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Discordance of umbilical coiling index between recipients and donors in twin-twin transfusion syndrome

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ABSTRACT

Introduction: To compare the intertwin umbilical cord coiling in twin-twin transfusion syndrome (TTTS) before fetoscopic laser treatment and to correlate these with Doppler findings in both twins.

Methods: We performed a prospective study using three-dimensional (3D) ultrasound with color Doppler imaging of the umbilical cord in TTTS. Coiling index was measured as a reciprocal value of one complete vascular coil. Ultrasound hypocoiling was thus defined as < 0.2 coils/cm and hypercoiling as > 0.6 coils/cm, respectively. Umbilical artery pulsatility index (PI) and peak systolic velocity, middle cerebral artery peak systolic velocity and ductus venosus PI of flow-velocity waveformes of both twins were measured.

Results: We included 65 women in the study. The average gestational age was 21.1 ± 2.7 weeks. In 65 recipients and 56 donors coiling index could be quantified. The median (interquartile range) coiling index of recipient twins was significantly higher than of donors, 0.55 (0.41–0.68) vs. 0.26 (0.2–0.5); P < 0.0001. The proportions of abnormal intertwin coiling were significantly (P = 0.0015) different. Out of 65 recipient with coiling indices evaluation, 1 (1.5%) showed hypocoiled and 27 (41.5%) hypercoiled cords. In contrast, 27 donor twins (48.2%) showed hypocoiled and 5 (8.9%) hypercoiled umbilical cords. There were no significant correlations between the fetal Doppler values and coiling indices.

Discussion: Evaluation of umbilical cord coiling index using 3D color Doppler in both twins complicated by TTTS is feasible in both, donors and recipients. Coiling indices differ significantly between recipient and donor twins and do not correlate with Doppler findings.

1. Introduction

In 1882 Friedrich Schatz published the first description of a case of twin-twin transfusion syndrome (TTTS) [1]. He also reported discordant umbilical cord appearance and noticed that the newborn twin with the polyhydramnios showed a greater twist of umbilical coils as compared to its co-twin. In general, TTTS complicated approximately 10% of monochorionic twins and is a consequence of blood shift from the donor to the recipient via placental anastomoses [2]. From the pathophysiological point of view hypovolemia activates the donor's renin-angiotensin system to restore the intravascular blood flow. In contrast the recipient shows blood volume overload combined with angiotensin transfer from the donor passed through connecting placental vessels resulting in chronic fetal hypertension [3].

There are a variety of hypotheses for the origin of cord coiling, such as fetal rotational movements, genetic factors, muscular fiber patterns in the umbilical arterial wall or fetal hemodynamic forces [4]. Monochorionic twins are genetically identical and TTTS offers a unique opportunity to neglect the hereditary influence and particulary highlight the hemodynamics in the development of cord coiling. Previously, two-dimensional ultrasound was used to investigate the intertwin coiling patterns in TTTS [5] and more recently recipients' umbilical artery elongation depicted by three-dimensional (3D) color Doppler emphasized the impact of fetal blood pressure on the cord anatomy [6].

The aim of our study was to compare 3D color Doppler sonographic coiling index between recipients and donors before laser therapy and to correlate these with Doppler findings in both twins.

2. Methods

Our center is a tertiary referral center for fetal medicine. All patients gave written informed consent to fetoscopic laser treatment and that their clinical data may be used for research purposes. Because this was a prospective observational study of standardized measurements, formal ethical approval was not required. TTTS staging was performed according to the Quintero criteria [7]. Ultrasound data from all

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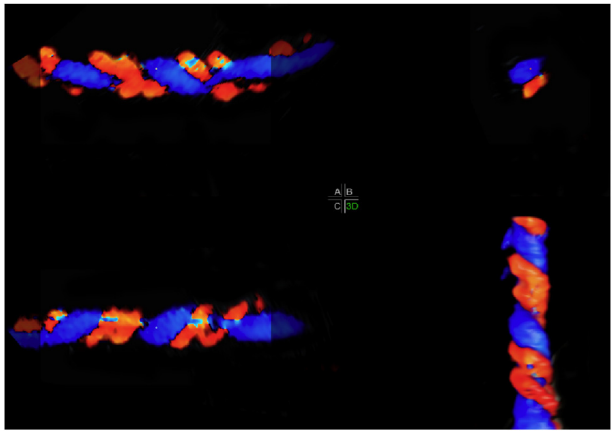

Fig. 1. Multiplanar mode showing 3D color Doppler ultrasound image demonstrating the three orthogonal planes and the rendered volume at the bottom right.

pregnancies were entered prospectively into our computer database (ViewPoint 5.6.8.428: ViewPoint Bildverarbeitung GmbH, Wessling, Germany). We acquired color Doppler 3D volumes of umbilical cords in TTTS cases on the day before or the day of laser therapy non-consecutively between May 2016 and July 2018. A standardized ultrasound setting was used for volume acquisition by a Voluson E10 (GE Healthcare, Milwaukee, WI). In recipients a 5 cm straight segment of the umbilical cord at the placental insertion was examined. In contrast the donors' cord volumes were stored as close to the placental cord insertion or alternatively, if present, the longest straight part of the cord was evaluated. When the most representative and motionless cord section appeared, 3D color Doppler volume was conducted using static 3D settings with a 30° sweep. Furthermore, single umbilical arteries were documented.

Multiplanar mode was used for offline analysis of the stored volumes. For the evaluation of the umbilical cord the scanning plane (x-axis) and the reconstructed orthogonal planes (y-and z-planes) were used to rotate and magnify the volume (Fig. 1). The technique described by Strong et al. was used to quantify umbilical cord coiling index [8]. Briefly, umbilical coiling index was calculated as the reciprocal of the distance between a complete artery coil. Therefore, we measured the distance from the inner edge of an arterial wall to the outer edge of the same artery of the next coil (Fig. 2). If the coiling index was too low to measure one complete pitch in one segment of 5 cm, we determined the coiling index as 0.2 (Fig. 3). Coiling index was defined as hypo- ($\leq$10th centile, 0.2 coils/cm), normo- (10^{th}-90^{th} centile, 0.2–0.6 coils/cm) and hypercoiled ($\geq 90^{th}$ centile, 0.6 coils/cm), respectively [9]. All 3D data sets were obtained by an experienced sonographer (CB) who performed

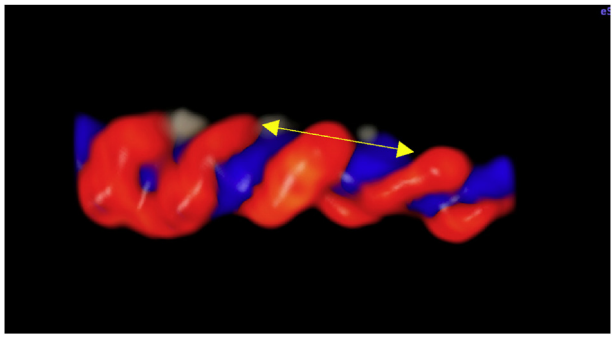

Fig. 2. 3D color Doppler ultrasound using rendering mode of a normocoiled umbilical cord. Depicting the coiling index the length from (cm) from the inner edge of an arterial wall to the outer edge of the same artery of the next coil was evaluated.

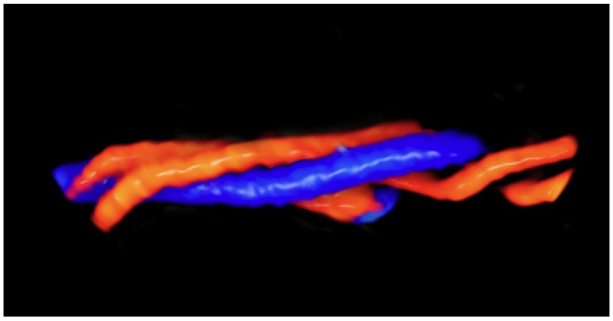

Fig. 3. Example of a hypocoiled umbilical cord in a donor twin. 3D Doppler ultrasound shows a typical pattern in which the vein (blue) was almost straight, whereas the arteries (red) twisted around the vein at a large distance. Therefore, the umbilical cord coiling index was 0.2.

measurements of the coiling indices as well. Furthermore, umbilical artery pulsatility index (PI) and peak systolic velocity, ductus venosus PI of flow-velocity waveformes and middle cerebral artery peak systolic velocity of both twins were measured and their correlation to the 3D coiling index was investigated.

2.1. Statistical analyses

Results are presented as mean ± standard deviation (SD) where a normal distribution was confirmed using the Kolomogorov-Smirnov test or as median and interquartile range (IQR). Simple linear regression and Pearson's correlation were used to investigate the relationship between coiling index and Doppler values. Wilcoxon signed rank sum test compared coiling indices in each twin pair. McNemar's test was used for comparing proportions. P-values < 0.05 were considered as statistically significant. All statistical analyses were performed with the IBM SPSS Statistics package (Version 22, SPSS, Inc., Chicago, IL, USA) and GraphPad Prism (Version 5, La Jolla, CA, USA).

3. Results

Overall, 65 monochorionic diamnotic twin pregnancies were investigated. The mean (± SD) gestational age at presentation was 21.1 ± 2.7 weeks. All women were treated with fetoscopic laser ablation. Baseline maternal characteristics and relevant pregnancy details such as Quintero stages at presentation are displayed in Table 1. There were two fetuses with a single umbilical artery.

In 65 recipients and 56 donors coiling indices could be quantified. The median (IQR) coiling index of recipient twins was significantly higher than of donors, 0.55 (0.41–0.68) vs. 0.26 (0.2–0.5); $P < 0.0001$.

The prevalence of abnormal intertwin coiling was significantly ($P = 0.0015$) different (Table 2). Out of 65 recipients with coiling indices evaluation, 1 (1.5%) had hypocoiled, and 27 (41.5%) showed hypercoiled (Fig. 4) cords. In contrast, 27 donor twins (48.2%) had

Table 1
Characteristics of the study population.

Maternal age, years	31.4 ± 5.6
Gestational age at ultrasound, weeks	21.1 ± 2.7
TTTS Stage:	
I°	8 (12.3)
II°	36 (55.4)
III°	19 (29.3)
IV°	2 (3)
V°	0
Single umbilical artery	1 Recipient, 1 Donor
Estimated weight discordance > 25%	13 (20%)

Data are given as mean (± SD) or n (%).

Table 2
3D Sonographic umbilical cord coiling pattern in recipient and donor twins.

	Recipient (n = 65)	Donor (n = 56)
Hypocoiled Umbilical artery	1 (1.5)	27 (48.2)
Normocoiled Umbilical artery	37 (57)	24 (42.9)
Hypercoiled Umbilical artery	27 (41.5)	5 (8.9)

Data are given as n (%).

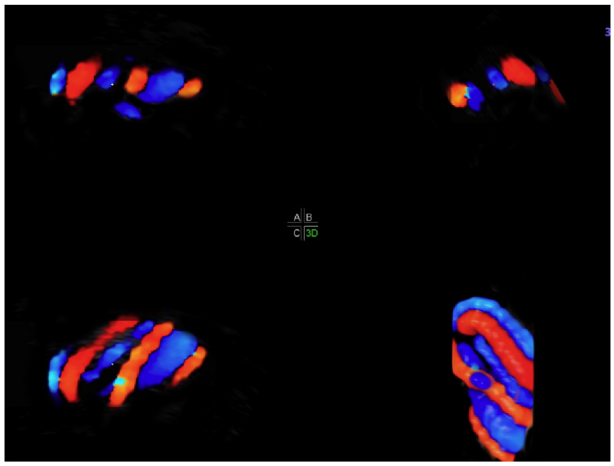

Fig. 4. Example of hypercoiled (coiling index 0.7) umbilical cord in a recipient twin using multiplanar mode.

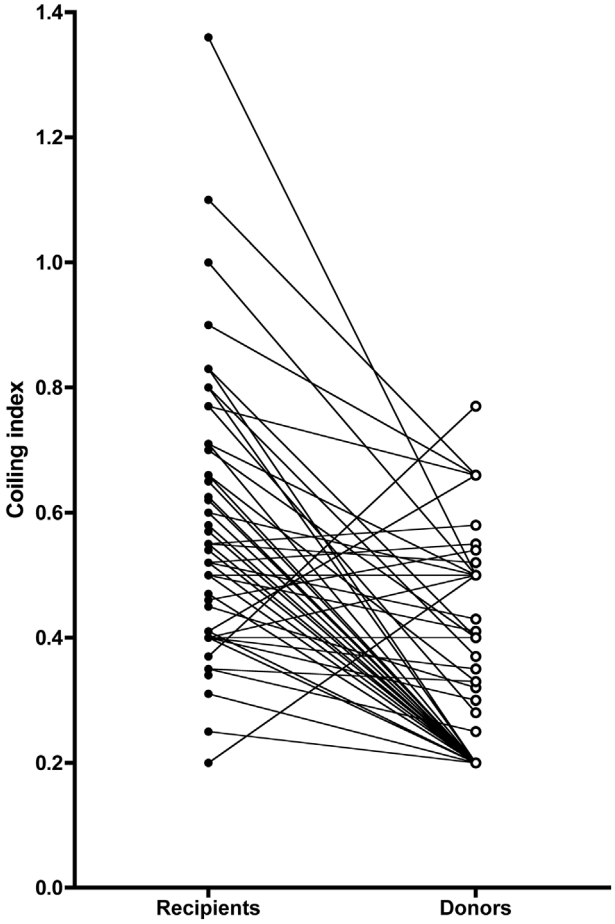

Fig. 5. Scatter plot of umbilical cord coiling index for each recipient-donor twin pair (n = 56).

Table 3
Correlation coefficient and P-values of coiling index and Doppler values.

	Coiling Index Recipient	Coiling Index Donor
Umbilical artery PI	r = −0.17, P = 0.17	r = −0.02, P = 0.83
Umbilical artery peak systolic velocity	r = −0.07, P = 0.56	r = 0.007, P = 0.95
Ductus venosus PIV	r = 0.10, P = 0.39	r = 0.24, P = 0.07
Middle cerebral artery peak systolic velocity	r = −0.01, P = 0.91	r = −0.25, P = 0.12

PI: pulsatility index; PIV: pulsatility index for veins.

hypocoiled and 5 (8.9%) showed hypercoiled umbilical cords. In Fig. 5 scatter plot of coiling indices for each recipient-donor pair is shown.

Furthermore, we found no significant correlations between coiling index and umbilical artery PI, umbilical artery peak systolic velocity, middle cerebral artery peak systolic velocity and ductus venosus PI, neither in donor nor in recipient twins (Table 3). Coiling indices were not significantly different in terms of Quintero stages in recipients and donors, respectively (data not shown).

4. Discussion

Our study shows for the first time that evaluation of umbilical cord coiling index using 3D color Doppler is feasible in both twins in pregnancies with TTTS. Values for coiling indices and coiling patterns differ significantly between recipient and donor twins and do not correlate with umbilical artery, middle cerebral artery or ductus venosus Doppler velocities.

Our results are in line with the findings of few publications which identified a striking discordance in coiling patterns in TTTS. Strong et al. [10] described postnatally in three monochorionic twin gestations that recipient twins had umbilical cords with at least twice as much vascular coiling as the corresponding donor twins. Our data also partly agree with the results from Cromi and coworkers [5]. They evaluated the umbilical cords of 21 monochorionic twin pregnancies with untreated TTTS using two-dimensional ultrasound. In all twin pairs, a discordant umbilical coiling pattern was observed with a prevalence of uncoiled or hypocoiled cords in the donor group and a higher proportion of hypercoiling and uncoordinated coiling in the recipient group [5]. However, the coiling indices in each twin pair and between recipient and donor groups were not compared. Recently, Donepudi and coworkers prospectively examined TTTS patients who underwent fetoscopic laser treatment [6]. Before the procedure, 3D color Doppler volume images of the recipient umbilical cords were acquired. They measured the umbilical artery length and found an arterial elongation in 52%. The authors concluded that these findings may reflect chronicity and severity of hypertension in the recipient fetus. It may be reasonable that the fetal blood volume overload and consecutive systematic hypertension are followed by increased cord coiling. However, the umbilical cord was studied only in recipients and the umbilical cord coiling index was not evaluated.

Reynolds and colleagues [11] reported in singletons that with every heartbeat a longitudinal distention of each umbilical artery occurred owing to the pulse pressure, which led to pressure changes in the umbilical vein. Consequently, venous blood flow from the placenta to the fetus was enhanced and increased with the number of coils. Predanic and coworkers [12] investigated the degree of cord coiling on blood flow of the umbilical vessels in 154 singletons at midgestation. They observed that increased umbilical coiling was associated with a decreased resistance to blood flow, increased peak systolic velocity in the umbilical arteries and increased umbilical venous blood flow. However, a review concluded, that umbilical coiling index indices does not significantly influence arterial Doppler flow in the cord [4]. This is in agreement with our findings which show no significant correlations

between the fetal Doppler measurements in the umbilical artery, middle cerebral artery as well as ductus venosus and coiling indices.

Interestingly, Coetzee and coworkers [13] analyzed umbilical coiling index on twins after birth to test whether coiling was influenced by zygosity. In 164 dichorionic and 64 monochorionic twin placentas coiling indices were not significantly different according to chorionicity. However, it seems unlikely that the coiling of the umbilical cord is genetically determined [14]. Unfortunately, the authors did not report any data on the prevalence of TTTS in their population.

3D color Doppler using multiplanar mode has the advantage that the investigator can view the umbilical cord in the transversal, sagittal and coronal planes at the same time. This is particularly useful if measurements as the coiling index have to be performed. We believe that more accurate measurements can be obtained using 3D ultrasound by rotating and magnifying the region of interest. This technique was especially beneficial in donors with the lack of amniotic fluid. Therefore, we were able to evaluate the coiling index in most cases in both, recipient and donor twins, thus allowing intertwin comparison, which is a strength of our study. However, owing to the fact that we are a referral center the lack of follow-up investigations after laser therapy is a limitation of our study. Unfortunately, we were not able to investigate whether the coiling index in recipients and donors changes after a successful intervention or perform color dye placental injections after birth as patients returned to their referring center one to two days after the procedure. In recipients we used a standardized approach and evaluated the cord at the placental insertion. However, due to the fact that the donor was stuck owing to severe oligo- or anhydramnios we had to restrict ultrasound volume imaging to parts of the umbilical cord which were accessible. It has been published that coiling was increased towards the fetal end of the cord in singletons [15] and coiling patterns were not always uniform over the entire cord length [16]. Therefore, the absolute values of the coiling index should be interpreted with caution, but the intertwin comparison with significant differences in hyper- and hypocoiling in recipients and donors, respectively, was striking.

In conclusion, our study shows for the first time a significant difference of umbilical cord coiling indices between recipient and donor twins using 3D color Doppler volume imaging. The prenatal measurement of coiling indices and intertwin comparison helps to understand the pathophysiology of TTTS and hemodynamics in both twins. Discordance of umbilical cord coiling in TTTS may reflect recipients' hyper- and donors' hypovolemia. Future studies are needed to evaluate whether first trimester coiling index discordance may be an early predictor for the development of TTTS and whether the coiling index in recipients and donors changes after a successful laser treatment.

Conflict of interest

None of the authors has a conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.placenta.2019.01.013.

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