



● *Original Contribution*

## CONTRAST-ENHANCED ULTRASONOGRAPHY IN SCLEROTHERAPY FOR OVARIAN ENDOMETRIAL CYST

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(Received 6 September 2017; revised 27 March 2018; in final form 29 March 2018)

**Abstract**—We investigated contrast-enhanced ultrasonography (CEUS) characteristics related to the perfusion pattern and parameters of the time–intensity curve of ovarian endometrial cysts (OECs) pre- and post-sclerotherapy. Forty-three patients with one-sided, single, untreated OECs underwent CEUS pre- and post-sclerotherapy. OEC wall thickness was measured by 2-D ultrasonography and CEUS, and CEUS enhancement patterns and time–intensity curve parameters before and after sclerotherapy were compared. OEC wall thickness remained essentially unchanged post-sclerotherapy. Wall thickness was significantly larger on 2-D ultrasonography than on CEUS. The OEC wall exhibited rapid enhancement and slow clearance both pre- and post-sclerotherapy. Wash-in and wash-out times remained unchanged. The wall exhibited iso-enhancement pre-sclerotherapy, but low and partially uneven enhancement post-sclerotherapy. Post-treatment, time to peak was delayed, peak intensity was reduced and perfusion slope was decreased. The contrast agent arrival time and area under the curve remained similar. CEUS enhancement patterns and quantitative parameters were altered post-sclerotherapy; thus, treatments involving sclerosing agent retention can help to improve the efficacy of sclerotherapy for OEC. (E-mail: [dongxq0451@163.com](mailto:dongxq0451@163.com)) © 2018 Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology.

**Key Words:** Contrast-enhanced ultrasonography, Ovarian endometrial cyst, Sclerotherapy.

### INTRODUCTION

Endometriosis is a refractory gynecologic disease (Chan et al. 2011), and its incidence in women of childbearing age is approximately 6%–10%. Endometriosis most commonly involves the ovaries, accounting for about 17%–44% of cases (Ramachandran et al. 2013) and can lead to ovarian endometrial cysts (OECs). The main clinical manifestations of OEC include dysmenorrhea, chronic pelvic pain, pelvic adhesions, pelvic mass and infertility (Lang 2001; Ramachandran et al. 2013; Wahd et al. 2014). Although the condition is benign, it is characterized by unlimited growth, angiogenesis, invasion and disruption of surrounding tissues, local or remote metastasis and other characteristics of malignant tumors (Cheng and Ji 2015; Wang and Guo 2014). In addition, it often affects women's psychological health and ability to work.

Ovarian endometrial cyst is a chronic and active disease that is also hormone dependent. Even with semi-radical or radical surgical treatment, its recurrence cannot be completely avoided (Zhang and Yao 2012). Most patients with OECs are women of childbearing age with fertility concerns. Thus, treating OECs by suppressing ovarian function with conservative drugs while also preserving patients' reproductive function is challenging (Moradi et al. 2014). Ultrasound-guided sclerotherapy is a minimally invasive treatment for OECs that has emerged in recent years. Although it does not avoid the problem of recurrence, it has become widely used as a clinical treatment for OECs, because it involves a small incision, is low in cost and can be repeated (Liu et al. 2013; Ma et al. 2015). Sclerotherapy can be performed with and without sclerosing agent retention, with treatment efficacies ranging between 45.5% and 90.6% and with a marked difference in outcome between the two types of sclerotherapy (Chan et al. 2003; Texidó et al. 2014; Yin et al. 2014).

The OEC wall consists of the stroma, endometrial glands and newly formed capillaries; sclerotherapy achieves its therapeutic effect by sclerosing the functional cells in

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the inner wall of the cyst and coagulating and occluding the newly formed capillaries (Wang et al. 2015; Zhao et al. 2010). Therefore, its therapeutic efficacy is determined by the degree of cyst wall sclerosis.

Contrast-enhanced ultrasonography (CEUS) is the best method for imaging the microvasculature. The contrast agent most commonly used currently is SonoVue, which contains SF<sub>6</sub> microbubbles with an average diameter of 2.5 μm; 90% of the microbubbles are less than 6 μm in diameter. These bubbles can easily pass through capillaries (Dai and Jiang 2008), thereby enabling the observation of blood flow in the OEC wall at a microvascular level pre- and post-sclerotherapy.

We previously conducted a preliminary analysis of CEUS-observed characteristics before and after sclerotherapy for OEC (Shao et al. 2015). However, pre-sclerotherapy CEUS was performed without punctures, whereas post-sclerotherapy CEUS was performed with sclerosing agent retention of about one-third of the primary cyst fluid. Thus, cyst volume differed before and after sclerotherapy, preventing comparison of wall thickness. Furthermore, the difference in the tension of the cyst wall (wall tension, which is determined by the volume of the cyst) may lead to errors in observations of OEC features on CEUS.

Therefore, in this study, we further investigated the differences in OEC characteristics and changes in OEC wall thickness on CEUS, before and after sclerotherapy, by designing experiments that could preserve cyst wall tension before and after the treatment.

## METHODS

### *Patient information*

Forty-three female patients with OEC admitted for advanced ultrasound-guided sclerotherapy from January 2013 to May 2015 were recruited for participation. All patients were married, had a 3-mo to 2-y history of the disease and had received no previous drug or surgical treatment. The condition was diagnosed by gynecologists based on symptoms, ultrasonography and laboratory tests. Patients with diseases with other surgical indications were excluded.

This study complied with the regulations of the Harbin Medical University medical ethics committee and the ethical principles of the World Medical Association Declaration of Helsinki.

### *Instruments and medications*

LOGIQ E9 color Doppler ultrasonography (GE Healthcare, Chicago, IL, USA) with CEUS software and time-intensity curve (TIC) analytical software (GE Healthcare) was employed. CEUS was conducted using a vaginal probe (Model, IC5-9 D, frequency: 4–11 MHz) and a disposable puncture needle (16/18 gauge × 20 cm; Hakko Co. Ltd., Nagano, Japan). Local anesthesia was achieved with a 2% lidocaine injection (Shanghai Hefeng Pharmaceu-

tical Co., Ltd., Shanghai, China). The endometrial cyst was washed with 0.9% saline solution (Tonghua Zhenghe Pharmaceutical Co., Ltd., Tonghua, China). Medical ethanol (95%) (Dezhou Anjie Gaoke Disinfection Products Co., Ltd., Dezhou, China) was used for sclerotherapy. To prevent inflammation, a combination of three anti-inflammatory drugs—etimicin (200 mg/4 mL; Wuxi Shanhe Pharmaceutical Co., Ltd., Wuxi, China), dexamethasone (5 mg/1 mL; Southwest Pharmaceutical Co., Ltd., Chongqing, China) and chymotrypsin (4000 U; Shanghai First Biochemical Pharmaceutical Co., Ltd., Shanghai, China)—were injected. The ultrasound contrast agent used was SonoVue (Bracco SpA, Milan, Italy); this lyophilized powder contained 59 g sulfur hexafluoride (SF<sub>6</sub>).

### *Pre-operative preparations*

Routine electrocardiography and clotting time, serum CA-125 levels and liver and kidney function tests were determined. Comprehensive pelvic examinations were performed using vaginal ultrasonography. The OEC location, size and wall thickness (measured from the medial margin to the lateral edge) were recorded, and the images were stored. Intravenous access was established through the median cubital vein. Patients were informed of the procedures, risks and technology used in sclerotherapy and CEUS, and signed an informed consent form.

### *Experimental design*

The volumes of all OECs were measured using 2-D ultrasound and calculated as cyst volume =  $\frac{1}{2}(a \times b \times c)$ , where  $a$ ,  $b$  and  $c$  were the diameters of the cyst on the orthogonal axes  $x$ ,  $y$  and  $z$ , respectively. The volume of medical ethanol used for sclerotherapy was calculated based on the volume of the cyst (usually one-third to one-half of the volume). Endometrial cyst fluid was completely aspirated, and the cyst was repeatedly washed with 0.9% saline. After injection and retention of a volume of 0.9% saline solution equivalent to the medical ethanol dose, the first CEUS was performed. Two hours after sclerotherapy using medical ethanol, CEUS was again conducted.

### *Sclerotherapy*

Patients were asked to empty their bladder before the procedure. The procedure was performed in the lithotomy position with routine disinfection. Under vaginal ultrasound guidance, a percutaneous transhepatic cholangiography (PTC) puncture needle was inserted into the cyst through the vaginal vault while avoiding the uterus and visible blood vessels. One end of the PTC needle was connected to a 20-mL syringe; the cyst fluid was aspirated, and this fluid volume was measured. The cyst was repeatedly washed with 0.9% saline solution until the fluid became clear. CEUS was performed immediately after injecting a volume of saline solution equivalent to the medical

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