Three-dimensional sonographic calculation of the volume of intracranial structures in growth-restricted and appropriate-for-gestational age fetuses

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Abstract

Intrauterine growth restriction (IUGR) has well-recognized perinatal and long term consequences. Because not all fetuses that are found to be small in utero have true growth restriction, the distinction of placental insufficiency from constitutional smallness has been one of the goals of fetal medicine over the last 20 years. Although intrauterine growth-restricted (IUGR) fetuses develop protective mechanisms, such as increased blood flow and oxygen uptake, they have an increased risk of developing signs of brain damage at birth.

Our study was a prospective observational study that aimed to analyze the possible existence of differences in the volume of fetal intracranial structures between IUGR (symmetric and asymmetric) and appropriate-for-gestational age fetuses in relation to MCA Doppler to determine cases with brain sparing effect and whether there is corresponding change in brain volume in relation to MCA Doppler changes.

In our study, 160 patients were included from those attending the Obstetrics and Gynecology department, fetal medicine unit at Kasr AL Aini hospital, Cairo University. We used VOCAL, which provides a semiautomatic delineation that frequently requires manual adjustments by the operator. VOCAL was selected instead of a multiplanar technique because this method requires less time to calculate volumes and has acceptable reproducibility. A technically successful measurement was obtained in all cases. Fetal brain volume data demonstrate a statistically significant linear increase of fetal brain volume relative to gestational age. Weekly increase in fetal brain volume is 20.51cm^3 for IUGR and 22.53 cm^3 for AGA. The fetal BV in IUGR is 296.366 cm^3. In AGA group the fetal BV is 335.284 cm^3.

Key words: IUGR; Doppler; Three-dimensional ultrasound; VOCAL

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Results

List of Abbreviations

2D: Two Dimensional

2DUS: Two Dimensional Ultrasonography

3D: Three Dimensional

3DUS: Three Dimensional Ultrasonography

AC/FL: Abdominal Circumference/Femur Length Ratio,

AC: Abdominal Circumference,

AFI: Amniotic Fluid Index

AGA: Average-for-Gestational-Age

APS: Anti phosphor Lipid syndrome

AREDF: Absent-Reversed end diastolic flow

BPD: Biparietal Diameter

BV: Brain Volume

CK: Creatine kinase

CNS: Central nervous system

CPR: Cerebro-placental ratio

CRI: cerebral resistance index

C/U: Cerbroumblical ratio

DV: Ducts Venuses

EFW: Estimated Fetal Weight

FGR: Fetal Growth Retardation

FHR: Fetal Heart Rate

GA: Gestational Age

GRIT: Growth Restriction Intervention Trial

HC/AC: Head Circumference/Abdominal Circumference Ratio,

HWL: Height width length

ICV: Intracranial volume

IGF-1: Insulin-Like Growth Factor-1

IGF-2: Insulin-Like Growth Factor-2

IL-6: Interlukin-6

IUGR: Intrauterine Growth Restriction

MCA: Middle Cerebral Artery

MRI: Magnetic Resonance Imaging

NBAS: Neonatal behavioral assessment scale

NICU: Neonatal Intensive Care,

NPV: Negative Predictive Value,

NS: No Significant Difference Between Groups,

NST: Non Stress Testing

PI: Pulsatility Index

PIH: Pregnancy Induced Hypertension

PPV: Positive Predictive Value,

RI: Resistance Index

sFlt-1: Soluble Fms-like tyrosine kinase1

S/D: Systolic/Diastolic

SGA: Small-for-Gestational-Age Fetuses

TNF-alpha: Tumor Necrosis Factor-Alpha

UA: Umbilical Artery

URI: Umbilical resistance index

UTI:Urinary tract infection

VLBW: Very Low Birth Weight

VOCAL: Virtual Organ Computer-aided Analysis

Introduction

Intrauterine growth restriction (IUGR) has well-recognized perinatal and long term consequences. Because not all fetuses that are found to be small in utero have true growth restriction, the distinction of placental insufficiency from constitutional smallness has been one of the goals of fetal medicine over the last 20 years **(Cruz-Martinez et al., 2009)**. The most widely used sign to identify placental insufficiency and consequently to diagnose IUGR is an elevated pulsatility index (PI) in the umbilical artery (UA) **(Lackman et al., 2001a; Lackman et al., 2001b)**. Small fetuses with normal UA Doppler findings are defined normally as small-for-gestational-age (SGA), and earlier reports suggested that they essentially might represent constitutionally small fetuses **(Soothill et al., 1999)**.

However, recent evidence suggests that this diagnostic category contains a proportion of cases with true forms of fetal growth restriction, where the degree of placental insufficiency is not reflected in the UA Doppler findings. Thus, studies over the last decade have provided evidence that, on average, SGA fetuses have significantly poorer perinatal outcomes **(McCowan et al., 2000; Doctor et al., 2001; Severi et al., 2002)**. In addition, a considerable proportion of these fetuses show abnormal neurobehavior neonatally **(Als et al., 1976; McCowan et al., 2002; Padidela and Bhat, 2003)** and abnormal neurodevelopmental tests in childhood, **(Figueras et al., 2008)** with features similar to those described for children who have IUGR **(Tolsa et al., 2004; Feldman and Eidelman, 2006)**. Because the identification of SGA fetuses with true growth restriction cannot be based on UA Doppler findings, assessment of fetal signs such as brain circulation changes could be used for these purposes **(Hershkovitz et al., 2000; Severi et al., 2002; Habek et al., 2007)**. Chronic fetal hypoxia is associated consistently with increased brain perfusion, which is also defined as brain sparing **(Scherjon et al., 1993)**. In clinical practice, brain sparing is identified by a middle cerebral artery (MCA) Doppler PI below the 5th percentile **(Dubiel et al., 2002)**. Recent studies have demonstrated that a proportion of SGA fetuses with MCA vasodilation have poorer perinatal outcome

(Hershkovitz et al., 2000; Severi et al., 2002) and a higher risk of abnormal neurobehavior neonatally **(Oros et al., 2007)** at 2 years of age **(Eixarch et al., 2008)**. These studies support the use of brain Doppler evaluation to distinguish SGA with growth restriction from constitutional smallness.

Although intrauterine growth-restricted (IUGR) fetuses develop protective mechanisms, such as increased blood flow and oxygen uptake, they have an increased risk of developing signs of brain damage at birth **(Fouron et al., 2001; Padilla-Gomes et al., 2007; Gonzalez et al., 2007; Benavides-Serralde et al., 2009)**. The brain is particularly sensitive to changes in oxygen and glucose concentration. Studies performed in neonates and in young adults born with intrauterine growth restriction have shown that signs of neurological damage can be manifested later in life as low scores in neuro developmental tests and reduced cognitive function **(Majnemer et al., 1993; Upadhyay et al., 2000; Tideman et al., 2007)**. Neonatal studies using brain biometry and volume segmentation have demonstrated the existence of selective growth restriction in certain brain regions **(Makhoul et al., 2004; Duncan et al., 2005)**, which could explain subsequent alterations in neurodevelopment. Whether these changes occur in utero is unknown.

Aim of the work

In the present study, we aimed to analyze the possible existence of differences in the volume of fetal intracranial structures between IUGR (symmetric and asymmetric) and appropriate-for-gestational age fetuses in relation to MCA Doppler to determine cases with brain sparing effect and whether there is corresponding change in brain volume in relation to MCA Doppler changes