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Evolution of Foetal echocardiography as a screening tool for prenatal diagnosis of congenital heart disease

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Abstract

Congenital cardiac anomalies are the most common anomalies, with an estimated incidence of about 4-13 per 1000 live births. Proper perinatal and neonatal management is dependent upon accurate prenatal diagnosis. Approximately 10% of fetuses with cardiac abnormalities have identified risk factors; hence, most of the anomalies occur in pregnancies without prenatal risk factors. Foetal echocardiography allows for prenatal diagnosis of congenital heart disease and serves as a routine screening tool for congenital heart defects. Advanced technology, has not only allowed more accurate and early detection of cardiac abnormalities but has also improved the care and outcome of selected fetuses with severe cardiac malformations or arrhythmias. It can also identify patients for in-utero cardiac interventions. Prenatal diagnosis of congenital heart disease has allowed for better counseling and preparation of families regarding the expected prenatal development of the foetus as well as the anticipated postnatal management strategy and prognosis.

Keywords: Foetal Echocardiography, Prenatal Diagnosis, Congenital heart disease, In-utero cardiac intervention.

Introduction

Over the past two decades, imaging has become the principle diagnostic tool in the prenatal detection of Foetal malformations. The introduction of real-time imaging has made in-utero evaluation of Foetal heart structure and function available as well. With a live birth incidence of 0.4-1.3%,^{1,2} congenital heart disease (CHD) comprises the most common form of major birth defect, being six times more common than chromosomal abnormalities and four times more common than neural tube defects.³ It accounts for approximately 20% of neonatal deaths and 50% of infant deaths and is seen four to five times more frequently in stillbirths.^{3,4} As a group, these defects account for significant neonatal morbidity and mortality, resulting in an economic burden on the health care system and a financial and emotional burden on the involved families.⁵

The purpose of this review article is to highlight:

1. Methods available for Foetal echocardiography

2. Examination of the Foetal heart

3. Foetal echocardiography as a screening tool used for in-utero diagnosis of abnormal Foetal cardiovascular structure and physiology;

4. Role of early Foetal echocardiography.

Methods available for Foetal echocardiography:

The examination of the Foetal heart utilizes B-mode (two-dimensional echocardiography), M-mode, spectral Doppler (pulsed wave and continuous wave) and colour Doppler flow mapping (two-dimensional Doppler echocardiography). These technical advances in sonographic instrumentation and analysis have allowed for in-depth anatomic and physiologic study of the Foetal heart both in its normal and malformed state.

The most important aspect of the echocardiographic examination is two-dimensional echocardiography which, when performed trans-abdominally allows the exact diagnosis of most cardiac abnormalities due to the high spatial and temporal resolution of modern real-time ultrasound machines in the demonstration of cardiac structures.⁶ High frequency probes improve the likelihood of detecting subtle defects.⁷

M-mode echocardiography has the advantage of superior temporal and spatial resolution and thus facilitates the exact measurement of cardiac walls, valves and chambers at a defined point in the cardiac cycle. However, over a period of time the B-mode has superseded the M-mode in terms of the spatial and temporal resolution and has improved to a great degree as to allow precise measurements and bypass the shortcomings of M-mode echocardiography, namely the complexity in obtaining the exact measuring position of the cursor and control during measurements. M-mode tracings of the atria and ventricles can delineate the Foetal rhythm and therefore, is used for the differential diagnosis of Foetal arrhythmias. In particular, a simultaneous record of Doppler waveform at the superior vena cava and the ascending aorta has become an important and useful method of assessing the interval between atrial and ventricular contractions.^{8,9} Identifying congenital complete heart block prenatally can prepare families and health care providers for the need for delivery at a tertiary center should the foetus require

temporary or permanent pacing after delivery. Beta stimulants and steroids have been reported as effective transplacental treatments for Foetal atrioventricular block.¹⁰⁻¹²

After two-dimensional echocardiography, colour coded echocardiography is the most important examination method in the diagnosis of cardiac anomalies. Simultaneous display of blood flow within the two-dimensional picture enhances the identification of vessels and allows a rapid overview for cardiac flow anomalies. Moreover, it increases the sensitivity of echocardiographic examinations as jets in regurgitation and valvular stenosis can be detected. The differentiation of complex cardiac abnormalities, especially those with obstructions of the outflow tracts is made easier and in selected cases analysis of the blood flow patterns allows for more differentiated assessment of prognosis.¹³

Examination of the Foetal heart:

Cardiac examination planes utilized in-utero are similar to those used in the postnatal period, although the airless lungs and less reflective ribs provide better access to the Foetal heart than after birth. This approach can be used from the 13th week of gestation onwards. A complete and thorough Foetal cardiovascular examination should include a segmental evaluation of the arrangement of the thoraco-abdominal organs and the entire Foetal heart and great vessels. Not infrequently, however, the operator must be flexible because Foetal position may alter the order in which the standard views are obtained. In addition to an unfavourable position, other factors that may affect the study and limit visualization include maternal obesity and oligohydramnios.¹⁴

Yoo et al.¹⁵ described a sequential segmental approach for the evaluation of Foetal heart using six basic sonographic views:

1. The transverse view of the Foetal upper abdomen is obtained to determine the arrangement of the abdominal organs, which, in most cases, provides the important clues to the determination of the atrial arrangement.
2. The four-chamber view is obtained to evaluate the atrio-ventricular junctions.
3. The views of the left and right ventricular outflow tracts are obtained to evaluate the ventricular-arterial junctions.
4. The three-vessel view and the aortic arch view are obtained for the evaluation of the arrangement and size of the great arteries, which provides additional clues to the diagnosis of the abnormalities involving the ventricular-arterial junctions and the great arteries.

At the beginning, the operator determines the position of the foetus and establishes abdominal situs by identifying

the right and left sides of the trunk. In the normal situation, the stomach should be visualized in the left side of the abdomen. Once the Foetal orientation has been established, the transducer can be tilted from its view of the abdominal circumference toward the Foetal head. As a result of this maneuver, images of the Foetal heart in the four-chamber view should be obtained. At this point, it is very important to make sure that the Foetal heart is situated in the middle of the chest with the cardiac apex on the same side of the body as the stomach. The Foetal heart should be without pronounced deviation to either the right or left thorax, because this could be an indication of a situs abnormality or other intra-thoracic congenital malformations.¹⁶

The four-chamber view is useful to assess the relative sizes of the cardiac chambers and to identify individual chamber anatomy. On exclusion of dextrocardia, the most posterior chamber closest to the spine is the left atrium with the septum secundum flap within it, and the chamber closest to the ventral abdominal wall is the right ventricle. In addition, the right ventricle should have coarse muscular trabeculations, including the moderator band visible toward its apex, which appears to foreshorten the right ventricular cavity. The chamber sizes at the level of the atrio-ventricular valves should be equal in size. The walls of the ventricles must be equal in size. Although, mild ventricular disproportion can occur as a normal variant, hypoplastic left heart syndrome and coarctation of aorta are important causes of this disparity.¹⁷ The echogenicity of the tricuspid and the mitral valve must be the same with the septal leaf of tricuspid valve insertion noted to be slightly more apically displaced than the left sided mitral valve. The valves should be noted to open and close completely. The inter-ventricular septum must be intact and the atrial septum must be intact except for the opening of foramen ovale, and the septum secundum flap in the left atrium should be seen coming and closing the foramen ovale. The pulmonary veins should be seen entering the left atrium. Whenever possible, it is important to see the four-chamber view from more than one orientation, including one that is perpendicular to the inter-ventricular septum, because the upper portion of the septum may be quite thin in normal foetuses, giving rise to a false-positive suspicion of a ventricular septal defect.¹⁸ Some views may reveal a small hypoechoic rim around the Foetal heart that can be mistaken for a pericardial effusion. An isolated finding of this type usually represents a normal variation.¹⁹ Cardiac rate and regular rhythm should be confirmed. The normal heart rate ranges from 120-160 beats per minute. Mild bradycardia is transiently observed in second trimester foetuses. Fixed bradycardia of heart rate especially below 110 beats per minute requires timely evaluation for possible heart block. Mild tachycardia (> 160 beats per minute) can occur as a normal variant during Foetal movement. Persistent

tachycardia, however, should be further evaluated for either possible Foetal distress or serious tachydysrhythmias.⁷

With the normal four-chamber view, conditions such as endocardial cushion defects, large ventricular septal defects, atrial septal defects, Ebstein's anomaly and left and right hypoplastic heart syndrome could be excluded but for outflow tract malformations, the long axis view of the left and the right ventricle needs to be obtained. Following the four-chamber view, to get the long axis view, we rotate the transducer towards the Foetal head. On this view, the anterior wall of the aorta should be continuous with the inter-ventricular septum without any breaks and the posterior wall of the aorta should be continuous with the mitral valve; and at the origin of the aorta, the atrio-ventricular valve must be visualized opening and closing. This view is classified as a five-chamber view. With this view, we can exclude high membranous ventricular septal defects, tetralogy of fallots, double outlet right ventricle, and transposition of great vessels. By rotating and sliding the transducer further towards the Foetal head, we should be able to obtain the view of the aortic arch with descending aorta and the three neck vessels originating from the apex of the aortic arch. After obtaining the aortic arch, moving the transducer towards the anterior abdominal wall slightly and tilting the transducer by 150, the view of the right ventricle can be obtained with the pulmonary trunk away from it and the ductus entering the aorta forming the ductal arch. Within the pulmonary artery, near its origin, the pulmonary valve should be visualized opening and closing. Except for the distal one-third of pulmonary artery, the remaining proximal two-third of pulmonary trunk should be parallel to one another and the pulmonary trunk and aorta should be equal in size in most instances. With this view, pulmonary stenosis of moderate to severe degree and pulmonary atresia would be excluded and the transposition of great vessels would be definitely excluded. The final view is to demonstrate the superior vena cava and the inferior vena cava entering the right atrium.

The sensitivity of the above-mentioned detailed Foetal echocardiographic examination at 22 weeks of gestation lies in the region of 80% for high-risk as well as low-risk collectively with a specificity approaching 100%.²⁰ However, conditions such as membranous coarctation of aorta, anomalous pulmonary venous drainage, mild degree of stenosis of outflow tract valves and the atrial and ventricular septal defects less than 3 mm are the ones which are likely to be missed which will not account for major morbidity or mortality by themselves, however still elude prenatal diagnosis.

The additional use of colour Doppler imaging in the segmented approach allows examination of the blood flow across the respective connections and especially facilitates identification of venous inflow and imaging of great arteries. Therefore, two-dimensional and colour coded Doppler

imaging are used simultaneously in Foetal echocardiography.³

Foetal echocardiography as a screening tool:

Screening programme for prenatal diagnosis of CHD using Foetal echocardiography is important as it allows not only improved counseling of families after a prenatal diagnosis of CHD, but also for proper perinatal and neonatal management as the neonate with a significant cardiac lesion will benefit from delivery at a tertiary care center where the expertise of paediatric cardiologists and cardiac surgeons are readily available²¹ as 50% of the congenital cardiac anomalies are considered easily amenable to surgery.³ Also, implementation of routinely offered Foetal echocardiography would lead to early diagnosis so that the parents can be informed about the severity and prognosis of the condition, before viability is reached. This in turn would enable them to make informed decisions about the further course of pregnancy, for example, avoidance of caesarean section for a lethal anomaly or continuation of pregnancy with delivery in a tertiary center. It would also improve the chances of survival of a baby with a critical congenital defect by ensuring that the necessary prenatal and postnatal care is provided.²¹ Precise knowledge of critical CHD can guide for Foetal cardiac catheter-based interventions. Several specialized centers offer catheter-based interventions in-utero to dilate stenosis of the pulmonary or aortic valves.²² The risk of aneuploidy associated with Foetal cardiac anomalies is much greater (ranging between 13% - 33%) than that associated with advanced maternal age.^{23,24} Knowledge of the Foetal karyotype allows for well-defined postnatal surgical intervention that may be altered by the finding of a devastating aneuploidy diagnosis. Also, when available, it provides an opportunity for thorough counseling regarding reproductive options and the assessment of the recurrence risk for future pregnancies.⁵ It should also be mentioned that a negative Foetal echocardiography could provide required reassurance to the family who had had a previous child with a congenital heart defect.²¹ In addition, the examination is safe and does not involve any invasive procedure.

Why the need for introducing Foetal echocardiography as a screening tool at 18-22 weeks of gestation to general population?

Only 10 percent of the fetuses with cardiac anomalies have identified risk factors, which includes family history of CHD (previous affected child; parents), coexisting maternal disease (e.g. type I diabetes mellitus, collagen vascular disease, or phenylketonuria), exposure to teratogens in early pregnancy such as lithium carbonate, retinoids, phenytoin, carbamazepine, valproic acid, paroxetine, infections such as parvovirus B19, rubella, coxsackie,

autoimmune antibodies such as anti-Ro (SSA), anti-La (SSB), hydrops, effusion, abnormal karyotype and extracardiac Foetal anomalies such as diaphragmatic hernia, exomphalos noted on a general Foetal sonogram. In such cases, detailed Foetal echocardiography is commonly done as part of the sonographic screening between 18 and 22 weeks of gestation.²⁵ However, most cases of CHD occur in pregnancies with no prenatal risk factors.⁷ Hence, basing referral for Foetal echocardiography on the presence of risk factors only excludes about 85% of foetuses with severe detectable heart defects from screening.²⁶

Generally, detailed Foetal echocardiography is not performed routinely for prenatal screening but is reserved for cases which are at high-risk for CHD, as it is a time consuming procedure that requires many two-dimensional cross-sectional views of the heart, additional Doppler and color flow investigations.²⁵ Also, skilled investigators with special experience in Foetal cardiology are needed. Consequently, cardiac abnormalities are among the major malformations that are most frequently missed in prenatal ultrasound examinations which is a cause for concern because undetected CHD increases the risk of early neonatal mortality.

Most of the centers use four-chamber view as a screening modality for evaluation of the Foetal heart and based on this view, vast majority of obstetricians develop a suspicion of anomalies of the Foetal heart, thereby initiating further detailed evaluation. However, four-chamber screening alone is not adequate to identify important abnormalities of the ventricular outflow tracts, great arteries and visceral and atrial situs and results in the sensitivity for detection of congenital cardiac anomalies to range between 5 and 60%.²⁷ The four-chamber view only allows the examination of a small aspect of the heart, namely the atria, the inter-atrial septum with the valve of the foramen ovale beating into the left atrium, both AV-valves which open and close, and the inter-ventricular septum with the inflow tracts. Other lesions in the region of the outflow tracts and the large vessels will generally not be detectable via the four-chamber view, including some severe anomalies which become symptomatic early after birth (transposition of the great arteries, tetralogy of fallot, pulmonary stenosis and atresia with ventricular septal defect, double outlet right ventricle and truncus arteriosus communis).

Multiple studies to date show that the detection rate of cardiac anomalies can be markedly increased by 30% by incorporating visualization of the outflow tracts and the great arteries into the examination compared with using four-chamber view alone.^{18,25} Following the technical improvements in ultrasonography in recent years, a systematic review carried out in 2005, found Foetal echocardiography close to 100% specific for diagnosing a normal foetus among unselected and low risk populations.²⁰

In conclusion with this, the screening study reported by the authors on 39,808 patients undergoing a thorough routine two-dimensional Foetal echocardiography at 22 weeks of gestation at the Antenatal Diagnostic Center of the National University Hospital, Singapore, revealed sensitivity of 85.4% for the detection of CHD and a specificity of 99.9% to rule out any such anomalies. Our positive and negative predictive rates were 87.7% and 99.9%, respectively.²⁸

Can early Foetal echocardiography between 13 and 15 weeks of gestation be used for general screening?

Though, the use of high resolution and high frequency trans-vaginal combined with trans-abdominal transducers between 13 and 15 weeks of gestation allows the demonstration of all cardiac structures and the detection of majority of cardiac defects,²⁹⁻³¹ its sensitivity is only above 60% which, however, is 20% lower than that of the trans-abdominal examination at 18-22 weeks gestation.²⁰ The lesser resolution of early echocardiography in relation to the small size of the Foetal heart may not always allow the detection of ventricular septal defects, double outlet right ventricle and tetralogy of fallot. The biggest disadvantage of first trimester echocardiography is the delayed progression of structural and functional cardiac changes in some forms of heart disease, which may only manifest at a later gestational age. Also, compared with trans-abdominal echocardiography between 18-22 weeks gestation, early echocardiography is less reliable and may result in a higher false-negative and false-positive rate³⁰⁻³² and needs to be supplemented by a second examination between 18 and 22 weeks of gestation. Furthermore, early echocardiography is more time consuming and requires a high level of training of the examiner. Therefore, it seems unjustified to use early Foetal echocardiography for general screening. On the other hand, it would be of great value to increase the examination quality in second trimester cardiac scanning, which should be performed by experienced examiners. This may allow the detection of 80% of cardiac defects.

Role of early Foetal echocardiography in high-risk pregnancies:

It is now well known that cardiac defects are found in increased frequency in the group of foetuses with thickened nuchal translucency (NT) detected by screening between 11 and 14 weeks gestation.³³⁻³⁵ Thus, NT screening could help to define a new high-risk group, which should receive a detailed Foetal echocardiography at or before 14 weeks of gestation as the risk of CHD is doubled over the background population if the NT measurement is between 2.5 and 3.5 mm, increasing to 26 times the background rate if the nuchal measurement is over 6.5 mm.³⁶ First trimester Foetal echocardiography should

also be offered to mothers at high risk of having children with CHD, with one or more first-degree relatives with cardiac defects³⁷ or those in whom cardiac defects are either inherited by mendelian rules alone, those with pre-gestational diabetes or diabetes diagnosed in early pregnancy and as a part of an early genetic sonogram service to women at-risk of chromosomal abnormalities due to advanced maternal age who have declined invasive testing. This should then be followed up at 18-22 weeks of gestation as a follow-up scan.³⁸

Future Developments:

Foetal echocardiography will play a big role as another modality in the assessment of Foetal well being besides multi-vessel Doppler studies, biophysical profile, amniotic fluid index and cardiotocography because when the foetus is in any kind of stress under conditions such as hypoxia, anaemia, abruptio, intrauterine infection, and preterm labour, cardiac output has to increase and in the foetus it is reflected by the right atrium enlarging, as the predominant side of the Foetal heart is the right chamber. The M-mode assessment of the heart chambers, the tricuspid ejection ratios and the precardiac load index obtained from the inferior vena cava is all going to play a significant role in the future in monitoring foetuses such as with intrauterine growth-restriction, twin-twin transfusion syndrome and cases of rhesus iso- immunization.

Team approach:

It is important to highlight that all members of the prenatal and early postnatal health care team, including the Foetal medicine specialist, geneticist, perinatologist, paediatrician, paediatric cardiologist and paediatric cardiac surgeon work together to provide care as a team. A Foetal Board comprising of the above mentioned multidisciplinary members must be constituted so as to review each case of Foetal malformation, refining the diagnosis, establishing management plans, and facilitating issues relating to the delivery of the patients. It is the authors' belief that the concept of the team approach not only capitalizes on the knowledge and expertise of the particular physicians in their respective fields, but also broadens the teams' competence in parental counseling as well as coordinating the planning of the prenatal and postnatal management of the patient.

Conclusion

As nearly 90% of all pregnancies in which the foetus has a cardiac abnormality are at no increased risk and as routine prenatal ultrasound scans almost always miss an isolated cardiac defect, appropriate detection of cardiac abnormalities can only be achieved by carrying out routine Foetal echocardiography in all foetuses in the second trimester, irrespective of the presence or absence of risk

factors for the development of congenital cardiac disease.

It must be remembered that Foetal echocardiography requires the use of high quality ultrasound machines and, in particular, the thorough training of the examiner. Therefore, the full potential of Foetal echocardiographic screening can only be reached with significant improvement in the level of training of all personnel involved in screening and by centralization of the examination in the second trimester.

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