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Growth patterns of monozygotic twin pregnancy complicated by Type-III selective fetal growth restriction

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KEYWORDS: Doppler; growth; monozygotic; selective; sFGR Type-3; sFGR Type-III; sIUGR

CONTRIBUTION

What are the novel findings of this work?

In monozygotic twin pregnancy with Type-III selective fetal growth restriction (sFGR), abnormal fetal growth of the smaller twin is evident from very early in gestation, while estimated fetal weight of the larger twin remains normal throughout pregnancy. Intertwin growth discordance remains stable across gestation. Normalization of umbilical artery Doppler is associated with improved growth of the smaller but not the larger twin.

What are the clinical implications of this work?

Type-III sFGR is a diagnosis that can be made early in the second trimester, as the growth-restricted twin is already abnormally small at 16 weeks of gestation. Because the dynamic flow pattern in the umbilical artery in these pregnancies has a direct impact on fetal growth, longitudinal umbilical artery Doppler monitoring is essential for risk stratification.

ABSTRACT

Objectives Little is known regarding fetal growth patterns in monozygotic twin pregnancy complicated by Type-III selective fetal growth restriction (sFGR). We aimed to assess fetal growth and umbilical artery Doppler

pattern in Type-III sFGR across gestation and evaluate the effect of changing Doppler flow pattern on growth and intertwin growth discordance.

Methods This was a retrospective cohort study of all Type-III sFGR pregnancies managed at nine fetal centers over a 12-year time period. Higher-order multiple pregnancy and cases with major fetal anomaly or other monozygosity-related complications at presentation were excluded. Estimated fetal weight (EFW) was assessed on ultrasound for each twin pair at five timepoints (16–20, 21–24, 25–28, 29–32 and > 32 weeks' gestation) and compared with singleton and uncomplicated monozygotic twin EFW. EFW and intertwin EFW discordance were compared between pregnancies with normalization of umbilical artery Doppler of the smaller twin later in pregnancy and those with persistently abnormal Doppler.

Results Overall, 328 pregnancies (656 fetuses) met the study criteria. In Type-III sFGR, the smaller twin had a lower EFW than an average singleton fetus (EFW Z-score ranging from –1.52 at 16 weeks to –2.69 at 36 weeks) and an average monozygotic twin in uncomplicated pregnancy (Z-score ranging from –1.73 at 16 weeks to –1.49 at 36 weeks) throughout the entire gestation, while the larger twin had a higher EFW than an average singleton fetus until 22 weeks' gestation and was similar in EFW to an average uncomplicated

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monochorionic twin throughout gestation. As pregnancy advanced, growth velocity of both twins decreased, with the larger twin remaining appropriately grown and the smaller twin becoming more growth restricted. Intertwin EFW discordance remained stable throughout gestation. On multivariable longitudinal modeling, normalization of fetal umbilical artery Doppler was associated with better growth of the smaller twin ($P = 0.002$) but not the larger twin ($P = 0.1$), without affecting the intertwin growth discordance ($P = 0.09$).

Conclusions Abnormal fetal growth of the smaller twin in Type-III sFGR was evident early in pregnancy, while EFW of the larger twin remained normal throughout gestation. Normalization of umbilical artery Doppler was associated with improved fetal growth of the smaller twin. © 2021 International Society of Ultrasound in Obstetrics and Gynecology.

INTRODUCTION

Approximately 7–14% of all monochorionic twin pregnancies^{1,2} are complicated by selective fetal growth restriction (sFGR), defined as intertwin estimated fetal weight (EFW) discordance exceeding 25% and one twin having EFW below the 10th percentile. One-fifth of all sFGR cases are categorized as Type-III sFGR³, which is characterized by intermittent absent or reversed end-diastolic flow (iA/REDF) in the umbilical artery of the smaller fetus, and unequal placental sharing with large intertwin artery-to-artery anastomoses (AAA)⁴. Although the outcome of Type-III sFGR is considered intermediate when compared with Type-I (normal umbilical artery Doppler) and Type-II sFGR (persistently abnormal umbilical artery Doppler), these pregnancies are at risk of unpredictable fetal death, primarily of the growth-restricted fetus, but often with subsequent demise of the normally grown cotwin. In cases of survival, the cotwin is at risk of severe brain injury after acute exsanguination^{5,6}.

We have shown previously that the risk of fetal death is associated with earlier onset of sFGR, but not with severity of EFW discordance between twins at the time of diagnosis⁷. However, little is known regarding the growth pattern of monochorionic twins with Type-III sFGR. Some of these pregnancies have shown umbilical artery Doppler normalization later in pregnancy^{8,9}, and the prognostic implications of this finding are unknown.

This study aimed to assess growth and umbilical artery Doppler patterns in monochorionic twin pregnancies complicated by Type-III sFGR across gestation and evaluate the effect of umbilical artery Doppler flow changes on growth and EFW discordance between twins.

METHODS

This was a retrospective cohort study, including a consecutive series of monochorionic diamniotic twin pregnancies

complicated by Type-III sFGR and managed longitudinally between 1 January 2008 and 1 July 2019 at nine fetal medicine centers. All cases, irrespective of gestational age at referral or diagnosis of Type-III sFGR, were included in this analysis. Type-III sFGR was defined as intertwin fetal EFW difference of 25% or more and fetal EFW of one twin below the 10th percentile in combination with iA/REDF in the umbilical artery of the smaller fetus during at least one ultrasound assessment⁴. Higher-order multiple pregnancies, cases complicated by major fetal structural or genetic anomaly and those with missing neonatal data were excluded from the analysis. Additionally, pregnancies complicated by twin–twin transfusion syndrome and twin anemia-polycythemia sequence at presentation were excluded.

The study protocol was approved by the research ethics board at each participating center. All participating centers had extensive experience with sonographic assessment and management of monochorionic twins and their associated complications.

All pregnancies underwent ultrasound assessment of fetal growth at least every 2 weeks. Additional surveillance strategies for Type-III sFGR varied between centers. The outcome and details of center-specific antenatal surveillance of pregnancies included in this cohort have been reported previously⁷.

For this study, EFW was assessed on ultrasound for each twin pair at five timepoints throughout gestation: 16–20, 21–24, 25–28, 29–32 and > 32 weeks, if available. In cases of spontaneous conception, gestational age was determined in the first trimester, based on the crown–rump length of the larger twin, whereas embryonic age was used for dating pregnancies conceived using *in-vitro* fertilization. EFW was calculated from fetal head circumference, biparietal diameter, abdominal circumference and femur length using the Hadlock formula¹⁰. Intertwin EFW difference was calculated using the following formula: (EFW of the larger fetus – EFW of the smaller fetus)/EFW of the larger fetus. Fetal growth in our cohort was compared with singleton growth according to Hadlock growth curves¹⁰. At the same gestational-age timepoints, the umbilical artery Doppler pattern was reviewed. Umbilical artery Doppler evolving from iA/REDF to persistently antegrade flow between diagnosis and delivery was categorized as normalization. Additional antenatal variables thought to impact fetal growth were collected, including maternal age at delivery, parity, mode of conception (spontaneous *vs* assisted reproduction) and maternal comorbidities, defined as any chronic medical condition.

Statistical analysis

The median (interquartile range (IQR)) EFW in monochorionic diamniotic twin pregnancies with Type-III sFGR, according to gestational-age timepoint, was calculated and compared with that of singleton¹⁰ and uncomplicated monochorionic twin¹¹ pregnancies; Z-scores were calculated accordingly. The effect of umbilical artery

Doppler on fetal growth was assessed by comparing EFW across gestation between pregnancies with Doppler normalization and those in which it remained persistently abnormal.

Linear regression models fitted using generalized estimating equation (GEE) were used to assess the effect of umbilical artery Doppler on EFW of smaller and larger twins, while accounting for the correlations between twin pairs and repeated measures. The association between intertwin EFW discordance and umbilical artery Doppler was evaluated using similar linear regression GEE approach, whose correlation structure was due to the longitudinal measurements of weight discordance. Multivariable models controlled for the potential confounding effects of gestational age (centralized by subtracting the mean from the original gestational-age data), maternal age, parity and mode of conception (spontaneous *vs* assisted reproduction). The final models included the effect of umbilical artery Doppler and potential confounders with a significant association with the outcome. In order to account for multicenter variability, we also conducted a GEE model step using linear mixed multilevel models, in which Level I was the repeated time measurement for each individual and Level II was the center effect. The effects of both levels were modeled using random intercepts. Both analyses excluded data from twins at timepoints after the occurrence of intrauterine fetal death. All analyses were performed using R (version 3.6)¹².

RESULTS

A total of 328 monochorionic diamniotic twin pregnancies (656 fetuses) met the study criteria⁷. Mean maternal age at delivery was 30.2 ± 4.9 years and median parity was 0 (IQR, 0–1). Maternal medical comorbidities were present in 38 (11.6%) pregnancies and conception using assisted reproductive techniques occurred in 32 (9.8%) cases. Mean gestational age at diagnosis of Type-III sFGR and inclusion in the study was 22.0 ± 4.6 (range, 14.7–32.7) weeks. Thirty-five pregnancies (10.7% of the entire cohort; 11.3% after exclusion of pregnancies that underwent selective reduction) were complicated by fetal death. Death of one fetus, always the smaller twin, occurred in 19 (5.8%) pregnancies, while 16 (4.9%) pregnancies were complicated by double fetal death. Mean gestational age at delivery was 31.8 ± 3.6 weeks. Mean birth-weight discordance between twins was $31.2 \pm 11.3\%$.

EFW of the smaller and larger twins at each gestational week, its comparison with singleton EFW and growth velocity of our cohort across gestation are presented in Table 1 and Figure 1. As early as at 16 weeks, median (IQR) EFW of the smaller twin was markedly lower than that of a singleton fetus at the same gestational age (Z-score, -1.52 (-2.42 to -0.85)). EFW of the larger twin, in contrast, was slightly higher compared with that of a singleton fetus at 16 weeks (Z-score, 0.92 (0.11 – 1.67)), but started to fall below the average

Table 1 Estimated fetal weight and estimated fetal weight Z-score of monochorionic diamniotic twin pregnancies complicated by Type-III selective fetal growth restriction, when compared with singleton and uncomplicated monochorionic twin pregnancies, across gestation

GA (weeks)	Estimated fetal weight (g)		Estimated fetal weight Z-score			
			Compared with singleton pregnancies*		Compared with uncomplicated monochorionic twin pregnancies†	
	Smaller twin	Larger twin	Smaller twin	Larger twin	Smaller twin	Larger twin
16	117 (100–131)	161 (148–165)	-1.52 (-2.42 to -0.85)	0.92 (0.11 to 1.67)	-1.73 (-2.60 to -1.00)	0.55 (-0.12 to 0.76)
17	137 (124–148)	179 (165–191)	-1.37 (-1.97 to -0.93)	0.61 (0.11 to 1.04)	-2.09 (-2.62 to -1.62)	-0.32 (-0.88 to 0.21)
18	158 (148–178)	225 (207–240)	-1.83 (-2.33 to -1.24)	0.74 (-0.08 to 1.53)	-2.43 (-2.79 to -1.72)	-0.11 (-0.73 to 0.41)
19	193 (185–210)	260 (237–279)	-1.80 (-2.25 to -1.22)	0.36 (-0.36 to 0.91)	-2.40 (-2.63 to -1.94)	-0.51 (-1.16 to 0.03)
20	228 (204–250)	329 (300–350)	-2.06 (-2.62 to -1.57)	0.61 (-0.16 to 1.16)	-2.50 (-3.05 to -1.99)	-0.18 (-0.84 to 0.32)
21	282 (245–298)	391 (352–424)	-2.03 (-2.54 to -1.49)	0.40 (-0.38 to 1.05)	-2.31 (-3.02 to -2.02)	-0.23 (-0.97 to 0.41)
22	318 (280–353)	460 (426–509)	-2.18 (-3.00 to -1.74)	0.22 (-0.36 to 0.92)	-2.56 (-3.15 to -2.00)	-0.32 (-0.84 to 0.46)
23	370 (322–416)	534 (483–572)	-2.49 (-3.01 to -1.82)	-0.03 (-0.64 to 0.68)	-2.59 (-3.22 to -1.98)	-0.44 (-1.11 to 0.07)
24	409 (365–470)	619 (568–669)	-2.66 (-3.27 to -1.98)	-0.01 (-0.51 to 0.63)	-2.83 (-3.31 to -2.16)	-0.51 (-1.07 to 0.05)
25	532 (482–562)	750 (684–807)	-2.16 (-2.84 to -1.88)	0.21 (-0.62 to 0.67)	-2.26 (-2.72 to -1.98)	-0.22 (-0.84 to 0.31)
26	574 (530–640)	841 (772–896)	-2.59 (-3.20 to -2.10)	-0.34 (-0.76 to 0.30)	-2.54 (-2.89 to -2.02)	-0.43 (-0.97 to 0.02)
27	661 (572–750)	964 (897–1052)	-2.59 (-3.28 to -2.07)	-0.27 (-0.74 to 0.48)	-2.48 (-3.09 to -1.87)	-0.41 (-0.87 to 0.19)
28	724 (608–824)	1089 (967–1222)	-2.95 (-3.76 to -2.22)	-0.33 (-1.20 to 0.27)	-2.60 (-3.28 to -2.01)	-0.45 (-1.17 to 0.33)
29	845 (706–941)	1268 (1148–1382)	-2.70 (-3.60 to -2.20)	-0.37 (-1.10 to 0.51)	-2.41 (-3.12 to -1.92)	-0.26 (-0.86 to 0.33)
30	929 (854–1020)	1381 (1258–1510)	-2.95 (-3.32 to -2.46)	-0.67 (-1.07 to 0.09)	-2.44 (-2.77 to -2.03)	-0.42 (-0.97 to 0.16)
31	1062 (967–1185)	1592 (1474–1707)	-2.84 (-3.27 to -2.23)	-0.27 (-0.74 to 0.12)	-2.27 (-2.64 to -1.78)	-0.19 (-0.65 to 0.27)
32	1155 (1017–1347)	1766 (1609–1929)	-3.07 (-3.66 to -2.35)	-0.39 (-1.22 to 0.15)	-2.26 (-2.74 to -1.60)	-0.15 (-0.69 to 0.42)
33	1328 (1138–1464)	1951 (1837–2092)	-2.89 (-3.51 to -2.32)	-0.52 (-1.06 to 0.05)	-2.00 (-2.58 to -1.58)	-0.09 (-0.44 to 0.34)
34	1446 (1263–1612)	2157 (1912–2330)	-2.89 (-3.49 to -2.24)	-0.47 (-1.23 to 0.09)	-1.92 (-2.41 to -1.46)	0.01 (-0.65 to 0.48)
35	1726 (1612–2006)	2297 (2272–2377)	-2.33 (-2.81 to -1.54)	-0.56 (-0.71 to -0.22)	-1.44 (-1.71 to -0.76)	-0.06 (-0.12 to 0.13)
36	1790 (1790–1790)	2476 (2476–2476)	-2.69 (-2.69 to -2.69)	-0.52 (-0.61 to -0.43)	-1.49 (-1.49 to -1.49)	-0.02 (-0.02 to -0.02)

Data are given as median (interquartile range). *Calculated by comparing with estimated fetal weight of singleton fetuses according to Hadlock growth curves¹⁰. †Calculated by comparing with estimated fetal weight of monochorionic twins according to growth curves for uncomplicated monochorionic twin pregnancies¹¹. GA, gestational age.

singleton EFW at 23 weeks (Z-score, -0.03 (-0.64 to 0.68)), albeit remaining above the 10th percentile for singleton fetuses. Overall, EFW Z-score of both twins decreased gradually between 16 and 30 weeks' gestation, suggesting a slower fetal growth velocity in monochorionic twin pregnancy with sFGR compared to singleton pregnancy. The EFW Z-score of the smaller fetus progressed from -1.52 at 16 weeks (approximately equivalent EFW \sim 7th percentile on singleton growth charts) to -2.95 at 30 weeks' gestation (EFW $<$ 1st percentile for singletons). EFW Z-score of the larger fetus progressed from 0.92 at 16 weeks (EFW \sim 90th percentile for singletons) to -0.67 at 30 weeks (EFW \sim 30th percentile for singletons). Although the intertwin EFW discordance increased slightly from $25 \pm 7.54\%$ at 16 weeks to $32 \pm 10.9\%$ at 30 weeks, this increase was not statistically significant ($P = 0.24$).

The comparison of EFW in monochorionic pregnancies with Type-III sFGR with that in uncomplicated monochorionic twin pregnancies is presented in Table 1. Similar to the comparison with singleton pregnancies, EFW of the smaller twin in monochorionic pregnancy with Type-III sFGR was significantly lower than that of a twin in uncomplicated monochorionic pregnancy at the same gestational age (EFW Z-score, -1.73 at 16 weeks increasing to -2.60 at 28 weeks). Although the growth-restricted fetus remained significantly smaller than the twin in uncomplicated monochorionic pregnancy, in the third trimester, this difference was less pronounced than when comparing the growth-restricted fetus with a singleton fetus (Z-score at 34 weeks of -1.92 vs -2.89 , respectively). The growth of the larger twin did not differ significantly when compared with a twin in uncomplicated monochorionic pregnancy. Similar to the comparison with singletons, EFW of the larger twin in monochorionic pregnancy with sFGR was slightly higher than that of the uncomplicated monochorionic twin at 16 weeks (Z-score, 0.55), but started to fall below the median at 17 weeks (Z-score, -0.32), albeit remaining well above the 10th percentile across gestation.

In 45 (13.7%) pregnancies, the umbilical artery Doppler flow of the smaller fetus normalized at a mean gestational age of 26.7 ± 4.2 weeks. This was more likely to occur in pregnancies that presented with abnormal

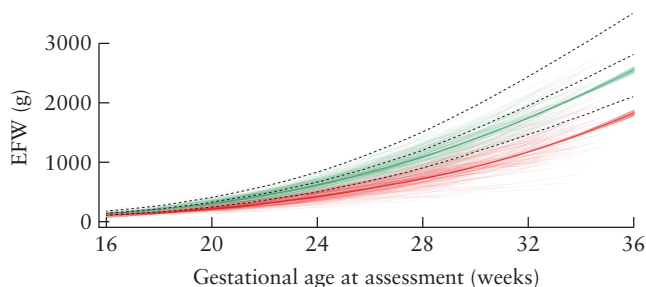


Figure 1 Estimated fetal weight (EFW) of the smaller (red) and larger (green) twins in monochorionic pregnancies complicated by Type-III selective fetal growth restriction and of singleton fetuses across gestation. 3rd, 50th and 97th EFW percentiles for singletons are shown (.....). Data for singleton fetuses derived from Hadlock growth curves¹⁰.

umbilical artery Doppler at an earlier gestational age (18.8 ± 4.0 vs 21.0 ± 4.8 weeks, $P = 0.003$). In pregnancies with normalized umbilical artery flow, EFW of the smaller and larger fetuses was significantly higher later in gestation compared with that in pregnancies with persistent iA/REDF (Figure 2). On multivariable longitudinal modeling, this effect on EFW remained

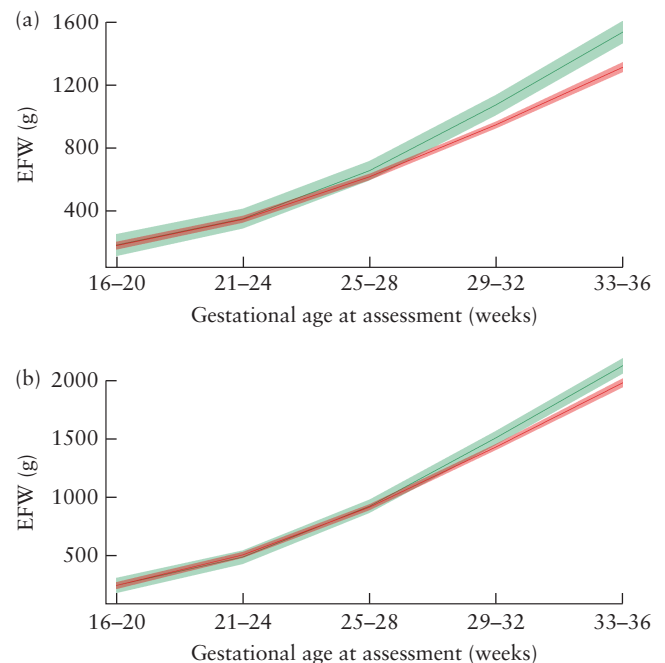


Figure 2 Estimated fetal weight (EFW) of the smaller (a) and larger (b) twins in monochorionic pregnancies complicated by Type-III selective fetal growth restriction across gestation, according to whether umbilical artery Doppler flow pattern normalized (green) or remained persistently absent or reversed (red) between diagnosis and delivery.

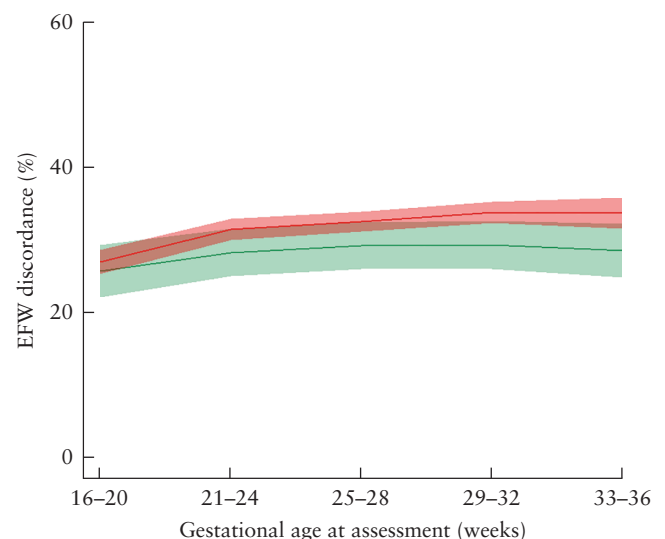


Figure 3 Estimated fetal weight (EFW) discordance in monochorionic twin pregnancies with selective fetal growth restriction across gestation, according to whether umbilical artery Doppler flow pattern normalized (green) or remained persistently absent or reversed (red) between diagnosis and delivery.

statistically significant for the smaller twin ($P = 0.002$) but not the larger twin ($P = 0.1$). Although EFW discordance was somewhat larger in twin pairs with persistent iA/REDF compared to those with Doppler normalization, this difference was not statistically significant ($P = 0.09$) (Figure 3). The additional analysis utilizing a multilevel model to account for intercenter variability yielded very similar results (data not shown).

DISCUSSION

In this cohort of monochorionic twin pregnancies complicated by Type-III sFGR, we found that the smaller twin had persistently and markedly lower EFW compared with singleton fetuses, from as early as 16 weeks' gestation, while the larger twin had slightly higher EFW compared with singleton fetuses until approximately 22 weeks. Beyond 22 weeks, the mean EFW of the larger twin fell below that of singleton fetuses, but remained appropriate for gestation, continuing to be above the 10th percentile for singleton pregnancies. Similar findings were observed when comparing fetal growth velocity between sFGR *vs* uncomplicated monochorionic twin pregnancy. However, although the smaller twin had substantially lower EFW in sFGR compared with uncomplicated monochorionic twin pregnancy, in the third trimester, this difference was less pronounced when compared with the EFW difference observed between the smaller twin in sFGR pregnancy and singleton fetuses; furthermore, EFW of the larger twin in sFGR pregnancy was only slightly below the median of the uncomplicated monochorionic twin EFW. Although growth velocity of both twins in sFGR pregnancies decreased across gestation, the intertwin growth discordance was stable. Normalization of umbilical artery Doppler was associated with significantly improved growth of the smaller twin, but did not affect the intertwin growth discordance.

Previous retrospective studies have confirmed that intrauterine growth of uncomplicated twin fetuses is reduced in comparison to singletons, starting from 26–32 weeks' gestation^{11,13–16}. This reduction is more evident in monochorionic than dichorionic twin pregnancy and with advancing gestational age¹⁴. In our cohort of pregnancies with Type-III sFGR, growth velocity of the larger twin deviated from singleton growth earlier in gestation, at approximately 23 weeks. This discordance pattern has been shown previously to be associated with high risk of adverse perinatal outcome¹⁷. Although twin-specific growth curves may have been beneficial¹⁸, we compared twin growth to singleton growth curves instead, as these represent optimal fetal growth. Additionally, before the third trimester, the differences between singleton and twin growth are not statistically significant, and their clinical significance remains to be shown^{16,18}.

The finding that intertwin growth discordance remained stable across gestation is not surprising. Indeed, the smaller fetus in Type-III sFGR has a small but otherwise healthy placenta. Therefore, the growth of this

twin is not expected to lag further with advancing gestation, which is seen in singleton or twin pregnancy with true placental insufficiency and vascular malperfusion. Similarly, the size of the large AAA, which helps sustain the growth of the smaller fetus, develops in line with overall placental development^{5,19}.

A few small cohort studies have demonstrated previously that the umbilical artery flow pattern of the smaller fetus can change throughout pregnancy in Type-III sFGR^{8,20} and that, in a minority of cases, the flow pattern can revert to normal at a more advanced gestational age⁵. Concordant with this evidence, in 13.7% of pregnancies in our cohort, umbilical artery Doppler changed from iA/REDF to antegrade flow. Normalization of Doppler flow was associated with improved growth of the smaller but not the larger twin. We hypothesize that normalization of the iA/REDF represents milder disease, in which the placenta is less unequally shared. In these placentae, the AAA may decrease in size with progressive placental growth, explaining why iA/REDF observed in the early second trimester disappears later on. In very unequally shared placentae, the smaller twin depends entirely on the blood exchange with the larger cotwin for its survival and angiogenetic factors may promote the growth of the AAA and persistence of the iA/REDF pattern. This observation needs to be confirmed in postnatal placental studies. Another possible explanation for alternating umbilical artery Doppler pattern may be the improved vascular development in the placental portion supplying the smaller twin with subsequent reduction in the placental resistance to blood flow and spontaneous regression or thrombosis of AAA. Lastly, it is possible that Type-I sFGR was misclassified as Type-III sFGR, as, in early gestation, iAEDF may be a normal finding. This hypothesis would also support the finding that, in fetuses with an earlier diagnosis of Type-III sFGR, umbilical artery Doppler was more likely to normalize. Because the dynamic flow pattern in the umbilical artery in Type-III sFGR has a direct impact on fetal growth, longitudinal umbilical artery Doppler monitoring is essential for risk stratification in monochorionic pregnancy with sFGR.

Strengths of our study include that it involved the collaborative experience of nine expert centers across North America, Europe and Asia and provides longitudinal data on almost twice as many Type-III sFGR pregnancies as has been included in the collective literature to date, thereby strengthening the validity of the findings. The longitudinal documentation of growth and Doppler changes across gestation enabled us to draw conclusions regarding their association that have not been described previously. Furthermore, our robust statistical methodology with correction for important confounders is noteworthy, particularly in the setting of fetal growth in twins, which is affected by independent maternal characteristics¹⁴. Nevertheless, the study has some weaknesses. Indeed, we were limited by the retrospective design and only included pregnancies from the second trimester of pregnancy onwards, as umbilical artery Doppler is not assessed in the

first trimester of pregnancy. The pregnancies that resulted in early fetal death were excluded by study design, leading to potential selection bias. Moreover, exclusion of pregnancies that underwent selective reduction (often those with more severe growth restriction and greater growth discordance) may have resulted in overestimation of fetal growth. Lastly, this study lacks placental injection studies and histological analysis. The collection of these data would have given more insight into the mechanism of Doppler normalization.

In conclusion, this cohort study shows that, in monochorionic twin pregnancy with Type-III sFGR, the smaller twin has lower EFW from a very early gestational age, while the larger twin has higher EFW early in pregnancy, when compared with singleton fetuses and uncomplicated monochorionic twins. As monochorionic pregnancy with Type-III sFGR advances, growth velocity of both twins decreases, with the larger twin remaining appropriately grown and the smaller becoming more growth restricted. Although the degree of growth discordance remains relatively stable across gestation, umbilical artery Doppler may normalize, in association with improved growth of the smaller twin.

COLLABORATORS

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Patrones de crecimiento del embarazo de gemelos monocoriónico complicado por una restricción selectiva del crecimiento fetal de tipo III

RESUMEN

Objetivos. Se conoce poco sobre los patrones de crecimiento fetal en el embarazo de gemelos monocoriónico complicado por la restricción selectiva del crecimiento fetal (RSCF) de tipo III. El objetivo de este estudio fue evaluar el crecimiento fetal y el patrón Doppler de la arteria umbilical en el RSCF tipo III a lo largo de la gestación y evaluar el efecto del cambio del patrón de flujo Doppler en el crecimiento y la discordancia del crecimiento de los gemelos.

Métodos. Este fue un estudio de cohorte retrospectivo de todos los embarazos con RSCF de tipo III tratados en nueve centros fetales durante un período de 12 años. Se excluyeron los casos de embarazo múltiple de alto orden o con anomalías fetales importantes u otras complicaciones relacionadas con la monocorionicidad en el cuadro clínico inicial. Se evaluó el peso estimado del feto (PEF) en la ecografía de cada par de gemelos en cinco momentos (16–20, 21–24, 25–28, 29–32 y >32 semanas de gestación) y se comparó con el PEF de gemelos monocoriales sin complicaciones. Más tarde en el embarazo se comparó la discordancia del PEF y el PEF entre gemelos entre los embarazos con Doppler normal de la arteria umbilical del gemelo más pequeño y aquellos con Doppler persistentemente anómalo.

Resultados. En total, 328 embarazos (656 fetos) cumplían los criterios del estudio. En el RSCF de tipo III, el gemelo más pequeño tuvo un PEF inferior al de un feto único medio (intervalo de la puntuación estándar de PEF entre -1,52 a 16 semanas y -2,69 a 36 semanas) y al de un gemelo monocoriónico medio en un embarazo sin complicaciones (intervalo de la puntuación estándar entre -1,73 a 16 semanas y -1,49 a 36 semanas) en toda la gestación, mientras que el gemelo de mayor tamaño tuvo un PEF superior al de un feto medio monocoriónico hasta las 22 semanas de gestación y fue similar en PEF al de un gemelo monocoriónico medio sin complicaciones en toda la gestación. A medida que avanzó el embarazo, la velocidad de crecimiento de ambos gemelos disminuyó, permaneciendo el gemelo más grande con un crecimiento adecuado y el gemelo más pequeño con una mayor restricción de crecimiento. La discordancia del PEF entre gemelos se mantuvo estable a lo largo de la gestación. En la modelización longitudinal multivariable, la normalización del Doppler de la arteria umbilical fetal se asoció con un mejor crecimiento del gemelo más pequeño ($P=0,002$) pero no del gemelo más grande ($P=0,1$), sin afectar a la discordancia de crecimiento entre gemelos ($P=0,09$).

Conclusiones. El crecimiento fetal anómalo del gemelo más pequeño en casos de RSCF de tipo III fue evidente desde el principio del embarazo, mientras que el PEF del gemelo más grande se mantuvo normal durante toda la gestación. La normalización del Doppler de la arteria umbilical se asoció a una mejora del crecimiento fetal del gemelo más pequeño.

单绒毛膜双胎妊娠合并 III 型选择性胎儿生长受限的生长模式

摘要

目标关于单绒毛膜双胎妊娠合并 III 型选择性胎儿生长受限 (sFGR) 的胎儿生长模式知之甚少。我们旨在评估妊娠期 III 型选择性胎儿生长受限 (sFGR) 中的胎儿生长和脐动脉多普勒模式, 并评估

改变多普勒血流模式对生长

和双胞胎间的生长不一致的影响。

方法这是一项回顾性队列研究, 研究对象为 12 年期间在九个胎儿中心治疗的所有 III 型选择性胎儿生长受限 (sFGR) 妊娠病例。高阶多胎妊娠和出现严重胎儿异常或其他单绒毛膜相关并发症的病例被排除在研究之外。在五个时间点 (妊娠 16-20、21-24、25-28、29-32 和 >32 周) 通过超声评估每对双胞胎的估计胎儿体重 (EFW), 并与单胎和简单的单绒毛膜双胎 EFW 进行比较。比较了妊娠后期较小双胞胎的正常脐动脉多普勒与持续异常多普勒情况下的估计胎儿体重和双胞胎之间估计胎儿体重不一致的情况。

Results 总体而言, 328 例妊娠 (656 个胎儿) 符合研究标准。在 III 型选择性胎儿生长受限 (sFGR) 病例中, 较小的双胞胎在整个妊娠期间的估计胎儿体重低于平均单胎胎儿 (EFW Z 评分范围从 16 周时的 -1.52 到 36 周时的 -2.69) 和正常妊娠中的平均单绒毛膜双胎 (Z 评分范围从 16 周时的 -1.73 到 36 周时的 -1.49), 而较大的双胞胎在妊娠 22 周前的估计胎儿体重高于平均单胎胎儿, 并且在整个妊娠期间的估计胎儿体重与平均未有并发症的单绒毛膜双胎相似。随着妊娠的进展, 双胞胎的生长速度都有所下降, 而双胞胎中较大的一个保持适当的生长, 较小的那个生长受到更多限制。双胞胎间估计胎儿体重不一致的程度在整个妊娠期间保持稳定。在多变量纵向建模中, 正常化的胎儿脐动脉多普勒与较小双胞胎的更好生长有关 ($P=0.002$), 但与较大双胞胎的生长无关 ($P=0.1$), 且不影响双胞胎生长不一致的情形 ($P=0.09$)。

选择性胎儿生长受限 (正常化的脐动脉多普勒与较小双胞胎的胎儿生长改善有关。