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A classification system for selective intrauterine growth restriction in monochorionic pregnancies according to umbilical artery Doppler flow in the smaller twin

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KEYWORDS: intermittent absent or reversed end-diastolic flow; monochorionic twins; selective intrauterine growth restriction

ABSTRACT

Objectives *To evaluate a classification of selective intrauterine growth restriction (sIUGR) in monochorionic (MC) twins based on the characteristics of umbilical artery (UA) Doppler flow in the smaller twin, in terms of association with clinical outcome and with the pattern of placental anastomoses.*

Methods *One hundred and thirty-four MC twins diagnosed with sIUGR at 18–26 weeks were classified as Type I (UA Doppler with positive diastolic flow,* n = *39), Type II (persistent absent or reversed end-diastolic flow,* n = *30) and Type III (intermittent absent or reversed end-diastolic flow,* n = *65). Perinatal outcome, placental sharing and the pattern of anastomoses were compared with those in 76 uncomplicated MC twins.*

Results *Mean gestational age at delivery was 35.5 (range, 30–38) weeks in controls, 35.4 (range, 16–38) weeks in Type I, 30.7 (range, 27–40) weeks in Type II (*$P < 0.0001$*) and 31.6 (range, 23–39) weeks in Type III (*$P < 0.0001$*) pregnancies. Fetal weight discordance was significantly higher in Type II (38%) and Type III (36%) than in Type I (29%) (*$P < 0.0001$*) pregnancies. Deterioration of the growth-restricted fetus occurred in 90% of Type II cases, compared with 0% and 10.8% of Types I and III, respectively (*$P < 0.001$*). Unexpected intrauterine fetal death of the smaller twin occurred in 15.4% of Type III cases, compared with 2.6% and 0% of Types I and II respectively (*$P < 0.05$*). Parenchymal brain lesions in the larger twin were observed in 19.7% of Type III cases and less than 5% in the other groups (*$P < 0.05$*). Placental discordance (larger/smaller) was 1.3 in controls, compared with 1.8, 2.6 and 4.4 in Types I, II and III, respectively (*$P < 0.01$*). The proportion of cases with arterioarterial anastomoses > 2 mm in diameter was 55% in controls, 70% in Type I, 18% in Type II (*$P < 0.01$*) and 98% in Type III (*$P < 0.01$*).*

Conclusion *sIUGR can be classified on the basis of umbilical artery Doppler into three types that correlate with different clinical behavior and different patterns of placental anastomoses. This classification may be of help in clinical decision-making and when comparing clinical studies. Copyright © 2007 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Selective intrauterine growth restriction (sIUGR) affects about 12–25% of monochorionic (MC) pregnancies[1]. The definition of sIUGR in MC twins is not universally established. Recent studies have used variable criteria in the definition, including estimated fetal weight[2–5], abdominal circumference[6] and/or the degree of fetal weight discordance[2,4,5,7,8]. sIUGR is increasingly recognized as an important complication of MC pregnancies, with a high risk of intrauterine demise and neurological adverse outcome[2–4,7–9]. In spite of an overall association with poor perinatal outcome, MC twins with sIUGR may present important differences in the natural history compared with singletons or dichorionic twins[4,6]. These differences are thought to result from the influence of the intertwin transfusion characteristic of MC twinning. The predominant direction and magnitude of

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blood flow interchange may vary substantially according to the pattern of placental anastomoses, which may lead to either beneficial or detrimental effects for the fetus with growth restriction[10]. Consequently, MC pregnancies with similar degrees of fetal weight discordance may be associated with remarkable differences in clinical behavior and outcome, and thus different clinical forms may coexist within the same diagnosis of sIUGR.

One parameter which best reflects the differences in intrauterine growth restriction (IUGR) in MC with respect to singletons or dichorionic twins is umbilical artery (UA) Doppler flow. The characteristics of UA Doppler flow may be strongly influenced by the existence of intertwin vascular connections, as shown by different studies in MC twins with twin–twin transfusion syndrome[11–13] or sIUGR[4,6,14–17]. In MC fetuses with IUGR, UA Doppler flow may show one of three main waveform patterns, as defined by the characteristics of diastolic flow: positive, persistently absent/reversed or intermittently absent/reversed[6,14–16]. The latter has also been defined as a cyclical pattern[14], and refers to a sign unique to MC twins resulting from the presence of transmitted waveforms from the larger into the smaller twin's cord due to the existence of placental large artery-to-artery (AA) anastomoses[14–16]. A characteristic feature of MC twins compared with other pregnancies is that the above Doppler patterns can be observed from very early in pregnancy and they normally remain unchanged until delivery[6,15,16]. More importantly, they have been strongly associated with important differences in clinical evolution and outcome[3,4,6]. Fetuses with positive UA diastolic flow are generally considered to have a benign prognosis, although there are no prospective studies addressing the outcome of this subgroup. Fetuses with persistently absent or reversed end-diastolic flow (AREDF) in the UA have been reported to have a high risk of hypoxic deterioration and consequently intrauterine demise[3,6,18]. Finally, in two recent studies we provided evidence that fetuses with intermittent absent or reversed end-diastolic flow (iAREDF) normally show an atypical clinical evolution with an increased risk of sudden death of the IUGR twin[4,16], and an increased rate of parenchymal brain damage in the normally grown twin[16].

We postulated that a classification of sIUGR in three types according to the above Doppler patterns might improve the accuracy of current definitions, and prospectively evaluated the association of such classification with the clinical outcome in a consecutive series of 134 monochorionic twins with sIUGR. We also evaluated the association of each Doppler pattern with the potential existence of differences in the distribution of placental anastomoses, which could help our understanding of the different outcomes.

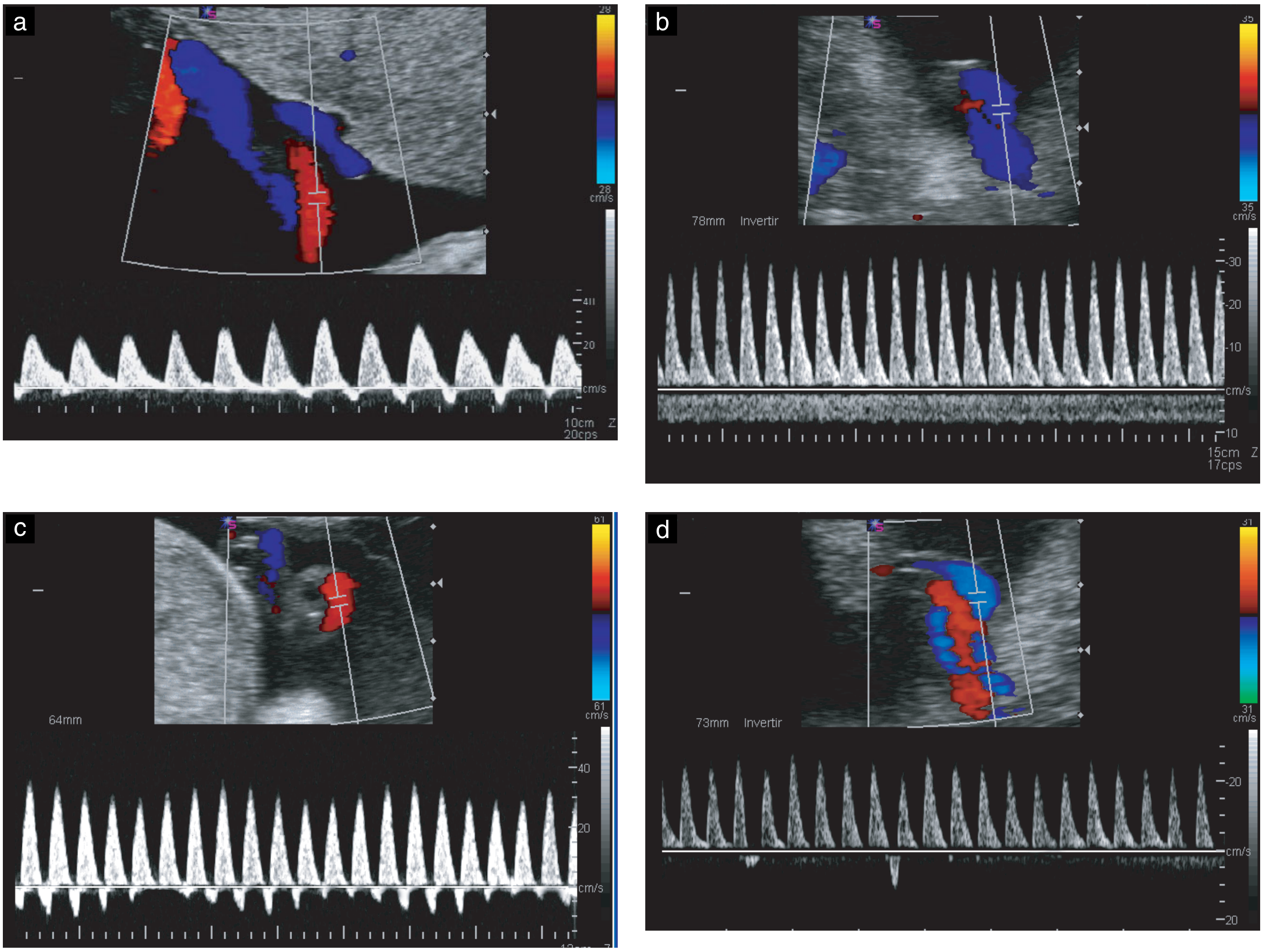
METHODS

This was a prospective study conducted over a 3.5-year period in three fetal medicine units as part of a larger project on MC pregnancy. The study protocols were approved by institutional review boards and the Ethics Oversight Committee of the European Commission, Fifth Framework Program (QLG1-CT-2002-01632, EuroTwin2Twin). All patients gave informed consent for placental collection. A total of 151 cases were diagnosed within 16 and 28 weeks' gestation during the study period. During 1 year, 17 of these were treated with laser within a prospective clinical study and subsequently excluded from analysis, which left a total of 134 cases. The first 21 cases with sIUGR described in this study have been reported in a clinical series on the association of iAREDF with neurological outcome[4].

sIUGR was defined as an estimated fetal weight below the 10^{th} percentile in one twin[19,20]. This was determined as $(A-B) \times 100/A$, where A is the estimated fetal weight of the larger twin and B is the estimated fetal weight of the smaller twin. Pregnancies with signs of twin–twin transfusion syndrome (TTS) were not included in this study. TTS was diagnosed on the basis of the following criteria: MC twin pregnancy; diagnosis established before 26 weeks; polyhydramnios in the recipient's sac (deepest vertical pool > 8 cm at < 20 weeks' gestation, > 10 cm at 20–25 weeks' gestation) and oligohydramnios in the donor's sac (< 2 cm); and discordant bladders, with a distended bladder in the recipient and a non-visible bladder in the donor during most of the examination.

Cases were subsequently classified into one of three types according to the characteristics of UA Doppler flow as evaluated on the first examination: Type I (positive end-diastolic flow in the umbilical artery), Type II (AREDF constantly observed during all the examination) or Type III (iAREDF). iAREDF was defined as the clear observation of AREDF alternating over a short period of positive diastolic flow, in the absence of fetal and maternal breathing (Figure 1). Doppler waveforms were always assessed by a minimum of three measurements at each UA with special care to avoid fetal or maternal movements. Pulsed Doppler examination of both UAs was performed in a free loop of the umbilical cord. The angle of insonation was zero or as near to zero as possible in all cases. All cases were followed and managed according to standard clinical protocols. Doppler investigation was repeated at all subsequent ultrasound examinations.

Fetal well-being was monitored mainly by Doppler examination, including serial evaluation of Doppler waveforms in the UA, middle cerebral artery and ductus venosus, in combination with fetal biophysical profile, and, from 28 weeks' gestation onwards, fetal heart rate patterns. Hospital admission was contemplated beyond 28 weeks if there was persistent AREDF in the UA Doppler examination, brain-sparing effect or abnormal ductus venosus Doppler flow. Fetal deterioration indicating the need for active management was defined as the presence of signs suggestive of severe hypoxia due to placental insufficiency, with a variable definition according to gestational age. Before 28 weeks, it was defined as absent or reversed atrial flow in the ductus venosus; after 28 weeks, it was defined by any of the following: persistent reversed end-diastolic



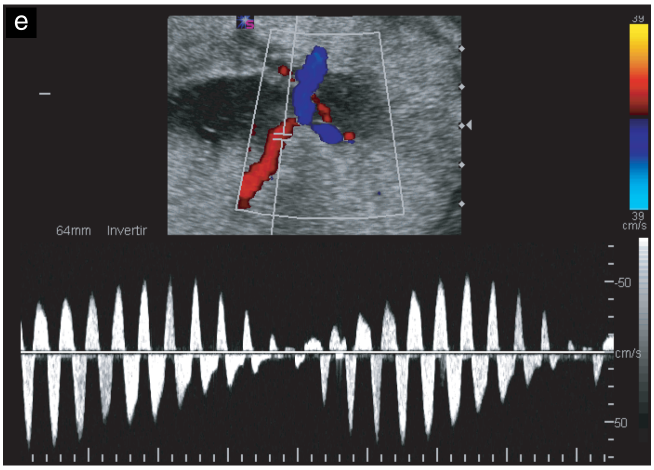


Figure 1 Different umbilical artery Doppler waveforms in monochorionic fetuses with selective intrauterine growth restriction and intermittent absent or reversed end-diastolic flow (iAREDF). (a) Typical image of iAREDF with cycles showing absent and/or reversed flow. (b,c) Using the fastest sweep speed allows better appreciation of the cyclical nature of the changes, as present in most cases, which may range from (b) absent to (c) clearly reversed diastolic waveforms. The systolic waveforms also show a characteristic oscillating aspect which results from the influence of the transmitted waveforms in the peak velocity. (d) In a proportion of cases, the intermittent appearance of absent or reversed waveforms is not cyclical and follows a more irregular pattern, occasionally appearing irregularly over periods of minutes rather than seconds. (e) The large placental arterioarterial anastomoses causing this Doppler phenomenon can virtually always be found and insonated[26], showing the characteristic bidirectional and periodic pattern resulting from the collision of the two systolic waveforms.

flow in the umbilical artery, ductus venosus pulsatility index (PI) persistently above two SD for gestational age, and/or persistently abnormal fetal heart rate traces and biophysical profile. The management protocol considered the option of fetoscopy-guided cord occlusion in the smaller twin if severe fetal deterioration was observed before 28 weeks. Timing of delivery was decided by the attending physicians.

Most neonates delivered at one of the institutions participating in the study. In a small proportion delivery occurred at the referring hospital and in these cases the perinatal outcome was retrieved from the managing physicians. Perinatal outcome was recorded in all groups. Unexpected fetal death was defined as fetal demise occurring in the absence of fetal deterioration at the last fetal evaluation, as defined above. All neonates underwent ultrasound brain scans on at least one, and preferably two, occasions, at or before the fourth day and at the age of 28 ± 7 days. Abnormal findings on ultrasound scan, suggesting parenchymal brain damage, were recorded, particularly if suggestive of periventricular leukomalacia[21].

Placental examination within 24 h after delivery was performed whenever possible. Fresh placentas including their vascularization were carefully examined. As a control group, the placentas from 76 uncomplicated MC twin pregnancies were studied. In a proportion of cases and in all controls, perfusion studies with dye were performed, as described previously[22]. The existence and type of anastomoses at the level of the vascular equator were recorded. For comparison among study groups, the pattern of anastomoses was assessed by means of a semiquantitative system. We recorded the presence of four types of anastomoses: artery to vein (AV), AA, AA larger than 2 mm, and vein to vein. AA anastomoses measuring > 2 mm were recorded in order to assess the proportion of large AA connections in each group. The cut-off of 2 mm was chosen arbitrarily. In previous studies we found that this cut-off differentiated reasonably well the large AA anastomoses present in virtually all cases with iAREDF[16].

After examination a digital picture of the whole placenta was taken and the image was analyzed with a software program to calculate the relative placental area for each fetus. All measurements were performed digitally by comparison with a standard (ruler) using Adobe Photoshop 6.0 software (Adobe Systems Inc., San Jose, CA, USA). The placental discordance (placental surface of the larger twin/placental surface of the smaller twin) was calculated. The ratio between fetal weight discordance and placental discordance was also calculated, in order to estimate the potential influence of placental anastomoses on the actual fetal weight discordance[23].

Chi-square or Fisher's exact test was used as appropriate for comparison of categorical variables. All continuous data were tested for normality, and are expressed as mean (range). One-way ANOVA (Bonferroni) was used for comparisons among study groups. $P < 0.05$ was considered significant. All statistical analyses were performed using SPSS version 13.0 (SPSS for Windows; SPSS Inc., Chicago, IL, USA).

RESULTS

Of a total of 134 cases included, 39 were classified as Type I, 30 as Type II and 65 as Type III. One Type I case progressed to absent end-diastolic flow (AEDF) at 30 weeks, but it was retained as Type I for analyses. No other changes in the pattern of UA Doppler flow were observed. The pregnancy course and perinatal outcome in the groups of sIUGR is summarized in Table 1. Type II and III pregnancies delivered significantly earlier than those defined as Type I ($P < 0.0001$) and consequently fetal birth weights were also lower ($P < 0.0001$). Fetal weight discordance was significantly higher in twins defined as Type II or III in comparison with Type I cases ($P < 0.0001$). Fetal deterioration as defined in this study, requiring active management, occurred in 90% of Type II cases, compared with 0% of Type I and 10.8% of Type III ($P < 0.0001$). In all cases, fetal deterioration was diagnosed on the basis of an abnormal ductus venosus, according to the criteria defined above. In 13 of these patients (nine Type II and four Type III) a cord occlusion was performed.

Unexpected intrauterine fetal death (IUFD) occurred in 15.4% (10/65) of Type III cases. In all 10 cases the smaller twin died, and in four of these the larger twin also died. In each case, IUFD occurred in fetuses with a previous scan showing normal PI values in the middle cerebral artery and in the ductus venosus. The median gestational age at diagnosis of fetal death was 24 (range, 20–30) weeks and the time between the last ultrasound scan and the diagnosis of fetal death was 5 (range, 0–7) days. Unexpected fetal death occurred in 2.6% of Type I cases

Table 1 Pregnancy course and perinatal outcome according to umbilical artery Doppler classification

Parameter	*Normal* (n = 76)	*Type I* (n = 39)	*Type II* (n = 30)	*Type III* (n = 65)
GA at diagnosis (weeks, mean (range))	—	23 (16–27)	20 (16–25)	22 (16–26)
GA at delivery (weeks, mean (range))	35.5 (30–38)	35.4 (16–38)	30.7 (27–40)*	31.6 (23–39)*
Birth weight (g, mean (range))				
Larger twin	2439 (1450–3530)	2385 (1200–3350)	1468 (760–2900)*	1713 (930–3450)*
Smaller twin	2187 (1260–3233)	1688 (800–2400)	787 (390–1360)*	1017 (450–2130)*
Fetal weight discordance (%, mean (range))	10 (1–22)	29 (25–37)*	38 (25–58)*	36 (25–64)*
In-utero deterioration of IUGR fetus (*n* (%))	—	0/39 (0)	27/30 (90.0)†	7/65 (10.8)
Unexpected IUFD (*n* (%))				
Larger twin	—	1/39 (2.6)	0/30 (0)	4/65 (6.2)
Smaller twin	—	1/39 (2.6)	0/30 (0)	10/65 (15.4)§
Intraventricular hemorrhage (*n* (%))				
Larger twin	—	0/38 (0)	1/30 (3.3)	2/61 (3.3)
Smaller twin	—	0/38 (0)	3/21 (14.3)‡	3/50 (6.0)
Parenchymal brain damage (*n* (%))				
Larger twin	—	0/38 (0)	1/30 (3.3)	12/61 (19.7)§
Smaller twin	—	0/38 (0)	3/21 (14.3)‡	1/50 (2.0)

*$P < 0.0001$ vs. uncomplicated and Type I; †$P < 0.0001$ vs. Type I and Type III; ‡$P < 0.05$ vs. Type 1; §$P < 0.05$ vs. Type I and Type II. GA, gestational age; IUFD, intrauterine fetal death; IUGR, intrauterine growth restriction.

and 0% of Type II ($P = 0.03$ and $P = 0.01$ respectively vs. Type III). The prevalence of parenchymal brain lesions on neonatal ultrasound scans in the larger twin was 19.7% in Type III pregnancies, compared with 0% in Type I and 3.3% in Type II ($P < 0.01$ and $P = 0.03$ respectively). Of 12 cases with brain lesions in Type III pregnancies, two occurred in single twin survivors and 10 in double twin survivors. The prevalence of parenchymal brain lesions on neonatal ultrasound scans in the smaller twin was 14.3% in Type II pregnancies, compared with 0% in Type I and 2.0% in Type III ($P = 0.04$ and $P = 0.07$ respectively). In the remaining fetuses the prevalence of parenchymal brain damage was below 5%.

The control group of 76 uncomplicated MC pregnancies used for placental comparisons had a mean gestational age at delivery of 35.5 (range, 30–38) weeks. Mean birth weights were 2439 (range, 1450–3530) g and 2187 (range, 1260–3233) g, and mean fetal weight discordance was 10% (range, 1–22%). The placenta was available for analysis in 95 (71%) cases, 23 Type I, 22 Type II and 50 Type III. Placental features are shown in Table 2. The discordance in the placental territories was 1.3 in controls, and it increased with each type: 1.8 in Type I, 2.6 in Type II ($P < 0.01$ vs. controls and Type I) and 4.4 in Type III ($P < 0.01$ vs. the other three groups). The ratio between fetal and placental discordance followed a similar pattern, from 0.94 in controls, to 0.79 in Type I, 0.71 in Type II ($P < 0.05$ vs. uncomplicated) and 0.44 in Type III ($P < 0.01$ vs. other three groups). The pattern of anastomoses differed in each study group (Table 2). Type I cases had a similar proportion of anastomoses to uncomplicated cases. Type II cases had a lower frequency of large AA anastomoses (18%; $P < 0.001$ vs. other groups). On the contrary, Type III cases had a significantly increased proportion of AA anastomoses of any size and of large AAs ($P < 0.01$ vs. other three groups)

DISCUSSION

This study provides evidence that UA Doppler patterns in MC twins with sIUGR can be used to classify three types with remarkable differences in clinical evolution and perinatal outcome. These types are also associated with placental features, which may help our understanding of the differences in clinical outcome. Our results illustrate the importance of using case definition criteria to allow comparison of clinical studies on sIUGR in MC twins. The classification proposed here provides a simple way of identifying different clinical forms within this condition.

The data confirm previous studies suggesting that UA Doppler changes in MC twins have a different evolution and significance than in other pregnancies[14–17]. In singleton and dichorionic twin pregnancies, UA Doppler flow is a key parameter for the diagnosis and surveillance of fetuses with IUGR secondary to placental insufficiency[24]. However, in MC twins with IUGR, the changes in UA Doppler waveforms cannot be interpreted in the same terms as in other pregnancies, as they represent a combination of the effects of placental insufficiency and those of the intertwin vascular connections[11–17]. Gaziano *et al.* noted that the prevalence of abnormal UA Doppler flow and reduced cerebrovascular Doppler ratios was increased in MC twins compared with dichorionic twins[17]. Vanderheyden *et al.* reported that in IUGR MC twins with persistent AEDF, the latency time between diagnosis of AEDF and delivery is significantly increased compared with that in singletons and dichorionic twins[6]. However, this increase was attributable to an earlier diagnosis of AEDF: 20 weeks in MC twins compared with 27 weeks in the other pregnancies. Similar findings have also been reported in studies describing the characteristics of iAREDF in MC twins[15,16]. Thus, UA Doppler changes in MC twins with sIUGR are present from very early in pregnancy but do not usually progress further.

Type I pregnancies as defined in this study seem to represent the lower end of the spectrum of severity. The good prognosis observed in this group is in agreement with a previous study by Huber *et al.*[18]. The authors reported the outcome of 54 twin pairs discordant for amniotic fluid, which could actually be classified as Type I according to the criteria defined in this study. The overall intrauterine mortality rate (5/108, 4.6%) is very similar to the 2.6% (2/78) reported here. In this study, only one of 39 fetuses (2.6%) classified as Type I developed AEDF during a mean observation period of 11 weeks. This suggests that, once the presence of positive diastolic flow is confirmed, patients can be reassured of a likely favorable outcome. Cases in this group were associated with patterns of anastomoses similar to those in uncomplicated MC

Table 2 Placental features and proportion of the types of placental anastomoses according to umbilical artery Doppler classification

Parameter	*Normal* (n = 76)	*Type I* (n = 23)	*Type II* (n = 22)	*Type III* (n = 50)
FW ratio (mean (range))	1.1 (1.0–1.29)	1.4 (1.3–1.6)*	1.6 (1.3–2.3)*	1.6 (1.3–2.7)*
PT ratio (mean (range))	1.3 (0.6–3.0)	1.8 (1.1–2.6)	2.6 (1.6–4.2)*	4.4 (1.8–19.0)‡
FW ratio/PT ratio (mean (range))	0.94 (0.38–1.73)	0.79 (0.57–1.37)	0.71 (0.48–1.05)†	0.44 (0.08–0.91)‡
Arteriovenous anastomoses (*n* (%))	71 (93)	22 (96)	22 (100)	44 (88)
Arterioarterial anastomoses (*n* (%))	61 (80)	18 (78)	16 (73)	50 (100)‡
Arterioarterial anastomoses of > 2 mm (*n* (%))	42 (55)	16 (70)	4 (18)*	49 (98)‡
Venovenous anastomoses (*n* (%))	15 (20)	5 (22)	3 (14)	12 (24)

Data on placental anastomoses represent the proportion of cases with at least one such type of anastomosis. *$P < 0.01$ vs. uncomplicated or Type I; †$P < 0.05$ vs. uncomplicated; ‡$P < 0.01$ vs. uncomplicated, Type I and Type II. FW, fetal weight; PT, placental territory.

pregnancies. In the presence of bidirectional fetal flow interchange, blood transfer from the larger twin may act as a 'rescue transfusion' of better oxygenated blood, which compensates for the effects of placental insufficiency in the smaller fetus[10,23]. The influence of such rescue transfusion is supported by a mean ratio between fetal and placental discordance of 0.79, whereas this ratio approached 1 in uncomplicated MC twins. A ratio below 1 suggests that the actual fetal weight discordance is lower than expected for the discordance of placental territories. We suggest that the lack of statistical significance between Type I and uncomplicated MC pregnancies ($P = 0.057$) might be due to the relatively small sample size, as the reduction is consistent with that observed in the other study groups.

Fetuses defined as Type II were characterized by a relatively constant clinical evolution. In a majority of cases the IUGR fetus showed progressive deterioration that led the managing physicians to consider active therapy before IUFD occurred. Placental analysis in this group showed a relatively similar distribution of anastomoses to that of Type I cases, but with a more severe form of placental discordance. This may help to understand the early onset of AEDV. On the other hand, and similar to Type I cases, the fetal weight/placental discordance ratio was significantly lower than in uncomplicated cases. Therefore, intertwin blood transfusion has a beneficial effect that compensates the placental insufficiency of the IUGR fetus, and is also likely to be responsible for the considerable prolongation of *in-utero* survival once the diagnosis of AEDV has been established. As previously reported[6] and confirmed in this study, the latency time between diagnosis and delivery in these fetuses is much longer than in singletons or dichorionic twins presenting with AEDV. However, in spite of an increased latency time, a substantial number of these cases deteriorate *in utero*[18], suggesting that from a certain gestational age intertwin blood flow interchange cannot completely compensate for the severe placental insufficiency of the IUGR fetus. In reality, although the perinatal outcome in this series might indicate to the contrary, Type II cases have the worst prognosis. However, contrary to what we observed in Type III fetuses, fetal deterioration in Type II MC twins (persistent AREDF) could be predicted in most cases by close fetal monitoring, allowing timely cord occlusion or elective delivery. Elective laser coagulation of the placental anastomoses for cases defined as Type II in this study has been proposed as an alternative to cord occlusion[3]. The potential benefit of this approach is being evaluated in an international clinical trial.

Finally, this study confirmed previous observations that MC twins presenting with iAREDF, and defined as Type III in this study, have a distinct condition among sIUGR MC twins[15,16]. We have reported that these pregnancies are characterized by an atypical clinical evolution of the IUGR twin, which normally fails to show Doppler signs suggesting fetal deterioration[4], as would be expected for fetuses with similar degrees of growth restriction. However, a proportion of these IUGR fetuses die unexpectedly[5], often hours or days after a normal examination. In addition, the larger twin has a significantly increased incidence of abnormal neonatal brain scans, suggesting white matter injury, even if both twins are born alive[6]. These complications are likely to result from the hemodynamic consequences of the large AA anastomoses producing the intermittent umbilical Doppler pattern. The existence of large AA connections is the distinctive feature of fetuses presenting with iAREDF, and classified as Type III in this study[14–16]. AA anastomoses behave as functional AV anastomoses[25], and they may strongly interfere with the natural history of the IUGR fetus[10]. In MC twins with sIUGR, the collision point where the two systolic waveforms meet is not equidistant from the two cord insertions, but shifted towards the smaller twin's cord[15,25]. Thus, the larger twin perfuses part of the fetoplacental volume of the smaller one, resulting in a particular type of 'rescue transfusion' that prolongs *in-utero* survival of the IUGR fetus. In fetuses with large AA connections, the increase in vessel diameter results in exponential increases in the volume flow per minute, and consequently these hemodynamic consequences are magnified. The fetal weight discordance to placental discordance ratio in this group (0.44) was remarkably lower than that in the other sIUGR groups (0.79 and 0.71), reflecting the important impact of large AA connections in fetal growth. However, a large AA anastomosis represents a highly unstable hemodynamic balance that facilitates the occurrence of acute fetofetal transfusion episodes in the presence of variations in fetal heart rate or blood pressure at any fetal side, as documented previously[2]. Such acute accidents might be responsible both for acute vascular overload of the smaller twin resulting in fetal death and for severe hypovolemic events in the larger twin causing fetal brain damage, as already suggested in an earlier report describing the existence of UA intermittent diastolic flow in MC twins[14]. Thus, although the natural history of Type III cases is associated with a better overall perinatal outcome than that of Type II cases, the actual prognosis may be worse because of the unpredictability of these adverse outcomes. Management of Type III fetuses represents a challenge, and studies to evaluate the potential impact of different clinical strategies are now under way.

In summary, we have proposed a classification based on the pattern of UA Doppler flow in the IUGR fetus, which may improve accuracy for the diagnosis of sIUGR in MC twins, and consequently allow better comparison of clinical studies on this condition. This study is limited by the sample size, although the rarity of these conditions precludes the accumulation of a large number of cases over a reasonable period for a clinical study. The relative prevalence of the types described here could be biased towards more severe cases because these were recruited from referral centers. For the same reason, we cannot exclude that the proportion of adverse events within each type might be somewhat magnified. It is likely that this classification needs refinement in the future, in order to span all the potential clinical variations of this complex condition. However, we believe that in its present form it helps in the recognition of individual differences observed in clinical practice in MC pregnancies complicated by sIUGR, and it correlates reasonably well with the clinical evolution and outcome in most cases.

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