Utilising ductus venosus Doppler waveform and four-chamber view to screen for foetal cardiac malformation in early second trimester of pregnancy

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Background Foetal echocardiography has become a diagnostic method to detect foetal congenital heart disease with high probability. However, it is not only time consuming and but also difficult to visualize outflow tract of foetus early in the second trimester of pregnancy, even for an experienced obstetric ultrasonographer. Recently, many methods for screening foetal cardiac anomalies were explored, but much more work is needed to develop an effective and suitable screening method. The aim of this study was to investigate the clinical significance of utilising the ductus venosus (DV) Doppler examination and the four-chamber view of heart to screen for foetal cardiac malformation in early second trimester of pregnancy.

Methods Heart and DV of 401 consecutive foetuses in early second trimester (12(+1)-17(+6) weeks) in high risk pregnancies were examined with Acuson 128 xp/10 or Sequoia 512 ultrasonic diagnostic systems. Absent or reversed flow during atrial contraction (A-wave) in the DV was defined as sufficiently abnormal to screen for foetal cardiac malformations. The foetal echocardiographic diagnosis was confirmed by postnatal echocardiography (or postmortem). The sensitivities of screening tests were compared among the three methods: DV Doppler examination, four-chamber view alone, and the combination of both techniques.

Results Satisfactory examinations were obtained in 383/401 foetuses (95%). Thirty foetuses with cardiac abnormalities were confirmed by neonatal echocardiography (or postmortem). The sensitivity of DV Doppler examination or four-chamber view alone is 63 % ( 19/30) and 60 % ( 18/30), respectively. The sensitivity of combining information, DV Doppler flow waveform and four-chamber view, to screen for foetal cardiac malformation is 83% (25/30) and significantly better than that of either DV Doppler flow waveform or four chamber view alone (P<0.05).

Conclusion Doppler flow waveform of DV can be used to screen for foetal cardiac malformation early in the second trimester. Combining information from Doppler flow waveform of DV and four-chamber view will improve the overall sensitivity of the screening.

pregnancy. Hence, it is necessary to develop other methods, to screen for foetal CHD in early second trimester of pregnancy, which are more effective and still suitable for general obstetric sonographers.

Over the last decade, extensive Doppler studies of the foetal circulation have demonstrated the importance of the ductus venosus (DV) in blood distribution during intrauterine life. The DV directs well-oxygenated blood from the placenta and umbilical vein directly to the myocardium and to the brain by preferential streaming through the foramen ovale to the left atrium. More recently, many studies suggest that major structural heart disease is associated with abnormal DV flow waveforms. The possible role of measuring the DV flow waveform as a screening method for CHD has been put forward, although much more work is needed to make the method reliable.

The aims of this study were to extend those observations to obtain greater insight into the role of DV Doppler examination as a screening method, and to investigate the clinical significance of utilising DV Doppler examination and four-chamber view to screen for cardiac abnormalities during early second trimester in foetuses at a high risk of CHD.

METHODS

Population
From August 2000 to March 2005, ultrasound examinations were carried out on 401 consecutive foetuses aged from 12(+1) weeks to 17(+6) weeks with high risk of CHD referred to our hospital for prenatal care and delivery.

Indications
Indications for foetal echocardiography were family history of CHD, increased nuchal translucency (>3.5 mm), suspected cardiac or extra cardiac anomalies at early second trimester scan, maternal pregestational diabetes, pregnancy affected by a chromosomal abnormality, exposure to teratogens, foetal arrhythmia or advanced maternal age (>35 years). All patients had signed informed consent prior to ultrasound examination.

Equipment
Ultrasound examinations were performed using two dimensional and colour Doppler flow imaging to direct spectral Doppler using an Acuson 128 xp/10 or Sequoia 512 ultrasonic imaging system (Acuson, Mountain View, CA USA) with 3.5 MHz or 6.0 MHz transducers. The lowest possible intensities of Doppler energy were used and always less than 100 mW/cm(2) (spatial peak temporal average). The recording speed utilized in the study was 50 cm/s to 100 cm/s.

Methods
The initial ultrasound examination consisted of determination of the number of foetuses and measurement of biparietal diameter, head circumference, femur length and abdominal circumference, which were used to confirm gestational age and estimate the foetal weight. Twin pregnancies were excluded from the study.

DV Doppler studies were carried out by two experienced obstetric ultrasonographers, prior to foetal echocardiography. A right ventral midsagittal plane of the foetal trunk was obtained and colour Doppler flow imaging used to visualize clearly the foetal venous circulation. Particular care was taken to distinguish the DV from the inferior vena cava and from the middle hepatic vein. The foetal DV has a slender profile and is trumpet shaped (Fig. 1). In the absence of foetal movement and of breathing, the spectral Doppler sample gate was placed where the DV originates from the umbilical vein. Care was taken to keep the interrogation angle as low as possible and always below 50°. The Doppler wall filter was set at 50 Hz. Consecutive high qualities DV waveforms were recorded. The normal Doppler flow waveform is characterized by a triphasic, unidirectional pattern: the velocity waveform is maximal during ventricular systole (S-wave), another peak is seen at early diastole (D-wave) and the nadir occurs at the end of diastole corresponding to atrial contraction (A-wave) (Fig. 2). Only absent or reversed flow during atrial contraction (A-wave) was defined as abnormal in this study. The time exposure to colour flow and Doppler ultrasound was limited to 5 minutes, and, if satisfactory waveforms could not be obtained within that time, the Doppler investigation ceased. Cases with unsatisfactory waveforms were not included in the study.

After completion of the DV Doppler examination, a four-chamber view was obtained for examination...
for foetal cardiac malformation by two other experienced doctors in foetal echocardiography (blind to the results of DV data collection). The data of screening was notes taken immediately. Then detailed foetal echocardiography was carried out for identification of positions and anatomic landmarks of the heart using a series of views including the left ventricular long and short axes view, outflow tract views, three vessels view as well as aortic and ductal arch views. Segmental examinations were performed in which the venous-atrial, atrioventricular, and ventriculoarterial connections were assessed in both right and left sides of the heart. In addition, the regions that separate portions of the heart were also examined, including the septum, ventricular walls and pericardium. M-mode examination was also performed to measure chamber and wall thickness, fractional shortening and ejection fraction of left ventricle as well as valve motion if possible. If necessary, spectral Doppler and colour Doppler flow imaging were used to demonstrate the direction and relative velocity of blood through vessels and cardiac chambers. The time spent performing detailed foetal echocardiography was less than 30 minutes.

Follow-up
Following ultrasonographical diagnosis and a follow-up echocardiography 4 weeks later, the parents of the foetus made their own decision concerning termination or continuation of pregnancy based on the information given by the doctors in obstetric cardiology. If the latter was chosen, foetal echocardiography was repeated every 4 weeks to term. All prenatal echocardiographic diagnosis was confirmed by postnatal echocardiography (or postmortem). When appropriate, the karyotype was determined.

Statistical analysis
Date were analysed by commercially available software (SPSS 11.0) using descriptive statistics. To assess the accuracy of foetal echocardiography, we reviewed the findings of autopsy, postnatal echocardiography and operative report where applicable. Standard statistical analysis was used to evaluate the sensitivity and the specificity as markers for foetal cardiac malformations. Comparison of the sensitivity between screening method of ductus venosus Doppler examination with the four-chamber view, DV Doppler flow waveform alone or four chamber view alone was made by comparison of proportions using of the χ² test. A P value <0.05 was accepted as significant.

RESULTS
The mean gestational age at the time of the first ultrasonographical study was (14.9±1.4) weeks (range 12(+1) to 17(+6) weeks), and 18 foetuses were excluded from the study because the Doppler examination was not satisfactory (15 cases) or twin pregnancies (3 cases). However, their heart structures were verified to be normal by foetal and neonatal echocardiography. The data from 383 (95%) foetuses were used in the study.

Thirty foetuses with cardiac abnormalities were confirmed by postmortem or neonatal echocardiography (6 cases of atrioventricular septal defect, 5 tetralogy of Fallot, 4 double outlet right ventricle, 3 Truncal artery anomalies, 3 ventricular septal defect, 2 transposition of great artery, 2 hypoplastic LV, 2 tricuspid atresia, 2 total anomalous pulmonary venous connection, 1 Ebstein anomaly). Fifteen foetuses had cardiac arrhythmias as well as 4 foetuses with pericardial effusion. Trisomy 21 was present in seven cases.

Absent or reversed flow during atrial contraction (Figs. 3, 4) was observed in 36 of the 383 foetuses with satisfactory Doppler examination. Among those, there were 19 with cardiac malformation (3 cases of atrioventricular septal defect, 3 tetralogy of Fallot, 4 double outlet right ventricle, 3 Truncal artery anomalies, 1 ventricular septal defect, 2 transposition of great artery, 2 hypoplastic LV, 1 Ebstein anomaly, Figs. 5, 6), 15 with arrhythmia without structural heart disease and 2 with massive pericardial effusion. However, 11 foetuses with structural heart disease (3 cases of atrioventricular septal defect, 2 tetralogy of Fallot, 2 ventricular septal defects, 2 tricuspid atresia, 2 total anomalous pulmonary venous connections,) did not display the abnormal DV flow pattern during atrial contraction. The sensitivity and specificity for detecting foetal cardiac malformation are 63% (19/30) and 99%, respectively.

Four-chamber view alone revealed the structure abnormalities in 18 of those foetuses. The sensitivity (60%) and specificity (99%) of the four-chamber view alone for screening foetal cardiac malformation was not significantly different (P>0.05), compared with that of the DV Doppler flow waveform alone.

Detail foetal echocardiography showed that 27 foetuses had cardiac abnormalities and 26 of those
were consistent with the postmortem or neonatal echocardiography. There was one false positive (ASD) and four false negatives (2 ventricular septal defect and 2 total anomalous pulmonary venous connection).

Combining data from the DV Doppler flow waveform and four-chamber view to screen for foetal cardiac malformation, 25 foetuses with cardiac malformation were suspected. The sensitivity (83%) is better than DV Doppler flow waveform or four chamber view alone, respectively (P<0.05).

DISCUSSION

The DV is a small but a key vessel, which connects the intraabdominal portion of the umbilical vein to the inferior vena cava and is located in the environs of confluence of venous channels leading toward the foetal heart. [10] It is one of the three physiological shunts determining blood distribution during intraterine life and plays an important role in the foetal circulation. The velocity pattern during the cardiac cycle shows much the same variation as in other precordial veins; however, there are two significant differences. The first is that the velocity in the DV is higher and the second is that the high forward velocity is maintained during atrial contraction.

Haemodynamically, the waveforms reflect the rapid change in pressure gradient between the umbilical vein and the right atrium. [14] The highest pressure gradient between the DV and right atrium occurs during ventricular systole when the lowered atrioventricular plane enables forward blood flow and filling of the atria. The subsequent early diastole is characterized by opening of the atrioventricular valves and passive filling of the atria. The foramen ovale closes during atrial contraction and the remaining atrial blood volume is actively pumped into the ventricle. This process, therefore, affects both right ventricular end-diastolic and central venous pressure. Consequently, any foetal cardiac malformation that can result in diastolic dysfunction or elevate the right atrial pressure may change the velocity flow pattern. The most striking feature is zero, or reversed, velocity during atrial contraction.

Over the last decade, Doppler studies of DV demonstrated that absent or reversed flow waveform of the DV was associated with foetal CHD, [15-18] arrhythmias and cardiomyopathy, [19] endstage hypoxia or increased right ventricular afterload. [20] Our results agree with those and show foetal pericardial effusion (>8 mm) may also be associated with absent or reversed flow waveform of the DV. Our study suggests that Doppler flow waveform of the DV alone can be used for screening for foetal cardiac malformations with a sensitivity of 63%. Although the exact mechanism by which abnormal DV waveforms occur is still unknown, most studies [7,10-18,21] on foetal circulation suggest that alteration of the Doppler flow pattern of the DV results from impaired cardiac performance, particularly from impaired diastolic function, or serious haemodynamic changes, such as augmentation of right atrial pressure. In hearts with markedly impaired diastolic function, atrial contraction occurs against increased impedance to forward flow. The proportion of blood ejected retrograde into the great veins is greater than when ventricular filling is unimpaired causing the transient flow reversal in the DV that constitutes the negative A-wave. [13] But a wide variety of cardiac structural abnormalities are associated with absent or reversed DV flow without heart failure, such as tetralogy of Fallot and other conditions in which heart failure develops only following the fall in pulmonary vascular resistance after birth. This may be related to many factors, such as immaturity of the foetal ventricles with less organized myocardial arrangement, fewer sarcomeres per unit mass, small diameter and operating at a significantly higher heart rate, allowing less time for inactivation of contraction when compared to the adult heart. [22,23] Therefore, there is an upward displacement of the end-diastolic pressure-volume relationship with a higher pressure at any volume. [13] These factors predispose the foetus to serious haemodynamic changes and elevated right atrial pressure when complicated by structural heart disease. The presence of anatomical defects, in addition to the relatively impaired ventricular filling, may alter the haemodynamics so that ‘cardiac dysfunction’ becomes manifest as an abnormal DV signal. [10,24] Our data support the concept and suggest that assessment of the Doppler flow waveform of DV is very important in the determination of foetal physiological or pathological changes and is a screening tool for foetal cardiac malformation.

In the study, 11 cases with cardiac malformation remained in which Doppler examination did not show zero or reversed flow in the DV. We speculate that those foetuses had not evolved to cardiac dysfunction or serious haemodynamic abnormality when examined. This suggests that Doppler examination of DV has its limitations and is insufficient in screening for foetal cardiac malformation. Therefore, foetal cardiac malformation cannot be excluded when the Doppler flow waveform is normal in DV Doppler examination.
Because it is easy to obtain and directly displays the structural abnormalities of the foetal heart, the four-chamber view is the choice to screen for foetal cardiac malformation. The four-chamber view alone can detect absent connections, such as mitral/tricuspid atresia, large septal defect, hypoplastic left/right heart syndrome, and atrioventricular septal defect. However, the role of the single view is insufficient because some cardiac malformations, such as tetralogy of Fallot, transposition of the great arteries, double outlet right ventricle (even pulmonary stenosis) may have normal four chamber views and are likely to be missed unless the scan is extended to include the outflow tracts. The literature suggests that if cardiac screening were confined to the four-chamber view, only 15% to 35.3% of foetal structural heart disease would be detectable. The four-chamber view alone has very high specificity, but low probability of detecting foetal cardiac malformation in the early of second trimester pregnancy.

Although the sensitivities of both Doppler flow waveform of DV and four chamber view in screening for foetal cardiac malformation were similar (63% vs. 60%), we found that both screening methods detected the same 12 foetuses with cardiac malformation, and Doppler flow waveform of DV displayed the abnormal waveform in another 7 foetuses whose four-chamber view was normal. The four-chamber view alone diagnosed another 6 foetuses with cardiac malformations in which the Doppler examination of DV was normal. Combining the DV Doppler flow waveform with four-chamber view to screen for foetal cardiac malformation, 25 cases with cardiac malformation were suspected. The sensitivity of screening test was increased from 63% or 60% to 83%.

Although it has some limitations, Doppler flow waveform of DV can be used to screen for foetal cardiac malformation in early second trimester. If the DV Doppler flow waveform of a foetus display is abnormal, then a detailed foetal echocardiogram should be carried out. Utilising data from (both) the Doppler flow waveform of DV and the four-chamber view could improve the overall sensitivity of screening for foetal cardiac malformation in early second trimester of pregnancy.

REFERENCES


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