OBSTETRICS

Impact of placental sharing and large bidirectional anastomoses on birthweight discordance in monochorionic twins: a retrospective cohort study in 449 cases

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BACKGROUND: In monochorionic twin pregnancies, the fetuses share a single placenta. When this placenta is unequally shared, a discordant antenatal growth pattern ensues resulting in high rates of perinatal morbidity and mortality. Understanding placental pathophysiology is paramount in devising feasible antenatal management strategies. Unequal placental sharing is not the sole determinant of birthweight discordance as there is no one-to-one relationship with placental share discordance. Placental angioarchitecture, especially the presence of large bidirectional anastomoses, is thought to affect this relationship by allowing for a compensatory intertwin blood flow.

OBJECTIVE: This study aimed to assess whether placental angioarchitecture can affect birthweight discordance in live-born monochorionic twins, the aim of our study was 2-fold: (1) to assess the relationship between birthweight discordance and placental share discordance and (2) to examine to what extent large bidirectional anastomoses can compensate for the effect of unequal placental sharing on birthweight discordance, with a subgroup analysis for umbilical artery Doppler flow patterns in cases with a birthweight discordance of ≥20%.

STUDY DESIGN: This was a retrospective cohort study that included monochorionic twin pregnancies observed in our center between March 2002 and June 2021, in which twins with a birthweight discordance of ≥20% were classified according to umbilical artery Doppler flow patterns of the smaller twin. We excluded cases with twin-twin transfusion syndrome and twin anemia polycythemia sequence. Monochorionic placentas of live-born twins were injected with dye, and images were saved for computer measurements of placental sharing and the diameter of anastomoses. Univariate linear regressions of the relationship between placental share discordance and birthweight discordance (both calculated as weight or share larger twin−weight or share smaller twin/weight or share larger twin×100%) and the relationship between arterioarterial and venovenous diameters and birthweight ratio/placental territory ratio were performed.

RESULTS: A total of 449 placentas were included in the analysis. Placental share discordance was positively correlated with birthweight discordance (β coefficient, 0.325; 95% confidence interval, 0.254−0.397; $P<.0001$). The arterioarterial diameter was negatively correlated with birthweight ratio/placental territory ratio (β coefficient, −0.041; 95% confidence interval, −0.059 to −0.023; $P<.0001$), meaning that an increase in arterioarterial diameter leads to less birthweight discordance than expected for the amount of placental share discordance. There was no relationship between venovenous diameter and birthweight ratio/placental territory ratio (β coefficient, −0.007; 95% confidence interval, −0.027 to 0.012; $P=.473$).

CONCLUSION: Birthweight discordance in monochorionic twins was strongly associated with placental share discordance. Large arterioarterial anastomoses can mitigate the effect of unequal placental sharing.

Key words: anastomoses, birthweight discordance, monochorionic twins, placental characteristics, selective fetal growth restriction

Introduction

In monochorionic (MC) twin pregnancies, the fetuses share a single placenta.[1] This shared placenta can give rise to different complications because of vascular anastomoses on its surface.[2] The most prevalent complication is a discordant antenatal growth pattern resulting in a birthweight discordance (BWD).[3,4] A large BWD is associated with increased rates of neonatal morbidity and impaired long-term neurodevelopment.[5−7] The antenatal classification of the severity of discordant antenatal growth (generally termed selective fetal growth restriction [sFGR]) proposed by Gratacós et al[8] in 2007 is based on umbilical artery (UA) end-diastolic flow patterns of the smaller twin and allows clinicians to estimate the prognosis. Type I is characterized by positive end-diastolic flow (pEDF), type II by persistent absent or reversed end-diastolic flow (A/REDF), and type III by intermittent A/REDF (iA/REDF). Types II and III have the most unpredictable clinical course and thereby still exhibit the highest rates of perinatal morbidity and mortality.

Understanding placental pathophysiology is paramount in devising feasible antenatal management strategies for pregnancies with discordant growth. The primary cause of a BWD in MC twins is generally considered to be unequal placental sharing.[9] However, it is not the sole determinant as there is no 1-to-1 relationship between placental share discordance and BWD.[10] Placental

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AJOG at a Glance

Why was this study conducted?

This study aimed to assess whether placental angioarchitecture can affect birthweight discordance (BWD) in monochorionic (MC) twins, as understanding placental pathophysiology is paramount in devising feasible antenatal management strategies for MC twins with a large growth discrepancy.

Key findings

Placental share discordance was strongly associated with BWD in MC twins. Large bidirectional anastomoses, in particular arterioarterial anastomoses, can compensate for unequal sharing. Cases with a large BWD and abnormal antenatal umbilical artery (UA) Doppler flow patterns show a distinct mechanism with increased importance of placental angioarchitecture.

What does this add to what is known?

Our study described a large cohort of MC twin placentas, with the inclusion of placentas from uncomplicated pregnancies and a subgroup analysis per UA Doppler flow pattern allowing for in-depth investigation of the distinct placental mechanisms for each pattern.

angioarchitecture, especially the presence of large bidirectional anastomoses, is thought to affect this relationship by allowing for a compensatory intertwin blood flow. This hypothesis was put forward by the previous finding that type III sFGR placentas have a relatively lower degree of BWD than expected for the amount of placental share discordance while also having a large arterioarterial (AA) anastomosis.[11] However, this large AA anastomosis also increases the risk of acute fetofetal transfusion after the demise of either twin. Hence, intensive fetal surveillance in type III is advised. This illustrates that each UA Doppler flow pattern as described by Gratacós et al[8] is considered to be an expression of a distinct placental mechanism that affects clinical decision making, particularly in types II and III. By further studying placental sharing and angioarchitecture, we can gain more etiologic knowledge on the origin of discordant antenatal growth that allows us to enhance our risk assessment and subsequent management approach in the future.

Therefore, the aim of this study was 2-fold: (1) to assess the relationship between BWD and placental share discordance (a measure for the amount of unequal placental sharing) and (2) to examine to what extent large bidirectional anastomoses (AA and venovenous (VV) anastomoses) can compensate for the effect of unequal placental sharing on BWD, with a subgroup analysis for each UA Doppler flow pattern as diagnosed prenatally in twin pairs with a BWD of $\geq$20%.

Materials and Methods

All MC twin placentas of live-born twins injected with colored dye in our center between March 2002 and June 2021 were eligible for inclusion. Placentas of monoamniotic (MA) twins, twins with twin-twin transfusion syndrome (TTTS), or twins with twin anemia polycythemia sequence were excluded because of their distinct pathophysiology and corresponding placental characteristics.[2,12] Moreover, we excluded MC triplet pregnancies, cases with twin reversed arterial perfusion, and/or other congenital abnormalities. Cases with unknown birthweights and cases in which placental measurements were impossible because of either maceration after fetal death (any single or double intrauterine fetal demise, selective reduction, or termination of pregnancy) or damage to the placenta because of manual removal were further excluded.

The following maternal and neonatal baseline characteristics were collected: maternal age, gravidity, parity, UA Doppler flow pattern (for cases with a BWD of $\geq$20% as this can be considered a postnatal expression of discordant antenatal growth), gestational age at birth, sex, delivery mode, birthweight, BWD (calculated as [birthweight larger twin−birthweight smaller twin]/birthweight larger twin$\times$100[13]), birthweight ratio (calculated as birthweight of larger twin/birthweight of smaller twin), proportion of neonates born small for gestational age (SGA) (defined as a birthweight of <10th percentile on Singleton growth curves),[14,15] and incidence of neonatal mortality (defined as death within 28 days after birth). The UA Doppler flow pattern was established in line with the Gratacós classification based on antenatal ultrasound with routine UA Doppler evaluations for MC twin pregnancies, distinguishing among pEDF, persistent A/REDF, and iA/REDF. As the UA Doppler flow pattern can change during pregnancy, the most prevalent type was chosen.[16] In our center, pregnancies with discordant antenatal growth are managed expectantly. In severe cases, a selective reduction is considered. Fetoscopic laser coagulation is not performed.

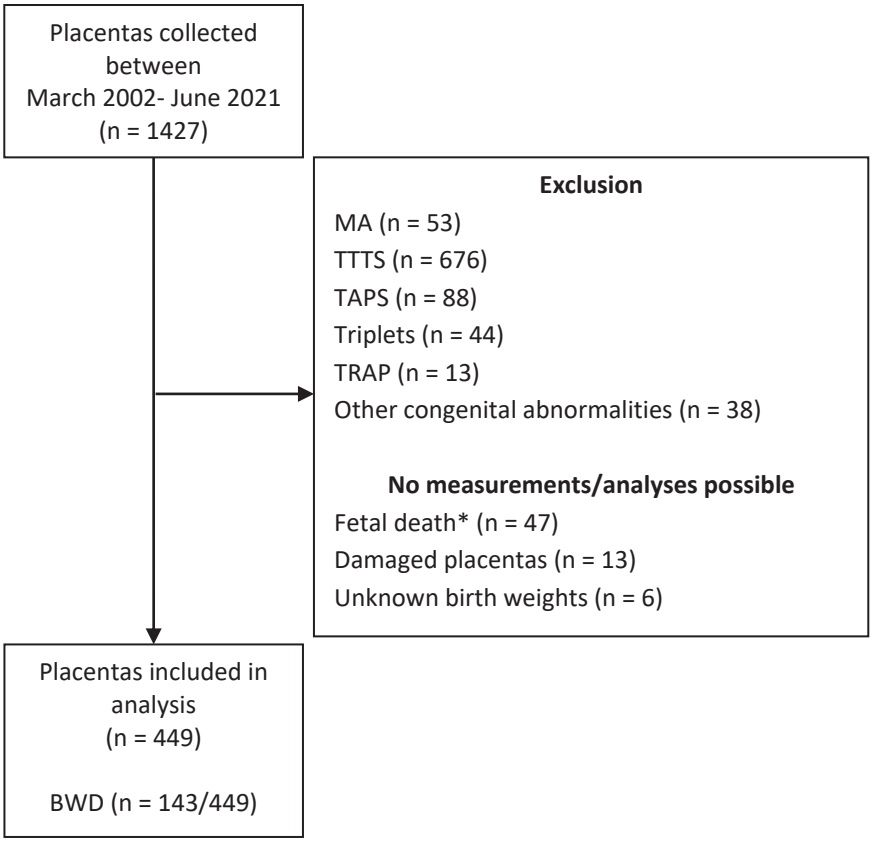
MC placentas are routinely injected with dye in our center as previously described.[17] After dye injection, placentas are photographed, and the images are digitally saved for computer analysis using ImageJ (version 1.57; National Institutes of Health, Bethesda, MA). The number of arteriovenous (AV) and venoarterial (VA) anastomoses were recorded from the firstborn twin to the secondborn twin. The number and total diameter of AA and VV anastomoses as well as the total number of anastomoses was also recorded. The proportion of fetuses with a velamentous or marginal (<1 cm from the margin of the placenta) cord insertion was documented for the smaller and larger twins. Fetal territories were demarcated by the margins of the twin-specific colored dyes and expressed by a percentage of the total placental surface. Placental share discordance was calculated as (placental share larger twin−placental share smaller twin)/placental share larger twin$\times$100. The

placental territory ratio was calculated similarly as birthweight ratio: placental share of larger twin/placental share of smaller twin. Part of these data was previously published in 2018.[11] Birthweight ratio/placental territory ratio was calculated. A value below 1 suggests a lower BWD for the given placental share discordance (ie, equal birthweights with an unequally shared placenta). A value above 1 suggests a higher BWD for the given placental share discordance (ie, discordant birthweights with an equally shared placenta).[18] We have chosen to report on both BWD and birthweight ratio and placental share discordance and placental territory ratio for comparability to other available studies reporting on similar parameters.

Statistical data were analyzed using IBM SPSS Statistics (version 25.0; IBM Corp, Chicago, IL). Data are presented as median (interquartile range [IQR]), number/total number (percentage), or number (percentage). To assess the first aim of our study, multivariate linear regression was performed to examine the relationship among placental share discordance, total AA diameter, total VV diameter, and BWD. To assess the second aim of our study, univariate linear regression was performed to examine the relationship between both total AA and total VV diameters and birthweight—to—placental territory ratio. We chose a different outcome measure than in the first aim, as the strong effect of placental share discordance on BWD can cloud the compensatory effect of AA and VV diameters that we want to research. Birthweight ratio/placental territory ratio eliminates this strong effect from the analysis by looking at BWD relative to placental share discordance and is an outcome parameter that is consistent with previous literature.[8,10,18] When a statistically significant ($P < .05$) association was found for both AA and VV diameters in univariate analysis, they were included in a multivariate linear regression model. A subgroup analysis per UA Doppler flow pattern in twin pairs with a BWD of ≥20% was performed for both aims. As VV anastomoses are rare, we did not include the total VV diameter in this subgroup analysis because of probable insufficient power. A P value of <.05 was considered statistically significant. The relationship among placental share discordance, BWD, total AA and VV diameters, and birthweight ratio/placental territory ratio for the total population and per UA Doppler flow pattern was plotted using RStudio (version 2021.9.2.382; RStudio, Boston, MA).

This retrospective study was approved and waived of the requirement for written informed consent by the ethics committee of the Leiden University Medical Center (protocol number G21.184) and funded by the Dutch Heart Foundation (grant number 2017T075). The funding source had no role in conducting the research or writing the research article.

FIGURE 1
Flowchart of study inclusion



*Either single/double IUFD or selective reduction/TOP.

Of the fetal death cases, 26 were diagnosed with selective fetal growth restriction antenatally (EFW of <10th percentile and EFW discordance of ≥25%) of which 4 were type I, 10 were type II, and 9 were type III (unknown in 2 cases).

BWD, birthweight discordance; *EFW*, estimated fetal weight; *MA*, monoamniotic; *TAPS*, twin anemia polycythemia sequence; *TRAP*, twin reversed arterial perfusion; *TTTS*, twin-twin transfusion syndrome.

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Results

Between March 2002 and June 2021, 1429 placentas were injected with colored dye. After applying the aforementioned exclusion criteria, 449 placentas were included for analysis (Figure 1). Of these 449 placentas, 152 (34%) had a BWD of ≥20%.

Baseline characteristics

Baseline characteristics for the total population and the subgroup of MC

TABLE 1
Baseline maternal and neonatal characteristics for the analyzed placentas, with the subgroup of monochorionic twins with a birthweight discordance of ≥20%

Characteristics	MC twins (n=898; 449 pregnancies)	BWD ≥20% (n=304; 152 pregnancies)
Maternal age (y)	32 (28–34)	31 (28–34)
Gravidity	2 (1–3)	1 (1–3)
Parity	1 (0–1)	0 (0–1)
UA Doppler flow pattern[a]		
pEDF	—	71 (50)
A/REDF	—	28 (20)
iA/REDF	—	44 (31)
Gestational age at birth (wk)	35.3 (32.1–36.3)	33.5 (31.0–35.8)
Female	448/894 (50)	150/304 (49)
Cesarean delivery	415/890 (46)	212/304 (70)
Birthweight (g)		
Smaller twin	1956 (1415–2350)	1381 (996–1796)
Larger twin	2350 (1792–2670)	2566 (1540–2010)
Small for gestational age		
Smaller twin	273/447 (61)	144/152 (95)
Larger twin	67/447 (15)	25/152 (16)
BWD (%)	13.3 (6.3–25.2)	30.2 (25.1–36.9)
Birthweight ratio	1.2 (1.1–1.3)	1.4 (1.3–1.6)
Neonatal mortality		
Smaller twin	11/423 (3)	7/141 (5)
Larger twin	4/282 (1)	2/140 (1)

Data are presented as median (interquartile range), number (percentage), or number/total (percentage).

A/REDF, absent or reversed end-diastolic flow; *BWD*, birthweight discordance; *iA/REDF*, intermittent absent or reversed end-diastolic flow; *MC*, monochorionic; *pEDF*, positive end-diastolic flow; *UA*, umbilical artery.

[a] Unknown in 9 twin pairs.

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twins with a BWD of ≥20% are summarized in Table 1. The median gestational age at birth was 35.3 weeks (IQR, 32.1–36.3) for the total population. The median birthweight in the smaller twin was 1956 g (IQR, 1415–2350) as opposed to 2350 g (IQR, 1792–2670) in the larger twin. BWD was 13.3% (IQR, 6.3–25.2), with a birthweight ratio of 1.2 (IQR, 1.1–1.3), meaning the larger twin had a 1.2 times higher birthweight than the smaller twin. Neonatal mortality occurred in 11 of 423 smaller twins (3%) and 4 of 282 larger twins (1%).

In the subgroup of MC twins with a BWD of ≥20% (n=152), 71 pairs (50%) presented with pEDF, 28 pairs (20%) presented with A/REDF, and 44 pairs (33%) presented with iA/REDF. The UA Doppler flow patterns were unknown in 9 twin pairs as no antenatal ultrasound was available. The median gestational age at birth for the subgroup was 33.5 weeks (IQR, 31.0–35.8), and 212 of 304 patients (70%) were delivered by way of cesarean delivery. The smaller twin had a median birthweight of 1381 g (IQR, 996–1796), and the larger twin had a median birthweight of 2566 g (IQR, 1540–2010). Of note, 144 of 152 smaller twins (95%) were born SGA compared with 25 of 152 larger twins (16%). The median BWD was 30.2% (IQR, 25.1–36.9), and the birthweight ratio was 1.4 (IQR, 1.3–1.6), implicating that the larger twin had a 1.4 times higher birthweight than the smaller twin. Neonatal mortality occurred in 7 of 141 smaller twins (5%) (of which 1 from a pregnancy with pEDF, 2 from a pregnancy with A/REDF, and 4 from a pregnancy with iA/REDF) and 2 of 140 larger twins (1%) (of which 1 from a pregnancy with pEDF and 1 from a pregnancy with iA/REDF).

Placental characteristics

Placental characteristics of the 449 MC twin pregnancies and the subgroup of 152 MC twin pregnancies with a BWD of ≥20% are presented in Table 2. AA anastomoses were present in the majority of placentas (411 of 449 [92%]), and VV anastomoses were present in 109 of 449 placentas (24%). The median AA diameter was 2.2 mm (IQR, 1.3–3.0), and the median VV diameter was 3.1 mm (IQR, 1.8–4.3). Of the smaller twins, 282 of 449 (63%) had a velamentous or marginal cord insertion, of which 175 of 282 (62%) were velamentous and 107 of 282 (38%) were marginal. This was the case for 104 of 449 larger twins (23%), with 34 of 104 velamentous (33%) and 70 of 104 marginal (67%). Median placental share discordance was 35.1% (IQR, 18.2–52.8), with 41% (IQR, 33–50) of the placenta for the smaller twin and 59% (IQR, 50–67) of the placenta for the larger twin. The placental territory ratio was 1.5 (IQR, 1.2–2.10), meaning that the larger twin had a 1.5 times larger placental share as opposed to the smaller twin. The birthweight ratio/placental territory ratio was 0.8 (IQR, 0.6–0.9), implicating a 0.2-times lower BWD than expected for the given placental share discordance.

Similarly, nearly all placentas of MC twins with a BWD of ≥20% had AA anastomoses (147 of 152 [97%]). VV anastomoses were present in 33 of 152 placentas (22%). The median AA diameter was 2.2 mm (IQR, 1.3–3.1),

TABLE 2
Placental characteristics of the analyzed placentas, including the subgroup of monochorionic twins with a birthweight discordance of ≥20%

Characteristics	MC twins (n=898; 449 pregnancies)	BWD ≥20% (n=304; 152 pregnancies)
Total anastomoses	10 (6–16)	10 (6–16)
AV anastomoses	4 (2–7)	4 (2–8)
VA anastomoses	4 (1–7)	4 (2–7)
Presence of AA anastomoses	411 (92)	147 (97)
>1 AA anastomoses	22 (5)	8 (6)
Total AA diameter (mm)	2.2 (1.3–3.0)	2.2 (1.3–3.1)
Presence of VV anastomoses	109 (24)	33 (22)
>1 VV anastomoses	17 (4)	4 (3)
Total VV diameter (mm)	3.1 (1.8–4.3)	3.3 (1.9–3.9)
Velamentous or marginal cord insertion		
Smaller twin	282 (63)	124 (82)
Larger twin	104 (23)	17 (11)
Placental share (%)		
Smaller twin	41 (33–50)	31 (25–40)
Larger twin	59 (50–67)	69 (60–75)
Placental share discordance (%)	35.1 (18.2–52.8)	55.4 (36.8–66.4)
Placental territory ratio	1.5 (1.2–2.1)	2.2 (1.6–3.0)
Birthweight ratio/placental territory ratio	0.8 (0.6–0.9)	0.7 (0.5–0.9)

Data are presented as median (interquartile range) or number (percentage).

AA, arterioarterial; *AV*, arteriovenous; *BWD*, birthweight discordance; *MC*, monochorionic; *VA*, venoarterial; *VV*, venovenous.

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and the median VV diameter was 3.3 mm (IQR, 1.9–3.9). Most smaller twins had a velamentous or marginal cord insertion (124 of 152 [82%]), of which 85 of 124 (69%) were velamentous and 39 of 124 (31%) were marginal. Of the larger twins, 17 of 152 (11%) had a velamentous or marginal cord insertion, of which 5 of 17 (29%) were velamentous and 12 of 16 (75%) were marginal. Median placental share discordance was 55.4% (IQR, 36.8–66.4), with 31% (IQR, 25–40) of the placenta for the smaller twin and 69% (IQR, 60–75) of the placenta for the larger twin. The placental territory ratio was 2.2 (IQR, 1.6–3.0), meaning that the larger twin had a 2.2-times larger placental share than the smaller twin. Birthweight ratio/placental territory ratio was 0.7 (IQR, 0.5–0.9), implicating a 0.3-times lower BWD than expected for the given placental share discordance.

Relationship placental sharing, arterioarterial and venovenous diameter, and birthweight discordance

The results from the multivariate linear regression of placental share discordance, total AA diameter and total VV diameter, and BWD (aim 1) for the total population and the subgroup with a BWD of ≥20% and available UA Doppler flow patterns (n=143) are shown in Table 3 and depicted in Figure 2. An increase in placental share discordance was associated with an increase in BWD (β coefficient, 0.325; 95% CI, 0.254–0.397; $P<.0001$) in the total population. Cases with pEDF demonstrated a similar positive correlation between placental share discordance and BWD (β coefficient, 0.214; 95% CI, 0.102–0.326; $P=.001$). In cases with A/REDF and iA/REDF, there was no significant association between placental share discordance and BWD, but for cases with A/REDF, there was a significant negative correlation between total AA diameter and BWD (β coefficient, −4.143; 95% CI, −7.103 to −1.182; $P=.006$).

Relationship birthweight ratio/placental territory ratio, arterioarterial and venovenous diameter

The results from the univariate linear regression of total AA and VV diameters and birthweight ratio/placental territory ratio (aim 2) are shown in Table 4 and depicted in Figure 2. The AA diameter, but not the VV diameter, was correlated with the birthweight ratio/placental territory ratio (β coefficient, −0.041; 95% CI, −0.059 to −0.023; $P<.0001$) for the total population, meaning that an increase in total AA diameter leads to less BWD than expected for the amount of placental share discordance. This was similar for cases with pEDF (β coefficient, −0.055; 95% CI, −0.098 to −0.011; $P=.013$) and cases with A/REDF (β coefficient, −0.180; 95% CI, −0.297 to −0.063; $P=.002$). The association between total AA diameter and birthweight ratio/placental territory ratio in cases with iA/REDF approached statistical significance (β coefficient, −0.053; 95% CI, −0.111 to 0.004; $P=.070$).

Comment

Principal findings

This study showed that there was a strong association between placental share discordance and BWD in live-born MC twins. However, the amount of BWD was smaller than the amount of placental share discordance. A larger AA diameter was shown to mitigate the effect of unequal placental sharing on BWD as reflected by a lower birthweight ratio/placental territory ratio with increasing diameter. Concerning the different UA Doppler flow patterns in

TABLE 3
Multivariate linear regression to evaluate the association between birthweight discordance and placental share discordance for the total population and per antenatal umbilical artery Doppler flow pattern for the twin pairs with a birthweight discordance of ≥20%

	Total population			pEDF			A/REDF			iA/REDF		
Characteristics		β coefficient (95% CI)	*P* value		β coefficient (95% CI)	*P* value		β coefficient (95% CI)	*P* value		β coefficient (95% CI)	*P* value
Placental share discordance (%)	35 (18–53)	0.325 (0.254–0.397)	<.0001	45 (30–60)	0.214 (0.102–0.326)	.001	56 (50–68)	0.018 (−0.157 to 0.193)	.840	66 (58–72)	0.136 (−0.037 to 0.310)	.124
Total AA diameter (mm)	2.2 (1.3–3.0)	0.470 (−1.106 to 2.047)	.559	1.7 (1.2–2.9)	−1.039 (−2.515 to 0.326)	.167	1.8 (1.1–2.4)	−4.143 (−7.103 to −1.182)	.006	2.8 (2.2–3.6)	−1.726 (−4.191 to 0.740)	.170
Total W diameter (mm)	3.1 (1.8–4.3)	−0.180 (−1.071 to 0.712)	.693									

Data are presented as median (interquartile range).

AA, arterioarterial; *A/REDF*, absent or reversed end-diastolic flow; *BWD*, birthweight discordance; *CI*, confidence interval; *iA/REDF*, intermittent absent or reversed end-diastolic flow; *pEDF*, positive end-diastolic flow; *UA*, umbilical artery; *VV*, venovenous.

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twin pairs with a BWD of ≥20%, cases with pEDF demonstrated similar associations as the total population in line with type I sFGR pregnancies also having a relatively uncomplicated course. As expected, cases with A/REDF and iA/REDF showed a distinct placental pathophysiology in which both did not show a significant association between placental share discordance and BWD, although compensation through a larger AA diameter (approaching statistical significance for iA/REDF) was present. This suggests increased importance of placental angioarchitecture.

Results in the context of what is known

Our results were in line with previous studies performed by Lewi et al[10] and Couck et al,[18] including 100 and 247 MC placentas, respectively. We confirmed the strong linear relationship between placental share discordance and BWD and the effect of a larger AA diameter in reducing the birthweight ratio/placental territory ratio in a substantially larger study population with a subgroup analysis per antenatal UA Doppler flow pattern. Moreover, Couck et al[18] found that a larger VV diameter decreases the amount of BWD for any given placental share discordance, independent of the AA diameter. We did not find this effect in our population, potentially because of the nearly double amount of placentas with VV anastomoses that we were able to include. In a study performed by Wang et al,[19] the presence of VV anastomoses was found to be negatively correlated with BWD in type III sFGR when corrected for gestational age at diagnosis and delivery. We were unable to conclude the effect of VV diameter in the subgroup analysis of the UA Doppler flow patterns, as only 9 pEDF, 6 A/REDF, and 12 iA/REDF placentas had a VV anastomosis. More research is necessary, preferably in a multicenter setting, to study the role of VV anastomoses.

In previous literature on the placental characteristics of the Gratacós types in sFGR, the large AA diameter was considered to be the compensation mechanism for unequal placental sharing primarily in type III placentas, as

TABLE 4
Univariate linear regression to evaluate the association between birthweight ratio/placental territory ratio and total arterioarterial and venovenous diameter per antenatal umbilical artery Doppler flow pattern in twin pairs with a birthweight discordance of ≥20%

Characteristics	Total population			pEDF			A/REDF			iA/REDF		
		β coefficient (95% CI)	*P* value		β coefficient (95% CI)	*P* value		β coefficient (95% CI)	*P* value		β coefficient (95% CI)	*P* value
Total AA diameter (mm)	2.2 (1.3–3.0)	−0.041 (−0.059 to −0.023)	<.0001	1.7 (1.2–2.9)	−0.055 (−0.098 to −0.011)	.013	1.8 (1.1–2.4)	−0.180 (−0.297 to −0.063)	.002	2.8 (2.2–3.6)	−0.053 (−0.111 to 0.004)	.070
Total VV diameter (mm)	3.1 (1.8–4.3)	−0.007 (−0.027 to 0.012)	.473									

Data are presented as median (interquartile range).

AA, arterioarterial; *A/REDF*, absent or reversed end-diastolic flow; *BWD*, birthweight discordance; *CI*, confidence interval; *iA/REDF*, intermittent absent or reversed end-diastolic flow; *pEDF*, positive end-diastolic flow; *UA*, umbilical cord; *VV*, venovenous.

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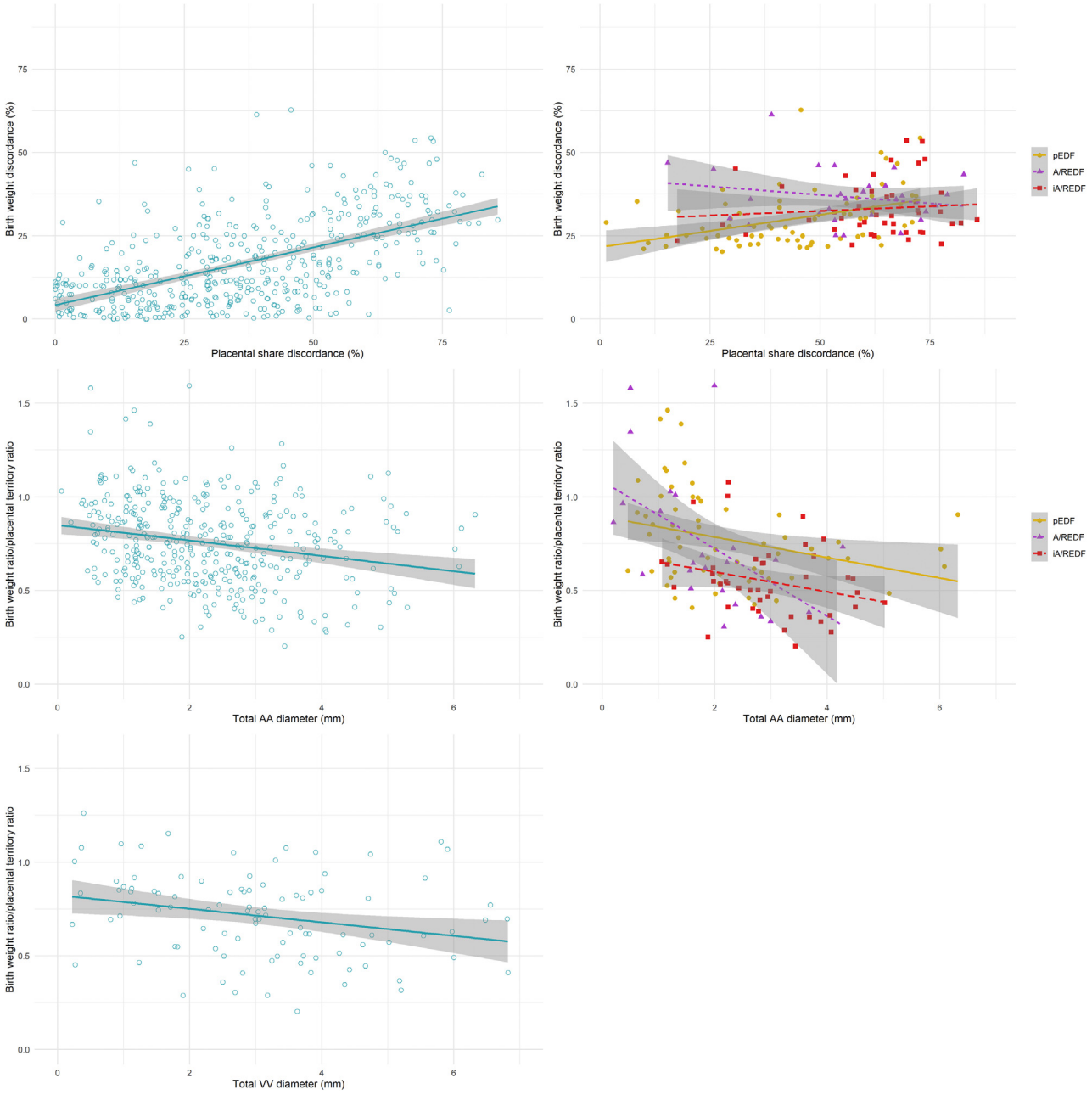
type III had both the largest AA diameter and the lowest birthweight ratio/placental territory ratio compared with type I and type II.[8,11] Our study demonstrated that in type I (pEDF) and type II (A/REDF), there is also compensation through the AA anastomoses. However, as the AA diameter is smaller in these types, they still demonstrate a higher birthweight ratio/placental territory ratio than reported in type III (iA/REDF).

The hazard in comparing studies using the Gratacós classification is the different scoring methods that are widely used. Some studies classify a pregnancy as type II or type III when abnormal UA Doppler flow patterns were observed on a single occasion,[20] others use the final classification before delivery,[19] and others use the most prevalent type of flows as we have done now and in the past.[11] UA Doppler flow patterns are dynamic and can change over time, presenting difficulty in determining the "definitive" Gratacós type.[16] International consensus is urgently needed to minimize this variation in diagnosis, as this currently clouds the exploration of pathophysiological mechanisms and hampers comparisons among studies.

Clinical implications

Our findings supported the hypothesis that large bidirectional anastomoses, in particular AA anastomoses, allow for an increased fetofetal blood flow and can thereby compensate for unequal placental sharing by way of a rescue transfusion from the larger twin to the smaller twin. Although beneficial for the growth of the smaller twin during pregnancy, large anastomoses can also pose a threat to either twin because of the risk of acute fetofetal transfusion potentially leading to fetal demise or neurologic damage.[8,21,22] This is especially thought to be the cause of the unpredictable clinical course of type III sFGR, which is reported to have the largest AA diameter.[8,11] This also determines the current management protocol in which fetal surveillance is advised. The knowledge from our current study can now lead to a more accurate risk assessment, especially if

FIGURE 2
Scatterplots depicting the relationship between placental sharing, AA and VV diameter and birth weight



AA, arterioarterial; *BWD*, birthweight discordance; *VV*, venovenous; *UA*, umbilical artery.

Groene. Placental sharing and birthweight in twins. Am J Obstet Gynecol 2022.

antenatal visualization of large, bidirectional anastomoses is further improved in the future.

Fetoscopic laser coagulation has been suggested for sFGR pregnancies with abnormal UA Doppler flow patterns to eliminate the risk of acute fetofetal transfusion by coagulating the large anastomoses.[23] However, our study further substantiates that the smaller twin also relies on these anastomoses for an additional blood supply from its co-twin. This rescue transfusion is lost when anastomoses are coagulated, resulting in high rates of fetal demise in the smaller twin (60%–77%).[24–27] Moreover, this phenomenon was observed in TTTS pregnancies where sFGR before laser was identified as a risk factor for fetal demise of the smaller twin.[28] In addition, fetoscopic laser

coagulation in sFGR pregnancies comes with more technical challenges than in TTTS because of the absence of an amniotic fluid discordance.

Research implications

This study has provided us a glimpse into the black box that is the MC placenta. However, its exact internal mechanisms are not yet fully understood. Future research should focus on volumetric measurements to more accurately quantify placental sharing. By early antenatal visualization of placental sharing and angioarchitecture (eg, with placental mapping by 3-dimensional color Doppler ultrasound or magnetic resonance imaging [MRI][29–32]), the knowledge from this study can be applied to formulate an individualized risk assessment and adapt the management strategy accordingly in the future. Moreover, pathologic examination of placental tissue, including placental weight, can provide more information on other potential causes of a BWD, such as antenatal placental insufficiency or maternal disease as reported in singletons with FGR.[33]

Strengths and limitations

Our study has limitations that should be taken into account when interpreting the data. First, its retrospective nature can introduce bias in the results. Moreover, as we are a specialized center, there might be an overrepresentation of severe cases with a large BWD. Importantly, reliable dye injection is only possible in cases with double survivors, automatically resulting in a selected population with relatively favorable outcomes as cases in which fetal demise or selective reduction occurred are generally the most severe cases. Lastly, it should be noted that we solely look at the placental surface in determining the sharing and not placental volume. Nevertheless, our study was strengthened by its large study population, the inclusion of placentas from twins with a broad range of BWD to explore, and the subgroup analyses per UA Doppler flow pattern in twins with a BWD of $\geq$20%, allowing for in-depth investigation of the distinct placental mechanisms for each type. As dye injection of placentas has been part of standard care in our center for nearly 20 years, we have a large dataset of placentas available, including digitally saved pictures that can be reviewed.

Conclusions

This study showed that BWD in MC twins is strongly associated with placental share discordance, but that large bidirectional anastomoses, particularly AA anastomoses, can mitigate the effect of unequal placental sharing (Video 1). Placentas from pregnancies with UA Doppler abnormalities show a distinct mechanism with a greater importance of placental angioarchitecture. ■

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