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Placental characteristics in monochorionic twins with selective intrauterine growth restriction in relation to the umbilical artery Doppler classification

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ABSTRACT

Introduction: The objective of this study was to evaluate the placental characteristics of monochorionic twin pregnancies with selective intrauterine growth restriction (sIUGR) classified according to the Gratacós classification based on umbilical artery Doppler measurements.

Methods: All consecutive placentas from monochorionic twin pregnancies with sIUGR, (defined as a birthweight discordance > 25% and/or an estimated fetal weight in one twin < 10th centile) examined between May 2002 and February 2018 were included in the study. Each placenta was injected with colored dye to study the angioarchitecture. Primary outcomes were placental share discordance and diameter of the arterio-arterial anastomoses in relation to the umbilical artery Doppler types of sIUGR (Gratacós classification).

Results: Of the 83 sIUGR twins included, 27 were classified as Gratacós type I, 24 as type II and 32 as type III. The median gestational age at delivery was 34.3 weeks for type I, compared to 31.2 weeks and 31.6 weeks for type II and type III respectively. A trend towards a higher placental share discordance in type III sIUGR was observed. The median arterio-arterial diameter was 1.7 mm (0.8–2.6) in type I, 1.7 mm (1.2–2.2) in type II and 2.8 (2.0–3.5) mm in type III ($p < 0.01$).

Discussion: Type III sIUGR placentas appear to be characterized by a larger diameter of the arterio-arterial anastomoses and a larger placental share discordance compared to type I and II sIUGR. The insights in the placental architecture of sIUGR placentas may offer new views on the pathophysiology of the disease.

1. Introduction

Monochorionic (MC) twin pregnancies are at increased risk of adverse perinatal outcome when compared to dichorionic twin pregnancies [1]. This increased risk is mainly caused by the vascular anastomoses on the surface of the shared placenta, allowing inter-twin blood transfusion between the two fetuses, which can lead to complications such as twin-twin transfusion syndrome (TTS), twin anemia polycythemia sequence (TAPS) or selective intra-uterine growth restriction (sIUGR) [2,3]. sIUGR occurs in 10–15% of MC twin pregnancies and results from both inter-twin blood flow and unequal placental sharing leading to severe growth restriction in the twin with the small placenta share.

In 2007, Gratacós et al. proposed a classification system for sIUGR [4] based on the umbilical artery (UA) Doppler flow in the smaller twin. Type I is characterized by positive UA Doppler flow, and is considered to have a benign prognosis. Type II is defined as a persistently absent/reversed UA end-diastolic flow (AREDF) and is associated with the highest perinatal mortality and morbidity. Lastly, type III is characterized by intermittent absent/reversed end-diastolic flow (iAREDF) and has an atypical clinical evolution with an increased risk of unexpected fetal demise of the smaller twin and an increased risk of cerebral injury in the larger twin [4–6].

Several studies previously described the placental angioarchitecture in MC twins with sIUGR [2,3,7,8]. However, no other studies, aside from Gratacós et al., in 2007, evaluated the association between placental characteristics and umbilical artery Doppler classification.

The aim of the study is to evaluate the placental characteristics in MC twins with sIUGR according to the Gratacós classification.

2. Methods

All placentas from MC pregnancies with a birthweight discordance > 25% and/or an estimated fetal weight in one twin < 10th

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centile consecutively examined at our specialized center between May 2002 and February 2018 were eligible for the study. We excluded MC pregnancies with co-existing TTS or TAPS, cases where the umbilical artery Doppler classification was not recorded, cases with incomplete placental data (either due to placental damage or loss of the placenta) and cases in which placental measurements on the digital picture could not be performed. Cases with single or double intra-uterine fetal demise (IUFD), defined as fetal death before 24 weeks of gestational age, were excluded when severe placental maceration made measurements impossible.

The following baseline characteristics were collected from our database: maternal age, gravidity, parity, gender, gestational age at diagnosis, gestational age at birth, mode of delivery, birth weight, birth weight discordance, intertwin hemoglobin (Hb) difference, perinatal survival and severe cerebral injury, defined as periventricular leukomalacia (PVL) ≥ grade 2, intraventricular hemorrhage (IVH) ≥ grade 3, ventricular dilatation, arterial or venous infarct or other severe cerebral injury. Birth weight discordance was calculated as follows: (birth weight larger twin – birth weight smaller twin)/birth weight larger twin x 100%. The Gratacós classification was established based on routine UA Doppler evaluations, with type I defined as a positive end-diastolic flow (PEDF), type II as AREDF and type III as iAREDF. iAREDF was identified within the same acquisition of UA Doppler and checked within a short interval in the same exam. The cord was assessed at the insertion site of the placenta. In case this was not possible, a free loop close to the insertion of the placenta was assessed. When the classification changed over time, the most prevalent type was chosen with help of an ultrasound operator.

Each of the MC placentas was routinely injected with colored dye to examine the pattern of placental anastomoses. Specific colors correlated with specific vessels, allowing for careful observation of different types of anastomoses. The cords of the twins were marked differently at birth: one clamp for the first born and two clamps for the second born twin. The fetal territories were demarcated by the margins of the twin-specific colored dyes and expressed by a percentage of the total placental surface. After the colored dye injection, the placentas were photographed and the images digitally saved for computer analysis. The placental measurements were conducted using Image J version 1.57.

We measured the diameter of each arterio-arterial (AA) anastomosis and venovenous (VV) anastomosis and we recorded the proportion of cases with an AA anastomosis > 2 mm in diameter. This specific cut-off was solely chosen in analogy with Gratacós et al. [4] to compare our results. The total AA or VV diameter was calculated in case the placenta possessed multiple AA or VV anastomoses by adding the subsequent diameters together. The umbilical cord insertion ratio was determined by dividing the total distance of the placenta by the distance between the two cord insertions. The umbilical cord insertions were divided into velamentous, marginal and (para)central [9]. The fetal weight ratio was calculated using the following formula: fetal weight larger twin/fetal weight smaller twin. Similarly, placental territory ratio was calculated by dividing the placental territory of the larger twin by the placental territory of the smaller twin.

Primary outcomes were the placental share discordance and the diameter of the AA anastomoses. The primary outcomes were compared according to the Gratacós classification system.

Data are presented as median (range). Data were analyzed using a Chi-square test for categorical variables, a Kruskal Wallis test for numerical variables and a GEE-analysis for survival data. A p-value < 0.05 was considered statistically significant. Statistical data was analyzed using IBM statistics v23.0 (SPSS, Inc., an IBM company, Chicago, IL, USA).

3. Results

A total of 109 placentas were eligible for the study based on the aforementioned inclusion criteria. Fifteen cases were excluded because

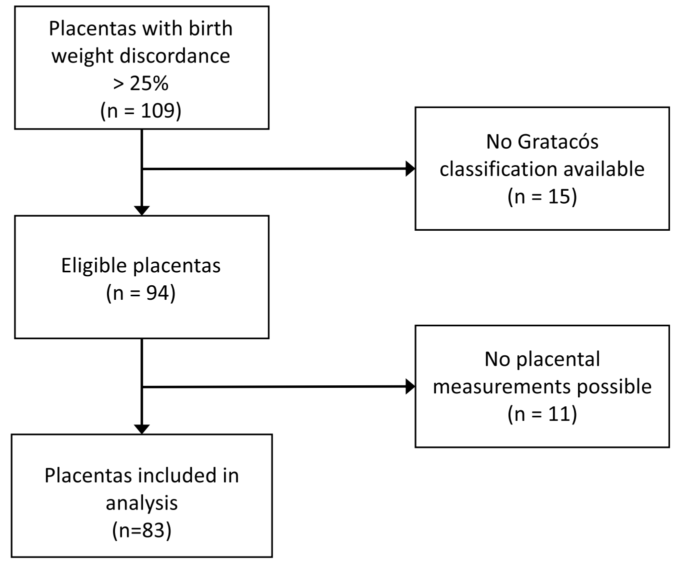

Fig. 1. Flowchart of placenta inclusion.

a Gratacós classification was not recorded and eleven cases were excluded because measurements could not be performed due to damage of the placenta, leaving 83 placentas to be included in the study (Fig. 1).

Of the 83 pregnancies and placentas included, 28 were classified as type I, 24 as type II and 31 as type III (see Fig. 2). Table 1 summarizes the baseline characteristics of the pregnancies according to the Gratacós classification. Type II and type III had a significantly lower gestational age at birth than type I. Gestational age at birth for type I was 34.3 (32.7–35.9) weeks compared to 31.2 (28.4–34.0) and 31.4 (28.8–34.1) weeks for type II and type III respectively ($p < 0.01$). Type II sIUGR cases demonstrated the highest birth weight discordance, namely 38.2% (31.7–44.7) as opposed to 32.8% (27.8–37.8) in type I and 31.9% (26.4–37.4) in type III ($p = 0.035$).

Table 2 summarizes the placental characteristics according to the Gratacós classification. At least one AA anastomosis was detected in all sIUGR placentas. In a few placentas (6.0%, 5/83), more than one AA anastomosis were present.

The diameter of the AA anastomoses was significantly higher in type III compared to type I and II, namely 2.8 mm (2.0–3.5) in type III versus 1.7 (0.8–2.6) in type I and 1.7 (1.2-2.2) in type II ($p < 0.01$). Moreover, type III demonstrated the highest proportion of AA anastomoses with a diameter larger than 2 mm, namely 77.4% as opposed to 42.9% in type I and 29.2% in type II ($p < 0.01$). The median fetal weight ratio was 1.5 (1.4–1.6) in type I, 1.6 (1.4–1.8) in type II and 1.5 (1.3–1.6) in type III ($p = 0.027$). The median placental territory ratio differed between the groups with 2.4 (1.7–2.9) in type I, 2.2 (1.5–2.9) in type II and 2.8 (2.2–3.5) in type III ($p = 0.044$). When dividing these (fetal weight ratio/placental territory ratio), type III sIUGR cases had a significantly lower ratio ($p = 0.025$), meaning that type III sIUGR cases have a lower fetal weight discordance than expected for the amount of placental territory discordance.

Mortality rate and the incidence of cerebral injury was low and similar in the three groups (Table 1). One twin pair (type I) had missing data concerning the perinatal mortality. In all cases, the cerebral injury affected the larger twin. The first case (type II) experienced an arterial infarction on the first day after birth. In the second case (type III) the cerebral injury was caused by ventricle dilatation one week after birth due to intraventricular hemorrhage grade 3. The last case (type III) suffered from a periventricular leukomalacia grade III which was not present antenatally but developed several weeks after birth.