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Cardiac function in early onset small for gestational age and growth restricted fetuses

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ABSTRACT

Objective: To examine cardiac function in appropriately grown, small for gestational age and intrauterine growth restricted fetuses and investigate the relationship between cardiac function and fetal arterial and venous Doppler parameters.

Study design: Myocardial performance index, isovolumetric contraction time, isovolumetric relaxation time, ejection time, and umbilical artery, middle cerebral artery and ductus venosus Doppler pulsatility index were measured for women between 24 and 32 weeks with small for gestational age and intrauterine growth restricted fetuses. Forty-eight appropriately grown, 11 small for gestational age and 12 intrauterine growth restricted cases were included. The relationship between cardiovascular parameters and gestation was defined and Doppler values converted to *Z*-scores in relation to gestational age.

Results: In small for gestational age fetuses and fetuses with intrauterine growth restriction the myocardial performance index was 0.66 (0.63–0.7) and 0.64 (0.60–0.67), respectively, and compared to appropriately grown fetuses, at 0.45 (0.43–0.47), was significantly increased ($p = 0.001$). No relationship was found between the myocardial performance index and arterial and venous Doppler *Z*-score.

Conclusion: Small for gestational age and intrauterine growth restricted fetuses demonstrate altered cardiac function in the late second and early third trimester of pregnancy. Importantly, the myocardial performance index is raised in small for gestational age fetuses before the arterial and venous Doppler abnormalities that characterize hypoxia are evident.

1. Introduction

Growth-restricted fetuses are at increased risk of short and long term morbidity [1] and death both in- and ex-utero [2]. Fetal growth restriction is most commonly due to placental insufficiency [3] and the resulting hypoxia leads to fetal blood flow being redirected to the brain and heart [4]. Fetal cardiac output is preferentially diverted in favor of the left ventricle [5]. When fetal hypoxia worsens, adaptive mechanisms result in abnormal arterial and venous flow [6].

The evaluation of placental function by umbilical artery Doppler velocimetry is used to distinguish between small for gestational age (SGA) and intrauterine growth restricted (IUGR) fetuses [7]. Some SGA fetuses with normal umbilical artery (UA) Doppler subsequently develop IUGR and hence have an increased risk of adverse perinatal outcome [8] and abnormal neurodevelopment [9].

Intrauterine growth restriction predisposes to lower cardiac compliance, increased arterial stiffness, increased cardiac afterload and end-diastolic ventricular filling. Abnormal cardiac function is postulated to be a potential marker for fetal condition in intrauterine growth restriction [10] and is associated with an increased risk of hypertension and vascular hypertrophy in postnatal life [11,12]. Biochemical (cardiac Troponin I) and echocardiographic signs of cardiac dysfunction (cardiac output, peak systolic velocity of the outflow tracts, and cardiac compliance) in the neonatal period predispose to premature adult cardiovascular disease and death [13,14].

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The myocardial performance index (MPI) measured by pulsed wave Doppler reflects both systolic and diastolic function as the sum of the isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) divided by the ejection time (ET) [15].

Raised MPI is seen in the initial stages of cardiac adaptation to IUGR [10], presumably secondary to hypoxia. It is uncertain how the cardiac indices change with gestation and whether they are related to fetal Doppler changes that are characteristic of hypoxia in IUGR. In this study we evaluate the MPI of preterm SGA and IUGR fetuses, and evaluate this in relation to fetal arterial and venous Doppler changes.

2. Materials and methods

2.1. Subjects and population

This was a prospective observational study conducted between December 2011 and September 2012 in the Fetal Medicine Department of a tertiary center. The study had ethics approval (09/H0308/5). Women were identified by members of the research team following clinically indicated ultrasound scans. Seventy-one women were recruited consecutively and formed three gestation groups: 24–26 weeks, 27–29 weeks and 30–32 weeks. Forty-eight were appropriate for gestational age (AGA), 11 were SGA and 12 had IUGR. All women gave written consent to the study.

SGA fetuses were defined as having an abdominal circumference (AC) ≤5th percentile [16] for gestational age but normal arterial and venous Doppler PI values [17]. IUGR fetuses, in addition to having AC <5th percentile, had abnormal UA Doppler at the time of recruitment. Gestational age was determined by fetal crown-rump length measurement at 11–13 weeks of gestation. All assessments were performed on the day of recruitment to the study.

2.2. Ultrasound and Doppler measurements

Measurements were performed on a Siemens Acuson S2000 (Mountainview, CA) machine using a 4–6 MHz curved transducer. All cardiac Doppler and biometry measurements were performed by one observer (WAH).

2.3. Fetal biometry

Fetal growth was determined at recruitment. Estimated fetal weight was calculated using biparietal diameter, head circumference, abdominal circumference and femur length [18].

2.4. Fetal peripheral circulation

UA Doppler pulsatility index (PI) was measured on a free-floating loop of the umbilical cord. The middle cerebral artery (MCA) PI was measured in a transverse view of the fetal head at the level of its origin from the circle of Willis. The ductus venosus (DV) PI was measured in a mid-sagittal or transverse section of the fetal abdomen. In all cases, the filter was set to the minimum setting. All Doppler PI measurements were converted to z-scores in relation to gestational week based on the mean and standard deviations reported for a reference group [17]. The Z score was derived from the value from which was subtracted the mean PI for that gestational week, divided by the standard deviation.

2.5. Fetal cardiac assessment (Doppler echocardiography)

The MPI was measured by obtaining a cross-sectional view of the fetal thorax at the level of the four-chamber view of the heart [10]. The Doppler gate (3 mm) was placed to include both the lateral wall of the ascending aorta and the mitral valve where views of the clicks of opening and closing of the valves are seen. The angle of insonation was as close as possible to zero degrees, in the absence of fetal movements. Images were recorded at a Doppler sweep velocity of 6 cm/s with the E/A waveform displayed as positive flow.

The MPI was calculated according to the formula: MPI = (ICT + IRT)/ET where the isovolumetric contraction time (ICT, ms) was calculated as the time from closure of the mitral valve to the opening of the aortic valve. Isovolumetric relaxation time (IRT, ms) was calculated as the time from closure of the aortic valve to the opening of mitral valve. Ejection time (ET, ms) or systolic time interval was calculated as the time from opening of the aortic valve to its closure. Z-scores were calculated from controls obtained within our study.

2.6. Statistical analysis

All calculations were performed using a statistical package SPSS 20 for Windows (Chicago, IL, USA). The cases were analyzed in three groups: AGA controls, SGA and IUGR. The Kruskal–Wallis test was used to compare the mean values between the groups with 95% confidence intervals (CI). Pearson correlations, T test and Mann–Whitney test were used to investigate the relationship between the fetal peripheral and cardiac circulations, gestational age and fetal heart rate (FHR). Normality was tested by the Shapiro–Wilk test.

3. Results

The mean gestational age at inclusion in the study was no different between the groups, but the IUGR group was recruited slightly later in gestation than was the case for AGA and SGA subjects (Table 1). Cardiac function assessment was not possible in two cases of the AGA group.

Table 1
Demographic and delivery characteristics.

Demographic and delivery characteristics	AGA	SGA	IUGR	Kruskal–Wallis test
No. cases	48	11	12	
Maternal age (median, range)	32 yrs (30–33)	28 yrs (20–33)	33 yrs (26–39)	$p = 0.277$
Gestational age at inclusion (median, range)	28 weeks (24–32)	28 weeks (24–32)	30 weeks (24–32)	$p = 0.042$
Estimated fetal weight at inclusion (median, range)	1260 g (635–2433)	878 g (443–1592)	1031 g (621–1410)	$p = 0.039$
Estimated fetal weight percentile at inclusion (median, range)	44.5 (20–80)	1.15 (0.6–5)*	1 (0.1–5)**	$p = 0.001$
Birth weight (median, range)	3080 g[a] (660–4380)	1300 g (500–2560)	1065 g (600–1745)[b]	$p = 0.001$
Birth weight percentile (range)	70 (10–99)	1 (1–5)*	1 (1–2)**	$p = 0.001$
Gestational age at delivery (median, range)	38 weeks (24–42)	34 weeks (27–38)	32 weeks[b] (27–36)	$p = 0.001$
Cesarean section rate (%)	41	82	100	

[a] In 4 of 48 AGA cases the postnatal details were not available.
[b] In 2 of 12 IUGR cases the postnatal details were not available.
* SGA vs AGA $p < 0.01$.
** IUGR vs AGA $p < 0.01$.