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Umbilical vein blood flow in fetuses with normal and lean umbilical cord

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ABSTRACT

Objective *To evaluate whether umbilical vascular coiling is correlated with the umbilical vein blood flow profile and to investigate if this is different between fetuses with a lean and those with a normal umbilical cord.*

Methods *Consecutive women with a singleton gestation who delivered at term and who underwent an ultrasound examination within 24 h from delivery were studied. Umbilical cord and vessel areas were calculated. Umbilical vein blood flow parameters were obtained by digital color Doppler velocity profile integration. After delivery, the umbilical coiling index was calculated.*

Results *One hundred and sixteen women were studied. Twelve (10.3%) had a lean umbilical cord (area < 10th centile). A significant correlation was found between the umbilical coiling index and the umbilical vein blood flow ($r = 0.67$, $P < 0.001$). A significant difference between fetuses with and without a lean cord was found in terms of: umbilical coiling index (0.18 ± 0.08 vs. 0.29 ± 0.09, $P < 0.005$), cord area (87.6 ± 5.1 mm^2 vs. 200.6 ± 34.6 mm^2, $P < 0.001$), Wharton's jelly amount (25.7 ± 10.3 mm^2 vs. 122.1 ± 33.4 mm^2, $P < 0.001$), umbilical vein blood flow (93.7 ± 17.8 ml/kg per min vs. 126.0 ± 23.4 ml/kg per min, $P < 0.001$), and umbilical vein blood flow mean velocity (6.6 ± 2.7 cm/s vs. 9.0 ± 3.6 cm/s, $P < 0.05$). The proportion of fetuses with an umbilical vein blood flow < 80 ml/kg per min was higher when the cord was lean than when it was normal (25% vs. 1.9%, $P < 0.01$).*

Conclusions *Lean umbilical cords differ from normal cords not only from a structural point of view but also in the umbilical vein blood flow characteristics. This could explain the increased incidence of intrapartum complications and fetal growth restriction among fetuses with a lean and/or hypocoiled cord.*

INTRODUCTION

Traditionally, umbilical vascular coiling has been considered a feature of the umbilical cord which protects it from compressive forces during labor[1,2]. Several authors have reported that hypocoiled or non-coiled umbilical cords at delivery are more frequently present in cases of adverse perinatal outcome[2–4]. Strong *et al.*[3] reported a higher incidence of interventional delivery for fetal distress in fetuses with a hypocoiled umbilical cord than in those with a normocoiled cord. Rana *et al.*[4] described a higher proportion of low cord blood pH and fetal heart rate disturbances in the former than in the latter group of fetuses. Furthermore, the antepartum identification of non-coiled umbilical cords appears to be a risk factor for suboptimal pregnancy outcome. Degani *et al.*[5] found a significant relationship between the sonographic umbilical coiling index and the Doppler flow characteristics in the umbilical vein of term fetuses. Recently, it has been demonstrated in humans and in animal experiments that the growth of the fetus is a function of the umbilical vein blood flow[6].

However, other morphologic features of the umbilical cord (i.e. umbilical cord size[7], umbilical artery morphology[8], presence of the Hyrtl anastomosis[9]) seem to play a role in the normal development of the fetus and placenta. Silver *et al.*[10] have noted a higher incidence of antepartum variable decelerations in fetuses with a small umbilical cord than in those with a normal umbilical cord in post-term pregnancy. Our group has reported that fetuses with a lean umbilical cord are at increased risk of being small for gestational age at birth and of having signs of distress at the time of delivery[7].

The purposes of this study were first, to evaluate whether umbilical vein blood flow measured by digital color Doppler velocity profile integration depends on the umbilical vascular coiling and, second, to investigate if fetuses with a lean umbilical cord have a different umbilical vein flow profile from those with a normal umbilical cord.

METHODS

Consecutive pregnant women who delivered at term and who underwent an obstetric ultrasonographic examination within 24 h before delivery were studied. Inclusion criteria were: (i) singleton gestation, (ii) intact membranes at the time

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of ultrasonography, (iii) delivery between 38 and 41 weeks of gestation, (iv) absence of congenital or chromosomal abnormalities, (v) normal amniotic fluid (vertical length of the largest amniotic fluid pocket > 3 cm at ultrasound), and (vi) absence of pregnancy complications (i.e. hypertensive disorders, diabetes). To avoid possible biases on the umbilical cord hemodynamics due to the effect of uterine contraction and advanced labor, patients with an effaced cervix, regular uterine contractions or a dilatation > 2 cm by digital examination were not considered eligible for this study. In all patients gestational age was determined by a reliable recollection of the last menstrual period and by an ultrasonographic examination before 14 weeks of gestation. The ultrasonographic evaluation included the measurement of fetal anthropometric parameters (biparietal diameter, abdominal circumference, femur length), the computation of umbilical cord and umbilical vessel cross-sectional areas, Doppler interrogation of the umbilical arteries and the estimation of blood flow through the umbilical vein. The umbilical cord measurements were obtained in a plane adjacent to the insertion into the fetal abdomen using the software of the ultrasound machine as previously described[11]. The surface area of Wharton's jelly was computed subtracting the total vessel area from the cross-sectional area of the umbilical cord. Intra- and interobserver variability were 4.3% and 5.1%, respectively[8]. An umbilical cord was defined as 'lean' when its cross-sectional area was below the 10th centile for gestational age[7]. Umbilical artery Doppler flow velocity waveforms were recorded when at least three consecutive waveforms showing a consistent pattern were obtained. The umbilical vein blood flow was measured by digital color Doppler velocity profile integration. This function specifies an arbitrary line on a playback color Doppler image, displays the waveform of the accuracy data concerning each pixel on the specified line as a profile, indicates changes in brightness as waveform data, and integrates data corresponding to several frames and displays it as a blood flow. Doppler parameters were obtained at three different parts of the umbilical cord. The mean of the parameters obtained was used for the purpose of statistical analysis. Mean flow velocity and flow volume per minute were computed. To allow comparisons among fetuses, the umbilical vein blood flow per minute was normalized for birth weight. The ultrasound examinations were performed with an Aloka Prosound 5500 unit (Aloka, Tokyo, Japan) equipped with a 3.5-MHz transducer. The pulsatility index and resistance index as well as the umbilical vein blood flow parameters were measured during fetal apnea and in the absence of uterine contractions.

Immediately after delivery the umbilical cord was examined. Umbilical cord measurements included the total number of vascular coils and the length of the umbilical cord. A coil was defined as a complete 360° spiral course of the umbilical vessels. The umbilical coiling index defined as the number of vascular coils in a given cord divided by its length was calculated. All placentae were weighed immediately after delivery.

All fetal heart rate tracing during labor was judged by an independent physician. Fetal heart rate disturbance was defined as repeated moderate to severe variable or late deceleration and prolonged bradycardia (for at least 8 min). Fetal growth retardation was considered as an infant birth weight below the 10th centile for gestational age[4]. Low Apgar score was defined as a 1-min Apgar score ≤ 3 and/or a 5-min Apgar score ≤ 6. This study was approved by the Human Research Review Committee.

Statistical analysis

Statistical analysis was performed using SPSS 7.0 (SPSS Inc., Chicago, IL, USA) and EpiStast 4.0 (EpiStat Services, Richardson, TX, USA). Mann–Whitney *U*-test or Student's *t*-test were used for comparison of continuous variables and proportions were analyzed using Fisher's exact test. Spearman rank correlation was used to correlate umbilical vein blood flow parameters and fetal or umbilical cord morphometric measurements. Statistical significance was achieved when P was < 0.05.

RESULTS

One hundred and sixteen pregnant women were included in the study, of whom 12 fetuses (10.3%) had a lean umbilical cord. The clinical characteristics of the study population according to the umbilical cord morphology are presented in Table 1. A significant correlation was found between the umbilical vein blood flow per minute normalized for fetal weight and the umbilical coiling index ($r = 0.67$, $P < 0.001$) (Figure 1). The regression equation for the umbilical coiling index (y) according to the umbilical vein blood flow (x) was: $y = -0.0602 + 0.0028x$. A significant correlation was found between the umbilical vein blood flow and the infant birth weight ($r = 0.61$, $P < 0.05$). No correlation was present between umbilical vein area and birth weight. No correlation was found between umbilical vein blood flow and placental weight.

Umbilical cord measurements and vessel blood flow parameters according to umbilical cord morphology are presented in Table 2. The proportion of fetuses with an umbilical vein blood flow < 80 mL/kg per min was higher among fetuses with a lean umbilical cord than among those with a normal umbilical cord (3/12 (25%) vs. 2/104 (1.9%); $P < 0.01$). The rate of fetuses with an umbilical coiling index < 15 was higher in the presence of a lean umbilical cord than in the case of a normal umbilical cord (5/12 (41.7%) vs. 5/104 (4.8%); $P < 0.05$). Of note, three of the five fetuses with a lean cord and umbilical coiling index below 15 had an umbilical vein blood flow < 70 mL/kg per min. These three fetuses were growth-retarded at delivery. One of the remaining two fetuses was delivered by an emergency Cesarean section due to severe fetal heart rate disturbances in labor.

DISCUSSION

The reason why the incidence of adverse perinatal outcome is increased among fetuses with hypocoiled umbilical cord has not been completely clarified. Several authors have attributed this to a reduced turgor and compression-resistant properties of the hypocoiled umbilical cord[3,4]. However, Dado *et al.*[12]

Table 1 Clinical characteristics of the study population according to the umbilical cord size

Characteristics	*Umbilical cord* *Normal* n = *104*	*Lean* n = *12*	P
Maternal age (years) (mean ± SD)	26.7 ± 4.5	29.0 ± 5.2	NS
Nulliparous, *n* (%)	34 (32.7)	4 (33.3)	NS
Smoking habit, *n* (%)	22 (21.2)	3 (25.0)	NS
Gestational age at delivery (weeks) (mean ± SD)	39.5 ± 1.0	39.7 ± 1.1	NS
Interval examination-to-delivery (h) (median, range)	7.7 (4–24)	7.1 (5–23.1)	NS
Birth weight (g) (mean ± SD)	3369 ± 446	3109 ± 568	0.06
Placental weight (g) (mean ± SD)	564 ± 96	525 ± 40	NS
Cesarean deliveries, *n* (%)	20 (19.2)	5 (41.7)	NS
Low Apgar score, *n* (%)	7 (6.7)	3 (25.0)	0.07
Fetal growth retardation, *n* (%)	8 (7.7)	4 (33.3)	< 0.05
Fetal heart rate disturbances, *n* (%)	7 (6.7)	3 (25.0)	0.07
Meconium stained amniotic fluid, *n* (%)	9 (8.7)	3 (25.0)	NS

NS, Not significant.

Table 2 Umbilical cord measurements and umbilical vessel blood flow characteristics according to the umbilical cord size

Characteristics	*Umbilical cord* *Normal* n = *104*	*Lean* n = *12*	P
Cord length (cm) (mean ± SD)	57.6 ± 10.3	57.2 ± 11.5	NS
Coiling index (mean ± SD)	0.29 ± 0.09	0.18 ± 0.08	< 0.005
Cord cross-sectional area (mm^2) (mean ± SD)	200.6 ± 34.6	87.6 ± 5.1	< 0.001
Artery cross-sectional area (mm^2) (mean ± SD)*	14.3 ± 5.4	13.3 ± 5.3	NS
Vein cross-sectional area (mm^2) (mean ± SD)	50.5 ± 20.2	35.2 ± 11.5	< 0.01
Wharton's jelly area (mm^2) (mean ± SD)	122.1 ± 33.4	25.7 ± 10.3	< 0.001
Artery pulsatility index (mean ± SD)	0.83 ± 0.14	0.85 ± 0.09	NS
Absolute vein blood flow (mL/min) (mean ± SD)	423.5 ± 93.2	293.6 ± 81.8	< 0.000
Vein blood flow for fetal weight (mL/kg per min) (mean ± SD)	126.0 ± 23.4	93.7 ± 17.8	< 0.001
Vein blood flow mean velocity (cm/s) (mean ± SD)	9.0 ± 3.6	6.6 ± 2.7	< 0.05

*Both arteries are considered (208 vs. 24). NS, Not significant.

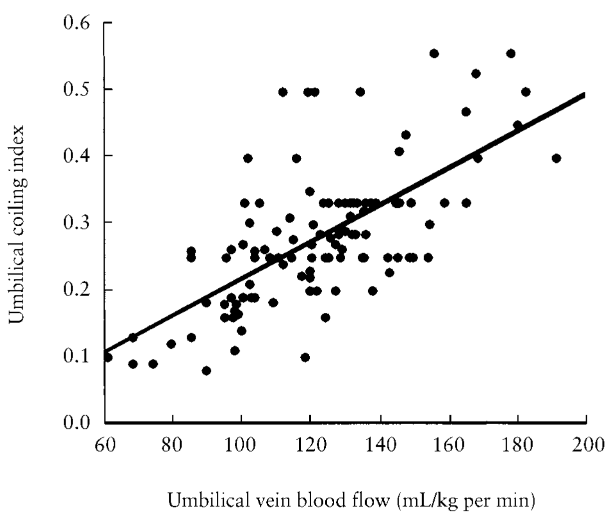

Figure 1 Correlation between vascular coiling and umbilical vein blood flow normalized for birth weight.

have recently conducted mechanical tests in which the umbilical arteries and vein were perfused, pressurized and subjected to compression, twisting and stretching while measuring venous flow, and concluded that non-coiled cords are not more susceptible to external compression, twisting or stretching than normally coiled umbilical cords.

The present study and that of Degani *et al.*[5] demonstrated that a significant correlation exists between the umbilical vascular coiling and umbilical vein blood flow. These findings support the hypothesis proposed by Reynolds[13] that the umbilical cord is a pistonless pulsometer pumping system. The fetal blood flows through the umbilical vein pumped by slight but definite decreases and increases in venous pressure that is generated from the force of the rising limb of the arterial pressure pulse. Therefore, the presence of arterial coils that surround the vein along the length of the cord provides multiple variations in an additive fashion.

The finding of hypocoiled and lean umbilical cord at delivery is not an uncommon one among small for gestational age neonates and among fetuses who had fetal distress in labor. The reason why these two umbilical cord characteristics frequently coexist is still unexplained. Malpas and Symonds[1] provided evidence that the helical structure of the umbilical cord is due to the spiral shape of some fibers constituting the vessel walls and suggested that this configuration enables the cord to withstand torsion without snarling. However, more recent investigations demonstrated that the Wharton's jelly also plays an important protective role for the umbilical vessels[14–16]. Scanning electron microscopy studies revealed that the Wharton's jelly presents a spongy network of interlacing collagen fibers in which the vessels are anchored by numerous thick collagen bundles[14]. Furthermore, several studies have speculated that the Wharton's jelly has a metabolic active role in maintaining the normal function of the umbilical cord vessels. Takechi *et al.*[15] demonstrated that some cells, similar to myofibroblasts and normally present in the Wharton's jelly, can function in both fibrogenesis and cell contraction, participating in the regulation of umbilical blood flow. Immunohistochemical studies showed that either the umbilical vessel walls or the Wharton's jelly composition are different in lean umbilical cords than in normal umbilical cords[16]. In addition, an altered morphology and ultrastructure of the umbilical cord components have been described in conditions frequently associated with a modification of umbilical artery blood flow[17]. In particular, it has been reported that the elastin content of the umbilical artery wall and the proportion of hyaluronic acid in the Wharton's jelly are significantly reduced in patients with pre-eclampsia[18], and that elastin gene expression is influenced by several factors such as cytokines (i.e. transforming growth factor-beta)[19] and vitamins (i.e. vitamin C)[20].

We speculate that the high proportion of vascular hypocoiling in lean umbilical cords is not an occasional finding but could be the consequence of an altered expression of genes responsible for the production of the structural constituent of the umbilical cord vessel walls and of the Wharton's jelly (i.e. elastin, collagen, hyaluronic acid).

The hypothesis that the morphology of the umbilical cord is most probably under genetic control is supported by the observation that the helical configuration of the umbilical cord has been reported to be present in the first trimester of gestation and that pathologic amounts of Wharton's jelly have been noted very early in gestation[21]. Furthermore, an increased incidence of aneuploidy has been reported among fetuses with a hypocoiled umbilical cord[22]. In addition, a lesser degree of chirality and a reduced amount of Wharton's jelly have been reported in umbilical cords with a single umbilical artery[23,24], a structural anomaly frequently seen in the presence of genetic and chromosomal disorders.

An important question is whether umbilical vein blood flow quantification can have clinical value in detecting those fetuses who will have an adverse perinatal outcome. Obviously, to be useful in clinical practice the umbilical vein blood quantification should give information during the second trimester of pregnancy. In the present study all measurements of the umbilical vein blood flow parameters were performed within 24 h of delivery, a situation that is not standard obstetrical practice. Barbera *et al.*[6] demonstrated that the umbilical vein blood flow for estimated fetal weight of the human fetus does not change significantly from 20 weeks of gestation to term. In addition, these authors found a significant correlation between the umbilical vein blood flow per kilogram, measured between 20 and 38 weeks of gestation, and anthropometric fetal measurements such as head circumference and abdominal circumference. Further prospective studies are needed to explore whether a quantification of the umbilical vein blood flow in the second trimester in a low-risk pregnancy can help in identifying a subset of fetuses at risk of growth restriction or of intrapartum complications.

Although the method used in the present study to estimate umbilical vein blood flow is simple, fast, and does not require computation (by the obstetrician), our results are very similar to those of others[5,6] who calculated the blood flow volume from parameters obtainable with any ultrasound machine equipped only with pulsed Doppler software. Indeed, no difference is present between the umbilical vein blood volume (mL/min per kg) reported by Degani *et al.*[5] and that of the present study (112 ± 25 vs. 122.7 ± 24.9).

This study has demonstrated that lean umbilical cords differ from normal cords not only from a structural point of view but also in umbilical vein blood flow characteristics, with the consequence of an altered blood supply to the fetus. This could explain the association of an increased incidence of fetal growth restriction with intrapartum complications among fetuses with a lean and/or hypocoiled cord.

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