The Value of Ultrasound in Diagnosing Umbilical Cord Knot and Its Effect on Fetal Perinatal Outcome

Abstract:

Objective:To analyse the prenatal diagnostic value of ultrasound in umbilical cord knot(UCK) and the correlation of UCK and fetal perinatal outcome.

Design:a systematic review,study-controlled.

Setting:the First Affiliated Hospital of Anhui Medical University.

Population or Sample: All fetuses born or induced in our hospital from January 2015 to December 2019.The UCK group(n=99) was the fetuses who were diagnosed as UCK after delivery,and the control group(n=200) was randomly selected from other normal fetuses.

Methods:Firstly, retrospective analysis was conducted on the prenatal ultrasound and clinical data of newborns or induced fetuses with UCK in our hospital from January 2015 to December 2019.The inclusion criteria included fetuses which delivered normally and stillbirth at 28 weeks or more and ultrasound examination and clinical data were complete.The exclusion criteria included incomplete prenatal ultrasound examination, clinical data and termination of pregnancy in the third trimester because of human factors.Diagnostic criteria of the prenatal ultrasound for UCK was that the accumulation of umbilical cord showed"clover or noose sign"by 2D ultrasound;Then the 3D structure of true UCK was presented by 3D ultrasound.The gold standard for diagnosis of UCK was that the clinician confirmed that there is UCK on the umbilical cord postpartum or post-induction.Secondly,the incidence of UCK and its relationship with fetal perinatal outcome were summarized and analyzed.Then,the value and image characteristics of prenatal ultrasound in diagnosing UCK were analyzed. Finally,the fetuses who were diagnosed as UCK after delivery were the UCK group, and the control group was 200 cases randomly selected from other normal fetuses.The differences of ultrasonic parameters and related clinical parameters were compared between the two groups by independent sample T-test (normal distribution) or rank sum test (skewed distribution) and binary logistic regression model.

Main Outcome Measures: Two-dimensional(2D) and three-dimensional(3D)

ultrasonic image characteristics and classification of umbilical cord knot(UCK).The differences of ultrasonic parameters and related clinical parameters.

Results:During 5 years, there were 40346 fetuses were born in our hospital, including 209 cases stillbirths in the third trimester.99 fetuses were confirmed with UCK by postnatal diagnosis (including 3 stillbirths died of UCK),accounting for 3% of the diagnosis of UCK.Prenatal 2D ultrasound showed 15 cases of suspicious UCK, of which 9 cases were diagnosed by 3D ultrasound and postnatal confirmed.It was difficult to display the characteristic images of UCK by two-dimensional ultrasound (2D-US).2D ultrasonic images can be classified as excessively distorted, stacked or cloverleaf.The three-dimensional ultrasound (3D-US) can clearly identify the true and false UCK,which can be divided into loose UCK,tight UCK,spiraling umbilical cord and twisted and stacked umbilical cord.The resistance index (RI) of middle cerebral artery (MCA) in the UCK group was lower than that in the normal control group ($P<0.05$).There were statistically significant differences in the maternal age, multiparty, gestational weeks, gestational diabetes mellitus (GDM), amniotic fluid volume and length of umbilical cord between the two groups ($P < 0.05$).

Conclusions: The incidence of UCK is only 0.25%, but mortality accounts for 1.4% of the fetal death in the third trimester.2D-US is combined with 3D-US can improve the prenatal diagnostic accuracy of UCK.With the maternal age,parity,amniotic fluid volume and cord length increased,the risk of UCK is increased.UCK should be excluded to avoid fetal adverse perinatal outcomes when fetal blood flow Doppler indicates the possibility of fetal hypoxia.

Keys: Umbilical Cord Knot.Ultrasonic Diagnosis.Risk Factors.Mortality.Perinatal Outcome

Funding statement

None.

Introduction

Up to now, there were many factors leading to fetal death in utero, for instance,

maternal complications or comorbidities, umbilical cord factors, placenta abnormality, amniotic fluid anomaly, unknown cause and so on.The umbilical cord factors was various, involving umbilical cord knots[1].

UCK was reported approximately ranging from 0.04% to 3% of all pregnancies[2]. Although the incidence of the UCK was rare, its complications were associated with serious consequences when it was formed and tightened, including premature birth, need for neonatal intensive care and fetal death[3]. Furthermore, fetuses with UCK had a 4-fold increased risk of stillbirth compared with fetuses without UCK[4].It was reported that the maternal age, anemia, obesity and past abortion[5] and some obstetric factors (e.g. polyhydramnios, diabetes, gravidarum, chronic hypertension, multiparty, long umbilical cord, male fetus, birth weight of the fetus,and genetic amniocentesis) were correlated with true UCK[6].

However,UCK was extremely difficult to diagnose antenatally in utero.UCK was easy to be misdiagnosed and overdiagnosed, which resulting in unnecessary clinical intervention, pregnant women anxiety, or serious consequences.Bohîlea et al[7] specified that the prenatal detection rate for UCK was 12%. At present, some case reports considered that three-dimensional ultrasound(3D-US),three-dimensional high-definition flow imaging, four-dimensional ultrasound(4D-US) were helpful for prenatal diagnosis of UCK[8].Even though the "hanging noose" sign has been reported as a highly specific two-dimensional ultrasound (2D-US) feature of UCK[9], 2D-US still had limitations for determining confidently the existence of true UCK and ruling out the possibility of a false negative result completely.

The purpose of this study was to analyze the incidence of UCK and its risk factors, the correlation between UCK and fetal perinatal outcome in late pregnancy, and the prenatal diagnostic value of 2D-US and 3D-US for UCK.

Materials and methods

Retrospective analysis was performed on newborns consecutive delivered at the First Affiliated Hospital of Anhui Medical University between January 2015 and December 2019, including natural delivery, caesarean section and natural stillbirth in

the third trimester.The inclusion criteria included fetuses which delivered normally and stillbirth at 28 weeks or more and ultrasound examination and clinical data were complete.The exclusion criteria included incomplete prenatal ultrasound examination, clinical data and termination of pregnancy in the third trimester duo to human factors.

Fetuses with UCK were confirmed after delivery by obstetrician.Firstly,the collected data were analyzed, including the causes of fetal death and the incidence of UCK during the third trimester and the effect of UCK on fetal perinatal outcome.Secondly, the detection rate and diagnostic accuracy of UCK by prenatal ultrasound were analyzed.The ultrasonic image characteristics and value of the prenatal 2D-US and 3D-US in diagnosing UCK were summarized and compared.Finally,fetuses which diagnosed as UCK postpartum were selected as UCK group,and 200 normal fetuses without UCK,which was randomly selected from normal births as the control group.Fetal ultrasonic and clinical parameters were collected and compared between the two groups.The following clinical characteristics were collected:maternal age, gestational age, mode of delivery, parity, fetal gender and fetal birth weight, gestational diabetes mellitus, maternal anemia, Apgar score, amniotic fluid volume, the length of the umbilical cord,and so on.Ultrasonic parameters included the ratio of the systolic peak and the end-diastolic velocity of blood flow (S/D), pulsatility index (PI) and the resistance index (RI)of middle cerebral artery (MCA) and umbilical artery.

Statistical analysis were performed with SPSS version 25. Statistical significance level was set at P value $<$ 0.05.The independent-sample *t* test or the Mann-Whitney Test was used to evaluate ultrasonic parameters. Binary logistic regression model was used to analyze the risk factors associated with the true UCK.

Results

Analysis of the natural fetal death in the third trimester

During this period, there were 40346 newborns in our hospital, including 209 cases of intrauterine fetal death during late pregnancy because of various causes. The

incidence of intrauterine fetal death was nearly 0.52% in late pregnancy. According to various maternal and fetal factors, the cause of maternal complications was up to 34.9%.Placental factors were second, accounting for 12.8%.Complications of the umbilical cord accounted for 11.0%(23/209), of which 3 fetuses dying from true UCK.

The UCK and fetal perinatal outcome in the third trimester

Fetuses with UCK were confirmed by obstetrician after delivery. The incidence of UCK was nearly 0.25% (99/40346). And 3 fetuses died from UCK in the third trimester, accounting for 13%(3/23) in fetuses dying of complications of umbilical cord and accounting for 1.4%(3/209) in fetal natural death in the third trimester.In 96 live fetuses with UCK, neonatal hypoxia was found in 7 postpartum fetuses which Apgar scores at 1 minute ranged from 4 to 7,returning to normal at 5 or 10 minutes.

The diagnosis of ultrasound for UCK

As shown in table 1, there were 99 fetuses with UCK confirmed after delivery in the 40346 fetuses.Two-dimensional ultrasound(2D-US) found 15 fetuses with suspicious UCK, in which 9 fetuses were diagnosed by Three-dimensional ultrasound(3D-US) and postnatal confirmed by obstetrician. It showed that the detection rate of 2D-US for UCK is as low as 15.2%.2D-US had low diagnostic accuracy for UCK,due to the lack of characteristic feature of UCK,then 3D-US had high positive diagnostic accuracy.2D-US showed different degree winding signs or ring signs (Fig 1: C1-A, C2-A, C3-A, C4-A),which were hinted suspicious UCK.The image of umbilical cord reconstructed by 3D-US can be directly displayed,which can be divided into the following structures.Loose UCK were defined as having UCK but umbilical cord gap exists(Fig 1: C1-B). Tight UCK were defined as having UCK and the disappearance of umbilical cord gap and compression of umbilical cord(Fig 1: C2-B).Spiral umbilical cord were defined as the umbilical cord spiraling without UCK (Fig 1: C3-B).And twisted umbilical cord were defined as umbilical cord twisted and stacked without UCK (Fig 1: C4-B).These all were confirmed after delivery.

As table 2 shown,statistical comparison of ultrasonic parameters was performed

using the independent-sample *t* test or the Mann-Whitney Test.The result showed that The resistance index (RI) of middle cerebral artery (MCA) in the UCK group was lower than that in the normal control group ($P<0.05$).However,others were not statistically significant.

Risk factor analysis of UCK

Table 3 showed the risk factors associated with true UCK. Maternal age of fetuses with the true UCK were significantly older than those without UCK. Gestational diabetes mellitus(GDM) showed statistical differences between the UCK group and the normal control group.There were statistically significant differences in parity and gestational weeks between the two groups.Fetuses with true UCK had more amniotic fluid volume and longer umbilical cord length than fetuses without UCK.Birth weight,fetal gender,maternal anemia and delivery mode were not significantly different between the study and control groups.

Discussion

The UCK and fetal perinatal outcome in the third trimester

With the improvement of fetal examination technology and treatment, the incidence of fetal death in utero decreased obviously. The most common cause of intrauterine fetal death remained maternal complications, for example,eclampsia and gestational diabetes.In this study,complications of umbilical cord led to 11.0% of fetal deaths, of which 3(13.0%) fetuses died of UCK.

Its morbidity was consistent with previous studies[2].Among the UCK group,the mortality of true UCK reached 3.0%(3/99).It meant that fetuses with UCK are at an increased risk of stillbirth once the UCK occurs and tightens.UCK may be responsible for fetal compromise which sudden and unforeseen fetal distress during delivery. In this study,7 fetuses with UCK developed hypoxia in postpartum.Although mother and prenatal fetal indicators were in the normal range,these fetuses had low Apgar scores at 1 minute.It may be the contribution of the fetal UCK. Timely prenatal intervention can be carried out by improving the prenatal ultrasonic diagnosis of UCK.Further,this can reduce the incidence of stillbirth and hypoxia or asphyxia caused by the

UCK.Therefore, it is crucial that try to improve the prenatal diagnosis of UCK and to prevent a disastrous outcome.

The availability of ultrasound in diagnosing UCK

However, the umbilical cord is a complex vascular structure with different twisting patterns and unstable spatial configuration.Wojciech Guzikowski et al.[10] showed a great usefulness of color Doppler ultrasound in the diagnosis of true UCK. According these study[11, 12],the prenatal diagnosis of UCK was incidental observation during the evaluation of amniotic fluid volume, at which time a suggestive "cloverleaf" pattern or a four-leaf clover may be present.It was reported that the"hanging noose"sign,visualization of a segment of the cord closely surrounded by a loop in prenatal 2D-US, was known as a highly specific feature of UCK[9]. However,as our results showed,2D-US image indicated typical "hanging noose" sign(F1:C3-A).UCK can be excluded with the help of 3D-US.UCK also has been described as an unusual multicolor umbilical cord pattern in the literature[6]. Nevertheless,it is still difficult to prenatal diagnosis of UCK by 2D-US because the prenatal 2D-US is lack of characteristic sign of UCK.In this study, the detection rate of 2D-US for UCK is as low as 15.2%.

3D-US combined with other ultrasound technologies has been widely used to prenatal diagnosis of placenta and umbilical cord pathologies[13, 14]. Abuhamad,A [15]suggested that two points were required for confirmation of a true UCK.The first of all, the suspected area on gray-scale ultrasound is visualized as a loop.Then,a full view of the UCK has been displayed by acquiring a color Doppler three-dimensional volume and rotating the volume along the x- and y-axes. In this study,the 3D-US excluded 6 cases of suspected the UCK on 2D-US, which were confirmed after delivery. Our study found suspicious UCK showed different degree winding signs or ring signs on 2D ultrasonic image.They were identified as loose UCK, tight UCK, spiral umbilical cord and twisted umbilical cord by 3D-US.Therefore,3D-US can more accurately differentiate from the false UCK and evaluate the tension degree of the true UCK when the prenatal diagnosis of true UCK is highly suspected on 2D-US.

Siristatidis et al.[16]showed that when the fetal oxygen saturation decreased to 37%,the fetal the resistance index (RI) of middle cerebral artery (MCA) decreased significantly.The fetuses developed hypoxic metabolism when the oxygen saturation dropped to 30% or lower.Our study found that the resistance index of middle cerebral artery in the UCK group was lower than that in the normal control group.However,the difference was not obvious.This may suggest that although there were the formation of UCK,the hemodynamic changes were not significant without tight UCK.

Analysis of risk factors associated with true UCK

Our study showed that male fetuses was not higher frequency of the formation of true UCK more often than females between the two groups.This result was inconsistent with previous literature[17].In addition,according to the study showed that if UCK was diagnosed before birth, cesarean section may be the best way to deliver the fetuses[18].However,Airas and Heinonen[5]thinked that monitoring vaginal delivery seemed to be a safe method for fetuses with true UCK.Our study found no differences in delivery patterns between the two groups.In the study group,cesarean delivery were the majority,which may be relevant to maternal previous history of cesarean.

Long umbilical cords were present in 4% of placentae, which increases the risk of true UCK and cord entanglement.Mothers with a history of an excessively long umbilical cord was proved to get increased risk of a long cord in subsequent pregnancies[19]. Our results showed that maternal age, parity,gestational diabetes mellitus,long cords and hydramnios were the risk factor of the formation of true UCK. Hydramnios at term was an independent risk factor for perinatal fetal death,and fetal surveillance was warranted in patients with hydramnios[20].However, the correlation between hydramnios and true UCK had not been found in Airas U and Heinonen S[5]study.The 3 fetuses who died of the true UCK were in late pregnancy.This may suggested that it is indispensable that prenatal real-time ultrasound provide appropriate monitoring to decide the optimal time of delivery to obstetricians.

Conclusion

Although the prenatal 2D-US signs of UCK are complex and lack of

characteristic sign,the reconstruction of umbilical cord 3D image is helpful for the prenatal diagnosis of suspicious UCK detected by 2D-US.In addition,it is helpful for the evaluation of fetal safety, early detection and timely intervention to prevent adverse consequences via combined with Doppler dynamic observation.

Funding

None.

Details of ethics approval

Not applicable.

Contribution to authorship

JF.G, Y.Z, WQ.Q, L.L, CF.G, WY.L and CX.Z conceived this study and collected relevant data, JF.G and CX.Z wrote the draft, CX.Z revised the manuscript.

Disclosure of interests

The authors declare that they have no conflict of interests.

Acknowledge

None.

References

Table 1. The value of 2D-US in diagnosing for UCK.

2D US	Postnatal diagnosis	
	With UCK	Without UCK
With UCK	9	6
Without UCK	90	40241

Table 2. The independent-sample t test or The Mann-Whitney Test of ultrasonic parameters in both study groups.

group	Number	Middle Cerebral Artery(MCA)			Umbilical Artery(UA)		
		PI	RI	S/D	PI	RI	S/D
UCK Group	99	1.21±0.18	0.75±0.07	4.34±1.41	0.76±0.15	0.55±0.08	2.28±0.44
Control Group	200	1.24±0.16	0.76±0.06	4.59±1.43	0.78±0.11	0.56±0.06	2.32±0.32
t/Z		1.812	1.988	-1.810	-1.857	-1.803	-1.712
P-Value		0.07	< 0.05	0.07	0.06	0.07	0.09

Table 3. Findings from simple logistic regression model analysis.

Risk factors		Group with UCK (n=99)	Group without UCK(n=200)	P-value
Maternal age(years)	< 20	1(1%)	0(0%)	
	20-30	47(47.5%)	137(68.5%)	
	31-40	43(43.4%)	62(31.0%)	
	> 40	8(8.1%)	1(0.5%)	P < 0.001
Parity(n)	1	29(29.3%)	91(45.5%)	
	2-4	61(61.6%)	103(51.5%)	
	> 4	9(9.1%)	6(3%)	P < 0.001
Gestational weeks	≥28and < 37	15(15.2%)	25(12.5%)	
	≥37and < 42	84(84.8%)	172(86%)	
	≥42	0(0%)	3(1.5%)	0.0227
Birth weight(g)	< 2500	11(11.1%)	15(7.5%)	
	2500-4000	79(79.8%)	180(90%)	
	> 4000	9(9.1%)	5(2.5%)	0.4368
Fetal gender	Male	62(62.6%)	103(51.5%)	
	Female	37(37.4%)	97(48.5%)	0.0695
Gestational diabetes mellitus		14(14.1%)	8(4%)	0.0029
Maternal anemia		10(10.1%)	19(9.5%)	0.8688
Amniotic fluid volume(ml)	< 300	12(12.1%)	47(23.5%)	
	300-2000	82(82.8%)	151(75.5%)	
	> 2000	5(5.1%)	2(1.0%)	< 0.001
Cord length	< 55	5(5.1%)	75(37.5%)	
	55-61	56(56.5%)	103(51.5%)	
	> 61	38(38.4%)	22(11%)	< 0.001
Delivery mode	Cesarean delivery	61(61.6%)	121(60.5%)	
	vaginal delivery	38(38.4%)	79(39.5%)	0.8524