SUPPLEMENTAL MATERIAL

Fetal Brain Volume Predicts Neurodevelopment in Congenital Heart Disease

Supplemental Table 1. Cardiac Class,[25] Diagnoses, and Cardiac Interventions for all CHD Participants	
Cardiac Diagnosis	**Cardiac Interventions**
Class I (Two ventricles with no aortic arch obstruction)	
d-TGA/IVS	1. Arterial switch operation, PDA ligation, PFO closure
d-TGA/IVS	1. Balloon atrial septostomy 2. Arterial switch operation
d-TGA/IVS	1. Arterial switch operation, ASD closure
d-TGA/IVS	1. Arterial switch operation, ASD closure, PDA ligation, pulmonary root reconstruction
d-TGA/IVS	1. Balloon atrial septostomy 2. Arterial switch operation, ASD closure, PDA ligation
d-TGA/VSD	1. Arterial switch operation, VSD and ASD closure
d-TGA/VSD with overriding and straddling tricuspid valve and RV hypoplasia	1. Arterial switch operation, PA banding, PFO and VSD closure
DORV, VSD	1. PA banding 2. PA band takedown, full repair with right ventricular outflow tract reconstruction, VSD closure, creation of fenestrated ASD, repair tricuspid valve
TOF/PS	1. TOF repair
TOF/PS	1. TOF repair
TOF/PS	1. TOF repair
TOF/PS, bilateral SVC	1. TOF repair
TOF/PS	1. Balloon dilation of pulmonary valve x 2 2. TOF repair
TOF/PS, right arch with aberrant origin of left subclavian	1. TOF repair, division of vascular ring
TOF/PA with MAPCAs	1. Multiple catheterizations to coil MAPCAs and to dilate/stent branch PAs 2. RV to PA conduit 3. TOF repair with VSD closure and RV to PA conduit replacement
TOF/PA with single large aortopulmonary collateral	1. TOF repair
Complete AV canal	1. Complete AV canal repair
Balanced transitional AV canal	1. Partial AV canal repair
Truncus arteriosus, AV canal	1. AV canal and truncus arteriosus repair with canal repair, RV to PA conduit, second ASD closure
Tricuspid stenosis, mildly hypoplastic RV, PS, VSD	1. Pulmonary valve balloon dilation
Dysplastic pulmonary valve	1. Resection of pulmonary valve, main PA patch, PDA ligation
Dysplastic pulmonary valve	1. PDA ligation, pulmonary arterioplasty
Class II (Two ventricles with aortic arch obstruction)	
Coarctation	1. Coarctation repair
Coarctation	1. Coarctation repair
Coarctation	1. Coarctation repair
Coarctation	1. Coarctation repair
VSD, coarctation	1. Coarctation repair, VSD and ASD closure
VSD, coarctation	1. VSD and PFO closure, aortic arch augmentation

DORV Taussig-Bing type with hypoplastic aortic arch	1. Balloon atrial septostomy 2. Arterial switch operation, aortic arch repair, VSD closure
DORV, d-TGA, coarctation	1. Arterial switch operation, coarctation repair, VSD closure
Interrupted aortic arch with aortopulmonary window	1. PA banding 2. Full repair with aortopulmonary repair and removal of PA bands
Severe AS	1. Fetal aortic valvuloplasty 2. PFO closure, Ross procedure, repair of ascending aortic aneurysm
Severe AS	1. Fetal aortic valvuloplasty 2. Postnatal aortic valvotomy
Severe AS with intact atrial septum	1. Fetal aortic valvuloplasty 2. Postnatal atrial needle transeptal puncture and aortic valvotomy 3. Aortic valve repair, ASD closure, endocardial fibroelastosis resection from LV, PDA ligation
Shone's complex	1. Balloon dilation of aortic valve
Class III (single ventricle without arch obstruction)	
Complex single ventricle physiology	1. Balloon atrial septostomy 2. PA banding, atrial septectomy, bidirectional Glenn
Complex single ventricle physiology	1. Stage 1 Norwood 2. Bidirectional Glenn
Complex single ventricle physiology	1. Postnatal details unavailable
Tricuspid atresia type 1B	1. Right sided modified BT shunt 2. Bidirectional Glenn 3. Fenestrated Fontan
Tricuspid atresia type 1C	1. Right modified BT shunt, PDA ligation, main PA transection with pulmonary valvectomy, oversewing main PA, complete atrial septectomy 2. Bidirectional Glenn and BT shunt due to left pulmonary vein stenosis
Severe Ebstein's anomaly	1. Right modified BT shunt 2. Bidirectional Glenn
Tricupsid atresia, pulmonary atresia	1. Right modified BT shunt 2. Bidirectional Glenn
Unbalanced AV Canal, DORV	1. PA banding
Class IV (single ventricle with arch obstruction)	
HLHS	1. Fetal aortic valve dilation 2. Atrial septal stent 3. Stage 1 Norwood 4. Bidirectional Glenn
HLHS	1. Stage 1 Norwood 2. Bidirectional Glenn
HLHS	1. Stage 1 Norwood 2. Bidirectional Glenn
HLHS	1. Stage 1 Norwood 2. Bidirectional Glenn
HLHS	1. Stage 1 Norwood 2. Bidirectional Glenn
HLHS with coronary fistula	1. Stage 1 Norwood 2. Bidirectional Glenn
HLHS with coronary fistula	1. Stage 1 Norwood 2. Bidirectional Glenn
HLHS, coarctation	1. Atrial septum dilation 2. Stage 1 Norwood

Critical AS with hypoplastic mitral valve and intact atrial septum	1. Stage 1 Norwood, repair of aortic dissection 2. Bidirectional Glenn

d-TGA = d-transposition of the great arteries; d-TGA/IVS = d-TGA with intact ventricular septum; TOF/PS = tetralogy of Fallot with pulmonary stenosis; TOF/PA = tetralogy of Fallot with pulmonary atresia; SVC = superior vena cava; MAPCA = major aortopulmonary collateral; AV = atrioventricular; AS = aortic valve stenosis; HLHS = hypoplastic left heart syndrome; VSD = ventricular septal defect; ASD = atrial septal defect; PDA = patent ductus arteriosus; PFO = patent foramen ovale; PA = pulmonary artery; RV = right ventricle

Supplemental Table 2. Alternative Hierarchical Regression Models to Predict Neurodevelopmental Outcomes in the CHD Group

Outcome	Variable	Beta Coefficient [95% CI]	Partial Adjusted R^2	Total Adjusted R^2
Bayley−III				
Cognitive composite	Total brain volume (per ml)*	0.28 [0.08, 0.48]	0.14	0.33
	Stroke or seizure	7.33 [−2.81, 17.47]	0.03	
	Length of stay (per day)	−0.11 [−0.19, −0.04]	0.21	
Language composite	Education, college or greater†	8.95 [1.48, 16.42]	0.09	0.22
	Total brain volume (per ml)*	0.32 [0.04, 0.60]	0.08	
Motor composite	Education, college or greater†	0.11 [−6.22, 6.45]	−0.03	0.35
	Cardiac class II	1.68 [−5.70, 9.06]	0.07	
	Cardiac class III	−8.70 [−17.22, −0.18]	−	
	Cardiac class IV	−4.53 [−13.37, 4.30]	−	

	Total brain volume (per ml)*	0.29 [0.06, 0.53]	0.12	
	Length of stay (per day)	−0.10 [−0.19, −0.01]	0.10	
Receptive communication	Education, college or greater†	1.75 [0.25, 3.24]	0.09	0.18
	Total brain volume (per ml)*	0.05 [−0.002, 0.11]	0.06	
Expressive communication	Education, college or greater†	1.19 [−0.17, 2.54]	0.05	0.21
	Total brain volume (per ml)*	0.06 [0.01, 0.12]	0.11	
	ECMO	−2.61 [−5.71, 0.49]	0.04	
Fine motor	Total brain volume (per ml)*	0.05 [0.003, 0.10]	0.08	0.26
	Birth weight (per kg)	0.49 [−0.53, 1.51]	−0.001	
	Length of stay (per day)	−0.02 [−0.04, −0.003]	0.10	
Gross motor	Education, college or greater†	0.24 [−0.85, 1.34]	−0.01	0.40
	Cardiac class II	−0.41 [−1.67, 0.84]	0.22	

	Cardiac class III	−2.26 [−3.79, −0.73]	−	
	Cardiac class IV	−2.22 [−3.61, −0.82]	−	
	Total brain volume (per ml)*	0.06 [0.01, 0.10]	0.12	
	ECMO	−2.71 [−5.24, −0.18]	0.08	
ABAS−3				
General adaptive composite	Total brain volume (per ml)*	0.49 [0.22, 0.76]	0.21	0.21

*Total brain volume refers to residual after adjustment of fetal total brain volume for sex and gestational age (linear and quadratic terms)

†Education refers to primary caregiver education

ECMO = extracorporeal membrane oxygenation

Bayley-III = Bayley Scales of Infant Development, Third Edition

ABAS-3 = Adaptive Behavior Assessment System, Third Edition

Supplemental Table 3. Stepwise Forward Selection Regression Models to Predict Neurodevelopmental Outcomes in the CHD Group

Outcome	Variable	Beta Coefficient [95% CI]	Partial Adjusted R^2	Total Adjusted R^2
Bayley-III				
Cognitive composite	Total brain volume (per ml)*	0.27 [0.08, 0.48]	0.14	0.33
	Length of stay (per day)	−0.11 [−0.19, −0.04]	0.21	
	Stroke or seizure	7.33 [−2.81, 17.47]	0.03	
Language Composite	Total brain volume (per ml)*	0.32 [0.04, 0.60]	0.08	0.22
	Education, college or greater†	8.95 [1.48, 16.42]	0.09	
Motor Composite	Total brain volume (per ml)*	0.29 [0.07, 0.52]	0.13	0.37
	Cardiac class II	1.67 [−5.60, 8.94]	0.07	
	Cardiac class III	−8.71 [−17.09, −0.34]	−	
	Cardiac class IV	−4.55 [−13.22, 4.12]	−	

	Length of stay (per day)	−0.10 [−0.19, −0.01]	0.10	
Receptive communication	Total brain volume (per ml)*	0.05 [−0.002, 0.11]	0.06	0.18
	Education, college or greater†	1.75 [0.25, 3.25]	0.09	
Expressive communication	Total brain volume (per ml)*	0.09 [0.04, 0.15]	0.18	0.18
	Birth weight	−0.71 [−1.85, 0.42]	0.05	
	ECMO	−2.95 [−6.09, 0.18]	0.01	
Fine motor	Total brain volume (per ml)*	0.06 [0.01, 0.10]	0.12	0.26
	LOS	−0.02 [−0.04, −0.005]	0.11	
Gross motor	Total brain volume (per ml)*	0.06 [0.02, 0.10]	0.15	0.45
	White race	1.39 [0.09, 2.70]	0.08	
	Cardiac class II	−0.44 [−1.62, 0.75]	0.25	
	Cardiac class III	−2.53 [−3.99, −1.06]	−	

	Cardiac class IV	−1.98 [−3.32, −0.64]	−	
	ECMO	−3.12 [−5.54, −0.71]	0.12	
ABAS-3				
General adaptive composite	Total brain volume (per ml)*	0.49 [0.22, 0.76]	0.21	0.21