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Selective intrauterine growth restriction in monochorionic twins: changing patterns in umbilical artery Doppler flow and outcomes

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KEYWORDS: Doppler flow; monochorionic pregnancy; selective intrauterine growth restriction; umbilical artery

ABSTRACT

Objectives *To describe changes in umbilical artery (UA) Doppler flow in monochorionic diamniotic (MCDA) twins affected by selective intrauterine growth restriction (sIUGR), to correlate Doppler findings with pregnancy course and perinatal outcome, and to report postnatal follow-up.*

Methods *This was a retrospective study of 140 MCDA twins with sIUGR. UA end-diastolic flow, defined as Doppler waveform pattern Type I (persistently positive), Type II (persistently absent or persistently reversed) or Type III (intermittently absent or intermittently reversed), was recorded at first examination and monitored weekly until double or single intrauterine fetal death (IUFD), bipolar cord coagulation or delivery. All neonates had an early neonatal brain scan, magnetic resonance imaging, when indicated, and neurological assessment during infancy. Rates (per 100 person-weeks) and hazard ratios (HR) of IUFD in the IUGR twin in each pregnancy were calculated considering UA Doppler pattern as a time-dependent variable.*

Results *At first examination, there were 65 cases with UA Doppler waveform pattern Type I, 62 with Type II and 13 with Type III. Of the 65 Type-I cases, 48 (74%) remained stable, while 17 (26%) changed to either Type II absent (14%), Type II reversed (9%) or Type III (3%). Of 62 Type-II cases (47 with absent and 15 with reversed flow), 33 (53%) remained stable (18 with absent and all 15 with reversed flow). The 29 Type-II absent cases which changed became Type II reversed (24/47, 51%) or Type III (5/47, 11%). All 13 Type-III cases remained stable. Compared with Type I, the risk of IUFD (adjusted for estimated fetal weight discordance and amniotic fluid deepest vertical pocket) was highest when the pregnancy was or became Type II reversed (HR, 9.5; 95% CI, 2.7–32.7) or Type II absent (HR, 4.3; 95% CI, 1.3–14.3). Mild neurological impairment was more prevalent in the IUGR twin than in the large cotwin (7% vs 1%, P = 0.02).*

Conclusions *Risk stratification based on UA Doppler is useful for planning ultrasound surveillance. However, patterns can change over time, with important consequences for management and outcome. Copyright © 2016 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Selective intrauterine growth restriction (sIUGR) affects approximately 10–15% of monochorionic (MC) twin pregnancies[1]. Diagnosis is based on an estimated fetal weight (EFW) in one twin of < 10th percentile[2,3], or an intertwin EFW discordance ≥ 25%[4]. This condition is of clinical significance due to the potential risk of intrauterine fetal death (IUFD) or adverse neurological outcome for both twins[5]. Unequal sharing of the placenta is the main cause of sIUGR[6,7], while clinical outcome is closely related to the characteristics of the placental vascular anastomoses[8].

Doppler evaluation of the umbilical artery (UA) in singletons and dichorionic twins is an established parameter for the diagnosis and surveillance of IUGR, secondary to

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placental insufficiency. In MC twin pregnancies complicated by sIUGR, UA Doppler waveforms represent the combined effect of placental insufficiency and placental vascular anastomoses[9]. According to the classification system[10] based on the characteristics of the diastolic flow in the UA, sIUGR MC twins exhibit three main waveform patterns: Type I (persistently positive), Type II (persistently absent or persistently reversed) and Type III (intermittently absent or intermittently reversed). These Doppler patterns are evident early in pregnancy and are associated with considerable differences in outcome, which is expected to be good for Type I, and with high risk of deterioration for Type II[10]. Type-III pregnancies are considered to have an intermediate prognosis, but are the most unpredictable and are at increased risk of antenatal brain injury[11,12].

The primary aim of this study was to describe the changes observed in UA Doppler flow patterns in a retrospective cohort of MC diamniotic (DA) twin pregnancies complicated by sIUGR. Secondary aims were to evaluate the impact of changes in UA Doppler findings in sIUGR twins on IUFD risk, while taking into account EFW discordance and amniotic fluid deepest vertical pocket (DVP) as further potential predictors of demise of the smaller twin, and to investigate the postnatal outcome of the cohort.

METHODS

We analyzed retrospectively 140 consecutive MCDA twin pregnancies complicated by sIUGR, referred before 26 weeks' gestation to our Fetal Therapy Unit at the Vittore Buzzi Children's Hospital, University of Milan in Italy, and examined between April 2004 and April 2012. All of the pregnancies had been diagnosed as MC on first-trimester ultrasound examination. At referral, both twins underwent a detailed evaluation of fetal anatomy, including fetal biometry and EFW, cardiac structure and function, DVP of amniotic fluid, placental location, cervical length and Doppler interrogation of the UA, fetal middle cerebral artery (MCA) and ductus venosus (DV). All examinations were performed by the same four operators (M.A.R., M.L., S.F. and V.S.) using a GE Voluson 730 Expert or GE E8 ultrasound machine (GE Medical Systems, Zipf, Austria), equipped with a 4–8-MHz probe. The diagnosis of sIUGR was made when the EFW was $< 10^{th}$ percentile in the smaller twin, or when the EFW difference was $\geq 25\%$ in the absence of twin-to-twin transfusion syndrome and twin–anemia polycythemia sequence. EFW was obtained according to Hadlock *et al.*[13] and intertwin EFW discordance was calculated using the formula (large twin EFW – small twin EFW) × 100/large twin EFW.

In the IUGR twin, UA Doppler waveforms were classified as Type I (end-diastolic flow persistently positive), Type II (flow persistently absent or persistently reversed) or Type III (flow intermittently absent or intermittently reversed). Intermittent absent or reversed flow was defined as UA waveforms showing cyclical positive, absent and reversed end-diastolic flow over a short time interval[14]. Doppler evaluations were performed in a free loop of the umbilical cord, and multiple waveforms of both UAs (with the exception of seven cases with a single UA) were obtained. The presence of intermittent absent or reversed flow in a free loop was always confirmed by sampling both UAs at the proximal portion of the umbilical cord, closest to the placental insertion[14]. When the two UAs showed different flow patterns (e.g. positive in one, absent in the other) the worse of the two was used to classify the UA Doppler pattern.

Peak systolic velocity and pulsatility index in the MCA were measured and recorded[15]. Doppler abnormalities in the DV were defined as absent or reversed a-wave end-diastolic velocity. Measurements were performed in the absence of fetal movements, with an angle of insonation as close to zero as possible.

Once the diagnosis of sIUGR had been established by fetal biometry, the UA Doppler pattern at first observation became the UA pattern baseline. The same routine was repeated at each examination, scheduled on a weekly basis, with more frequent examinations in the presence of reversed UA flow or abnormal DV waveform.

Before viability (24 weeks), in the presence of a severely compromised IUGR twin (defined as persistently absent or reversed end-diastolic flow in the UA combined with persistently absent or reversed a-wave in the DV), active management with bipolar cord coagulation (BCC) for selective termination was considered. Thirteen cases of BCC included in the present study have been described previously[16].

After viability, the timing of delivery was decided by the attending hospital on the basis of local protocols, taking into consideration gestational age and fetal condition. Fetal deterioration in the IUGR twin was defined by reversed flow in the UA, abnormal a-wave in the DV, or abnormal pulsatility index in the MCA. Anhydramnios and growth arrest in the smaller twin were also considered as signs of fetal deterioration.

The pattern of UA Doppler flow observed ≤ 1 week prior to a double or single IUFD, BCC or delivery was recorded as UA pattern at last examination. Magnetic resonance imaging (MRI) was performed in the surviving twin 2 weeks after all single IUFDs, and in all cases of cerebral injury suspected on ultrasound.

All pregnancies were delivered in hospitals with second- or third-level neonatal care units, and all liveborn neonates underwent an early brain scan. An abnormal scan was an indication for cerebral MRI regardless of gestational age. Chronic lung disease, necrotizing enterocolitis, and Stage-III retinopathy of prematurity were considered as severe neonatal morbidities. All surviving infants were followed up with serial neurological examinations by a pediatric neurologist-psychiatrist, which is routine care in Italy. Postnatal follow-up ranged from 12 months to 7 years (median, 24 months) and was recorded for all neonates/infants.

Neurological impairments were classified as severe, moderate or mild[17]. Patients classified as having severe impairment were those with: motor deficits impairing their ability to walk (cerebral palsy Level 3–5), development quotient < 70, severe behavioral disorder (autism) or bilateral sensorineural deficit (bilateral deafness or blindness). Children classified as having moderate disability were those with: motor deficits not impairing their ability to walk (cerebral palsy Level 2), development quotient of 70–84, behavioral disorders (attention deficit and/or hyperactivity) or unilateral sensorineural deficit. Children classified as having mild disability were those with: minor motor deficits (clumsiness), transient motor delay (with prospect of normalization) or isolated language impairment[18].

For all infants, the results of the neurological examinations were obtained for neuromotor and neurodevelopmental data. Rate of intact survival was defined as the number of infants surviving without complications or impairment, divided by the total number of infants (i.e. 140 IUGR and 140 large twins).

The study complied with our institution's research guidelines for clinical observational studies.

Statistical analysis

For univariate analyses, the Kruskal–Wallis test was used to compare continuous variables across sIUGR UA Doppler flow pattern types, and Fisher's exact test for categorical variables. In order to evaluate Doppler pattern changes over time (monitored weekly), distributions of UA end-diastolic flow at first and last examination were compared.

Given the different lengths of follow-up among the pregnancies, to investigate the association of IUFD of the IUGR twin with selected clinical characteristics (UA Doppler pattern, EFW discordance and amniotic fluid DVP), we calculated the person-time at risk (person-weeks) from first examination to time of BCC, IUFD or delivery. UA Doppler pattern was treated as a time-dependent variable (i.e. in the event of pattern change, women contributed person-weeks to more than one Doppler pattern)[19], while EFW discordance and DVP were taken only at the first examination. We then calculated the IUFD rates (per 100 person-weeks) and 95% CIs for the IUGR twins.

Finally, hazard ratios (HR) for IUFD in IUGR twins were calculated using univariate and multivariable Cox regression models, including the covariates UA Doppler pattern (time-dependent), EFW discordance (< 25%, ≥ 25%) and amniotic fluid DVP (≥ 2 cm, < 2 cm). Gestational age was used as the time scale and, since women entered the study at different gestational ages, left-truncation (i.e. delayed entry) was taken into account by beginning follow-up on the date of first examination[20]. BCC and delivery were treated as censoring events. After fitting Cox models, the proportional hazards assumption was tested on the basis of Schoenfeld residuals.

$P < 0.05$ (two-tailed) was considered statistically significant. All analyses were performed with Stata 13 statistical software (StataCorp LP, 2013, College Station, TX, USA).

Table 1 Maternal and fetal characteristics at diagnosis of selective intrauterine growth restriction in 140 monochorionic diamniotic twin pregnancies

Characteristic	*Value*
Maternal	
Maternal age (years)	33 (19–42)
Nulliparous	84 (60)
IVF pregnancy	7 (5)
Prenatal invasive diagnosis	58 (41)
Fetal	
GA at diagnosis (weeks)	19 (17–25)
EFW discordance ≥ 25%	115 (82)
UA Doppler pattern at diagnosis	
Persistently positive (Type I)	65 (46)
EFW discordance ≥ 25%	51/65 (78)
Persistently absent or reversed (Type II)	62 (44)
EFW discordance ≥ 25%	55/62 (89)
Persistently absent	47/62 (76)
Persistently reversed	15/62 (24)
Intermittently absent or reversed (Type III)	13 (9)
EFW discordance ≥ 25%	9/13 (69)
Length of follow-up (weeks)	12 (8–16)

Data are given as median (range), *n* (%) or *n*/*N* (%). EFW, estimated fetal weight; GA, gestational age; IVF, *in-vitro* fertilization; UA, umbilical artery.

RESULTS

Among a total of 1230 MCDA twin pregnancies referred to our hospital from April 2004 to April 2012, there were 140 complicated by sIUGR.

Table 1 summarizes the maternal and fetal characteristics at the time of diagnosis of sIUGR. At last examination (≤ 1 week prior to double or single IUFD, BCC or delivery), a total of 46 (33%) cases showed a pattern of UA Doppler flow that had changed from that recorded at first examination, all cases with such change having originally been either Type I (of which 17/65 (26%) changed) or Type II with absent flow (of which 29/47 (62%) changed) (Table 2). There were no significant differences between these 46 cases with respect to gestational age at diagnosis, EFW discordance or amniotic fluid DVP, compared with those remaining unchanged, and the median follow-up time was the same (12 weeks) in cases with stable patterns and in those which changed patterns.

Table 3 summarizes the pregnancy course and perinatal outcome according to UA Doppler pattern at first examination. Double IUFD complicated 10 (7%) pregnancies, at a median gestational age of 24 (range, 18–32) weeks. Single IUFD, always involving the IUGR twin, occurred in eight (6%) pregnancies, at a median gestational age of 25 (range, 22–32) weeks. Five of these eight cases were managed expectantly, with serial ultrasound examinations and MRI performed 2 weeks after the cotwin's death. These five large cotwins were delivered at a median gestational age of 36 (range, 31–39) weeks and had normal neurological development. Two other IUGR twin deaths, occurring at 26 and 32 weeks, were managed by elective delivery of the large twins. The twin born at 26 weeks, weighing

Table 2 Change in umbilical artery Doppler pattern in 140 intrauterine growth-restricted monochorionic diamniotic twins

First examination	Last examination				
		Type II			
	Type I	Absent	Reversed	Type III	Total
Type I	48 (74)	9 (14)	6 (9)	2 (3)	65 (100)
Type II					
Absent		18 (38)	24 (51)	5 (11)	47 (100)
Reversed			15 (100)		15 (100)
Type III				13 (100)	13 (100)
Total	48 (34)	27 (19)	45 (32)	20 (14)	140 (100)

Data are given as *n* (%). Type I, persistently positive; Type II, persistently absent or reversed; Type III, intermittently absent or reversed.

980 g, had intraventricular hemorrhage Grade ≥ 3 and died soon after birth. The other, weighing 1980 g at delivery at 32 weeks, survived but developed severe neurological morbidity (multicystic encephalomalacia, with spastic bilateral cerebral palsy affecting all four limbs). In the eighth case, after death of the IUGR twin at 24 weeks, the large twin suffered severe cerebral injury and the family chose to terminate the pregnancy. There were two additional cases of antenatal cerebral injury (extensive subcortical ischemic lesion in one; intraventricular hemorrhage Grade IV in the other) in ongoing twin pregnancies, in both cases affecting the smaller twin. One neonate died soon after birth, while the other survived with severe neurological morbidity.

Overall, 20/140 (14%) IUGR cases underwent BCC. The survival rate for the large twin after the procedure was 16/20 (80%): two suffered IUFD and two miscarried. There was one additional miscarriage, in a Type-I pregnancy (with cervical length 18 mm at first examination). One hundred and twenty women had at least one live birth, with a median gestational age at delivery of 32 (interquartile range, 29–33) weeks. Neonatal death occurred in 26 (9%) of the 280 twins, with an overall survival rate of 80/140 (57%) in the small twin, and of 111/140 (79%) in the large.

Table 4 summarizes the neurodevelopmental outcome of surviving infants. Mild neurological impairment was more prevalent in the small twin than in the large cotwin (7% *vs* 1%, $P = 0.02$). Overall, the intact survival rate was 67/140 (48%) among the IUGR twins and 103/140 (74%) among the large twins ($P < 0.001$).

Table 5 considers the IUGR twins and shows the number, rate (per 100 person-weeks) and crude and adjusted HRs for IUFD according to UA Doppler pattern type, EFW discordance and amniotic fluid DVP. The overall IUFD rate was 1.8 per 100 person-weeks. The highest rate was observed when the pregnancy was (or became) UA Doppler pattern Type II reversed (6.9 per 100 person-weeks), followed by Type II absent (3.1 per 100 person-weeks). The univariate and multivariable Cox analyses confirmed the high IUFD relative risk for these two patterns (adjusted HR = 9.5 for Type II reversed and HR = 4.3 for Type II absent).

Table 3 Pregnancy course and perinatal outcome according to umbilical artery (UA) Doppler pattern at first examination in affected twin in 140 monochorionic diamniotic twin pregnancies with selective intrauterine growth restriction (sIUGR)

Outcome	Type I (n = 65)	Type II absent (n = 47)	Type II reversed (n = 15)	Type III (n = 13)	Total (n = 140)	P*
Double IUFD	2 (3)	6 (13)	2 (13)	0 (0)	10 (7)	0.10
IUGR twin IUFD	1 (2)	3 (6)	3 (20)	1 (8)	8 (6)	0.03
BCC of IUGR twin†	3 (5)	10 (21)	5 (33)	2 (15)	20 (14)	0.005
Large twin loss after BCC	0 (0)	4 (9)	0 (0)	0 (0)	4 (3)	
TOP (both twins)‡	1 (2)	2 (4)	0 (0)	1 (8)	4 (3)	0.40
TOP (large twin only)‡	0 (0)	1 (2)	0 (0)	0 (0)	1 (1)	
Miscarriage	1 (2)	0 (0)	0 (0)	0 (0)	1 (1)	1.00
GA at delivery (weeks)§	33 (31–35)	30 (27–33)	30 (27–33)	32 (30–33)	32 (29–33)	0.006
Birth weight (g)						
IUGR twin (n = 97)	1328 (940–1670)	765 (570–1205)	650 (540–930)	1190 (910–1480)	1040 (730–1480)	< 0.01
Large twin (n = 120)	2039 (1515–2303)	1400 (980–1920)	1350 (950–1880)	1640 (1300–2100)	1650 (1200–2200)	< 0.01
Neonatal death						
IUGR twin	8 (12)	5 (11)	3 (20)	1 (8)	17 (12)	0.77
Large twin	4 (6)	3 (6)	2 (13)	0 (0)	9 (6)	0.59
Overall survival						
IUGR twin	49 (75)	21 (45)	2 (13)	8 (62)	80 (57)	< 0.001
Large twin	57 (88)	31 (66)	11 (73)	12 (92)	111 (79)	0.02
Severe neonatal morbidity						
IUGR twin	3 (5)	2 (4)	1 (7)	1 (8)	7 (5)	0.77
Large twin	3 (5)	0 (0)	0 (0)	0 (0)	3 (2)	0.52

Data are given as *n* (%) or median (interquartile range). Type I: persistently positive; Type II: persistently absent or reversed; Type III: intermittently absent or reversed. *Kruskal–Wallis test or Fisher's exact test, for continuous or categorical variables, respectively. †Three Type I and 10 Type II with absent flow at first examination underwent BCC following change in pattern to Type II reversed. ‡One large twin terminated for cerebral injury after intrauterine fetal death (IUFD) of intrauterine growth-restricted (IUGR) cotwin with pattern Type II absent; four terminations of entire pregnancy by maternal choice. §Pregnancies with at least one live birth ($n = 120$). BCC, bipolar cord coagulation; GA, gestational age; TOP, termination of pregnancy.

Table 4 Neurodevelopmental outcome in surviving infants from 140 monochorionic diamniotic twin pregnancies with selective intrauterine growth restriction (sIUGR)

Outcome	*sIUGR twin (n = 80)*	*Large twin (n = 111)*	*Total (n = 191)*	P
Severe neurological morbidity	5 (6)	6 (5)	11 (6)	1.00
Spastic bilateral cerebral palsy				
Affecting inferior limbs	2	2	4	
Affecting four limbs	2	3	5	
Bilateral deafness	1	1	2	
Moderate neurological morbidity	2 (3)	1 (1)	3 (2)	0.57
Unilateral deafness	1	0	1	
Attention deficit hyperactivity disorder	1	1	2	
Mild neurological morbidity	6 (7)	1 (1)	7 (4)	0.02
Total intact survival rate	67/140 (48)	103/140 (74)	170/280 (61)	< 0.001

Data are given as *n* or *n* (%).

Table 5 Number, rate (per 100 person-weeks) and hazard ratios (HR) for intrauterine fetal death (IUFD) of affected twin in monochorionic diamniotic twin pregnancies with selective intrauterine growth restriction, according to selected clinical characteristics

Variable	*Person-weeks at risk*	n	*Rate* (95% CI)*	*HR† (95% CI)*	P	*HR_{adj}‡ (95% CI)*	P
IUFD	1285.1	23	1.8 (1.2–2.7)				
UA Doppler pattern							
Type I	712.1	4	0.6 (0.2–1.5)	1.0 (Reference)		1.0 (Reference)	
Type II absent	287.6	9	3.1 (1.6–6.0)	4.8 (1.5–15.9)	0.009	4.3 (1.3–14.3)	0.02
Type II reversed	116.7	8	6.9 (3.4–13.7)	11.4 (3.4–38.9)	< 0.001	9.5 (2.7–32.7)	< 0.001
Type III	168.7	2	1.2 (0.3–4.7)	2.0 (0.4–11.1)	0.42	2.9 (0.5–16.1)	0.23
EFW discordance							
< 25%	293.3	1	0.3 (0.05–2.4)	1.0 (Reference)		1.0 (Reference)	
≥ 25%	991.8	22	2.2 (1.5–3.4)	6.7 (0.9–50.0)	0.06	4.9 (0.6–38.3)	0.13
Amniotic fluid DVP							
≥ 2 cm	1108.9	16	1.4 (0.9–2.4)	1.0 (Reference)		1.0 (Reference)	
< 2 cm	176.3	7	4.0 (1.9–8.3)	2.4 (1.0–6.0)	0.054	1.4 (0.5–3.6)	0.48

*n/100 person-weeks. †Crude hazard ratio (Cox model). ‡Adjusted hazard ratio, from a Cox model containing all three variables: umbilical artery (UA) Doppler pattern (time-dependent), estimated fetal weight (EFW) discordance and amniotic fluid deepest vertical pocket (DVP) (both at first examination).

DISCUSSION

In this series of MCDA twin pregnancies with sIUGR, UA Doppler waveform patterns in the IUGR twin changed during pregnancy in 26% of Type-I cases and in 62% of Type-II cases with absent flow, while they remained unchanged in Type-II reversed and Type-III cases. As regards the impact of these changes on outcome, higher risk for IUFD was found in cases that were (or became) pattern Type II reversed and pattern Type II absent.

The study confirms the importance of a classification system based on UA Doppler pattern to predict perinatal outcome in MC twins complicated by sIUGR, but also questions the assumption that the Type-I pattern remains unchanged during pregnancy. Of the two major studies addressing this issue, after pattern assignment at enrolment, one[10] found a change in just one of the 39 Type-I cases described, while the other[11] found no change in any of the 31 cases. Type-I pregnancies are thus generally considered to have a good outcome, with a low risk of IUFD in the small twin (3–5%) and survival rates of around 95%. In our cohort, as in the abovementioned studies, the 74% of Type-I cases which remained stable had an intrauterine mortality rate of 5%. However, unlike the two previous studies, our study found that over a quarter of Type-I cases changed into worse patterns indicative of increasing placental dysfunction, and this change made the outcome less favorable. Of the nine cases worsening to Type II with absent flow, one was complicated with death of the IUGR twin at 24 weeks and severe cerebral injury in the large twin, and three with very preterm delivery for arrested growth. The six cases progressing to Type II with reversed flow clearly needed appropriate management (three with cord occlusion and three with elective preterm delivery).

sIUGR Type II is known to be at high risk of deterioration, leading obstetricians to consider active management before the occurrence of IUFD. Of the 30 cases described by Gratacos *et al.*[10], fetal deterioration (defined as abnormal venous Doppler, persistent reversed flow in the UA or abnormal biophysical profile) occurred in 90% of cases. The management options comprised selective feticide before 28 weeks (performed with cord occlusion in 9/30 cases) and preterm elective delivery after 28 weeks. No unexpected deaths were observed in this cohort.

The only study of expectant management in Type-II sIUGR cases ($n = 27$), by Ishii *et al.*[11], reported death rates of 29.6% in the smaller twin and 22.2% in the larger. In our 62 Type-II pregnancies (47 with absent and 15 with reversed flow at first examination) we observed a rate of IUFD of 10% in the smaller twin and 13% in both twins. All the deaths in Type-II cases with absent flow occurred without the typical fetal deterioration in Doppler indices observed in singleton IUGR pregnancies, with DV Doppler flow preserved. The abovementioned studies[10,11] treated the Type-II pattern as a unique, homogeneous category. Our results instead show that the risk of IUFD was higher for pattern Type II reversed compared with that for Type II absent, highlighting the need to differentiate these cases at all times.

Type-III pattern is unpredictable, given the hemodynamic implications of the large placental artery-to-artery anastomoses[14,21]. Gratacos *et al.* reported an IUFD rate for the small twin of 15.4% and a high incidence of parenchymal brain lesion in the cotwin[10]. Results were similar in the series described by Ishii *et al.*[11] as regards IUFD in the smaller twin (15.4%), with a cerebral injury rate in the larger surviving twin of 38.5%. Interestingly, our cohort contained far fewer Type-III cases than did those of Gratacos *et al.*[21] and Lopriore *et al.*[22] (whose prevalence was around 40%), and was closer to the 14.8% observed by Ishii *et al.*[23]. Leaving aside these differences, which may be connected to the type of population, our study shows that, even with meticulous examination of both UAs, Type-III pattern can be missed early in pregnancy (increasing, in our cohort, from 9% initially to 14% at last examination). These apparently failed diagnoses may be explained by intermittent patterns with longer periods; it has also been documented that the size of the arterioarterial anastomoses and the degree of placental share may correlate with the prominence of the intermittent pattern[14]. All these variables may have played a masking role, preventing early identification of sIUGR Type III, and point to the importance of correct diagnosis, given the perinatal risk reported.

An increased risk of postnatal cerebral injury has been observed in MC twins complicated with sIUGR and/or discordant birth weight[24], whereas a recent review based on postnatal cranial ultrasound data reported severe cerebral injury in only approximately 8% of liveborn infants[25]. Although, in accordance with other series[26], the IUGR twins did not show increased incidence of severe cerebral injury compared with the larger twins, this study did find that mild neurological impairment was more frequent in the IUGR infants.

Our study has both strengths and limitations. Its strength lies in it being a large series, followed by the same experienced sonographers, providing scrupulously documented long-term outcomes. It is limited by consisting of a retrospective cohort covering an 8-year period, with the possibility that a few Type-III cases were misclassified as Type II. Moreover, being a tertiary care series, it may be susceptible to referral bias. Finally, its retrospective nature and lack of a homogeneous, standardized follow-up may have resulted in underestimation of the incidence of impairment.

In conclusion, this study confirms that stratifying Doppler patterns in MC twin pregnancies complicated with sIUGR helps to guide ultrasound surveillance. Even with strict monitoring, however, a certain number of IUFDs is inevitable, and raises the much-debated issue of how best to manage these pregnancies. While the management of Types II and III is by now a recognized clinical challenge, involving complex issues such as selective feticide, parental choice and the risks of very preterm delivery, our study also shows the importance of bearing in mind that a significant proportion of Type-I patterns can deteriorate, thereby presenting the same problems as Types II and III in terms of management options and outcome.

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