RBMOnline - Vol 11. No 2. 2005 232–235 Reproductive BioMedicine Online; www.rbmonline.com/Article/1674 on web 14 June 2005

Article

Subendometrial power Doppler quantification: a new classification proposal

Mirela Jimenez obtained her MD degree in 1983 and the specialist degree in Obstetrics and Gynecology 3 years later at the Faculty of Medicine, Hospital de Clínicas de Porto Alegre (Universidade Federal do Rio Grande do Sul) in Brazil. She is currently engaged in research towards her PhD degree at the same University. At present she is also Physician in Obstetrics and Gynecology at the Hospital de Clínicas de Porto Alegre. Her current research interest lies mainly in contraception.

Dr Mirela Jimenez

MF Jiménez, EP Passos, PAP Fagundes, JA Magalhães, R Palma-Dias, JSL Cunha-Filho[1]
Human Reproduction Centre, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
[1]Correspondence: Rua Ramiro Barcelos, 2350/1135, 90035–003 Porto Alegre, RS, Brazil. Tel: +55 51 21018117; e-mail: sabino@via-rs.net

Abstract

Fifty-two women with regular menses were enrolled in the study. The patients were not allowed to use non-steroidal anti-inflammatory drugs within 24 h of any examination. All patients were examined during the mid-luteal phase (6–9 days after ovulation, according to previous ultrasound record). Power Doppler energy levels were classified into five categories according to the per cent area of sub-endometrial signal: I (<10%), II (10–25%), III (25–50%), IV (50-75%) and V (>75%). The colour Doppler signal was considered positive when it reached at least the endometrial basal layer. The picture of the endometrium was analysed and the regions of interest were identified and marked for further analysis. Each recorded image was then independently evaluated and classified by three blinded observers. According to the power Doppler classification, age, body mass index (BMI) and endometrial thickness were analysed, and no significant differences were observed among them. The Kappa test (0.70) demonstrated an excellent agreement among examiners (P = 0.0001). This study has validated a very simple and cost-effective classification for sub-endometrial vascularization. This method of quantification may potentially be of use, and its relevance to clinical practice should be explored.

Keywords: *classification, endometrial vascularization, power Doppler, power Doppler energy*

Introduction

Power Doppler energy (PDE) is a new modality in ultrasound technology currently being used in several medical specialties, with important diagnostic and therapeutic applications.

PDE uses the amplitude of the Doppler signal instead of the mean frequency shift. Background noise, which can pose difficulties in examination using traditional colour Doppler, is easily distinguishable from true blood flow when using power Doppler. Moreover, due to its enhanced accuracy, PDE could be employed to detect image areas of low blood flow that are currently undetectable by colour Doppler imaging. PDE results from the scattering of ultrasound waves from red blood cells in arteries, arterioles, venules and veins, and thus depicts microvascularization of a specific tissue (Amso *et al*., 2001).

In gynaecology, PDE is useful to detect and examine areas with microvasculature such as the endometrium and the ovaries. The study of intra-endometrial vascularization may be useful to assess one of the factors of endometrial receptiveness for embryo implantation. Moreover, the lowest impedance of uterine blood flow occurs in the luteal phase, probably indicating increased blood flow to the uterus around the presumed time when implantation might occur (Steer *et al*., 1990).

Moreover, women with adequate endometrial thickness but small PDE tended to have unfavourable reproductive outcomes (Yang *et al*., 1999). Nonetheless, the usefulness of this new method has one important and unsolved problem: its quantification, necessary to ensure comparable assessment and classification among different gynaecology diseases.

Some investigators have attempted to demonstrate and validate a number of quantitative or semi-quantitative methods for the measurement of PDE (Amso *et al*., 2001; Järvelä *et al*., 2003).

Other authors described a PDE quantification software that measures the power Doppler indices calculated in a specific area. Calculated indices showed low intra-observer and inter-observer variation for ovary and endometrium, and acceptable levels for small structures such as the follicle (Amso *et al.*, 2001). Computer software measurements, associated with endometrial thickness, were used as a predictive of endometrial receptivity. The authors concluded that the software measurement might serve as a factor indicative of endometrial receptivity for embryo implantation (Yang *et al.*, 1999).

However, due to the lack of a specific computer software and because the results could not be reproduced by other investigators, it has been difficult to use this method. The aim of this study is to describe a new PDE classification using a simple and reproducible method, based on a categorical sub-endometrial microvascularization analysis.

Materials and methods

Design

A prospective cross-sectional study was performed with patients from Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil.

Subjects

The study population (sample) was composed of 52 fertile volunteer women. The inclusion criteria were: (i) regular menses (menstrual cycle varying from 24 to 35 days); (ii) age <40 years; (iii) normal serum TSH, FSH and prolactin concentrations (day –3).

Contraceptive pills or any kind of hormonal preparation had not been used during the previous 3 months and any intrauterine device had been removed at least 3 months earlier. Patients were not allowed to use non-steroidal anti-inflammatory drugs within 24 h of any examination. The exclusion criteria were: pregnancy, acute or chronic inflammatory pelvic disease, menorrhagia of unknown cause, cervicitis, cervical dysplasia or genital tumour. All patients underwent gynaecological examination and had a Pap smear in the previous 12 months.

Study protocol

All subjects were examined during one cycle, with daily ultrasound, so as to assess follicular development for confirmation of ovulation. Then, they were examined in the mid-luteal phase, 6–9 days after the day of ovulation, for the assessment of endometrial thickness and power Doppler measurement by ultrasound scans. The study was approved by the Ethics Committee of Hospital de Clínicas de Porto Alegre (no. 02-127) and all subjects signed an informed consent form.

Power Doppler classification

The sonography equipment consists of a SONOACE 9900 (Medison SA, Seoul, Korea). PDE was performed via the transvaginal route by the same investigator (P.A.P.F.). The settings for power Doppler sonography were standardized for the highest sensitivity in the absence of apparent noise using a high pass filter at 50 Hz, pulsed repetition frequency at 750 Hz, and moderate long persistence. The lowest possible measurable velocity was below 5 cm/s. A picture was captured and the image was marked for further analysis. Moreover, the ultrasound probe was equipped with a native harmonic system that improves image resolution.

Power Doppler energy results were classified into five categories according to percentage sub-endometrial signal area: I (<10%), II (10–25%), III (25–50%), IV (50–75%) and V (>75%).

Each recorded image was then independently evaluated and classified by two (JAM and RPD) blinded ultrasound specialists.

Statistics

Comparisons among the categorical classification and the group characteristics were done by the Kruskal–Wallis test. The probability of chance agreement among three sonography examiners was assessed using the Kappa test ($P < 0.05$ was considered significant). A value of 1 indicates perfect agreement (after allowing for this probability of chance agreement) between ratings; 0 indicates no agreement other than what can be attributed to chance, and a negative value indicates less than chance agreement. Non-parametric Spearman correlation was performed to identify any correlation between endometrial thickness and uterine power Doppler signal. The five categories were chosen as it was suspected that the distribution of the results was not Gaussian (this was confirmed by the results – see below).

Results

In this study, 52 women were evaluated in the mid-luteal phase. The median (percentiles) of age (years) and body mass index (BMI) (kg/m^2) were 28 (27–31) and 22 (21–24) respectively. As far as parity is concerned, of the 52 patients (100%) who comprised the sample, 19 (37%) had no children; 11 (21%) had one; 14 (27%) had two; and 8 (15%) had three children. In terms of abortion occurrences, 22 patients (42%) of the sample reported no occurrences; 30 patients (58%) reported, at least one occurrence.

According to the power Doppler classification, age, BMI and endometrial thickness were analysed and there were no significant differences among them (**Table 1**).

The Kappa test (0.70) indicated excellent agreement among the observers ($P = 0.001$).

In order to investigate a correlation between endometrial thickness and PDE, a Spearman's rho was carried out. The analysis was not statistically significant.

Discussion

This study demonstrated excellent agreement among different examiners, allowing this power Doppler energy quantification

Table 1. Median (range) of age, body mass index (BMI) and endometrial thicknesses in the midluteal phase in 52 subjects according to the classification of the power Doppler energy; group I (<10%), group II (10-25%), group III (25-50%), group IV (50-75%) and group V (>75%). There were no statistically significant differences between the groups.

	Group I (n = *18)*	*Group II* (n = *19)*	*Group III* (n = *9)*	*Group IV* (n = *4)*	*Group V* (n = *2)*
Patient distribution by category (%)	34.6	36.5	17.3	7.7	3.8
Age (years)	28.5 (19–41)	27.5 (19–40)	30.5 (21–41)	26.0 (24–32)	25.5 (22–29)
BMI (kg/m^2)	23 (18–28)	22 (18–36)	22 (18–27)	21 (19–22)	22 (20–24)
Endometrial thickness (mm)	7 (3–10)	8 (3–13)	7 (4–9)	8 (7–8)	7 (5–9)

to be used as a very simple and useful classification for the study of sub-endometrial microvascularization.

Only two subjects were found with sub-endometrial power Doppler signal greater than 75% (class V). This could be because no patients with blood flow enhancing pathologies (pregnancy, acute or chronic inflammatory pelvic disease, menorrhagia of unknown cause, cervicitis, cervical dysplasia or genital tumour) were included.

Patients with fibrosis, endometrial pathologies or adenomyosis were not included in this study; therefore, care should be taken in extrapolating the results to gynaecological conditions, as such conditions could impede or modify the proposed classification.

Quantification of the PDE in ultrasound machines has been an issue of interest in recent years and has ranged from subjective methods to quantitative techniques (Bhal *et al.*, 1999; Contart *et al.*, 2000).

The same authors (Contart *et al.*, 2000) evaluated the power Doppler sub-endometrial vascularization and used it as a parameter for the prognosis of embryo implantation in patients who underwent intracytoplasmic sperm injection (ICSI). The endometrium was divided into four equal quadrants and classified as grade I, II, III or IV according to the visualization of the power Doppler in the quadrants. The colour Doppler signal was considered to be positive when it reached at least the basal layer of the endometrium. The endometrial thickness and pulsatility index of uterine artery were similar for the four grades. The results demonstrated that isolated evaluation of endometrial vascularization with power Doppler is not an important factor for the prediction of pregnancy in an ICSI programme. The same group of researchers (Baruffi *et al.*, 2002) used a scoring system as a method for the prognosis of embryo implantation with seven parameters. The use of this score method could not identify a population with greater uterine receptivity for embryo implantation in an ICSI programme.

The association between endometrial blood flow and endometrial thickness was evaluated in a prospective study in women undergoing IVF. Blood flow was determined by a power Doppler technique: the signal was converted and the image processed. The area of the vascular signal was manually demarcated and automatically calculated and expressed in mm^2. The authors concluded that, in addition to endometrial thickness, PDE might be a factor indicative of endometrial receptiveness (Yang *et al.*, 1999).

No association was found between endometrial thickness and PDE (Spearmen's rho not significant), probably because all ultrasound scans were performed during the same cycle period and the subjects were homogeneous in terms of demographic characteristics.

The sub-endometrial PDE was classified into these five categories, because as was suspected and was confirmed by the results, the distribution was not Gaussian. Consequently, the most accurate method to illustrate sub-endometrial PDE is using the quartile allotment.

In addition, a new software package that quantifies power Doppler energy was tested to evaluate the quantification of vascularization in specific areas in the uterus and ovary. Calculated indices showed low intra-observer and inter-observer variability for ovary and endometrium and acceptable levels for small structures such as the follicle (Amso *et al.*, 2001).

Future studies could be implemented in order to determine vascular changes during the early follicular, mid-follicular and peri-ovulatory phases of normally cycling fertile women as well as facilitate comparisons within and between individuals. Moreover, there is great interest in predicting endometrial receptiveness and embryo implantation in assisted reproduction. Three-dimensional ultrasound was used to obtain quantitative data on endometrial volume and sub-endometrial blood flow, and may be a useful tool in the prediction of pregnancy rate (Wu *et al.*, 2003).

Due to the lack of specific computer software, other investigators could not reproduce these results. This study showed a strong correlation, with Kappa correlation test over 0.70, making this power Doppler quantification a very simple, reproducible, cost-effective and useful classification.

The main focus of this paper was to present and test a simple and reproducible power Doppler classification. It was decided to perform only one ultrasound scan using only one ultrasound equipment in order to control several biases that could interfere the results: ultrasound equipment and adjustment, menstrual cycle day, inter-observer experience and time of day.

Future applications of this method may include studies of corpus luteum perfusion and monitoring of placental perfusion in normal or growth-restricted fetuses. In reproductive medicine, studies of the vasculature may be helpful in monitoring follicular and endometrial changes in women with infertility before and during their treatment.

In conclusion, a very simple classification for the quantification of endometrial microvascularization has been validated. This method of quantification is promising and its relevance to clinical practice could be further explored in different patients and in others clinical conditions in gynaecology.

Acknowledgements

We are grateful for the financial support received from 'Fundo de Incentivo à Pesquisa e Eventos', Hospital de Clínicas de Porto Alegre (FIPE-HCPA), 'Programa de Pós-Graduação em Medicina: Ciências Médicas–UFRGS' and from the 'Conselho Nacional de Desenvolvimento Científico e Tecnológico' (CNPq), Brazil. We are also grateful for the editorial support provided by the Graduated Research Group, Hospital de Clínicas de Porto Alegre, Brazil.

References

Amso NN, Watermeyer SR, Pugh N *et al.* 2001 Quantification of power Doppler energy and its future potential. *Fertility and Sterility* **76**, 583–587.

Baruffi RL, Contart P, Mauri AL *et al.* 2002 A uterine ultrasographic scoring system as a method for the prognosis of embryo implantation. *Journal of Assisted Reproduction and Genetics* **19**, 99–102.

Bhal PS, Pugh N, Chui D *et al.* 1999 The use of transvaginal power Doppler ultrasonography to evaluate the relationship between perifollicular vascularity and outcome in in-vitro fertilization treatment cycles. *Human Reproduction* **14**, 939–945.

Contart P, Baruffi RL, Coelho J *et al.* 2000 Power Doppler endometrial evaluation as a method for the prognosis of embryo implantation in an ICSI program. *Journal of Assisted Reproduction and Genetics* **17**, 328–334.

Järvelä I, Sladkevicius P, Tekay AH *et al.* 2003 Intraobserver and interobserver variability of ovarian volume, gray-scale and colour flow indices obtained using transvaginal three-dimensional power Doppler ultrasonography. *Ultrasound Obstetrics and Gynecology* **21**, 277–282.

Steer CV, Campbell S, Pampiglione JS *et al.* 1990 Transvaginal colour flow imaging of the uterine arteries during the ovarian and menstrual cycles. *Human Reproduction* **5**, 391–395.

Wu HM, Chiang CH, Huang HY *et al.* 2003 Detection of the subendometrial vascularization flow index by three-dimensional ultrasound may be useful for predicting the pregnancy rate for patients undergoing in vitro fertilization–embryo transfer. *Fertility and Sterility* **79**, 507–511.

Yang JH, Wu MY, Chen CD *et al.* 1999 Association of endometrial blood flow as determined by a modified color Doppler technique with subsequent outcome of in-vitro fertilization. *Human Reproduction* **14**, 1606–1610.

Received 15 December 2004; refereed 19 January 2005; accepted 21 April 2005.