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Placental volume, vasculature and calcification in pregnancies complicated by pre-eclampsia and intra-uterine growth restriction

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ABSTRACT

Objective: Pre-eclampsia (PET) and intrauterine growth restriction (IUGR), often associated with impaired placental function, are among the most common conditions contributing to increased perinatal mortality and morbidity. This study investigates if three dimensional power Doppler (3DPD) of the placenta and computerised analysis of placental calcification is different between PET/IUGR and normal pregnancies.

Study design: This was a prospective cohort study involving 50 women with pre-eclampsia and/or IUGR, or with IUGR only from 24 to 40 weeks' gestation. 3DPD ultrasound was used to calculate placental volume, vascularisation index (VI), flow index (FI) and vascularisation-flow index (VFI). Following each scan the percentage of placental calcification was also calculated, by computer analysis. Results were compared with normal (control) values, and findings correlated with maternal and fetal Doppler parameters and placental histology.

Results: Volume, VI, and VFI are not influenced by gestational age in PET/IUGR pregnancies. FI was found to increase with gestational age ($p = 0.009$) and was lower than normal in the total study group from 24 to 30 weeks ($p = 0.006$). In the pregnancies affected by PET, whether or not IUGR was present, all three indices were lower than normal values between 24 and 30 weeks (VI: $p = 0.038$, FI: $p = 0.004$, VFI: $p = 0.015$). Vascularisation and flow indices were less than the normal 50th centile in the majority of cases of utero-placental insufficiency ($p = 0.047$), and vascularisation and vascularisation flow indices were lower in cases of accelerated placental maturation ($p = 0.016$ and 0.041 respectively). Placental volume greater than the 50th centile between 24 and 30 weeks was associated with the presence of infarction on histology ($p = 0.021$). Flow index ($p = 0.002$) and vascularisation flow index ($p = 0.036$) were lower in the presence of bilateral uterine artery notches. Calcification, similar to the control group, was related to an increasing UAPI ($p = 0.041$) and MCA PI <5th centile ($p = 0.010$).

Conclusions: The study findings suggest that there may be a role for 3DPD placental assessment of volume, vascularisation and blood flow and computer analysis of placental calcification in the identification and management of PET/IUGR pregnancy.

Introduction

Pre-eclampsia (PET) and intrauterine growth restriction (IUGR), conditions resulting from ischaemic placental disease [1], necessitate obstetric interventions for delivery. Both conditions are associated with increased perinatal mortality and morbidity, with IUGR identified as the most common cause of stillbirth [2,3]. The cause of PET (affecting approximately 6–8% of all pregnancies [4]) can be either maternal, placental or both. Maternal PET results from the interaction between a normal placenta and maternal microvascular disease. Placental PET results from poor placentation. In the pre-clinical phase (before 20 weeks gestation), there is reduced utero-placental circulation capacity and in the clinical phase the placenta becomes more hypoxic. In the more severe cases, (usually of early-onset, i.e. before 34 weeks gestation [5]), fetal hypoxia and stillbirth can occur. IUGR can develop as a result of a primary placental pathology or from maternal disease which affects the placenta, e.g. PET (with poor placentation). The majority of cases of IUGR will have significant placental pathology, including pre-eclampsia related changes [6].

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Previous studies to assess blood flow density in placental volumes have shown the flow index (FI) to be reduced in the most severe cases of placental impairment [7], and all three vascularisation and blood flow indices to be reduced in IUGR [8]. Recent studies have concentrated on first trimester assessment. This study sets out to assess if placentae of pregnancies complicated by PET and/or IUGR on ultrasound differ from normal and to investigate if there is a role for 3DPD studies in the management of pregnancies complicated by PET, +/−IUGR and in pregnancies complicated with IUGR only in the second and third trimester.

We also investigate the role of computer analysis, as an alternative to Grannum grading, to identify placental calcification in PET/IUGR pregnancies. This is done using a novel, 2D ultrasound imaging software tool, the 'placentometer' which was developed in the School of Medicine and Medical Sciences, University College Dublin [9].

Materials and methods

This was a case-controlled longitudinal study. With institutional ethical approval and maternal written consent 35 women with suspected IUGR and 15 women with PET, with or without growth restriction were recruited to the study. Criteria for PET were a diastolic blood pressure reading of 90 m/Hg or more and proteinuria of >0.3 g in a 24 h urine collection or urinalysis protein reading of +1 or above. Criteria for IUGR were reduced growth velocity in the abdominal circumference and/or an estimated fetal weight on or below the 10th centile for gestational age plus/minus increased umbilical artery Doppler pulsatility index (PI) or absent end diastolic flow. Gestational age at the time of the scans ranged from 24 + 4 to 40 weeks. The number of scans per patient (1 to 3) depended on the gestational age at recruitment (total number of scans 66).

All scans were performed transabdominally using a Voluson 730 Expert ultrasound machine (GE Medical Systems, Austria), equipped with curved array transducers. A 2–7 MHz transducer was used to acquire all two dimensional (2D) images, and a 4–8 MHz transducer was used to acquire the three dimensional (3D) images. Each scan incorporated assessment of placental site, fetal biometry and estimation of fetal weight. Doppler studies of the umbilical artery (UA), middle cerebral artery (MCA) and uterine artery (UtA) were performed, and PI calculated.

The 3DPD placental image saved at each scan was subsequently analysed to calculate volume, vascularisation index (VI), flow index (FI) and vascularisation-flow index (VFI) using the Virtual Organ Computer-aided AnaLysis (VOCAL^{TM}) software (3 dimensional Sonoview, GE Healthcare) [10]. Once each image was rotated 180° a shell contour was displayed and volume automatically calculated and accepted. 'Contour Histogram' was then selected from the VOCAL menu. This allowed the calculated histogram to appear on the screen, displaying the vascular indices VI, FI and VFI (Fig. 1). In four cases it was not possible to obtain an adequate 3DPD image of the placenta. One of these cases had an upper anterior placenta and the position was upper posterior in the other 3 gestational age at the time of these 4 scans ranged from 31 + 1 to 38 + 1 weeks.

To calculate the percentage of placental calcification, using the placentometer, the region of interest (ROI) was first selected, by drawing an outline around the placenta using a pointing device controlled by the mouse. Pixels were recorded following the mouse movements and were then joined into line-segments. These segments were finally combined to form a continuous outline. The ROI included the basal, body and surface areas of the placenta. A slider was then used to alter the intensity threshold for defining calcification within the ROI. The next stage in the process was the creation of a flood-filing algorithm which produced a secondary reference map used in a quantification algorithm. When all the relevant areas of calcification were highlighted metric

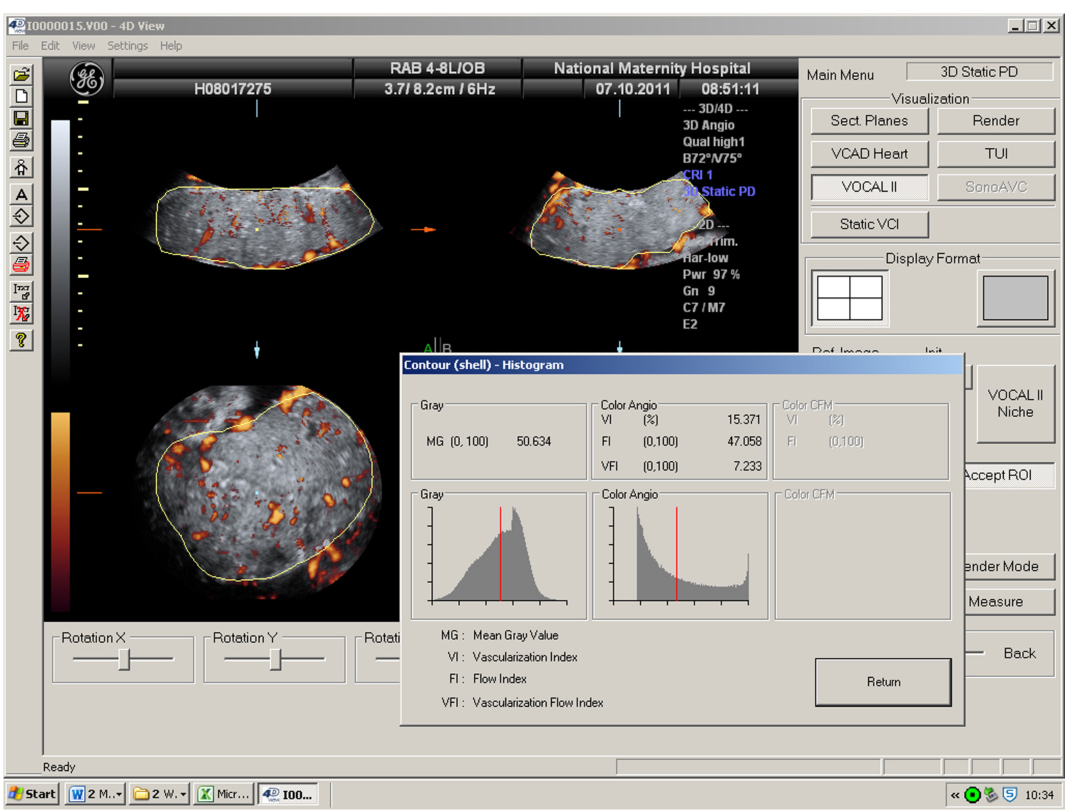

Fig. 1. 3D power Doppler histogram demonstrating the placental vascular indices [VI (15.371%), FI (47.058) and VFI (7.233)].