Fetal Hemodynamics of Intrauterine Growth Restriction by Phase Contrast MRI and MR Oximetry

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Target Audience: Professionals involved in management of intrauterine growth restriction pregnancies; Radiologists; Developmental Scientists

Purpose: We sought to compare phase contrast MRI and T2 mapping measurements of blood flow and oxygen content in the major vessels of appropriate for gestational age (AGA) and small for gestational age (SGA) fetuses, and to evaluate the utility of fetal MRI hemodynamic measurements against conventional Doppler markers of intrauterine growth restriction (IUGR).

Methods: In this prospective IRB approved study we obtained informed consent for late gestation fetal cardiovascular MRI using a commercial 1.5T MRI system (Siemens Avanto). We measured fetal body and brain weight by segmenting a 3D-SSFP acquisition. Blood flow and oxygen saturations were measured in the major fetal vessels using phase contrast MRI with metric optimized gating and T2 mapping with motion correction according to our previously published technique.[1] Fetal oxygen delivery (DO_2) and consumption (VO_2) were calculated using an estimated haemoglobin concentration based on population averages.[2] We recorded clinical fetal monitoring results (Middle Cerebral Artery and Umbilical Artery Pulsatility Index, Cerebro-Placental Ratio, umbilical cord blood gases and Apgar scores) and the placental histopathology results. A student t-test (GraphPad Prism) was used to compare parameters for the two groups with $p<0.05$ indicating a significant difference. We used linear regression to look for any correlations between measured variables. A Chi-squared test was performed to assess the relative prevalence of significant placental abnormalities in the two groups.

Results: There was one stillbirth of a fetus with known IUGR in the setting of pre-eclampsia. The remaining subjects were all born in good condition. Fetuses were divided into two groups according to estimated fetal weight (EFW) with fetuses below the 10th percentile defined as SGA and those above the 10th percentile as AGA. There were 10 SGA and 30 AGA fetuses. There was no difference in mean gestational age (GA) between the two groups. The results of the flow measurements are shown in Table 1. Brain weight was reduced in SGA fetuses and brain weight was inversely correlated with SVC flow (R^2=0.35, P=0.0013). Figures 1 and 2 show that mean T2 values, fetal DO_2 and VO_2 were significantly lower in SGA fetuses than AGA fetuses. Placental pathology revealed lower placental weight in the SGA group (SGA: 313 ± 113g, AGA: 453 ± 70g, P=0.008). Placental weight correlated with DO2 (R^2=0.38, P=0.007) (Figure 3) and descending aorta T2 values (R^2=0.41, P=0.004), and was inversely correlated with SVC flow (R^2=0.27, P=0.03). When the placental histology was analyzed for the presence of established findings associated with significant IUGR, we found a higher prevalence of placental abnormality in the SGA group (P=0.02). Comparison of cord blood gases in the two groups revealed lower UV and UA PO_2 in the SGA group ($UVPO_2$: P=0.04, $UAPO_2$: P=0.005), but there was no correlation between cord gases and prenatal hemodynamic parameters. The Apgar scores for the two groups were not significantly different. There were no significant differences in Doppler parameters between the two groups and no significant correlations between the MRI measurements and Doppler parameters or Apgar scores.

Measurements	Group	Mean	SD	P value	Significance
Gestation Age (weeks)	AGA	35.2	0.7	0.8	NS
	SGA	35.5	2.7		
Estimated Weight (Kg)	AGA	2.7	0.3	0.002	Significant
	SGA	1.8	0.6		
Brain Weight (g)	AGA	294	29	0.02	Significant
	SGA	241	56		
CVO (ml/min/kg)	AGA	465	57	0.2	NS
	SGA	522	126		
MPA (ml/min/kg)	AGA	244	40	0.2	NS
	SGA	289	87		
AAO (ml/min/kg)	AGA	213	44	0.6	NS
	SGA	201	59		
SVC (ml/min/kg)	AGA	137	35	0.003	Significant
	SGA	214	58		
DA (ml/min/kg)	AGA	184	40	0.08	NS
	SGA	235	74		
DAO (ml/min/kg)	AGA	255	41	0.6	NS
	SGA	262	67		
PBF (ml/min/kg)	AGA	69	40	0.0001	Significant
	SGA	32	9		
UV (ml/min/kg)	AGA	129	31	0.01	Significant
	SGA	102	28		

Table 1. GA, EFW, brain weight and major vessel flows in the two groups (CVO: combined ventricular output, MPA: main pulmonary artery, AAO: ascending aorta, SVC: superior vena cava, DA: ductus arteriosus, DAO: descending aorta PBF: pulmonary blood flow, UV: umbilical vein.

Discussion: When compared with the AGA group, the SGA fetuses in this study had lower UV blood flow, PBF and oxygen saturations and higher SVC flows. This is in keeping with the redistribution of the circulation in response to acute hypoxia previously shown in fetal lambs and by conventional cordocentesis oximetry and Doppler studies in human IUGR.[3,4] The placental histology results are consistent with a high incidence of IUGR in the SGA fetuses, as is the reduction in DO2 we found in these fetuses with MRI. The associated drop in fetal VO2 may reflect fetal metabolic adaptation to reduced oxygen delivery, with a resulting slowing of fetal growth. Furthermore, despite the presence of "brain sparing physiology", placental insufficiency also appeared to limit brain growth in these fetuses. While we found significant differences between the two groups in terms of MRI fetal hemodynamic parameters and a strong correlation between these parameters and placental weight, there were no significant differences between the two groups by conventional Doppler parameters and no correlation between conventional monitoring and placental abnormalities. This is consistent with known poor sensitivity and specificity of conventional Doppler parameters in the setting of late-onset IUGR and suggests that our MRI approach may have clinical utility in identifying fetuses with this condition.[5] As late-onset IUGR is associated with suboptimal neurodevelopmental outcomes, modification of delivery timing remains of interest in this group.

Conclusion: We showed a high incidence of placental abnormalities in SGA fetuses in keeping with IUGR. SGA was associated with MRI evidence of expected fetal hemodynamic adaptions to hypoxia that were undetected by conventional Doppler assessment. Whether the enhanced detection of late-onset IUGR by MRI could improve patient outcomes remains unknown, but we propose that further investigation of this approach is warranted.

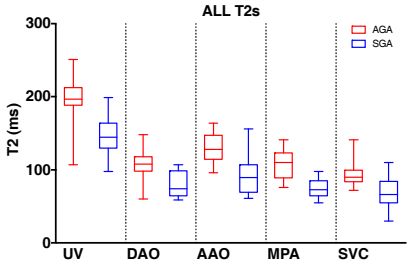

Figure 1. T2 values in major vessels in SGA and AGA groups

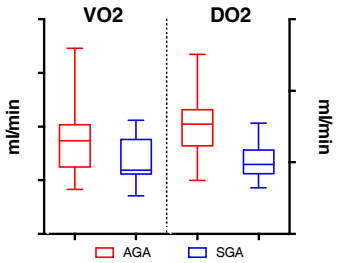

Figure 2. Calculated VO2 and DO2 in SGA and AGA groups

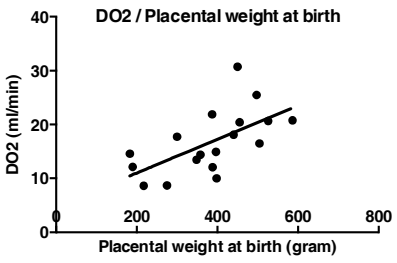

Figure 3. Correlation between calculated DO2 with placental weight after birth.

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