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Original Article

Diagnostic utility of three-dimensional power Doppler ultrasound for postmenopausal bleeding

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ABSTRACT

Objectives: We evaluated the role of three-dimensional power Doppler ultrasound (3D PD-US) to detect endometrial lesions in women with postmenopausal endometrial bleeding.
Materials and methods: In this prospective observational study, from January 2009 to November 2012, we recruited 225 postmenopausal women with postmenopausal uterine bleeding who met the study criteria. Women who had hematologic disease, chronic medical diseases, or nonuterine pelvic diseases were excluded. Prior to endometrial biopsy, the patients underwent a baseline transvaginal ultrasound screening. The vascular indices and endometrial volumes were calculated with 3D PD-US and compared with the endometrial histopathology.
Results: Among the endometrial histopathologic findings of 174 women, atrophic endometrium was the most common finding (30.5%). Endometrial malignancy was confirmed in 28 cases (16.1%), and endometrial hyperplasia was diagnosed in 17 cases (9.8%). The prevalence of endometrial cancer was high in patients who had endometrial thickness >9.5 mm ($p < 0.001$) and volume greater than 4.05 mL ($p < 0.001$). For the endometrial carcinoma only, the cutoff values of vascular index, flow index, and vascular flow index for predicting malignancy were 13.070, 12.610, and 3.764, respectively. For endometrial hyperplasia, endometrial thickness and vascular flow index were significant findings.
Conclusion: Endometrial vasculature and volume can be obtained using 3D PD-US. The diagnostic usefulness of 3D PD-US for endometrial diseases is promising in women with postmenopausal endometrial bleeding.

Introduction

Postmenopausal bleeding is a common symptom in general gynecological practice. The incidence of vaginal bleeding in postmenopausal women is approximately 10% immediately after menopause and 5% of all cases of menopause [1,2]. Various benign genital causes of postmenopausal vaginal bleeding include atrophic vaginitis, endometrial and cervical polyps, endometrial hyperplasia, pyometra, and submucosal fibroids. However, 10% of all women presenting with postmenopausal bleeding may have endometrial malignancy. Clinical investigations for those patients are mainly directed to exclude malignant and premalignant lesions [3,4].

In the United States, endometrial cancer is the most common type of gynecological cancer, and it is ranked fourth among all types of cancer and seventh among all causes of death by cancer [5]. Cancers in the female reproductive organs account for 15.2% of all types of cancer; however, endometrial cancer comprises only 1.9% of all types of cancer, but the incidence is increasing with the increased average lifespan and popularity of hormone replacement therapy [6]. Endometrial cancer occurs in both the pre- and postmenopausal periods, peaking when patients are in their 50s, and postmenopausal uterine bleeding is the most common symptom of endometrial cancer [3].

To our knowledge, endometrial sampling and histopathologic review can provide a tentative diagnosis [7]. Transvaginal ultrasound as a noninvasive scan is the most commonly used first-line

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investigation for women with postmenopausal endometrial bleeding before endometrial sampling. Usually, a thick endometrium is indicative of further invasive evaluations such as endometrial sampling and/or hysteroscopy [8,9]. However, conventional two-dimensional (2D) ultrasound cannot assess all possible endometrial pathologies. The recent developments with ultrasound equipment enable new imaging techniques for volume scanning. Unlike 2D ultrasound, three-dimensional (3D) ultrasound visualizes the whole endometrium on a coronal plane and can integrate Doppler imaging to display the vascularity in the interested areas.

In this study, we applied 3D power Doppler ultrasound (3D PD-US) in women with postmenopausal endometrial bleeding and calculated various ultrasonographic vascular markers. Thus, we aimed to determine the useful markers to predict endometrial disease and evaluate the usefulness of 3D PD-US in postmenopausal bleeding.

Materials and methods

Patients

We recruited all 225 women who visited the obstetrics and gynecology departments of three university hospitals from January 2009 to November 2012 with a chief complaint of abnormal postmenopausal endometrial bleeding. The study was conducted prospectively in women who met the criteria. Menopause was defined as amenorrhea for at least 12 months. Patients with bleeding that originated from the cervix, vagina, or vulva were not considered for the observation. Among them, 174 patients were evaluated for prospective correct diagnosis for bleeding after excluding patients who had systemic and hematologic disorders, previous endometrial diagnosis, uterine bleeding due to disorders in the pelvis other than in the uterus, or postmenopausal hormone therapy. All women underwent physical examinations such as weight and body mass index (BMI) evaluation, history, gynecologic evaluation, and basic laboratory tests. Ethical approval for further evaluation and use of data was granted by the Institutional Review Board of Kosin Medical Center.

Ultrasound investigation

The patients underwent 2D transvaginal ultrasound scanning as the initial investigation to evaluate the endometrium. Routine ultrasound was used for the diagnosis of the anatomical cause of endometrial bleeding, such as uterine fibroid. The endometrial thickness was measured at its thickest point in an anteroposterior dimension from one basal layer to other in a midsagittal plane. Then, adjunctive 3D PD-US (Voluson E8; GE Healthcare, Zipf, Austria) was carried out using uniform ultrasound modes, and the obtained volume data were transferred to one investigator (A. Kim) for volume and Doppler analysis. The settings were as follows: frequency, 5 MHz; power Doppler gain, −5; dynamic range, 20–40 dB; edge, 1; persistence, 2; color map, 5; motion filter, 1; and pulse repetition frequency, 0.8 kHz. When a midsagittal view of the uterus was obtained, the power Doppler mode was turned on. The area of interest was the endometrium. The 3D mode was then activated, and the area of interest was adjusted. Three-dimensional volumetric data were obtained using automatic sweep, with the angle being set to 120° to ensure that a complete endometrial volume was included. The patients were asked to hold their breath during volume acquisition. The multiplanar display was used to ensure that the area of interest had been captured in its entirety. After 3D volume storage, direct ultrasound examination was performed to reduce examination time and patient discomfort. All 3D volume data that were transferred were analyzed with a desktop computer equipped with Virtual Organ Computer-Aided Analysis (VOCAL) software, which can calculate the targeted volume and vasculatures. The results of the adjunctive 3D PD-US assessment did not affect subsequent clinical management procedures because the clinicians did not know the 3D PD-US results.

The manual mode of the VOCAL contour editor was used to cover the 3D volume of the endometrium with 15° rotation steps. The A-plane (sagittal view of the uterus) was rotated, and the myometrial–endometrial junction from the fundus to the internal cervical os was outlined in each rotation image (12 slices). Then, the histogram demonstrated only the endometrium and showed the endometrial volume with vascular indices (Figure 1). The three automatically calculated vascular indices of the endometrium included the vascularization index (VI), flow index (FI), and vascularization flow index (VFI).

Endometrial sampling

Within 1 week after ultrasound examination, endometrial biopsy was performed by cervical dilatation and curettage in participating women after signed informed consent was obtained. In the lithotomy position, the patient was prepared with povidone–iodine topical antiseptic solution and draped. After sedation, the cervix was dilated with a Hegar dilater, and the endometrium was curetted. The endometrial specimens were reviewed by pathologists for final diagnosis.

Statistical analysis

All results are presented as mean and standard deviation values according to the distribution of data or number with %. The Komologorov–Smirnov test was used to evaluate the normal distribution of the continuous data. Comparisons between two groups were carried out with the Student t test. The receiver operating characteristic curve was applied to calculate the predictive value of the endometrial parameters for endometrial cancer or endometrial hyperplasia. SPSS version 19.0 (SPSS Inc., Chicago, IL, USA) was used for statistical calculations, and $p < 0.05$ was considered statistically significant.

Results

Among 225 patients who had undergone 2D and 3D PD-US, 174 completed the endometrial biopsy for diagnostic confirmation (Table 1). In total, 146 patients (83.9%) showed a benign endometrium, which could be of the following types: (1) proliferative endometrium, (2) secretory endometrium, (3) glandular stromal dissociation, (4) endometritis, (5) endometrial atrophy, (6) endometrial polyp, and (7) endometrial hyperplasia. The most common diagnosis among the benign diseases was endometrial atrophy (53 cases, 30.5%). However, endometrial malignancy was confirmed in 28 cases (16.1%). Among these, 25 cases were diagnosed with adenocarcinoma, while two cases were of squamous cell carcinoma and one was of serous carcinoma.

Table 1 shows the comparison of clinical characteristics including ultrasonographic data. In the malignant group, the mean age was higher than that of the benign group (59.27 years and 61.04 years, respectively; $p = 0.023$). Thus, there was a significant difference in the interval since menopause in the two groups (mean, 9.24 years vs. 11.26 years; $p = 0.003$). Patients with a malignant endometrium tended to have a higher BMI (mean, 27.32 kg/m^2 vs. 29.28 kg/m^2; $p = 0.16$).

In the endometrial evaluation with 2D ultrasound, the valuable measurement was endometrial thickness. The endometrial thickness was thicker in malignant cases than in benign cases (mean,