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Color Doppler myocardial imaging demonstrates reduced diastolic tissue velocity in growth retarded fetuses with flow redistribution

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ABSTRACT

Objectives: In fetuses suffering from intrauterine growth retardation with cerebroplacental redistribution (IUGR CPR), the diastolic heart function may be particularly susceptible to hypoxemia as described in postnatal pathological conditions. Using the newly introduced ultrasound technique, color Doppler myocardial imaging (CDMI), we investigated the correlation between diastolic tissue velocities and diastolic blood flow velocities and compared diastolic myocardial tissue velocities in fetuses with IUGR CPR and normal fetuses.
Study design: Peak early and active atrial tissue velocities (E' and A') were acquired from both ventricular free walls in 18 fetuses with IUGR CPR and 42 normal fetuses. In 35 normal fetuses, blood flow across the atrio-ventricular valves was also recorded. Umbilical artery (UA), middle cerebral artery (MCA) and ductus venosus (DV) flows were obtained in all fetuses. Nonparametric tests were used for statistical analysis.
Results: There was a tendency towards increased E' and A' with fetal age in normal pregnancies. No correlation between tissue velocity and blood flow velocity was established. IUGR CPR fetuses had significantly lower E' and A', but when indexing to heart length, only A' remained significantly lower. E'/A' ratio was increased in the left ventricle but unchanged in the right.
Conclusion: CDMI is easily applicable during standard fetal echocardiography and provides new information on the diastolic properties of the fetal myocardium. In fetuses with IUGR CPR, diastolic tissue velocities are abnormal and especially A' may be a marker of diastolic dysfunction.

1. Introduction

In intrauterine growth retarded (IUGR) fetuses with cerebroplacental flow redistribution (CPR) the scarcity of oxygen and nutrients has consistently been shown to negatively affect cardiac function, ranging from sub-clinical systolic dysfunction to overt heart failure [1,2] and cardiovascular deterioration may directly account for the increased perinatal mortality seen in this high risk patient group [3,4].

Whereas most studies in IUGR fetuses have focused on systolic performance, diastolic function may be more susceptible to hypoxemia and thus a more sensitive early marker for fetal compromise. Diastolic flows through the atrio-ventricular valves have previously been investigated in normal [5,6] and in pathological pregnancies [7–9]. Diastolic filling of the ventricles is a two step phenomenon comprising an early passive filling (E) that depends on a number of factors such as active ventricular relaxation, elastic recoil and pressure–volume characteristics, and a late filling (A) following atrial contraction. Thus, basic measures of diastolic function usually include the peak-E velocity, the peak-A velocity and the E/A ratio. Whereas E velocities dominate in healthy children and adults, the opposite is typical in early fetal life [10]. But as peak E velocity during pregnancy normally increases more than A velocities, the E/A ratio tends to increase during fetal maturation. In IUGR fetuses, however, data have been diverse with some studies reporting decreased and others increased E/A ratios [1,7,11–13].

With the introduction of color Doppler myocardial imaging (CDMI), assessment of regional myocardial function has become possible. In CDMI, signals from low velocity and high density structures generate a complete two-dimensional map of myocardial motion throughout the cardiac cycle. This quantitative assessment of myocardial function is superior to flow measurements, not only due to the elimination of beat-to-beat variability, but also because tissue velocities are less preload-dependent [14]. We have previously used CDMI to study systolic function in growth retarded fetuses with brain sparing [2]. The purpose of this study was to examine the correlation between diastolic flow and

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myocardial velocities in normal fetuses and to compare diastolic tissue velocities in fetuses with IUGR CPR with age-matched normal fetuses.

2. Material and methods

Eighteen fetuses with IUGR and CPR were included. Five were twin pregnancies (three dichorionic and two monochorionic). The monochorionic pregnancy showed no sign of intrauterine twin-to-twin transfusion syndrome and the postnatal hemoglobins were normal (and indeed lowest in the larger twin). Two fetuses were excluded, one with postnatally diagnosed Down's syndrome and one with a postnatally diagnosed tiny ventricular septal defect. Forty-two normal singleton fetuses comprised the control group. Of these, 35 fetuses had only one scan around 29 weeks of gestation (the cross-sectional group), whereas seven fetuses were scanned monthly from mid-gestation to birth (the follow-up group). Overall, 69 normal scans were acquired. The same groups of fetuses have earlier been reported regarding the systolic function [2]. Cardiac examinations were performed with a Vivid 7 ultrasound unit equipped with a 1.5–4 MHz, MS3 phased array transducer (GE Healthcare, Horten, Norway) during fetal quiescence with the ultrasound beam parallel ($<10^\circ$) to the interventricular septum in the four-chamber view with the apex pointing either directly towards or away from the transducer. In the cross-sectional normal group only, peak E and A velocities were measured at sweep speed 50 mm/s with the sample volume at the tip of both atrioventricular valves. CDMI recordings were acquired with frame rates between 175 and 215 per second. Early and late tissue velocities (E' and A') were calculated off line as means of three consecutive heart cycles by placing a 2 mm $\times$ 2 mm sample area at the basal part of the left and right ventricular free walls (Fig. 1). The sample area was fixed to the same myocardial segment throughout the cardiac cycles. Systole and diastole were visually defined by the opening and closure of the atrioventricular valves. As a surrogate measure of heart size, the length of the heart was measured from the basis to the apex in the same four-chamber view.

Extracardiac blood flow measurements and fetal biometry were performed with either a Vivid 7 or a Voluson 730 Expert equipped with a 2–5 MHz real time broadband curved array transducer (RAB2-5L) (Kretz, GE Medical Systems, Zipf, Austria). In all fetuses the pulsatility index (PI, (peak systolic velocity − minimum diastolic velocity)/averaged velocity over one cardiac cycle) of the umbilical (UA) and the medial cerebral artery (MCA) were measured as means of two to three cycles. Finally, the ductus venosus A wave flow pattern was obtained. Fetal weight was calculated with the Hadlock formula based on head size, abdominal circumference and femur length [15].

Statistical analysis was performed with Stata (Intercooled Stata 9.0 for Windows, StataCorp LP, College Station, TX, USA). For comparison of cases and controls only one scan per normal fetus from approximately week 29 in normal fetuses ($n = 41$) was used. Mean and 95% confidence intervals were calculated for each tissue velocity parameter. Mann–Whitney's test was used to compare cases and controls. A p-value < 0.05 was considered significant. The correlations between tissue velocities and gestational age were tested with Spearman's rank test and the hypothesis of no correlation was tested with the sign test. For correlation between tissue and flow velocities a linear regression model was used. To assess intra- and inter-observer variability, 10 scans were reanalyzed by the same observer and a second observer. The variability is expressed as proportional mean difference and 95% limits of agreement ($\pm 1.96 \times$ SD) according to Bland and Altman [16].

The study was approved by the Danish Council of Ethics and the Danish Data Protection Agency. All women gave informed written consent.

3. Results

A total of 87 ultrasound scans were performed. Only one scan was excluded because of poor image quality (normal fetus). Mean age of the control fetuses was 28^6 (28^5–28^6) (weeks^{days}) and estimated weight was 1332 (1294–1370) g. Mean age of the growth retarded fetuses was 29^3 (28^3–30^3) and the estimated weight 850 (701–999) g.

Tricuspid flow was obtained in 97% and mitral flow in 94% of the 35 normal fetuses that were scanned on only one occasion (the cross-sectional group). Mean right E and A flow velocities were 42.5 (40.8–44.2) and 57.2 (54.8–59.7) cm/s and mean left E and A were 40.4 (38.2–42.5) and 53.8 (51.3–56.3) cm/s. The mean right and left E/A ratios were 0.75 (0.73–0.77) and 0.75 (0.70–0.77).

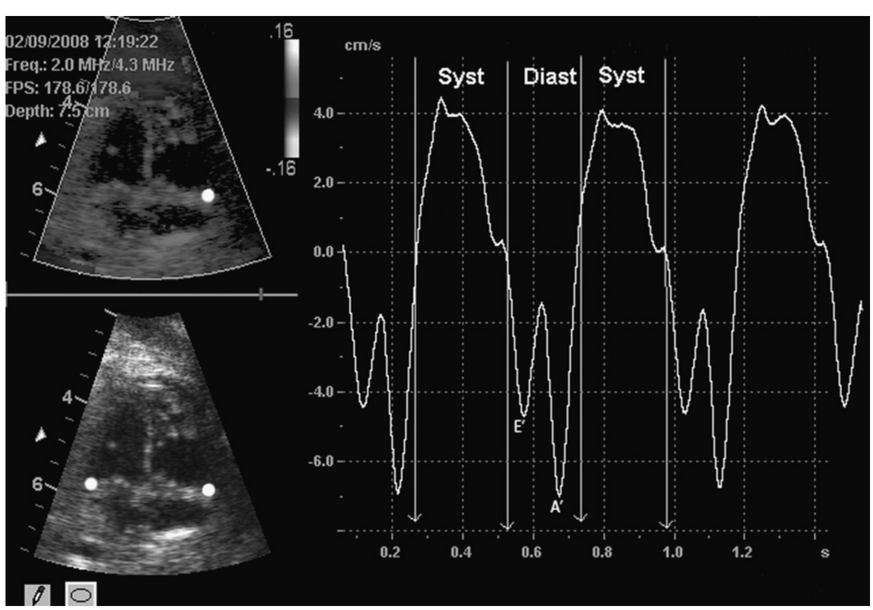

Fig. 1. On the top left the circle in the basal ventricular wall of the right ventricle corresponds to the velocity curve on the right hand side. The two circles (bottom left) show the placement of the sample areas in both ventricles.