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Model of hypoplastic left heart in the fetal lamb created using a percutaneous transhepatic technique - preliminary experience

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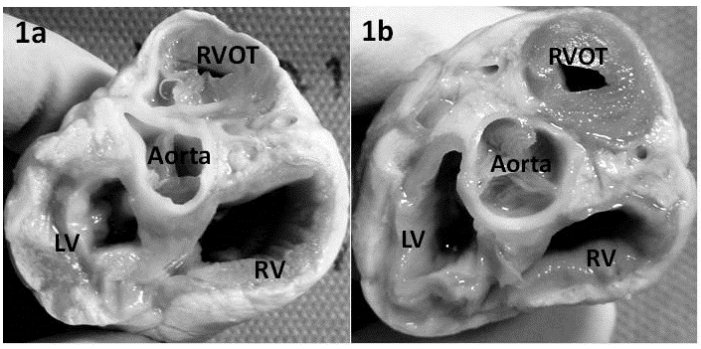
Introduction: Reduced blood flow into the fetal left ventricle (LV) may underlie development of Hypoplastic Left Heart Syndrome (HLHS), for which palliative surgery is the only treatment option. Currently there is no HLHS model in a large fetal mammalian animal for testing and clinical translation of new therapy. We have recently published a percutaneous trans-hepatic technique to catheterise the fetal heart, which could be utilised to produce an animal model of HLHS. Using a percutaneous trans-hepatic technique to deliver an occluder into the fetal heart, we aimed to create a fetal lamb model of HLHS by occluding the foramen ovale (FO).

Methods: Three fetal lambs (110-117days, term=147days) under maternal general anaesthesia were used. Under ultrasound guidance, the fetal hepatic vein was percutaneously punctured through the maternal abdomen using a 14GA IV-cannula. A coronary catheter and guidewire were inserted and advanced into the fetal IVC and right atrium. An Amplatzer Duct Occluder II (ADO II 4x4mm, St Jude Medical) was delivered to occlude the fetal FO. In 2 fetuses, a self-expandable stent (8x12 mm Superflex-DS 4Fr deliverable stent, Opti-Med Inc. Germany) was positioned across the FO first, and the ADO II was anchored within the stent. Serial ultrasounds were performed to monitor cardiac development. Euthanasia and post-mortem examination was performed 3 weeks after. A twin fetus which did not undergo the procedure was used as control for comparison. Morphometric measurements were made on digital images (Image J1.48b, NIH) of transverse sections of the heart at the level of atrioventricular valves.

Results: All 3 fetal lambs survived well to 3 weeks without any fetal compromise. At post-mortem examination, the LV lumen was markedly reduced (Fig 1a) with lower LV/right ventricular (RV) chamber volume ratio, LV/RV lumen area ratio and increased septal thickness at level of atrioventricular valves (Table), compared with the control fetal heart (Fig 1b).



Conclusions: Occlusion of the fetal FO using percutaneous catheterisation leads to phenotype simulating HLHS. Our results demonstrate the potential to develop the world's first large animal model of HLHS, critical for understanding the cardiac and pulmonary consequences and devising new therapies.

Fetal hearts	Ratio of heart weight/body weight (g/kg)	Ratio of LV/RV chamber volume	Ratio of LV/RV lumen area	Septal thickness (cm)
Occluded FO 1	3.7	0.63	0.79,	0.44
Occluded FO 2	4.5	0.30	0.88	0.45
Occluded FO 3	4.7	0.23	1.02	0.53
Control (n=1)	4.1	1.0	1.54	0.23