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Original Research

Contrast enhanced ultrasound in diagnosis of endometrial carcinoma and endometrial hyperplasia

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Abstract: The present study was aimed to compare application of contrast enhanced ultrasound (CEUS) in diagnosis of endometrial carcinoma (EC) and endometrial hyperplasia (EH). A total of 81 patients with EC and simple EH were selected in this study. Among all patients, 39 cases were diagnosed as EC and 42 cases were diagnosed with EH. All patients were diagnosed by CEUS examination. The diagnosis of EC and EH was also confirmed by endometrial biopsy. CEUS was conducted for all patients. Eendometrial thickness was measured and the mean arrival time, time-to-peak, enhancement time, arrival intensity, peak intensity, enhancement intensity, rising rate, washout half-time and clearance half-time were recorded. Myometrial invasion was categorized into 2 stages <50% and >50%. No significant difference was observed in clinical basis between the two groups. Endometrial thickness of EC was significantly higher than that of EH, P<0.05. Results of CEUS parameters showed that in EC patients, all values of arrival time, time-to-peak, washout half-time and clearance half-time were all shorter in EC group compared with those in EH patients, P<0.05. And values of peak intensity, enhancement intensity, and rising rate were also lower in EC patients than those in EH patients, P<0.05. Diagnostic accuracy of CEUS in myometrial invasion for EC was shown showed that 26 of 30 cases were diagnosed as myometrial invasion <50% by CEUS and 7 of 9 cases were diagnosed as myometrial invasion >50%. The total diagnostic accuracy of CEUS is 82.62% (33/39). We conducted a comparison study to analyze different diagnostic effects of CEUS for EC and EH. The study may give more clinical basic data in the field of CEUS application in diagnosis of EC and can give a reference to the difference between EC and EH.

Key words: Contrast enhanced ultrasound; Diagnosis; Endometrial carcinoma; Endometrial hyperplasia.

Introduction

Endometrial carcinoma (EC) is one of the most common gynecological cancer which usually occurs in perimenopausal women around 50 years old (1,2). In 2012, the number of newly diagnosed EC cases in Europe was nearly 100,000, with an age standardized incidence of 13.6 per 100,000 women (3). During the years, the incidence rate of EC shows a rising tendency and the 5-year survival rate decreased gradually (4). Most patients with EC are diagnosed as stage I, thus preoperative assessment will be helpful to treatment for EC. Common diagnostic methods, such as curettage scraping (5), hysteroscopy (6), MRI (7), PET/CT (8) or traditional transvaginal ultrasound (9), all have their advantages as well as their insufficiency. However, the rates of misdiagnosis and missed diagnosis are still very high (10). For example, in clinical, EC is easy to be confused with endometrial hyperplasia (EH), which is defined histologically as abnormal over growth of endometrial glands (11).

Recently, contrast-enhanced ultraultrasound (CEUS) has attracted scholars' attention for its potential in diagnosis of EC. CEUS uses a microbubble contrast agent, such as SonoVue or Levovist, and has been applied in the discrimination of benign from malignant adnexal masses and its application is now gradually getting more and more widely (12,13). During the past 10 years, CEUS has been significantly improved the diagnostic test accuracy of ultraultrasound in examining gynecological diseases, such as ovarian tumors (14). Application of CEUS to determine myometrial invasion and cancer stage in EC has also been reported in recent years; however relevant studies are still very inadequate. In the present study, we conducted a comparison study to analyze the diagnostic efficacy of CEUS in EC and EH.

Materials and Methods

Subjects

A total of 81 patients with endometrial carcinoma and simple endometrial hyperplasia who went to Second Affiliated Hospital of Fujian Medical University during 2011~2016 were selected in this study. Among the patients, 39 were diagnosed as EC and 42 were diagnosed with EH. All patients were diagnosed by CEUS examination. The diagnosis of EC and EH was also confirmed by endometrial biopsy. Patients who had a history of radiochemotherapy treatment, hypertension, and heart disease or drug allergies were excluded. Detailed clinical basic information was shown in Table 1. The study protocol was approved by Ethics Committee of Second Affiliated Hospital of Fujian Medical University. Written informed consent was obtained from all patients.

Contrast enhanced ultrasound

Contrast-enhanced ultrasound was conducted by two experienced sonographers. The diagnostic ultrasound system was Philips ATL 3000 ultrasound system (ATL 3000; Phillips Healthcare, Bothell, WA) which was equipped with a 4-8 MHz transvaginal transducer using a low mechanical index (<0.1). Contrast-specific imaging mode was used for postcontrast scanning. Before CEUS, Regular ultrasound was performed for all patients. All ultrasound scans were saved in the hard drive of the machine in digital imaging.

The contrast agent used in this study was SonoVue (Bracco, Geneva, Switzerland), which mainly contained sulfur hexafluoride gas microbubbles with a phospholipid monolayer coating. Before the examination, a 20-G cannula was used to obtain venous access. The agent diluted prior in 5 ml of 0.9% saline was administered at a concentration of 8 microlitres/ml followed by an additional 5 ml of physiologic saline solution to flush the cannula. The dose of SonoVue injection was 2.4 ml.

Color Doppler flow imaging was used to detect the tumor's nutrient blood signal and the endometrial neoplasms were characterized by heterogeneous echo patterns within the uterine cavity, with or without myometrial invasion. The endometrial thickness was measured as the maximum diameter of the endometrium in the midsagittal plane. Myometrial invasion was measured from the endometrial myometrial interface to the deepest edge of the tumour extension into the myometrium and was categorized into 2 stages <50% and >50% (15). Following parameters were recorded or calculated: The mean arrival time, the time interval from administration of the contrast agent to its visual observation in the tumour vessels; time-to-peak; enhancement time, peak time to arrival time; arrival intensity, peak intensity; enhancement intensity, peak intensity to arrival intensity; rise time and rising rate, enhancement intensity/enhancement time, washout half-time and clearance half-time.

Statistical analysis

The measurement data was expressed by mean ± SD. Enumeration data were analyzed by chi square test and independent continuous variables were compared using the Student t-test. It was considered to be statistically significant when P-value was less than 0.05. All calculations were made using SPSS 18.0.

Results

Basic clinical information

A total of 39 patients were diagnosed with EC with the mean age of 58.43±7.12 years, while the 42 EH patients had a mean age of 56.34±6.81 years. All other characteristics including weight, body mass index, nulliparity rate and postmenopausal rate showed no significant difference between the two groups (Table 1).

Table 1. clinical basic information of the two groups of patients.

Groups	EC (n=39)	EH (n=42)
Age, years	58.43±7.12	56.34±6.81
Weight, kg	65.33±10.54	63.16±10.28
Body mass index, kg/m^2	26.47±5.88	25.32±6.14
Nulliparity	14 (35.9%)	16 (38.1%)
Postmenopausal status	26 (66.7%)	29 (69.0%)

Table 2 endometrial thickness and CEUS parameters in EC and EH patients.

Groups	EC	EH
endometrial thickness, cm	1.93±0.24*	1.31±0.48
mean arrival time, second	14.32±3.21*	16.21±5.46
time-to-peak, second	22.44±4.39*	25.65±5.14
washout half-time, second	69.64±18.53*	74.85±16.46
clearance half-time, second	79.13±12.35*	88.32±14.17
peak intensity, dB	28.37±6.82*	31.66±6.19
enhancement intensity, dB	20.57±5.64*	22.15±5.11
rising rate, dB/second	1.94±0.18*	2.27±0.32

*P<0.05, compared with the EH group.

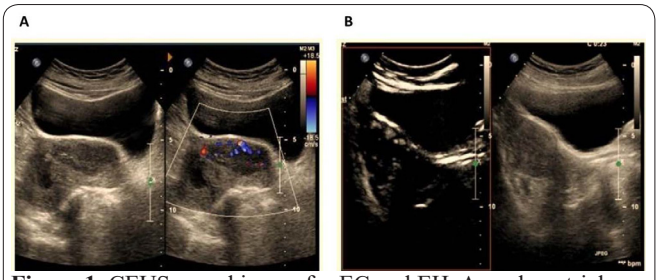

Figure 1. CEUS sound image for EC and EH. A. endometrial carcinoma; B. endometrial hyperplasia.

Comparison of CEUS results for EC and EH

As shown in Table 2, endometrial thickness of EC was significantly higher than that of EH, P<0.05 (Figure 1). CEUS parameters were also compared. Results showed that in EC patients, arrival time was earlier than that in EH patients, P<0.05. What's more, values of time-to-peak, washout half-time and clearance half-time were all shorter in EC group compared with those in EH patients, P<0.05. Values of peak intensity, enhancement intensity, and rising rate were also lower in EC patients than those in EH patients, P<0.05.

Comparison of Pathology Results and CEUS of myometrial invasion for EC

Diagnostic accuracy of CEUS in myometrial invasion for EC was shown in Table 3. Results showed that 26 of 30 cases were diagnosed as myometrial invasion

Table 3. Diagnostic accuracy of CEUS in myometrial invasion for EC.

CEUS diagnosis	Histological stage		Total
	<50% (n=30)	>50% (n=9)	
<50%	26	2	28
>50%	4	7	11

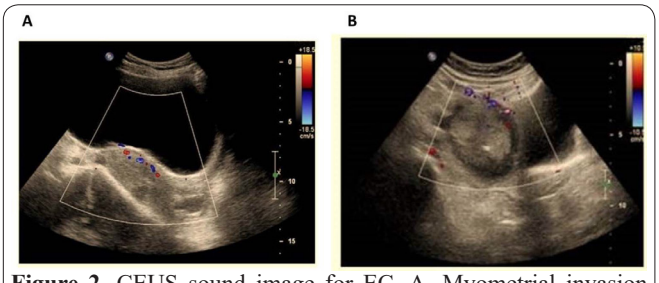

Figure 2. CEUS sound image for EC. A. Myometrial invasion <50% in endometrial carcinoma. B. Myometrial invasion >50% in endometrial carcinoma.

<50% (Figure 2A) by CEUS and 7 of 9 cases were diagnosed as myometrial invasion >50% (Figure 2B). The total diagnostic accuracy of CEUS is 82.62% (33/39).

Discussion

In recently years, CEUS has been widely adopted in diagnosis of more and more diseases such as liver cancer (16), splenic artery steal syndrome (17) and Esophageal Varices (18). Diagnosis value of CEUS in endometrial carcinoma was also gradually noticed by scholars. In China, many clinicians start to use CEUS in diagnosis in various of uterine lesions like uterine fibroid or EH (19,20). However compared with application of CEUS in other fields, its use in diagnosis of EC and EH still needs more researches.

In the present study, 39 patients with endometrial carcinoma and 42 patients with simple endometrial hyperplasia were selected to conducted a comparison study to analyze the diagnostic efficacy of CEUS in EC and EH. Contrast enhanced ultrasound was conducted on all patients. Results showed that after contrast agent administration, the brightness of the power Doppler signal and the amount of recognisable vascular areas increased in each tumor in visual evaluation (15). The tumor base, position, and boundary were shown more clearly compared with traditional ultrasound. Evaluation results showed that endometrial thickness of EC was significantly higher than that of EH. Results of CEUS parameters showed that in EC patients, all values of arrival time, time-to-peak, washout half-time and clearance half-time were shorter in EC group compared with those in EH patients. And values of peak intensity, enhancement intensity, and rising rate were also lower in EC patients than those in EH patients. Diagnostic accuracy of CEUS in myometrial invasion for EC was also analyzed. Results showed that the total diagnostic accuracy of CEUS is 82.62%.

Several similar studies were conducted. Liu et al compared diagnosis of CEUS in EC and EH and found that all CEUS parameters of EC were lower than those of EH, which was in consistent with the present study (20). Liu et al studied Imaging of endometrial carcinoma using contrast-enhanced sonography and obtained a diagnostic accuracy of 85.3% for CEUS (21). Song et al demonstrated that CEUS parameters of EC were all higher than normal myometrium except for enhancement time and arrival intensity, and the total diagnostic accuracy of CEUS is 68.6% (15). The present study also has some limitations, for example the sample size is small, and more related uterine lesions can be studied and compared.

In conclusion, we conducted a comparison study to analyze different diagnostic effect of CEUS for endometrial carcinoma and endometrial hyperplasia. The study may give more clinical basic data to application of CEUS in diagnosis of EC and can give a reference to the difference between EC and EH in diagnosis by CEUS.

Ethics, consent and permissions

Ethical approval was given by the medical ethics committee of The Second Hospital of Hebei Medical University.

Consent for publication

All of the authors have Consented to publish this reaserch.

Author's contribution

Each author has made an important scientific contribution to the study and has assisted with the drafting or revising of the manuscript.

Interest conflict

All of the authors have no conflict of interest in this research.

Availability of data and material

All data and material is available.

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