187 The role of maternal lymphatic markers in fetal diagnosis of critical congenital heart disease

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OBJECTIVE: Abnormal fetal nuchal translucency (NT) measurement during pregnancy is associated with critical congenital heart disease (CCHD). Markers of lymphatic function have also been related to increased NT and may point to a potential underlying causative link between CCHD and NT. The objective of this study was thus to investigate whether maternal lymphatic markers drawn at the second trimester screening are associated with CCHD in the infant.

STUDY DESIGN: Retrospective case-control study of non-diabetic pregnant women in the California Prenatal Screening Program between 2009 and 2010 who had banked second trimester serum samples (n = 39,784). CCHD data in infants was captured by linking data to birth certificate and hospital patient discharge records maintained by the Office of Statewide Health Planning and Development. These records code diagnoses and procedures using the International Classification of Diseases codes (ICD9). The following diagnostic codes were used to define CCHD: 745.0-745.3, 745.6, 746.0-746.3, 746.7, 747.1, 747.4. Second trimester samples were assayed using a standard-sensitivity Milliplex Map kit (Millipore) for vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF) AA/BB, and PDGF AB run on a Luminex-100 (all in pg/ml). Markers were log transformed for analysis. Crude and adjusted logistic models (odds ratios (ORs) and their 95% confidence intervals (CI)) were used to evaluate the association between lymphatic markers and CCHDs. Models were adjusted for the other biomarkers, maternal race/ethnicity, age, BMI and hypertensive disorder.

RESULTS: 93 CCHD cases and 194 controls were selected for lymphatic marker analysis. The crude and adjusted OR for log VEGF, log PDGF AB/BB and log PDFG AA are presented in the Table.

CONCLUSION: Increased maternal PDGF AA but not VEGF and PDGF AB/BB is associated with CCHD in the infant. These data add further evidence for a role of lymphatic function in predicting CCHDs in pregnancy.

Table: Crude and adjusted OR for lympatic markers and CCHD

	univariate OR	95% CI	Multivariate OR	95% CI
Log VEGF	1.07	0.94-1.22	1.08	0.94-1.24
Log PDGF AA	1.83	1.05-3.2	2.41	1.06-5.44
Log PDGF AB/BB	0.93	0.6-1.45	0.58	0.32-1.05

188 Neonatal outcomes for pregnancies complicated by fetal cardiac anomalies according to attempted route of delivery

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OBJECTIVE: To examine the role of attempted route of delivery on neonatal outcomes in fetuses with congenital cardiac anomalies.

STUDY DESIGN: Singleton and multiple gestations with fetal cardiac anomalies and delivery greater than 34 weeks were analyzed from the Consortium on Safe Labor, a retrospective cohort study of electronic medical records. Fetal cardiac anomalies were determined using ICD 9 codes and organized based on morphology. Cases with more than one cardiac defect were analyzed in each group. Stillbirths and aneuploidies were excluded. Neonatal outcomes were determined for each type of fetal cardiac anomaly. Composite neonatal morbidity (serious respiratory morbidity, sepsis, birth trauma, hypoxic ischemic encephalopathy, and neonatal death) was compared between attempted vaginal delivery (VD) and planned cesarean delivery (CD) for prenatal and postnatal diagnosis. We used multivariate logistic regression to calculate adjusted odds ratio (aOR) for composite neonatal morbidity controlling for race, parity, BMI, insurance, gestational age, maternal disease, single or multiple anomalies, and maternal drug use.

RESULTS: There were 2,166 neonates with 2,701 fetal cardiac anomalies. Rates of cardiac anomaly prenatal diagnosis were generally similar to rates reported in the literature with the majority not diagnosed prenatally (Table). Neonatal death occurred in 8.4% of 107 neonates with conotruncal defects. Serious respiratory morbidity occurred in 56.2% of 89 neonates with left ventricular outflow tract defects. In our cohort 76.3% of 2,166 neonates underwent attempted VD and 23.7% planned CD. Planned CD compared to attempted VD was not associated with decreased composite neonatal morbidity for all prenatally diagnosed (aOR 0.99, 95% CI 0.77-1.27) as well as postnatally diagnosed fetuses (aOR 1.67, 95% CI 0.86-3.24).

CONCLUSION: The majority of fetal cardiac anomalies were not prenatally diagnosed and were associated with increased rates of neonatal morbidity. Planned cesarean delivery for fetal cardiac anomalies was not associated with decreased neonatal morbidity.

Most common fetal cardiac anomaly classifications and corresponding neonatal outcomes

Description	Fetal anomaly with prenatal diagnosis n/A(%)	Fetal anomaly with postnatal diagnosis n/A(%)	Percent prenatal detection available in current literature	Neonatal death n/N(%)	Serious respiratory morbidity n/N(%)	NICU admission over 72 hours n/N*(%) *Missing outcome data
Conotruncal defects N=107 neonates A=112 anomalies	38(33.9)	74(66.1)	41.7-85.2	9(8.4)	54(50.5)	45/100(45.0)
Ventricular septal defects N=660 neonates A=660 anomalies	76(11.5)	584(88.5)	12.9-68.6	13(2.0)	144(21.8)	189/621(30.4)
Atrial septal defects N=1453 neonates A=1453 anomalies	132(9.1)	1321(90.9)	12.9	30(2.1)	518(35.7)	625/1358(46.0)
Congenital anomalies pulmonary artery N=256 neonates A=256 anomalies	27(10.5)	229(89.5)	10.0	8(3.1)	123(48.0)	158/238(66.4)
Left ventricular outflow tract obstruction (LVOTO) defects N=89 neonates A=97 anomalies	41(42.3)	56(57.7)	25.7-97.6	5(5.6)	50(56.2)	35/83(42.2)
Right ventricular outflow tract obstruction (RVOTO) defects N=84 neonates	55(65.5)	65(77.4)	19.2-68.6	3(3.6)	36(42.9)	36/76(47.4)
A=84 anomalies						

189 Fetal tolerance of labor in pregnancies complicated by growth restriction and abnormal umbilical artery Doppler

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OBJECTIVE: To quantify the rate of cesarean section secondary to fetal distress in pregnancies complicated by growth restriction with and

without abnormal fetal umbilical artery (UA) Doppler findings when compared to normal pregnancies.

STUDY DESIGN: Retrospective analysis of 297 pregnancies complicated by intrauterine growth restriction from 2009-2015 at two affiliate hospitals in the same large metropolitan area. All growth restricted fetuses with abnormal UA Doppler were identified (n=84) after exclusions for known aneuploidy, fetal demise, cardiac anomalies and missing delivery data. A cohort with growth restriction and normal UA Doppler (n=213) were selected in a 2:1 ratio. Information regarding demographic data, maternal comorbidities, neonatal outcomes, mode of delivery, and indication for cesarean section were collected from the medical record. Odds ratios for cesarean section, adjusted for gestational age using a multivariate logistic regression model, were calculated for both groups compared to all non-growth restricted deliveries at the main delivery institution in 2015.

RESULTS: There was a higher rate of cesarean section for fetal distress in growth restricted fetuses with abnormal Doppler when compared to normal Doppler (52.4% vs 17.4%; p=<0.0001). When compared to the non-growth restricted delivery population, there was an overall increased risk of cesarean section with both the normal Doppler group (OR 1.6; CI=1.2-2.1) and the abnormal Doppler group (OR 12.7; CI=5.8-28.1). There was a further increased risk when evaluating cesarean section for fetal distress in both normal (OR 3.7; CI=2.5-5.3) and abnormal (OR 16.6; CI=9.6-28.5) Doppler groups. A sub-group analysis of the normal Doppler group with oligohydramnios was found to have an increased rate of cesarean section (54.6% vs. 39.6%; p=0.07), but this was not statistically significant. Of patients that were eligible for induction, 76.2% (n=99) of the normal Doppler group and 35.0% (n=7) of the abnormal Doppler group had a successful vaginal delivery.

CONCLUSION: Fetal growth restriction confers an elevated risk of cesarean section for fetal distress, which is further increased in the presence of abnormal UA Doppler. However, there remains an acceptable rate of vaginal delivery in these groups and induction is a potential option for eligible patients.

190 Risk of donor demise after laser therapy for twin-twin transfusion when complicated by growth restriction and abnormal umbilical artery Doppler

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OBJECTIVE: Donor twin abnormal umbilical artery (UA) Doppler and growth restriction are common ultrasonographic findings in twin-twin transfusion syndrome (TTTS) and indicate fetal compromise. This study aims to investigate the natural course of these findings after laser surgery for TTTS and the prognostic ability of either resolution or persistence of abnormal UA Doppler with and without intrauterine growth restriction (IUGR) to predict fetal demise.

STUDY DESIGN: A retrospective cohort study of all monochorionic-diamniotic multi-fetal gestations diagnosed with TTTS undergoing laser surgery at a single large metropolitan referral center from 2010-2016. The estimated fetal weight was measured preoperatively and the UA Doppler was measured both pre- and postoperatively. Odds ratios were calculated for each group for risk of intrauterine fetal demise compared to the preoperative normal UA Doppler group. Post-operative odds ratios were calculated with an intent to treat analysis including patients with a donor demise prior to the post-operative ultrasound.

RESULTS: There were 83 women who met inclusion criteria and 81 had delivery data available for analysis. Forty-three (51.8%) patients had abnormal donor twin UA Doppler preoperatively and thirty-three (39.8%) were diagnosed with IUGR. However, thirteen (30.2%) had normalization of the UA Doppler postoperatively (median=8 days). Abnormal preoperative UA Doppler was associated with an increased risk of donor demise (OR: 1.91; 0.50-7.29), which was further elevated in the presence of IUGR (OR: 6.3; 1.93-20.62). If the UA Doppler remained abnormal postoperatively, the risk of donor demise further increased (OR: 4.44; 1.02-19.38) and was highest if IUGR was also present preoperatively (OR: 16.0; 4.21-60.86).

CONCLUSION: Laser treatment for TTTS can lead to rapid resolution of abnormal UA Doppler post-operatively. However, persistence of abnormal UA Doppler findings, especially in the presence of IUGR, is a significant risk factor for donor intrauterine demise.

Risk of donor demise with abnormal UA Doppler and IUGR findings

	Pre-op normal (n=38)	Pre-op abnormal (n=43)	Pre-op abnormal w/o IUGR (n=19)	Pre-op abnormal + IUGR (n=24)	Post-op normal (n=45)	Post-op abnormal (n=31)	Post-op abnormal w/o IUGR (n=11)	Post-op abnormal + IUGR (n=20)
Donor IUFD (%)	6 (15.8)	18 (41.9)	5 (26.3)	13 (54.2)	3 (6.7)	20 (64.5)	5 (45.5)	15 (75.0)
Odds ratio		3.84 (1.33-	1.91 (0.50-7.29)	6.3 (1.93-20.62)	0.38 (0.09-	9.70 (3.10-30.35	4.44 (1.02-19.38)	16.0 (4.21-
(95% CI)		11.10)			1.64)			60.86)

191 Maternal poly-alloimmunization does not increase the severity of fetal anemia

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OBJECTIVE: Maternal poly-alloimmunization has been proposed to increase the risk of fetal anemia. The objective of this study was to compare the severity of fetal anemia in a cohort of pregnant women with single or multiple maternal red blood cell antibodies.

STUDY DESIGN: IRB approval was obtained for a retrospective cohort study of women with alloimmunization from a single institution over a 6-year period (2008-2014). Subjects evaluated by middle cerebral artery Doppler velocimetry studies for elevated antibody titers were included. Clinical data extracted from the medical record included number and type of antibody, time to first Doppler > 1.5 MoM, fetal hematocrit, and clinical outcomes. Descriptive statistics, 2-tailed t-test and hazard analysis were performed using SPSS (Cary, NC) for data analysis.

RESULTS: Of 163 subjects, 120 (74%) had a single antibody and 43 (26%) had >1 antibody. Doppler velocimetry >1.5MoM was present in 19 subjects (16%) with a single antibody and 14 subjects (33%) with multiple antibodies (p=0.04). Anti-D was the only antibody more frequently associated with elevated Doppler values (39% vs 20%; p=0.04). Hazard analysis revealed a median survival time to Doppler velocimetry >1.5MoM of 34.7 (95% CI 30.9 - 38.5) weeks with a single antibody and 31.6 (95% CI 29.8 - 33.3) weeks with multiple antibodies (p=0.15). The median survival time was 31.1 weeks (95% CI 29.5 - 32.8) in the presence of Anti-D antibodies, compared to 35.4 weeks (95% CI 29.1 - 41.8) with all other antibodies (p=0.04). The survival time for subjects poly-alloimmunized with anti-D (31.6 weeks; 95% CI 24.8 - 38.3) was comparable to subjects poly-alloimmunized without anti-D (31.6 weeks; 95% CI 28.4 - 34.7) (p=0.77). Fetal hematocrit measured during percutaneous umbilical vein sampling did not differ between subjects with a single antibody or multiple antibodies (21.3+/-10.3 vs. 17.7+/-9.6; p=0.52).