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Isolated single umbilical artery: evaluating the risk of adverse pregnancy outcome

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ABSTRACT

Objective: To evaluate if isolated single umbilical artery (SUA) diagnosed on second-trimester ultrasound has an independent risk association with adverse pregnancy outcomes.
Study design: We compared 136 singleton pregnancies with isolated SUA with 500 consecutive singleton pregnancies with a three-vessel cord (3VC). Pregnancies complicated by chromosomal abnormalities and other congenital malformations were excluded. The rates of intrauterine growth restriction (IUGR) defined as birth weight less than the 3rd percentile, small for gestational age (SGA) fetuses, defined as a birth weight lower than the 10th percentile and the incidence of very preterm deliveries before 34 weeks of gestation were compared between the two groups. Multivariable logistic regression analysis was performed to evaluate the risk association between SUA and adverse pregnancy outcomes, while controlling for potential confounders.
Results: Fetuses with isolated SUA had significantly lower birth weight (2942.5 ± 783.7 vs. 3243.7 ± 585.6 g, $p = 0.002$), and were delivered at an earlier gestational age (38.7 ± 3.4 vs. 39.5 ± 2.2 weeks, $p < 0.001$), when compared to fetuses with a 3VC. Fetuses with isolated SUA were at higher risk for IUGR (15.4% vs. 1.8%, $p < 0.001$), SGA (20.6% vs. 4.4%, $p < 0.001$) and very preterm delivery (6.6% vs. 1.4%, $p = 0.002$). Using a multiple logistic regression model, isolated SUA was shown to be an independent risk factor for IUGR (adjusted OR = 11.3, 95% CI 4.8–25.6; $p < 0.001$) and very preterm delivery (adjusted OR = 5.0, 95% CI 1.8–13.8; $p = 0.002$).
Conclusions: The presence of isolated SUA is independently associated with an increased risk for IUGR, SGA and very preterm delivery.

Introduction

The absence of one umbilical artery, which represents the most common anatomical abnormality of the umbilical cord, is found in 0.2–2.0% [1–4] of deliveries. The pathogenesis of this condition, known as single umbilical artery (SUA), is uncertain. Aplasia or atrophy of the missing vessel has been suggested in the etiology [5]. Fetuses with SUA are considered at increased risk of chromosomal and structural abnormalities and increased adverse perinatal outcome, such as perinatal mortality, growth restriction and preterm labor [2,3,6,7]. Despite these associations, controversy exists regarding the clinical significance of SUA as an isolated finding in a low-risk patient population. Some of the current literature did not demonstrate an increased risk of IUGR in anatomically normal fetuses with SUA and the authors suggested that the remaining artery in SUA fetuses carries twice the blood volume of an artery in a 3VC [4,8,9]. Other studies reported that the finding of SUA is associated with increased incidence of fetal growth restriction, prematurity and perinatal mortality and recommended serial sonograms for fetal growth and close obstetric follow-up [3,10–13].

While other authors have placed much emphasis on the association between SUA and aneuploidy or co-existing anomalies [1,2,5–7,10–12], the aim of our study was to estimate the rates of adverse pregnancy outcome in a low-risk patient population. Therefore, we included only fetuses without known chromosomal

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abnormalities and associated major congenital anomalies and evaluated the risk of intrauterine growth restriction (IUGR), small for gestational age (SGA) fetuses and the incidence of deliveries before 34 gestational weeks compared to a control group of 500 fetuses with a three-vessel cord (3VC) using a robust, prospectively obtained database.

Materials and methods

This is a retrospective cohort study of consecutive patients, with a two-vessel umbilical cord, who received second-trimester ultrasonography at our tertiary referral center between 2004 and 2011 as part of routine antenatal care. Study approval was obtained from the institutional review board of the Medical University of Vienna (ECS 1160-2013). Demographic information, maternal medical and obstetrical history, ultrasonographic findings, and genetic screening or diagnostic results are entered into a prospective perinatal database at the time of the ultrasound examination for all patients seen at our institution. Additionally, all pregnancy and neonatal outcome information, assessed by a neonatologist, was entered into this database. A SUA was diagnosed by visualizing two vessels on a cross section of the umbilical cord. If necessary, color flow mapping was used to visualize the umbilical arteries adjacent to the fetal bladder. When SUA was suspected, a detailed second trimester fetal anomaly scan was undertaken according to routine clinical practice and the patients were offered fetal karyotyping. Doppler flow indices of the uterine and the umbilical artery were performed in all cases at 20–25 weeks of gestation. We measured the Pulsatility Index (PI) of the umbilical artery in each fetus together with PI flow measurements and notch evaluation of the uterine arteries was obtained. All measurements were performed in accordance to the guidelines of the International Society for Ultrasound in Obstetrics and Gynecology (ISUOG) (www.isuog.org).

Primary outcomes included the risk of IUGR, small for gestational age fetuses (SGA), intrauterine fetal death (IUFD) and very preterm delivery in cases of isolated SUA.

Estimation of fetal weight was calculated by applying the Hadlock formula using composite measures of fetal biometry [14]. IUGR was defined as birth weight less than the 3rd percentile and SGA was defined as a birth weight less than the 10th percentile. Very preterm delivery was defined as a delivery before 34 gestational weeks and IUFD was defined as fetal death at 20 weeks or more of gestation.

The institution's perinatal database was the used to identify 500 consecutive pregnancies with a 3VC, which were seen during the same time period at our institution's outpatient clinic. All baseline characteristics as well as the incidence of the primary outcomes were compared between patients with and without isolated SUA. Additionally we controlled for potential confounders such as obesity, defined as a BMI >30, tobacco use, gestational diabetes with insulin treatment, hypertension and methadone abuse. Given the known risk of adverse pregnancy outcome in fetuses with aneuploidy and severe malformations, all cases with chromosomal abnormalities and major fetal anomalies were excluded.

Statistical analysis

In this cohort study we used descriptive statistics for analyses of patients' demographic data. Values are given as mean (standard deviation [SD]) when normally distributed or as median (range) at presence of skewed distribution. Student's *t*-test was used to compare continuous variables, and Chi square test and Fisher's exact test was used to compare categorial variables. For multivariable analysis a logistic regression model was used entering preterm birth or presence of IUGR as dependent variable and risk factors as covariates. The statistical software SPSS 18.0 for Windows (SPSS 18.0, SPSS Inc, Chicago, IL, USA) was used for statistical analyses. *p*-Values of <0.05 were considered statistically significant.

Results

In total, 209 cases of SUA were identified during the 8-year study period, giving an incidence of 1.4% in our patient population. Seven (3.3%) fetuses showed chromosomal abnormalities (Trisomy 21 ($n = 1$), Trisomy 18 ($n = 4$), Trisomy 9 ($n = 1$) and chromosomal mosaicism ($n = 1$)). All fetuses with karyotype aberrations showed other malformations affecting the central nervous system ($n = 2$), the heart ($n = 4$) or the urogenital system ($n = 1$). Twenty (9.6%) chromosomally normal fetuses presented with other major structural anomalies: Ten fetuses showed congenital heart defects (atrioventricular valve dysplasia ($n = 2$), Tetralogy of Fallot ($n = 3$), double outlet right ventricle ($n = 2$), ventricular septal defect ($n = 3$)). In 10 cases structural malformations affected the following systems: musculoskeletal ($n = 2$), gastrointestinal ($n = 1$), urogenital ($n = 4$) and central nervous system ($n = 3$). Additionally, 18 (8.3%) twin pregnancies were observed (dichorionic ($n = 16$); monochornionic ($n = 2$)). Cases with congenital malformations, chromosomal anomalies and multiple pregnancies were excluded from the cohort. Additionally 28 (13.4%) patients had to be excluded because they were referred from other hospitals for a second opinion sonogram and data on pregnancy outcome was missing. In total, 136 fetuses showed single umbilical artery as an isolated finding and delivered at our center. These cases were used for analysis. Maternal demographics and pregnancy characteristics for our population are shown in Table 1. Twenty-five (18.4%) women opted for prenatal karyotyping revealing normal test results. The remaining pregnancies resulted in healthy infants, therefore no additional karyotypes were obtained in the postnatal period. Patients with fetuses with isolated SUA were found to have a comparable BMI at the time of ultrasound examination and similar rates of hypertension, preeclampsia, gestational diabetes, tobacco use and substance abuse compared to patients with a 3VC ($n = 500$).

Patients with isolated SUA delivered earlier than patients without SUA (38.7 ± 3.4 weeks vs. 39.5 ± 2.2 weeks, mean difference: 0.8 weeks, $p = 0.002$) and birth weights were significantly lower in neonates with SUA (2942.5 ± 783.7 g vs. 3243.7 ± 585.6 g, mean difference 301.2 g, $p < 0.001$) compared to the 3VC group. Results of the univariate analyses are provided in Table 2. The rate of very preterm delivery before 34 weeks of gestation was increased in pregnancies with SUA ($p = 0.002$) even after controlling for BMI >30, hypertension, preeclampsia, gestational diabetes, cigarette smoking and methadone abuse (Table 3). Patients with isolated SUA were at increased risk for IUGR compared to those without SUA (15.4% versus 1.8%; $p < 0.001$) (Table 2). The association between SUA and IUGR

Table 1
Patients' characteristics ($n = 636$).

	N or mean	% or SD
Maternal age (years)	28.6	6.5
Gravidity	2.7	1.6
Parity	1.1	1.1
Gestational age at ultrasound (weeks)	21.4	4.7
BMI > 30	84	13.2%
Diabetes	51	8%
Preeclampsia	9	1.4%
Cigarette smoking	173	27.2%
Substance use	13	2%
Fetal sex (female)	306	48.1%

BMI, body mass index, SD, standard deviation.