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Correspondence

Sonohysterography and liquid-based cytology in menopausal patients with abnormal endometrium

To the Editor,

We read with great interest the article by Kim et al [1] regarding three-dimensional power Doppler ultrasound (3D PD-US) for postmenopausal bleeding. In postmenopausal women with abnormal uterine bleeding, the authors observed higher vascular indices in patients with malignant endometrial lesions when compared with other benign diseases. On the basis of their findings they concluded that 3D PD-US is a promising diagnostic tool in patients with abnormal uterine bleeding.

We agree with their conclusions, the availability of 3D ultrasound has introduced a new way of studying pathologies in both obstetric and gynaecologic fields. In addition power Doppler examination offers the unique possibility to visualize and quantify blood flow at the same time [2].

Our major concern with the current article is that the authors adopt endometrial biopsy performed by cervical dilatation and curettage as the gold standard. Actually, it was observed that in 10–25% of patients, dilatation and curettage alone may miss an existing endometrial pathology [3,4]. Consequently their results might have underestimated the prevalence of malignancies or coexisting pathologies.

The sensitivity and specificity of a test are usually determined by comparison with a reference test (gold standard), which is supposed to be the most accurate way to detect the disease. During the past decades hysteroscopic-guided biopsy has become the tool of choice for the evaluation of the endometrial cavity in cases of abnormal uterine bleeding.

Usually the causes of abnormal uterine bleeding are benign in both pre- and postmenopausal women, however, an early identification of precancerous conditions is essential above all in postmenopausal patients. Thus it is imperative to identify a relatively noninvasive, low-cost method that can reliably identify cases that require surgical intervention. According to Modesitt [5] any woman older than 45 years of age with abnormal uterine bleeding or with known risk factors should undergo immediate endometrial sampling as part of her evaluation. Consequently, the ideal method should include a morphological examination of the endometrial stripe and endometrial sampling at the same time.

In a pilot study we evaluated the accuracy of a new diagnostic approach of uterine cavity by combining sonohysterography (SHG) and liquid-based endometrial cytology in order to obtain an early detection of precancerous lesions of the uterus in postmenopausal women.

Postmenopausal women with an abnormal or a poorly defined endometrial interface, as seen during baseline transvaginal ultrasound (TVUS), were included in the study. We considered an endometrial thickness of 4 mm, as the cut-off point, to differentiate the condition of hypo-atrophy from oncology risk conditions. SHG followed by hysteroscopy was offered to selected patients.

SHG was performed by the same authors in the same session or within 2 weeks later. A standard bivalve vaginal speculum was put in place, and the cervix was cleansed with povidone–iodine. A 5-F catheter with a 1-mL balloon (Silicone Balloon HSG Catheter, Cook (R), Milan Italy) was used for saline instillation during SHG. This catheter was modified by cutting the tip in order to improve the quantity of sample obtained during the procedure. It was carefully inserted into the cervical canal up to the internal os and connected to a 20-mL syringe. Firstly, sampling was performed by repeated, combined delicate infusion, and vacuum aspiration using 5 mL of physiologic saline solution through the catheter.

The washing solution coming from the uterine cavity was collected and poured into a vial containing 30 mL of Cytolyt (Cytyc Corporation, Boxborough, MA, USA).

With concomitant TVUS examination, 10–20 mL physiologic saline solution was slowly injected to distend the endometrial lumen. Concomitantly, the distention was observed by TVUS, and continued until the entire cavity was clearly visible.

During hysteroscopy cytological sampling was performed by brushing using the Endoflower device (RI-MOS, Mirandola, Modena, Italy).

After the endometrial sampling, the tip of the device was immersed in the Cytolyt vial (Cytyc Corporation) where it was vigorously stirred in order to facilitate the cell releasing. Histological sampling was performed using the Endoram device (RI-MOS, Modena, Italy). All cytological and histological samples were then sent to the laboratory.

Sixty-five postmenopausal women undergoing TVUS in our center were included in the study. Mean age was 57.8 ± 5.7 years; mean body mass index was 24.8 ± 4.2 kg/m^2.

We detected and characterized an endocavitary pathology, with SHG, in 57 patients (87.7% of all patients), in eight cases the examination was negative. The following hysteroscopy test confirmed the endocavitary pathology in all the 57 women: 33 (50.8%)

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Table 1
Diagnostic accuracy parameters of TVUS and SHG for endometrial polyps, myomas, and endometrial hyperplasia (EH). TVUS and SHG were compared using hysteroscopy (as a gold standard).

		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Endometrial polyps	TVUS	75.8 (58.9–87.6)	0	83.3 (67.1–92.8)	0
	SHG	100 (89.6–100)	88.9 (74.5–96)	97.1 (85.1–99.8)	100 (89.6–100)
Myomas	TVUS	50 (21.3–78.7)	0	83.3 (49.2–97.4)	0
	SHG	90 (65.2–98.5)	100 (78.1–100)	100 (78.1–100)	88.9 (63.9–98.9)
Endometrial hyperplasia	TVUS	100 (85–100)	0	32.1 (16.6–52.4)	0
	SHG	100 (78.1–100)	100 (78.1–100)	100 (78.1–100)	100 (78.1–100)

Note: The numbers in parentheses are the limits of the 95% confidence interval. NPV = negative predictive value; PPV = positive predictive value; SHG = sonohysterography; TVUS = transvaginal sonography.

endometrial polyps, 10 (15.4%) myomas, 10 (15.4%) endometrial hyperplasia, three (4.6%) patients had myomas and polyps, and one (1.5%) had endometrial cancer.

Table 1 shows diagnostic accuracy parameters and their confidence intervals (CIs) for the two imaging methods evaluated and for each of the three diagnostic groups considered in this study: endometrial polyps, myomas, and endometrial hyperplasia.

Among samples obtained during SHG, 46 (70.8%) showed adequate for liquid-based endometrial cytology analysis, the remaining 18 (27.7%) were inadequate. All hysteroscopic samples obtained by the Endoflower device proved adequate. Hysteroscopic biopsies were inadequate for histological examination in 44 out of 65 cases (67.7%).

In one case endometrial liquid-based cytology on washing solution coming from the uterine cavity during SHG evidenced endometrial hyperplasia with atypia. The evaluation of the biopsy and cytology obtained by hysteroscopy demonstrated endometrial adenocarcinoma. Interestingly, the patient was symptomatic with abnormal uterine bleeding and the endometrial thickness observed at TVUS measured 4.5 mm.

In our study SHG proved high diagnostic accuracy in the identification of endometrial pathology.

Independently of the sampling method, endometrial liquid-based cytology, compared with endometrial biopsy, was diagnostic in a considerably much higher percentage of cases (70.8% for samples obtained through SHG and 100% for samples achieved through hysteroscopy vs. 32.3% of biopsies). In 67.7% of cases, biopsy provided inadequate results. However, when biopsy was adequate, a perfect cytology–histology diagnostic concordance was observed.

The integrated approach SHG plus endometrial liquid-based cytology might be considered a reliable outpatient procedure in the management of patients with abnormal endometrial bleeding or, more in general, those presenting abnormal or a poorly defined endometrium during TVUS.

The low invasiveness and the rapidity of execution of the integrated diagnostic procedures led to an increased tolerability for the woman. Patients may obtain, in a single session, a complete diagnostic process based on three different tests, avoiding the long waiting lists typical of more invasive procedures. Nonetheless, further studies conducted on larger scales are required to validate this less invasive procedure.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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Maria Elisabetta Coccia, Francesca Rizzello*, Fiamma Cammilli, Palma Berloco, Eleonora Castellacci
Department of Clinical and Experimental Biomedical Sciences, University of Florence, Florence, Italy

* Corresponding author. Department of Clinical and Experimental Biomedical Sciences, University of Florence, Largo Brambilla, 3, Florence, Italy.
E-mail address: francesca.rizzello@gmail.com (F. Rizzello).