

Antenatal Detection of True Knot in the Umbilical Cord – How Accurate Can We Be?

Pränataler Nachweis eines echten Nabelschnurknotens – Wie treffsicher sind wir?

Authors

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ABSTRACT

Background Umbilical cord knot (UCK) is associated with increased risk of fetal death, but is usually diagnosed only after delivery. Our objective was to examine the accuracy of prenatal ultrasound in the diagnosis of UCK and the outcomes of these pregnancies.

Methods A prospective study was performed on 56 patients in which UCK was suspected during a routine level-II anatomical scan (study group). Data included demographics, pregnancy outcome, and short-term neonatal follow-up. The control group included pregnant women with normal pregnancy without UCK in a 4:1 ratio matched for gestational age at delivery.

Results True knot was observed postnatally in 54 out of 56 fetuses (detection rate of 96.4%). Gestational age at diagnosis of UCK was 22.1 ± 3.1 weeks. The female to male ratio was 1:1 in both groups. Maternal age and parity were significantly higher in pregnancies with UCK compared to controls. The mean gestational age at delivery was 37.1 weeks of gestation in the UCK group. There was no difference in the birthweight percentile. 47 patients (87%) underwent induction of labor. There were no differences in the rate of cesarean section or Apgar scores. No neonate with UCK needed ventilation. None suffered from seizures and none needed brain imaging. There were no cases of fetal or neonatal death in the pregnancies with UCK.

Conclusion There is a high detection rate of UCK during targeted scan of the umbilical cord performed during the level-II anatomical scan. Careful pregnancy follow-up and early term delivery may result in excellent obstetrical outcomes.

ZUSAMMENFASSUNG

Hintergrund Der Nabelschnurknoten (UCK) ist mit einem erhöhten Risiko für intrauterinen Fruchttod verbunden, wird jedoch normalerweise erst nach Entbindung diagnostiziert. Unser Ziel war es, die Genauigkeit des pränatalen Ultraschalls bei der Diagnose des UCK und das Schwangerschafts-Outcome zu untersuchen.

Methoden Eine prospektive Studie wurde an 56 Patienten durchgeführt, bei denen ein UCK während eines routinemäßigen anatomischen Scans der Stufe II (Studiengruppe) vermutet wurde. Die Daten umfassten demografische Daten, den Schwangerschaftsausgang und eine kurzfristige Nachbeobachtung von Neugeborenen. Die Kontrollgruppe umfasste schwangere Frauen mit normaler Schwangerschaft ohne UCK in einem Verhältnis von 4:1, mit Matching nach Schwangerschaftswoche bei Entbindung.

Ergebnisse Echte Knoten wurden postnatal bei 54 von 56 Föten beobachtet (Nachweisrate 96,4%). Das Gestationsalter bei Diagnose des UCK betrug $22,1 \pm 3,1$ Wochen. Die Weiblich:Männlich-Ratio betrug in beiden Gruppen 1:1. Das mütterliche Alter und die Parität waren bei Schwangerschaften mit UCK im Vergleich zu den Kontrollen signifikant höher. Das mittlere Gestationsalter bei Entbindung betrug in der UCK-Gruppe 37,1 Schwangerschaftswochen. Bei der Perzen-

* Both authors equally contributed to this study.

tile des Geburtsgewichts gab es keinen Unterschied. Bei 47 Patienten (87 %) wurde die Geburt eingeleitet. Es gab keine Unterschiede in der Kaiserschnitttrate oder bei den Apgar-Scores. Keines der Neugeborenen mit UCK musste beatmet werden. Keines litt unter Krampfanfällen, noch war eine Hirn-Bildgebung erforderlich. Bei den Schwangerschaften mit UCK gab es keine Fälle von fetalem oder neonatalem Tod.

Schlussfolgerung Es gibt eine hohe Detektionsrate von UCK bei der gezielten Untersuchung der Nabelschnur, die bei der anatomischen Level-II-Untersuchung durchgeführt wird. Eine sorgfältige Betreuung der Schwangerschaft und eine frühe Entbindung können zu einem hervorragenden geburtshilflichen Outcome führen.

Introduction

Umbilical cord knot (UCK) is a obstetrical phenomenon observed in 0.3–2.1 % of all deliveries [1, 2]. The entire course of the umbilical cord is not routinely examined during pregnancy. Therefore, most cases are diagnosed only following delivery. UCK is associated with a 4–8 times higher rate of fetal mortality [1–4]. Therefore, the antenatal diagnosis of UCK is of clinical importance. These pregnancies are classified as high-risk pregnancies, necessitating meticulous follow-up and early term induction of labor [2, 3].

The prenatal sonographic diagnosis of UCK can be made using 2DUS demonstrating a transverse section of the umbilical cord surrounded by a loop of umbilical cord creating the “hanging noose” sign [5]. Limited studies on a small number of pregnancies examined the accuracy of ultrasound in the detection of UCK. Earlier studies concluded that UCK are easily missed during routine prenatal 2-dimensional ultrasound (2DUS) [5, 6]. The addition of three-dimensional and four-dimensional ultrasound (3DUS) improved the accuracy of prenatal diagnosis to up to 62.5 % [7–9]. False-positive diagnosis may be due to the detection of a conglomerate of loops of umbilical cord, or a tortuous course of the vessels inside the umbilical cord. False-negative diagnosis may be due to a posterior location of the knot behind the fetal body, technical difficulties such as maternal habitus or fetal position, or the creation of the knot after the scan [8].

The objective of the present study was to characterize pregnancies in which UCK was suspected antenatally and to compare the perinatal outcomes to controls without UCK.

Methods

A prospective study was conducted from 2016 to 2019 including all singleton pregnancies in which UCK was suspected. The study was approved by the institutional review board of our medical center.

The entire course of the umbilical cord was evaluated during the routine level-II anatomical scan. Diagnosis of UCK was made using 2DUS demonstrating a transverse section of the umbilical cord surrounded by a loop of umbilical cord that creates the “hanging noose” sign [5] (► Fig. 1a, b). Confirmation was made by applying 3 D/4 D color Doppler ultrasound and rotating the volume along the x- and the y-axes until full view of the knot was displayed (► Fig. 2a, b). All patients were followed at the ultrasound unit along with the high-risk outpatient clinic in our hospital. The patients in our study were examined every 2 weeks from the first diagnosis until 32 weeks of gestation and twice a week following

32 weeks of gestation, with induction of labor at about 37–38 weeks of gestation.

Sonographic suspicion of tightening of the umbilical cord was based on color Doppler ultrasound measurements of a smaller diameter of the arteries and the veins at the suspected area of tightening of the UCK compared to a place with no suspected tightening. Demonstration of fluid within the loops of the umbilical cord inside the knot decreased the suspicion of tightening of the knot (► Fig. 3).

Data included maternal age, gravidity, parity, date of diagnosis of UCK, pregnancy outcomes including induction of labor, mode of delivery, birth weight, and neonatal treatment including: need for oxygen, ventilation, neonatal seizures.

The control group included pregnant women with a normal pregnancy without UCK in a 4:1 ratio matched for gestational age at delivery, who delivered just before or after the patients included in the study group (n = 216).

Statistical analysis

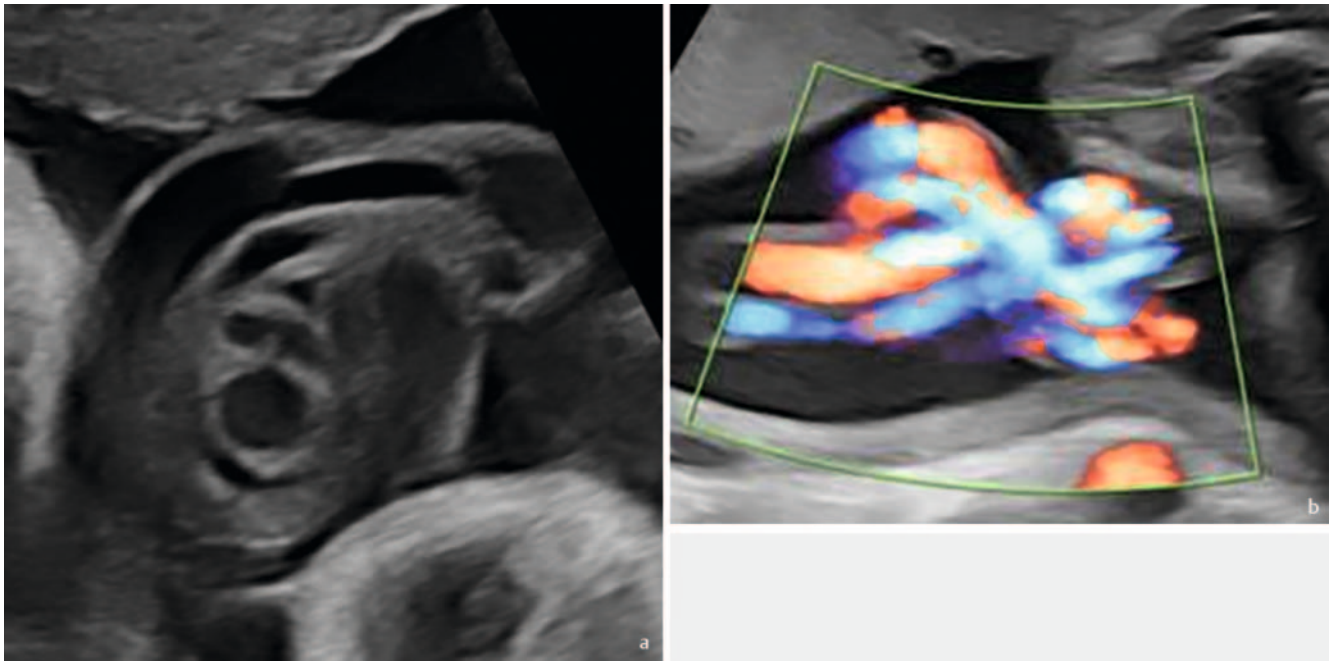
Normality of the data was tested using the Shapiro-Wilk or Kolmogorov-Smirnov test. Data are presented as median and interquartile range (IQR) or mean and standard deviation, depending on the normality of the data. Comparison between unrelated variables was conducted with Student’s t-test or Mann–Whitney U-test, as appropriate. The chi-square and Fisher’s exact tests were used for comparison between categorical variables. Correlation between variables was conducted using either Pearson or Spearman’s rank correlation as appropriate. Significance was accepted at $p < 0.05$. Statistical analyses were conducted using the IBM Statistical Package for the Social Sciences (IBM SPSS v.23; IBM Corporation Inc, Armonk, NY, USA).

Results

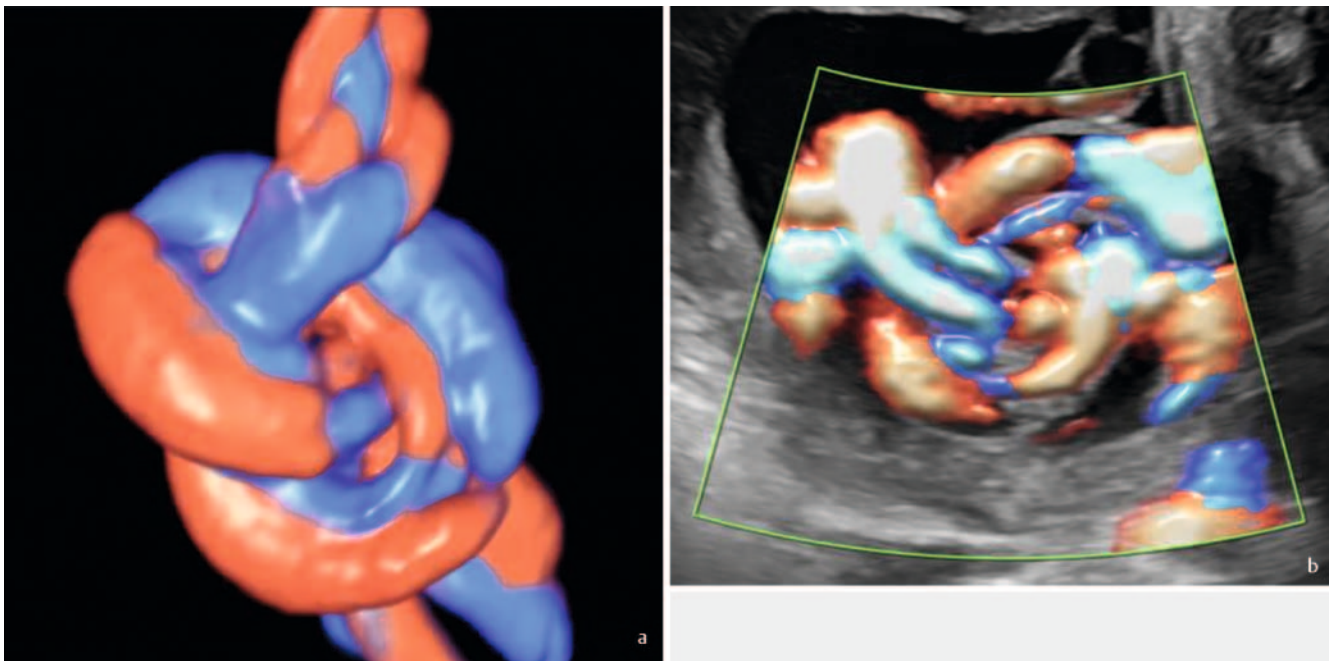
56 pregnancies were suspected of having UCK during pregnancy in the study period with 54 being diagnosed with UCK following delivery (► Fig. 4), thus demonstrating a sonographic prenatal accuracy of 96.4 %.

The demographic characteristics of the study population are presented in ► Table 1. Maternal age and parity were significantly higher in the pregnancies with UCK compared to the controls. Polyhydramnios was observed in only one pregnancy.

Doppler analysis revealed normal flow in the umbilical cord with the highest systolic-diastolic ratio of 2.7 ± 0.6 and the highest pulsatility index of 0.9 ± 0.16 . The flow in the middle cerebral



► **Fig. 1** **a** 2-dimensional sonographic demonstration of umbilical cord knot at 36 weeks of gestation. **b** 2-dimensional color Doppler sonographic demonstration of umbilical cord knot at 28 weeks of gestation.



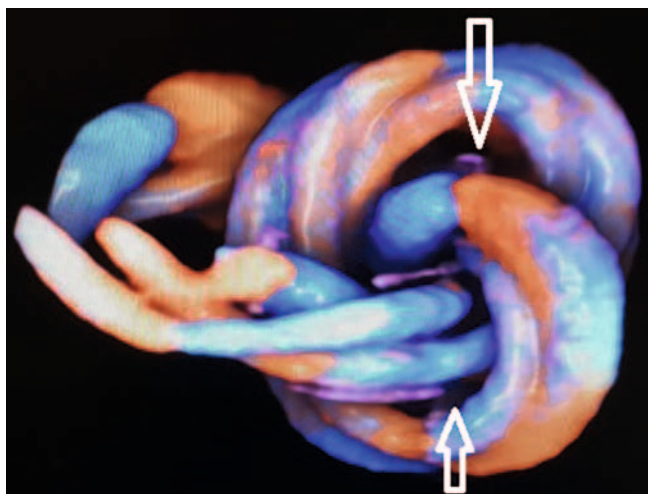
► **Fig. 2** **a** 3-dimensional color Doppler demonstration of umbilical cord knot at 28 weeks of gestation. **b** 4-dimensional color Doppler demonstration of umbilical cord knot at 33 weeks of gestation.

artery had the highest peak systolic velocity of 33.7 ± 0.3 and the lowest pulsatility index of 1.5 ± 0.63 .

The perinatal outcomes are presented in ► **Table 2**. There was no difference in the birth weight percentile between the two groups.

47 patients with UCK (87%) underwent induction of labor. Two patients delivered spontaneously at $36 + 2$ weeks of gestation and

another patient delivered spontaneously at $40 + 2$ weeks of gestation. Four additional patients had a planned cesarean section. There was no difference in the rate of overall cesarean sections between the patients with UCK and the control group in general, and no difference in the rate of cesarean section due to a non-reassuring fetal monitor.



► **Fig. 3** 3-dimensional color Doppler demonstration of umbilical cord knot at 27 weeks of gestation. Arrows point to fluid within the loops of the knot ruling out tightening of the knot.

► **Table 1** Demographic characteristics of the study population.

	true knot (n = 54)	control group (n = 216)	p-value
age mean ± SD	33.8 ± 3.6	30.7 ± 6.2	<0.0001
age ≥ 35 % (N)	44.4 % (24)	24.5 % (53)	0.004
gravidity mean ± SD	3.2 ± 2	2.7 ± 2.2	0.09
parity mean ± SD	1.65 ± 1.57	1.3 ± 1.9	0.2
parity > 0 % (n)	81.5 % (44)	50.5 % (109)	<0.0001
gestational age at diagnosis of knot mean ± SD	22.1 w ± 3.1 w	–	–

The neonatal Apgar scores were similar in the neonates with UCK and the control group. No differences were found between the groups regarding the need for oxygen supplementation, mechanical ventilation, seizures, or indications for brain imaging for the neonates. There were no cases of fetal or neonatal death in both groups.

The two false-positive cases included a 36-year-old G7P3 patient who was diagnosed with UCK at 20 weeks of gestation, and delivered spontaneously with no induction of labor at 36 + 2 weeks a 2745-gram healthy boy; and a 35-year-old G3P1 who was diagnosed with UCK at 22 weeks of gestation, and delivered by cesarean section due to breech presentation at 37 + 1 weeks a 2600-gram healthy boy.

Discussion

The present study demonstrated that meticulous analysis of the umbilical cord may detect true knot with a high detection rate of 96.4%. Careful antenatal follow-up of these high-risk pregnancies



► **Fig. 4** Detection of umbilical cord knot at delivery.

along with delivery at early term resulted in live, healthy, adequate-for-gestational-age neonates.

Previous studies, mainly retrospective, described several risk factors for UCK including increased maternal age and increased parity [1, 2, 4, 13], as also demonstrated in our study. Increased parity may be associated with increased maternal age. Other risk factors included polyhydramnios, observed only in one patient in our study, diabetes mellitus, not observed in the present study, and male predominance [1, 4]. We found similar rates of males and females with UCK.

The patients in our study were examined every 2 weeks from the first diagnosis until 32 weeks of gestation and twice a week after 32 weeks of gestation, with induction of labor at about 37 weeks of gestation. Color Doppler ultrasound was performed in order to rule out tightening of the umbilical cord at the area of the UCK. A few previous case reports have described intrauterine growth restriction caused by chronic tightening of the UCK [14–16]. A larger study by Raisanen et al. reported an increased risk of 3.17 for small-for-gestational-age neonates due to UCK [3]. During careful follow-up we did not reveal tightening of the umbilical cord and indeed all neonates were adequate for gestational age with no significant differences with respect to the control group. Therefore, according to the results of the present study, UCK did not adversely affect fetal weight.

The main reason for induction of labor at early term was the concern of acute tightening of the UCK leading to sudden fetal

► **Table 2** Perinatal outcomes of pregnancies with UCK compared to controls.

	true knot (n = 54)	control (n = 216)	p-value
gestational age at delivery mean ± SD	37.1w ± 5.4 d	37.1w ± 6 d	0.6
mode of delivery % (n)			0.4
▪ NVD	64.8 % (35)	57.9 % (125)	
▪ operative Delivery	7.4 % (4)	5.1 % (11)	
▪ cesarean Section	27.8 % (15)	37 % (80)	
indication for C-section % (n)			
▪ NRFHR	20 % (3/15)	15 % (12/80)	0.7
▪ previous cesarean	20 % (3/15)	25.9 % (21/80)	0.75
▪ maternal request	13.3 % (2/15)	3.7 % (3/80)	0.18
▪ malpresentation	33.3 % (5/15)	27.2 % (22/80)	0.54
▪ other	13.3 % (2/15)	28.7 % (23/80)	0.34
birth weight gr mean ± SD	2844 ± 390	2724 ± 487	0.06
birth weight percentile mean ± SD	47.6 ± 23	42.3 ± 27.2	0.19
gender % (n)			0.8
▪ male	51.9 % (28)	53.7 % (116)	
▪ female	48.1 % (26)	46.3 % (100)	
apgar 5 min median (range)	9.9 (7–10)	9.9 (0–10)	0.53
apgar 5 min ≤ 7 % (n)	1.9 % (1)	1.4 % (3)	1
arterial pH mean ± SD	7.25 ± 0.05	7.25 ± 0.08	0.93
arterial pH ≤ 7.1 % (n)	0 % (0/54)	3.5 % (3/84)	1
venous pH mean ± SD	7.3 ± 0.06	7.28 ± 0.06	0.3
venous pH ≤ 7.1 % (n)	0 % (0/7)	1.1 % (1/89)	1

NVD: Normal vaginal delivery; NRFHR: Non-reassuring fetal heart rate.

death. Previous retrospective studies reported up to an eight-fold increase in the risk of fetal death due to a tightened UCK [1–4, 17, 18]. Although some reported intrauterine fetal demise in the second trimester [15, 19], Linde et al. reported an odds ratio of 5.19 regarding perinatal death at term compared to 1.65 at preterm [4]. In order to prevent complications of prematurity on the one hand and fetal death on the other hand, we recommended induced labor at about 37 weeks of gestation.

We assume that the meticulous follow-up along with the earlier induction of labor lead to the overall good neonatal outcomes. This assumption is enforced by the fact that there was no meconium, no need for ventilation support, no seizures, and no perinatal death among the study group. Similarly, an earlier study by Maher et al. found no differences in umbilical cord gas values between newborns with and without true knots [20]. The rate of overall cesarean sections, as well as the rate of urgent cesarean

sections due to a non-reassuring fetal monitor were similar in the study group and the control group. Importantly, more cesarean sections due to maternal request were performed in the study group, but the difference did not reach statistical significance. This may be attributed to the maternal anxiety and fear of perinatal death directly related to the antenatal detection of UCK. Nevertheless, the overall rate of cesarean section did not differ between the pregnancies with UCK and the control group.

No specific causes were found for the two false-negative cases. We assume that a conglomerate of loops of umbilical cord resembled UCK and lead to the false diagnosis.

We acknowledge several limitations in this study. The number of pregnancies with UCK is relatively small, limiting the strength of the statistical analysis. However, this is one of the largest prospective studies on UCK. There is no common protocol regarding the follow-up of these pregnancies. Due to previous reports of intrauterine growth retardation and fetal death [1–4], we examined these patients every two weeks after 32 weeks of gestation, and did not perform randomization to routine follow-up and strict follow-up. Due to previous reports of fetal death at term [1–4], we recommended induction of labor at early term and did not perform randomization to verify whether induction of labor at early gestation significantly reduces fetal death. Another limitation is the lack of information about false-negative cases, that may be caused by technical obstacles or due to formation of the knot after the targeted scan.

In summary, sonographic examination of the umbilical cord at mid-trimester may identify true knots in the umbilical cord with a high detection rate. It may be prudent to recommend careful follow-up with color Doppler ultrasound, followed by induction of labor at early term in order to attain good outcomes in these high-risk pregnancies.

Conflict of Interest

The authors declare that they have no conflict of interest.

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