Preliminary fetal hemodynamic patterns in late gestation fetuses with common forms of cyanotic congenital heart disease by phase contrast MRI and T2 mapping

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Target Audience: The presented data will be useful for health professionals in field of obstetrics, neonatology, paediatric cardiology and radiology, as well as researchers in imaging and developmental science.

Purpose: We sought to determine the hemodynamics of late gestation fetuses with common forms of cyanotic congenital heart disease (CHD), using a combination of phase contrast (PC) magnetic resonance imaging (MRI) and MR oximetry by T2 mapping.

Methods: The major vessels of 33 normal late gestation fetuses (mean GA: 36.3 weeks SD 1.3 weeks) and 51 fetuses with five common forms of cyanotic CHD (mean GA 35.8 weeks SD 2.1 weeks) were studied with PC MRI according to our previously published technique[1,2]. T2 mapping was also performed in 66 of the 84 fetuses. Oxygen saturations (SaO2) were calculated using gestational age appropriate population average hematocrits[3] with conversion from T2 to SaO2 performed according to adult blood T2 relaxometry[4]. Blood flow and SaO2 were expressed as means with ± 2SD. Hemodynamic parameters were compared using a Student t-test (GraphPad Prism) with $p<0.05$ considered significant.

Results: Mean vessel flows and SaO_2 measured by MRI compared with normal reference[1] data are shown in Table 1. Figure 1 illustrates the SaO2 in the normal fetal circulation and in three types of CHD.

Table 1. Blood flow and oxygen saturation in the major vessels of normal human fetuses and fetuses with cyanotic congenital heart disease

	Blood flow in ml/min/kg (mean ± SD; n)								Oxygen Saturation in % (mean ± SD; n)				
	CVO	AAO	MPA	SVC	DAO	UV	DA	PBF	UV	AAo	MPA	DAo	SVC
Normal	469 ± 57 (33)	208 ± 42 (33)	246 ± 40 (33)	137 ± 33 (33)	237 ± 44 (33)	130 ± 31 (33)	180 ± 52 (33)	71 ± 33 (33)	80 ± 5 (33)	59 ± 6 (33)	52 ± 7 (33)	53 ± 6 (33)	45 ± 6 (33)
HLHS	429 ± 119 (14)	56 ± 53 (13)	368 ± 121 (14)	141 ± 42 (15)	220 ± 62 (14)	120 ± 37 (14)	298 ± 110 (12)	78 ± 43 (12)	80 ± 10 (5)	48 ± 4 (3)	48 ± 8 (4)	50 ± 9 (5)	36 ± 10 (5)
TOF	482 ± 80 (12)	387 ± 88 (12)	84 ± 51 (11)	129 ± 35 (12)	261 ± 84 (11)	140 ± 53 (11)	78 ± 117 (6)	79 ± 89 (8)	68 ± 13 (10)	53 ± 11 (9)	50 ±16 (5)	50 ± 11 (10)	38 ± 12 (8)
TGA/IVS	498 + 102 (13)	272 + 62 (13)	211 + 49 (13)	170 + 72 (13)	250 + 60 (13)	133 + 25 (13)	133 + 55 (11)	83 + 90 (10)	71 + 8 (7)	46 + 13 (7)	53 + 13 (7)	49 + 10 (7)	39 + 11 (7)
Ebstein's Anomaly	285 ± 115 (5)	207 ± 58 (5)	150 ± 212 (2)	101 ± 16 (5)	162 ± 57 (6)	112 ± 40 (6)	110 ± 125 (2)	71 ± 69 (2)	78 ± 10 (6)	46 ± 2 (4)	44 ± 0 (1)	45 ± 8 (6)	33 ± 5 (4)
Tricuspid Atresia	414 ± 53 (7)	229 ± 102 (7)	173 ± 115 (7)	138 ± 46 (7)	195 ± 44 (7)	80 ± 41 (7)	125 ± 82 (6)	73 ± 43 (7)	73 ± 8 (5)	47 ± 11 (5)	50 ± 13 (3)	47 ± 11 (5)	36 ± 12 (5)

HLHS- Hypoplastic left heart syndrome, TOF- Tetralogy of Fallot, TGA/IVS- Transposition of the great arteries with intact ventricular septum, CVO- combined ventricular output, AAo- ascending aorta, MPA- main pulmonary artery, SVC- superior vena cava, DAo- descending aorta, UV- umbilical vein, DA- ductus arteriosus, PBF- pulmonary blood flow

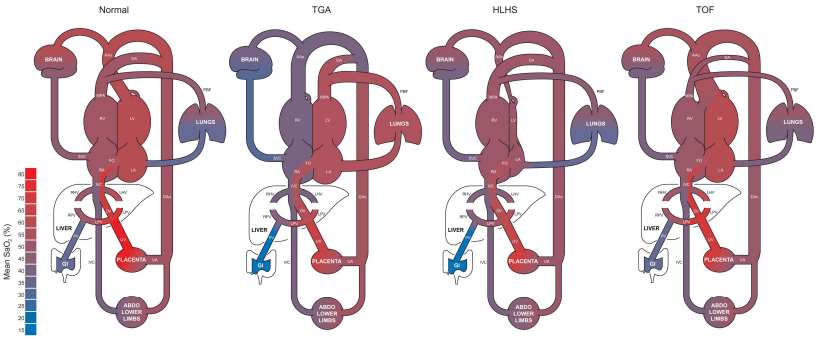

Figure 1: Oxygen saturations in typical examples of the normal late gestation human fetus (left) and three common forms of congenital heart disease by MRI.

Fetuses with single ventricle physiology (SV) had lower CVO than normals ($p<0.02$), while the lowest CVO was found in fetuses with Ebstein's anomaly ($p<0.0001$). SV physiology is also associated with lower placental blood flow ($p<0.03$). SVC flow (and therefore cerebral blood flow) and PBF are reasonably stable across all patient groups. HLHS fetuses have lower AAo ($p<0.0001$) and higher MPA ($p<0.0001$) and DA flow ($p<0.0001$) while TOF has higher AAo ($p<0.0001$) and lower MPA ($p<0.0001$) and DA flow ($p<0.001$) The SaO_2s throughout the fetal circulation are lower in CHD than in normals, including lower umbilical venous SaO2 ($p<0.01$) and AAo SaO_2 ($p<0.0001$).

Discussion: While there are some limitations of our technique relating to the reliance on assumed hematocrit and the general challenges of fetal MRI, these limitations probably apply equally to each patient group and a compelling picture of the hemodynamic impact of CHD emerges. The low CVO in SV patients is in keeping with previous ultrasound findings and presumably reflects an upper limit on the compensatory increase in cardiac output provided by the functioning ventricle in these fetuses. Their ability to maintain normal cardiac output is likely to be further affected by the presence of significant atrio-ventricular valve regurgitation, as demonstrated in the Ebstein's anomaly group. Placental blood flow is known to be dependent on blood pressure, which in turn is impacted by cardiac output, and this presumably explains the lower UV flow in SV patients. Low CVO does not explain why the fetuses with tricuspid atresia had lower placental blood flow than other SV patients. The reason for this is unclear, and the result may be spurious, resulting from the small sample size. The changes in the distribution of AAo and MPA flow in TOF and HLHS are expected in the setting of the right (TOF) and left (HLHS) ventricular outflow tract obstruction that characterize these lesions. The reduction in UV SaO2 found in many fetuses with CHD may result from placental abnormalities, which appear to be very common in fetuses with CHD[5]. However, the reduction in AAo SaO_2 is also due to failure of the normal streaming of oxygenated blood from the placenta to the left ventricle and aorta via the ductus venosus and foramen ovale (see Figure 1).

Conclusion: PC MRI and T2 mapping confirm previously suspected alterations in fetal hemodynamics resulting from CHD and provides some insight into the potential hemodynamic drivers of fetal dysmaturation that characterize subjects with these common birth defects.

References:

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