Rates of adverse outcomes in AGA neonates misdiagnosed as FGR and unexposed controls

Outcome	AGA birth- FGR US	CTL	Unadjusted p-value (Chi²)	Adjusted Odds Ratio (95% C.I.)
Preterm delivery	19/78 (24.4%)	28/702 (4.0%)	<0.001	7.13 (3.55-14.3)
NICU admission	20/78 (25.6%)	87/702 (12.4%)	0.001	2.60 (1.42-4.74)
Cesarean delivery	23/78 (29.5%)	186/702 (26.5%)	NS	1.18 (0.69-2.04)
Neonatal death	1/78 (1.3%)	0/702	-	-
5 min. Apgar<4	0/78	0/702	-	-

221 Impact of inclusion of fetal growth restriction in severe preeclampsia diagnosis

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OBJECTIVE: Based on the newest ACOG guidelines (2013), fetal growth restriction (FGR) is no longer a criterion for diagnosis of preeclampsia (PE) with severe features. This study examines the impact of including FGR as criteria for the diagnosis of PE with severe features on neonatal and maternal outcomes.

STUDY DESIGN: Retrospective cohort of women with PE at a tertiary care center from 2011-2015. Inclusion criteria was diagnosis of PE <37 weeks. Women with preeclampsia with neither severe features (blood pressure $\geq$ 160/110 or a serum laboratory abnormality) nor FGR were excluded. Exposure groups include PE with severe features and no FGR (SPEnoFGR), PE with FGR and no severe features (SPEbyFGR), and PE with severe features plus FGR (SPE+FGR). The primary outcome was perinatal death (stillbirth or neonatal death). Secondary outcomes were abruption, delivery for non-reassuring fetal heart tones (NRFHTs), intrapartum or postpartum eclampsia, and a composite of adverse maternal outcomes (cardiomyopathy, ICU admission, intubation, and readmission for hypertension). Groups were compared with ANOVA and χ^2, as appropriate.

RESULTS: Of the 618 women included, 527 (85.3%) were SPEnoFGR, 20(3.4%) were SPEbyFGR, and 70(11.3%) were SPE+FGR. The gestational age at delivery was earliest with SPE+FGR (31.1 wks) and latest in SPEbyFGR (35.5 wks). In spite of this, the presence of FGR in PE with or without other severe features was associated with an increased incidence of perinatal death (p<0.01). Presence of FGR in PE with or without other severe features was also associated with an increased incidence in delivery for NRFHTs (p<0.01). Maternal outcomes did not differ significantly between groups.

CONCLUSION: Although utilizing FGR as a severe feature would reclassify relatively few cases of PE, the presence of FGR has a significant impact on neonatal mortality.

Neonatal and maternal outcomes with FGR included in SPE diagnosis (presented as n (%))

	Severe Preeclampsia no FGR	Severe Preeclampsia FGR only	Severe Preeclampsia plus FGR	P value
	n=527	n=21	n=70	
Perinatal death	24 (4.6%)	2 (9.5%)	11 (16.4%)	<0.01
Stillbirth	16 (3.0%)	1 (4.8%)	4 (5.8%)	0.47
Neonatal death	11 (2.1%)	1 (4.8%)	7 (10.5%)	<0.01
Abruption	5 (1.0%)	0	2 (2.9%)	0.32
Non-reassuring fetal heart tones	40 (7.6%)	5 (23.8%)	23 (32.9%)	<0.01
Adverse maternal outcomes	35 (6.6%)	1 (4.8%)	3 (4.3%)	0.72
Eclampsia (intrapartum/postpartum	3 (0.6%)	0	0	0.77

222 Global transcriptomic analysis of human placenta in the setting of intrauterine growth restriction (IUGR) using RNA sequencing (RNA-Seq)

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OBJECTIVE: Appropriate fetal growth is linked to normal placental development and function. Identification of key pathogenic pathways that may be responsible for the increased morbidity and mortality of fetuses with IUGR is critical. We performed a genome-wide transcriptome RNA-seq analysis to discover placental villous trophoblast transcripts differentially expressed in the setting of preeclampsia (PE) as opposed to idiopathic IUGR.

STUDY DESIGN: Total RNA was extracted from 25 placental villous tissue samples of women with: 1) idiopathic PTB (iPTB, n=5, GA: 32±1wks; 2) idiopathic IUGR (n=5, GA: 29±1 wks); 3) severe PE & normal fetal growth (sPE, n=8, GA: 30±1 wks); 4) sPE & IUGR (n=7, GA: 30±1 wks). All IUGR fetuses had birthweights <10% (85% were at <3%) and abnormal Dopplers. Cord blood Insulin-like growth factor 1 (IGF-1) was measured as a marker of IUGR. RNA-seq was performed using the Illumina platform. Following data curation and quality control, statistical analyses were performed using 'DESeq2' and 'edgeR' (FDR<0.1).

RESULTS: Relative to iPTB, idiopathic IUGR resulted in altered expression of 3,908 placental transcripts. Relative to iPTB, placentas of sPE & IUGR exhibited altered expression of 1,639 genes. This group profile was consistent with significantly lower cord blood IGF-1 levels in idiopathic IUGR vs. iPTB newborns (P<0.001). Conversely, 576 genes were differentially expressed in the setting of sPE alone. Overall, the global transcriptional profiles of sPE and sPE & IUGR placentas were highly similar, with differential expression of <10 genes. In contrast, idiopathic IUGR differed from sPE & IUGR by 91 transcripts and from sPE & normal fetal growth by 543 transcripts. Idiopathic IUGR was associated with dysregulation of gene sets related to cell cycle regulation, oxidative phosphorylation, and insulin growth factor regulation. sPE was linked to pathways associated with altered adipokine signaling, lipid and sugar metabolism, and amyloid precursor processing.

CONCLUSION: The transcriptome of villous trophoblasts of pregnancies complicated by sPE and sPE & IUGR is remarkably similar, implying that in sPE, IUGR cannot be linked to a markedly different gene expression profile. The large variability of placental transcriptome in idiopathic IUGR emphasizes again the heterogeneity of the growth restricted phenotype.

223 Fetal growth restriction is associated with different patterns of placental abnormalities in twin and singleton pregnancies

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OBJECTIVE: The rate of fetal growth restriction (FGR) is higher in twin compared with singleton pregnancies. However, the mechanisms underlying FGR may differ between twins and singletons. Our aim was to compare the placental findings between twin and singleton pregnancies complicated by FGR.

STUDY DESIGN: This was a retrospective cohort study of all singleton and twin SGA (birth weight <10th%) newborns delivered in a single tertiary referral center between 2001-2015. SGA was diagnosed in twins and singletons using the recently published NICHD twins- and

singletons-based growth charts, respectively. Placental abnormalities were compared between twins and singletons and were classified into maternal vascular malperfusion, loss of integrity, fetal vascular malperfusion, and chronic inflammation.

RESULTS: 1) A total of 1,282 SGA newborns were identified during the study period, of whom 365 (28.5%) were twins. 2) The rate of any placental pathology was lower for SGA twins compared with SGA singletons (38.1% vs 67.8% p<0.001), mainly due to a lower rate of maternal malperfusion lesions (4.1% vs. 42.1% p<0.001). 3) On multivariable regression analysis, SGA in twins was associated with lower odds of any placental abnormality (OR 0.29, 95%-CI 0.23-0.38) and maternal vascular malperfusion (OR 0.06, 95%-CI 0.04-0.10) (TABLE). 4) Plurality was not associated with the risk of fetal vascular malperfusion lesions and chronic villitis (TABLE).

CONCLUSION: SGA in twin pregnancies is less likely to be associated with maternal vascular malperfusion lesions compared with SGA in singletons. These findings may imply that the mechanisms underlying fetal growth FGR in twins differ from those in singleton pregnancies.

Placental Abnormality Associated with SGA in Twins vs. SGA in Singletons

Placental abnormality	SGA in twins vs. SGA in singletons [OR (95%-CI)]
Any placental abnormality	0.29 (0.23-0.38)
Maternal vascular malperfusion	0.06 (0.04-0.10)
Maternal vascular loss of integrity	0.56 (0.28-1.12)
Fetal vascular malperfusion (fetal thrombotic vasculopathy)	0.78 (0.58-1.04)
Chronic inflammation (chronic villitis)	0.66 (0.42-1.02)

224 Perinatal outcomes of twin twin transfusion syndrome based on gestational age at time of selective fetoscopic laser photocoagulation

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OBJECTIVE: Selective fetoscopic laser photocoagulation (SFLP) remains the treatment of choice for twin twin transfusion syndrome (TTTS). Little is known about perinatal outcomes after SFLP treatment for TTTS when stratified by gestational age (GA) at the time of SFLP treatment. Our objective is to describe gestational-age-at-treatment specific perinatal outcomes after SFLP treatment for TTTS.

STUDY DESIGN: Data on all consecutive pregnancies diagnosed with TTTS (n=640) and treated by SFLP between 2008-2014 were reviewed. Exclusion criteria included fetal malformations, known chromosomal anomalies, and triplet gestations. Patient demographics and perinatal outcome data were collected. Data was stratified and compared based on GA at time of SFLP. ANOVA, T-test, and Chi-square tests were used as indicated.

RESULTS: The average GA at the time of evaluation, SFLP, and delivery was 20.42 ± 2.53, 20.9±2.6, and 30.1±4.2 weeks, respectively. 63% (n=403/640) were Quintero Stage III TTTS and 37% (n=238) had selective IUGR. Overall survival was 91% (n=582) with 76% (n=485) donor survival and 88% (n=560) recipient survival. The rate of preterm delivery <28 weeks and <34 weeks were 26% (n=169) and 83% (n=529), respectively. There was no significant difference in Quinetro stage among groups (table). With increasing GA at SFLP, there was a significant increase in donor and recipient survival, gestational age at delivery, and a significant decrease in rate of pregnancy loss, preterm delivery <28 weeks, and double and single fetal demise in TTTS treated with SFLP.

CONCLUSION: Regardless of Quintero stage, earlier GA at the time of SFLP in TTTS is associated with higher rate of adverse pregnancy outcome and lower survival. This information is important in patient counseling. Further studies are needed to identify predictors of outcome.

Comparison of perinatal outcome in TTTS treated with SFLP stratified by gestational age at procedure

Variables	16 weeks	17 weeks	18 weeks	19 weeks	20 weeks	21 weeks	22 weeks	23 weeks	24 weeks	25 weeks	26-27 weeks	P-value
Number of cases - n (%)	30 (4.7)	56 (8.8)	82 (12.8)	75 (11.7)	100 (15.6)	83 (13)	73 (11.4)	47 (7.3)	40 (6.3)	34 (5.3)	20 (3.1)	
Quintero stage												0.161
I - n (%)	1 (3)	5 (9)	12 (15)	11 (15)	21 (21)	12 (14)	17 (23)	10 (21)	12 (30)	9 (26)	4 (20)	
II - n (%)	5 (17)	5 (9)	10 (12)	7 (9)	11 (11)	9 (11)	8 (11)	6 (13)	3 (8)	8 (24)	1 (5)	
III - n (%)	21 (70)	45 (80)	52 (63)	53 (71)	62 (62)	54 (65)	42 (58)	28 (60)	21 (52)	12 (35)	13 (65)	
IV - n (%)	3 (10)	1 (2)	8 (10)	4 (5)	6 (6)	8 (10)	6 (8)	3 (6)	4 (10)	5 (15)	2 (10)	
Number of live births												0.005
0 - n (%)	7 (23)	6 (11)	11 (13)	10 (13)	10 (10)	5 (6)	5 (7)	2 (4)	1 (3)	1 (3)	0 (0)	
1 - n (%)	11 (36)	12 (21)	11 (13)	16 (21)	17 (17)	18 (21)	7 (10)	12 (26)	9 (22)	3 (9)	3 (13)	
2 - n (%)	12 (40)	38 (86)	60 (73)	49 (65)	73 (73)	60 (72)	61 (84)	33 (70)	30 (75)	30 (82)	17 (85)	
Delivery less than 24 weeks - n (%)	6 (20)	7 (12.5)	11 (13.4)	11 (14.7)	11 (11)	5 (6)	5 (6.8)	0 (0)	0 (0)	0 (0)	0 (0)	0.003
Delivery less than 28 weeks - n (%)	11 (36.7)	24 (42.9)	25 (30.5)	21 (28)	28 (28)	14 (16.9)	14 (19.2)	14 (29.8)	13 (32.5)	4 (11.8)	1 (5)	0.004
Donor survival - n (%)	14 (46.7)	38 (67.9)	61 (74.4)	52 (69.3)	77 (77)	65 (78.3)	63 (86.3)	36 (76.6)	32 (80)	30 (88.2)	17 (85)	0.003
Recipient survival - n (%)	21 (70)	50 (89.3)	70 (85.4)	62 (82.7)	86 (86)	73 (88)	66 (90.4)	42 (89.4)	37 (92.5)	33 (97.1)	20 (100)	0.054
Gestational age at delivery - weeks	28.0 ± 5.57	28.74 ± 4.66	29.43 ± 4.66	29.88 ± 4.57	29.99 ± 4.09	30.8 ± 3.51	31.15 ± 3.85	29.93 ± 3.69	30.53 ± 3.75	32 ± 2.84	31.54 ± 2.52	<0.0001

225 Timing of fetal death and pregnancy outcome in twin twin transfusion syndrome after laser

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OBJECTIVE: Single-fetal demise (SFD) in monochiorionic/diamniotic twins (MCDA) can pose substantial risks for the surviving co-twin, including increased risk of fetal loss, preterm delivery, neurovascular injury, and end-organ damage. In laser (SFLP) treated twin twin transfusion syndrome (TTTS)(10-15% of MCDA), SFD occurs in up to 20%. Little is known about pregnancy outcome in SFLP treated TTTS patients based on timing of SFD.

STUDY DESIGN: Data on all consecutive pregnancies diagnosed with TTTS (n=640) and treated by laser surgery and had SFD between 2008-2014 were reviewed. Exclusion criteria included fetal malformations, known chromosomal anomalies, and triplet gestations. Patient demographics and perinatal outcome data were collected. Data was stratified and compared based on timing of fetal death into 2 groups: immediate fetal death intra-operatively or day 1 post SFLP and fetal death within 7 days of SFLP. ANOVA, T-test and Chi-square tests were used as indicated.

RESULTS: 17% (111/640) had SFD with 82% (n=91) being donor demise and 18% (n=20) being recipient demise. Mean gestational age (GA) of demise and delivery was 24.4±4.6 and 30.7±4.2 weeks, respectively. 70% (n=78) were Quintero stage III at time of SFLP with 53% (n=59) selective fetal growth restriction (sIUGR). Rate of preterm delivery (PTD) at <28 weeks, <34 weeks and pregnancy loss in SFD pregnancies was 24% (n=27), 78% (n=86), and 4.5% (n=5), respectively. 41% (n=46) had immediate SFD and 84% (n=92) had death within 7 days of SFLP. In comparing pregnancy outcome in SFD within 7 days (table), there was a significantly higher rate of PTD <28weeks, lower GA at delivery and lower recipient birth weight as compared to SFD >7 days post SFLP. There was no significant difference among groups in staging, sIUGR, GA at evaluation, and PTD <34weeks. Similarly, there was no significant difference in all data variables when stratified based on immediate postoperative demise.

CONCLUSION: TTTS pregnancies post SFLP complicated with SFD within 7 days of procedure are at higher risk of adverse pregnancy