Reliability of First-Trimester Ultrasonic Biopsy for the Evaluation of Placental and Myometrial Blood Perfusion and the Prediction of Preeclampsia

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Abstract

Objective: Low placental vascularization measured by three-dimensional (3-D) ultrasound with power Doppler can predict preeclampsia. We evaluated the reliability and reproducibility of the ultrasonic sphere biopsy (USSB) technique to evaluate placental and subplacental myometrium vascularization in the first trimester.

Methods: We performed a secondary analysis of a case-control study nested in a prospective cohort of women with a singleton pregnancy undergoing ultrasound at 11 to 14 weeks' gestation. Women who developed preeclampsia (n = 20) and randomly selected controls (n = 60) were compared. Other controls (n = 60) were also randomly selected to evaluate intra- and inter-observer reproducibility. Using 3-D power Doppler, the vascularization index (VI), flow index (FI), and vascularization flow index (VFI) were measured from the volume of the whole placenta and the subplacental myometrium and from their respective USSB. Pearson's correlation coefficients (cc) with their *P*-values were calculated.

Results: We observed that USSB is reliable in estimating the vascularization of the whole placenta in the first trimester (cc of VI 0.83; of FI 0.62; and of VFI 0.78; $P < 0.001$ for all) but was not as reliable for estimating subplacental myometrium vascularization (cc of VI 0.71; of FI 0.35; and of VFI 0.73). Measurement of placental vascularization using USSB showed good to excellent intra- and inter-observer reproducibility (cc of VI 0.86 and 0.85, respectively; of FI 0.75 and 0.75, respectively; and of VFI 0.83 and 0.83, respectively; $P < 0.001$ for all). Finally, we observed that women who subsequently developed preeclampsia had lower placental USSB VI (2.1 vs 4.8, $P = 0.02$), FI (32.4 vs. 42.5, $P = 0.002$), and VFI (0.8 vs. 2.1, $P = 0.01$) than controls.

Conclusion: First-trimester USSB of the placenta using 3-D power Doppler is a reliable and reproducible procedure for estimating placental vascularization and could be used to predict preeclampsia.

Key Words: Pregnancy, preeclampsia, placenta, ultrasound, three-dimensional, doppler

Competing Interests: None declared.

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Résumé

Objectif : La détection d'une faible vascularisation placentaire par échographie 3D couplée au Doppler de puissance est un facteur prédicteur de prééclampsie. Nous nous sommes penchés sur la fiabilité et la reproductibilité de la technique de biopsie sphérique par échographie dans le contexte de l'évaluation de la vascularisation placentaire et sous-placentaire au premier trimestre.

Méthodologie : Nous avons effectué une analyse secondaire d'une étude cas-témoin tirée d'une cohorte prospective de femmes enceintes d'un fœtus unique ayant subi une échographie entre la 11^{e} et la 14^{e} semaine de la grossesse. Les femmes qui ont développé une prééclampsie (n = 20) ont été comparées à un groupe témoin de patientes sélectionnées aléatoirement (n = 60). Un autre groupe témoin de patientes (n = 60) ont aussi été sélectionnées aléatoirement pour évaluer la reproductibilité intra- et interobservateur. Nous avons calculé l'indice de vascularisation (IV), l'indice de flux (IF) et l'indice de flux vasculaire (IFV) à partir d'une échographie 3D couplée au Doppler de puissance du placenta entier et du myomètre sous-placentaire, ainsi que de leurs biopsies sphériques par échographie respectives. Le coefficient de corrélation de Pearson et la valeur *P* ont été calculés.

Résultats : Nous avons observé que la biopsie sphérique est une méthode fiable pour estimer la vascularisation du placenta entier au premier trimestre (coef. de Pearson : IV : 0,83; IF : 0,62; IFV : 0,78. $P < 0{,}001$ pour tous), mais qu'elle ne permet pas d'estimer avec fiabilité la vascularisation du myomètre sous-placentaire (coef. de Pearson : IV : 0,71; IF : 0,35; IFV : 0,73). La reproductibilité intra- et interobservateur de la mesure de la vascularisation placentaire par biopsie sphérique était bonne à excellente (coef. de Pearson : IV : 0,86 et 0,85, respectivement; IF : 0,75 et 0,75, respectivement; IFV : 0,83 et 0,83, respectivement. $P < 0{,}001$ pour tous). Enfin, nous avons observé que par rapport aux témoins, les femmes qui ont développé ultérieurement une prééclampsie présentaient des valeurs inférieures à la biopsie sphérique par échographie du placenta entier pour l'IV (2,1 c. 4,8; $P = 0{,}02$), l'IF (32,4 c. 42,5; $P = 0{,}002$) et l'IFV (0,8 c. 2,1; $P = 0{,}01$).

Conclusion : La biopsie sphérique du placenta effectuée au premier trimestre par échographie 3D couplée au Doppler de puissance est une méthode fiable et reproductible pour estimer la vascularisation placentaire et peut être utilisée pour prédire le développement d'une prééclampsie.

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INTRODUCTION

Preeclampsia is a multisystem disorder of pregnancy associated with placentation disorders, mainly in the severe and early-onset forms of the disease.[1,2] An early diagnosis of impaired placentation could help in the identification of women at high risk for preeclampsia. Uterine artery Doppler velocimetry has been typically used to estimate placental insufficiency related to incomplete transformation of uterine spiral arteries and the risk of preeclampsia.[3,4] Using three-dimensional ultrasound with power Doppler velocimetry, we observed that first-trimester vascularization indices for the whole placenta and for the subplacental myometrium were lower in women who developed preeclampsia.[5] The predictive values of those indices could be superior to uterine artery Doppler velocimetry.[5–7] However, measurement of the volume and vascularization of the entire placenta requires manual drawing of the contour of the placenta in several planes; this is time-consuming (up to 30 minutes per patient) and requires expertise. Therefore, VIs of the entire placenta and of the subplacental myometrium may not be clinically useful for prediction of preeclampsia.

The virtual ultrasonic sphere biopsy technique, a shorter procedure, could be used to estimate the vascularization of the placenta or the sub-placental myometrium.[8] Dar et al. used the ultrasonic sphere biopsy technique to estimate the vascularization of the utero-placental space in the first trimester and observed that women who subsequently developed preeclampsia had lower values of VI, flow index, and vascularization flow index than controls.[8] We aimed to evaluate the reliability and reproducibility of the USSB technique to evaluate placental and subplacental myometrium vascularization in the first trimester in relation to the prediction of developing preeclampsia.

ABBREVIATIONS

cc	correlation coefficients
FI	flow index
USSB	ultrasonic sphere biopsy
VFI	vascularization flow index
VI	vascularization index

METHODS

We performed a secondary analysis of a case-control study nested in a prospective cohort of pregnant women recruited between March 2010 and May 2011. Women with singleton pregnancies were recruited at 11 to 14 weeks of gestation. Women with multiple pregnancies, fetuses with suspected lethal malformations or chromosomal anomalies, and women with pregnancies that ended in spontaneous abortion before 20 weeks were excluded from analysis. After consent, ultrasound was performed at between 11+0 weeks and 13+6 weeks. The crown—lump length was measured, and 3-D sweeps of the entire placenta were acquired using Voluson E8 ultrasound equipment (GE Medical Systems Inc., Milwaukee, WI) equipped with a 4 to 8 MHz transducer. Identical pre-established instrument power settings were used in all cases (angio mode: cent; smooth: 4/5; FRQ: normal quality; density: 7; enhance: 16; balance: 175; filter: 2; actual power: 100% dB; pulse repetition frequency: 0.6 kHz, gain colour: −7.2 dB; WMF = low1).

Gestational age was calculated from the date of the last menstrual period, unless the difference between this calculation and the age indicated by first trimester ultrasound was more than five days. Participants were followed until delivery, and medical records were reviewed for perinatal data, including birth weight, gestational age at delivery, and diagnosis of preeclampsia. Preeclampsia was defined as a systolic blood pressure of 140 mm Hg or more and/or a diastolic blood pressure of 90 mm Hg or more on at least two occasions four hours apart after 20 weeks of gestation, combined with proteinuria (300 mg or more in 24 hours or at least 2+ on dipstick analysis if no 24 hours collection was available).[9,10] Medical records of each case with suspected hypertensive disorder were reviewed, and the diagnosis was validated by a maternal-fetal medicine subspecialist. Cases of preeclampsia diagnosed and delivered before 37 weeks' gestation were considered preterm, and all cases delivered at or after 37 weeks' gestation were deemed term preeclampsia.[2,11–13] Each woman with preeclampsia was matched according to parity and maternal age with three controls who delivered at term without pregnancy complications, including preeclampsia, intrauterine growth restriction, or placental abruption. Another subgroup of 60 women was randomly selected for evaluation of intra- and inter-observer reproducibility.

For each case and control, both placental and subplacental myometrium VI, FI, and VFI were assessed with virtual