OC26: CARDIAC FUNCTION IN SPECIFIC CONDITIONS

OC26.01
Fetal cardiac output: measurement by four dimensional power Doppler and artificial neural networks. Results from a sheep model

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Objectives: Non invasive measurement of fetal vascular flow remains an elusive matter, accuracy of current tools is very limited and relies mainly in operator skills. The aim of our study was to develop a tool for indirect flow measurement, accurate and repeatable, by using power Doppler signal, Real time three dimensional ultrasound (4DPD) and mathematical image data simulation and adjustment tools based on artificial neural networks (ANN).
Methods: Six pregnant sheep with adequately controlled gestational age of 125 days (near term) were surgically instrumented to access fetal ascending aorta by transventricular catheterization. Cardiac output was measured by Fick thermodilution, as well as by pulsed Doppler. Several sets of 4DPD volumes were taken during the procedure. Measurements were stored in an electronic datasheet. Pearson's correlation coefficient and simple linear regression were obtained. Linear equation matrix were generated and obtained data was evaluated through an error adjustment process by employing an artificial neural network software (ANN).
Results: A total of 30 sets of measurements in controlled conditions were collected during the study period. A mean of six measurements by cardiac cycle were digitally obtained from the velocity curve. A six by six matrix of data was designed for every measurement. Mean velocity at every time was calculated and compared to actual data, intraclass correlation coefficient (95% CI) was 0.9 (0.73–0.99). ANN predicted calculated measurements in 99% of cases.
Conclusions: 4DPD might be a reliable, accurate, non invasive tool for fetal vascular flow measurement.

OC26.02
Maternal hyperglycemia affects first trimester fetal cardiac function in normal hearts

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Objectives: In vitro animal studies suggest that hyperglycemia impairs fetal cardiac function early in gestation by affecting neural crest signaling. We aimed to study if evidence of first trimester myocardial dysfunction is detectable in fetuses of women with pregestational diabetes mellitus (DM).
Methods: Women with DM had fetal echocardiography at 11–14 weeks' gestation (GA) using a segmental approach. Cardiac preload, diastolic function, global myocardial performance and placental afterload were studied by Doppler of the ductus venosus (DV), mitral and tricuspid E/A ratios, left and right ventricular Tei index and umbilial artery (UA) respectively. DM patients were matched for GA, UA and DV Doppler with normal controls.
Results: After exclusion of structural cardiac anomalies 60 DM and 60 controls were studied at 12.6 weeks (11.1–13.6). UA and DV pulsatility indices (median 2.22 and 0.99) and nuchal translucency was (median 1.5 mm) were similar between cases and controls. DM patients had lower mitral E/A ratios [0.55 ± 0.08 vs. 0.52 ± 0.08 in controls, $P = 0.03$). Left and right ventricular Tei indices were significantly higher in diabetics [0.51 ± 0.08 vs. 0.48 ± 0.1; 0.51 ± 0.08 vs. 0.45 ± 0.08 in controls, $P < 0.04$ and < 0.001]. This lower global myocardial performance was due to prolonged myocardial relaxation especially in diabetics with a HbA1c > 7. (0.001 for all parameters). No correlation between cardiac performance parameters and DV and UA indices were observed.
Conclusions: We demonstrate significant differences in first trimester diastolic myocardial performance in fetuses of diabetic mothers compared with non-diabetic controls. The decrease in myocardial performance was more marked with increasing hyperglycemia, and appears independent of preload and afterload. Impaired neural crest signaling offers a biologically plausible explanation and our ability to document these changes this early in pregnancy opens potential new avenues to monitor and modify maternal glycemic control before cardiac remodeling such as myocardial hypertrophy develops.

OC26.03
Bioinformatic analysis of genes regulating myocardiocyte contractile function in a rabbit model of cardiac dysfunction due to intrauterine growth restriction

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Objectives: To assess the existence of functional differences in blocks of genes regulating key steps in the contractile machinery of the myocardiocyte in a rabbit model of cardiac dysfunction due to fetal growth restriction (FGR).
Methods: A FGR model was created in 5 pregnant rabbits, 40–50% of uteroplacental vessels of one horn were ligated at 25d of gestation, and cesarean section was performed at 30d. Fetal cardiac function assessment was performed in 15 cases and controls before delivery including: ductus venosus (DVPI) and aortic isthmus pulsatility index (AoIPI),left ejection fraction (EF) and isovolumetric relaxation time (IRT). After delivery, hearts of 6 pairs of cases and controls were selected at random and gene expression profile was analyzed with a rabbit DNA microarray in ventricular tissue. Genes involved in key elements of mycoardiocyte contractility, including calcium homeostasis and sarcomere contractiliy were analyzed with two kinds of bioinformatics analysis: differential single-gene expression analysis and FatiScan analysis to assess coordinated differences in blocks of genes involved in complex functions.
Results: DVPI, AoIPI and IRT were significantly increased in FGR (Table 1). FatiScan analysis demonstrated the sarcomeric M-band structure, including critical genes in sarcomere structure and function such as titin, obscuring and myomesisn, was significantly over-expressed in FGR versus healthy control hearts.
Conclusions: Cardiac dysfunction in a rabbit model of FGR is associated with functional changes of genes regulating myocardiocyte contractility. Since these genes are also involved in genetic cardiomyopathies, these findings support further research to elucidate the presence of epigenetic changes leading to permanent cardiac dysfunction in FGR.

OC26.03: Table 1. Cardiac function parameters in study groups

	Control	*Ligature*	P
DVPI	0.75 (0.25)	1.33 (0.75)	0.008
AoIPI	3.05 (0.45)	3.85 (1.16)	0.019
EF (%)	89.1 (8.2)	82 (24.6)	n.s.
IRT (ms)	38.1 (7.7)	50.1 (12.4)	0.004

OC26.04
Cardiac function between 11 and 35 weeks' gestation and nuchal translucency thickness in trisomy 21 fetuses

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Objectives: The increased nuchal translucency (NT) is a marker for trisomy 21 (Tri21) and for cardiac defects (CHDs), Cardiac dysfunction has been postulated in Tri21 fetuses. We aimed to study cardiac function throughout gestation in these fetuses.
Methods: Echocardiography was performed on 49 trisomy 21 fetuses and 190 eukaryotic controls with normal hearts, (86 with a normal NT and 104 with a NT $\geq 95^{th}$ percentile), between 11 and 35 weeks' gestation. Measurements included: E- and A-wave peak velocity, E/A velocity ratio and E/TVI ratio over the atrioventricular valves, myocardial performance index, semilunar valves peak velocity (PVel)and acceleration time (AT), stroke volume (SV) and cardiac output (C) and the ductus venosus pulsatility index for veins at 11–14 weeks' gestation (DVPIV).
Results: 11–13.9 weeks' gestation: In Tri21 fetuses the semilunar valve PVels and tricuspid valve (TV) A-wave velocity were significantly reduced and TV E/A ratio and DVPIV significantly increased compared to normal NT controls. 14 and 21.9 weeks' gestation: Aortic PVel, mitral (MV) and TV E- and A-wave velocities and MV E/TVI were significantly reduced in Tri21 fetuses without CHD compared to controls. 22 and 35 weeks' gestation: In Tri21 fetuses with normal hearts the TV E- and A-wave velocity, right ventricular SV, aortic PVel and left ventricular CO were significantly reduced compared to normal NT controls.
Conclusions: Tri21 fetuses have abnormal cardiac function irrespective of the NT thickness or presence of CHD. We found evidence for increased preload in early gestation with increased afterload thereafter along with biventricular systolic and diastolic dysfunction.

OC26.05
Assessment of longitudinal myocardial function of the right ventricle in fetuses with congestive heart failure using tissue Doppler imaging

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Objectives: The aim of this study was to analyze the systolic and diastolic myocardial function of the right ventricle (RV) in fetuses with congestive heart failure (CHF) using tissue Doppler imaging (TDI).
Methods: Myocardial function of the RV was assessed in 42 normal fetuses and 67 fetuses with CHF between 27 and 39 weeks' of gestation. Detailed echocardiography combined with pulse and tissue Doppler was performed in all cases. To determine the degree of CHF, cardiovascular score (CVS) was evaluated on each subject. TDI data was obtained at the level of 4-chamber view by placing the sample volume at the lateral part of the tricuspid annulus. Pre-ejection (S1), systolic (S2), early diastolic (E′) and late diastolic (A′) myocardial velocities were assessed. Ratio of peak velocities in early and late diastole (E′/A′), ratio of peak velocities in early diastole measured by pulse and tissue Doppler (E/E′) and Tei-index were also calculated.
Results: The CVS in fetuses with CHF ranged from 8 to 0 (mean 6 ± 1.5). This parameter strongly correlated with TDI-Tei-index ($r = -0.62$; $P < 0.01$). TDI-Tei-index was significantly higher in the group with CHF compared to normal (0.76 ± 0.11 vs. 0.53 ± 0.08; $P < 0.001$). Ratio E/E′ was also greater in fetuses with CHF (10.5 ± 2.3 vs. 5.8 ± 1.1; $P < 0.01$). In subgroup with CHF and CVS > 5 mean E′ was significantly lower than in fetuses without CHF (3.8 ± 0.41 vs. 6.2 ± 0.59; $P < 0.001$) and S1 was elevated (12.3 ± 1.5 vs. 5.2 ± 1.3; $P < 0.01$), however mean S2, A′ and E′/A′ were within normal limits. In fetuses with CVP ≤ 5 the following changes of myocardial velocities were noted: E′ significantly decreased or absent (mean 1.2 ± 0.9), A′ significantly increased (mean 15.4 ± 2.3), S2 and E′/A′ significantly decreased (mean 2.4 ± 0.8 and 0.38 ± 0.09 respectively). A decrease in all myocardial velocities was associated with poor outcome.
Conclusions: Our results validate the potential clinical applicability of TDI technique in assessment of cardiac function in fetuses with CHF.

OC26.06
Fetal circulatory dynamics in presence of simple TGA

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Objectives: To characterize the prenatal circulatory dynamics of simple transposition of the great arteries (TGA).
Methods: A study group of 36 fetuses with TGA was compared to 77 normal fetuses (controls) matched for gestational age. In all cases, Doppler recordings and diameter measurements were available above the aortic and pulmonary valves as well into the ductus arteriosus (DA). Blood flow through the lungs (flow above the pulmonary valve minus net flow through the DA) was calculated. In the TGA group, flow through the foramen ovale (FO) was assumed to be equal to the net flow through the DA. Second (T2) and third (T3) trimester data were analyzed separately.
Results: The mean gestational ages of the control and TGA groups were 24.3 ± 4 and 23.4 ± 2.7 respectively for T2, 31 ± 3.7 and 33 ± 2.6 respectively for T3. Table 1 summarizes the actual cardio-circulatory data observed in the two groups. Contrarily to the control group, the TGA shows a preponderant LV throughout T2 and T3, a higher lungs flow in T2, a lower QRV and an elevated QFO in T3.
Conclusions: The distribution of CCO of fetuses with TGA is quite different from normals. The clinical implications of these specific features, especially at the level of the lungs, deserve further investigations.