles, which demonstrates a linear increase with gestation.[2] Thus, a concept of biventricular combined cardiac outputs is necessary to understand and assess the fetal cardiac function.

2. Assessment of Fetal Cardiac Function

Fetal cardiac function has been estimated using echo-

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Table 1 Echocardiographic parameters for assessment of fetal cardiac function

Variables	Modalities	Abnormalities	Significance
Diastolic parameters			
MV inflow (E/A ratio)	PW Doppler	Uniphasic	LV diastolic dysfunction
		E/A ↓	LV diastolic dysfunction
		E/A ↑	Left volume loading, External compression
TV inflow (E/A ratio)	PW Doppler	Uniphasic	RV diastolic dysfunction
		E/A ↓	RV diastolic dysfunction
		E/A ↑	Right volume loading, External compression
DV: A-wave, PI	PW Doppler	absent/reversal	Diastolic dysfunction, Tricuspid regurgitation
IVRT	PW Doppler, Tissue Doppler	prolonged	Diastolic dysfunction
E/e′	PW Doppler, Tissue Doppler	↑	Diastolic dysfunction
Systolic/Global parameters			
CTR, CTAR	B-mode	increased	cardiac dilatation
FS/EF	M-mode	decreased	Reduced contractility, Volume loading
		Increased	Reduced afterload, Increased contractility
SV/CO	PW Doppler, B-mode	Decreased	Reduced contractility, Reduced filling
		Increased	Volume loading, Reduced afterload
Tei index	PW Doppler, Tissue Doppler	Increased	ET ↓, IVRT ↑, IVCT ↑

CO, cardiac output; CTAR, cardio-thoracic area ratio; CTR, cardio-thoracic ratio; DV, ductus venous; EF, ejection fraction; ET, ejection time; FS, fractional shortening; IVCT, isovolumetric contraction time; IVRT, isovolumetric relaxation time; LV, left ventricle; MV, mitral valve; PW, pulsed wave; RV, right ventricle; SV, systolic volume; TV, tricuspid valve

cardiographic methods such as M-mode, B-mode, color flow mapping, and pulsed wave Doppler.[3–6] In addition, recent studies have reported the utility of tissue Doppler imaging (TDI) in fetal echocardiography, which enables to assess the myocardial motion.[7–9] However, established parameters for fetal cardiac function remain to be unresolved. Table 1 shows variables which have been reported in the literature and used in clinical studies in these days.

M-mode echocardiography has been widely used to assess the contractile performance of the fetal myocardium. The most widely used parameters to assess the fetal cardiac function are either fractional shortening (FS) or ejection fraction (EF), and these were reported not to change significantly across gestational ages.[10] Although many investigators have reported the fetal contractile performance of both ventricles using FS or EF, there are many limitations to assess FS or EF in the fetal life: first, the orientation of the M-mode cursor should be at right angles to the ventricular septum, which depends on the fetal position; second, the right ventricle tends to contract by shortening along its long axis rather than in its short axis, which makes impossible to assess the contractile performance in the right ventricle precisely; third, the length of fetal ventricles is not constant at twice the diameter of the ventricles, which relationship is fundamental assumption to calculate EF by using the common formula by Teichholtz.[11]

The cardiac output (CO) or stroke volume (SV) of both left and right sides of the heart has been measured using pulsed Doppler echocardiography, in which studies flows across the atrioventricular valves or the right and left ventricular outflow tract were measured.[12, 13] These studies showed a marked increase in CO with advancing gestation and that the output of the right ventricle was usually higher than that of the left. Although the measurement of CO or SV is possible, these parameters are not used in daily practice because of lack of feasibility and reproducibility.

Tei index, so called "myocardial performance index (MPI)" is a parameter measuring global myocardial function, which is defined as the sum of the isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) divided by ejection time (ET).[14] The MPI is a reliable early marker of fetal cardiac dysfunction and is considered to indicate the initial stages of cardiac adaptation

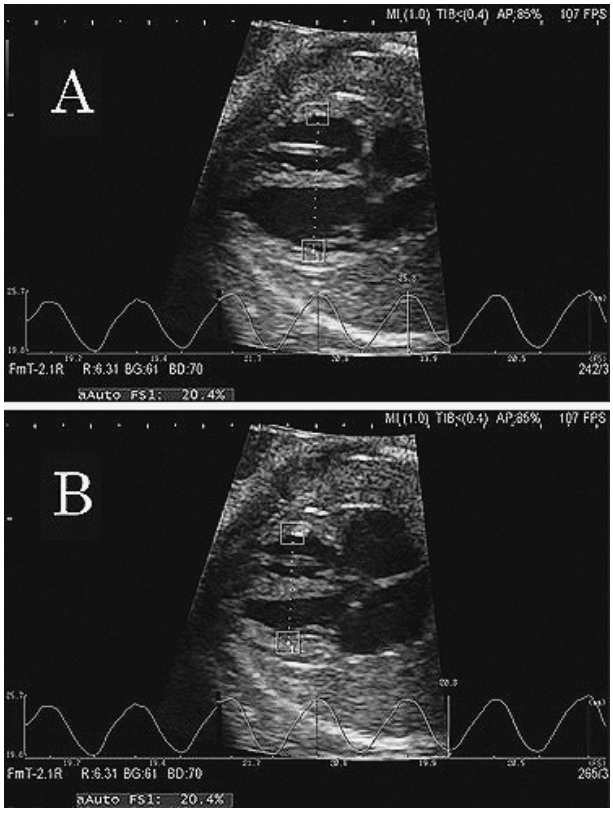

Fig. 1 The ultrasonogram of Auto FS measurement. The region-of-interest follows the myocardium contracting in the minor axis direction and the major axis direction.

for various perinatal complications. Impaired ventricular dysfunction is associated with higher MPI values,[15] frequently due to a prolongation of the IRT, which is generally accompanied by a reduced ET, with the ICT. The MPI has been used to demonstrate fetal cardiac dysfunction including twin-to-twin transfusion syndrome (TTTS),[16–18] congenital heart malformations,[19, 20] fetal growth restriction (FGR).[21–23]

3. Development of a Novel Technique to Assess Fetal Cardiac Function

3.1. Automatic FS measuring method (Auto FS)

Although FS calculated using the conventional M-mode is currently the main method that is generally used to evaluate the fetal cardiac function,[4, 24, 25] there are some limitations to obtain the data due to fetal position and movement. Therefore, we recently developed an automatic FS measuring method (Auto FS), which uses a 2DT method for tracking fetal heart motion, wherein the Auto FS can be calculated automatically[26] (Fig. 1). Auto FS in both right and left ventricles decreased significantly with gestational age. Furthermore, this novel technique enables us to obtain combined-Auto FS, which may indicate biventricular contractile performance.

The ventricle contracts not only in the short axis direction but also in the long axis direction,[27–29] Considering it, FS using the M-mode that measures temporal changes on the same straight line cannot measure the fetal cardiac contraction rate at the same site during both the systolic and diastolic phases. 2DT method can track the heart muscles, which contract in the long axis direction, by setting the ROI on the heart muscle using the four-chamber view. That is, Auto FS measures the contract rate in consideration of myocardial movement in the long axis direction.

Each Auto FS had a negative correlation with the number of gestational age. The negative correlation with the number of gestational age could be explained by the influence of the increased intracardiac pressure in correlation with the number of gestational age[2] and by the increase in afterload due to the increased circulatory blood flow of the fetus.

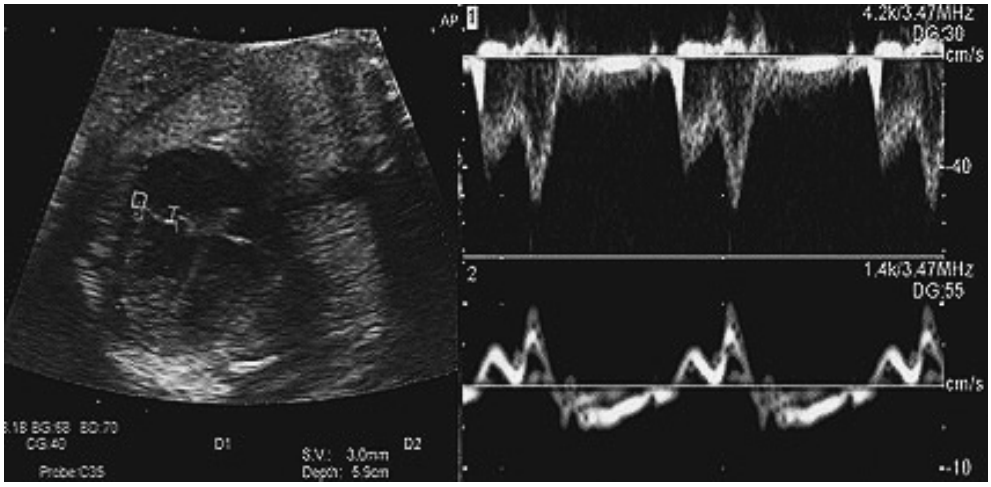

Fig. 2 The ultrasonogram for assessment of E/e' by the Dual gate Doppler method. The upper Doppler waveform is obtained using pulsed wave Doppler imaging, whereas the lower waveform is obtained using tissue Doppler imaging. In the Dual gate Doppler method, velocities of E and e' wave are measured in the identical cardiac cycle.

3.2. E/e' by dual gate Doppler method

Assessment of fetal cardiac function focusing on diastolic function is still challenging in the fetal echocardiographic field. The ratio of E/e', the conjunction with early mitral annular velocity (e') and mitral early peak filling velocity (E), is one of the echocardiographic parameters for diastolic function, and its application is recommended to adult echocardiography.[30–32] The literature concerning reference values of fetal E/e' is, however, limited.[33, 34] Dual gate Doppler (DD) method is a technology that enables to assess two Doppler waveforms simultaneously at any separate two locations. Using DD method, it is possible to measure E/e' of the same heartbeat, showing blood flow and TDI waveform in real time. Therefore, we adapted DD method to assess fetal diastolic cardiac function[35] (Fig. 2).

By using this novel technique, both left and right E/e' showed significant negative correlations with gestational age. The reason why progressive decline of fetal E/e' value along with gestational age is considered that the rate of increment of velocity of e' wave along with gestational age is higher than that of E wave, and the increment of e' velocity contributes to the decrease of E/e'.

Physiologically high E/e' at earlier gestation might reflect myocardial immaturity. The descending of each E/e' with advancing gestation seemed to imply the increase of cardiac compliance owing to fetal myocardial functional mature with biometrical growth. In other words, we speculated that the serial change of fetal E/e' in this study shows evolution of cardiac diastolic function in the prenatal period.

4. Future Prospect for Assessment of Fetal Cardiac Function

Assessment of fetal cardiac function using a number of modalities is still ongoing. In other words, we, physicians, do not yet have optimal tools to assess clinical condition of a fetus in the mother adequately. However, many investigators continue to explore and study from various points of view. Further investigation is still needed.

Conflicts of interest: None declared.

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