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Original Article

Correlations of evaluation of fallopian tube patency via four-dimensional contrast-enhanced ultrasound with serum inflammatory factors

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Abstract: Objective: To investigate the correlations of evaluation of fallopian tube patency via four-dimensional contrast-enhanced ultrasound (CEUS) with serum inflammatory factors. Methods: A total of 40 patients with primary infertility treated in our hospital from March 2015 to September 2017 were selected and divided into CEUS group and laparoscope group according to the diagnosis and treatment methods. The evaluation effect on fallopian tube patency, diagnostic results for specific condition of fallopian tube obstruction, duration time and pain degree of patients were compared between the two diagnostic methods, and complications of the two diagnostic methods were recorded. The correlations of fallopian tube patency with serum inflammatory factors were analyzed, and the correlations of passing time of contrast agent through the fallopian tube with serum high-sensitivity C-reactive protein (hs-CRP) and interleukin-1 (IL-1) were also analyzed. Results: The difference in diagnostic rate of fallopian tube obstruction between CEUS group (62.5%) and laparoscope group (70.0%) was not statistically significant ($P > 0.05$). Meanwhile, the diagnostic results for specific condition of fallopian tube obstruction had no statistically significant differences between CEUS group and laparoscope group ($P > 0.05$). However, compared with laparoscope group, CEUS group showed significantly shorter examination duration time ($P < 0.05$), lower pain degree of patients during diagnosis ($P < 0.05$) and the total proportion of complications during diagnosis of fallopian tube obstruction ($P < 0.05$). Moreover, the levels of hs-CRP and IL-1 in patients with fallopian tube obstruction were obviously lower than those in patients without fallopian tube obstruction ($P < 0.05$), and the passing time of contrast agent of four-dimensional CEUS through the fallopian tube was positively correlated with serum hs-CRP and IL-1 levels ($P < 0.05$). Conclusion: Four-dimensional CEUS has the same effectiveness as laparoscopy in the diagnosis of fallopian tube obstruction, but it has higher safety and fewer complications and causes less pain in patients. At the same time, the longer of the passing time of contrast agent through the fallopian tube, the more obvious of the chronic inflammatory response, the higher of the risk of fallopian tube obstruction.

Keywords: Four-dimensional contrast-enhanced ultrasound, fallopian tube, serum inflammatory factors, fallopian tube obstruction

Introduction

Infertility is a kind of common gynecological disease, and the proportion of fallopian tube-derived infertility is getting higher and higher with the changes of people's life style [1]. Studies have confirmed that the obstruction, distortion, stiffness and uncoordinated peristalsis of fallopian tube lumen due to various reasons will lead to fallopian tube dysfunction, resulting in female infertility [2]. In recent years, the proportion of infertility in the population is even as high as 10% [3], among which fallopian tube obstruction is the most important contributing factor, so the effective diagnosis of fallopian tube patency is of great value for the guidance of clinical treatment [4].

At present, there are many clinical diagnostic methods for fallopian tube patency, among which hysterosalpingography is commonly used, but it is not the first choice in clinic due to a certain radioactivity [5]. In addition, hydrotubation combined with microscopic observation can viasulize the observation and treatment of fallopian tube intuitively, but it is expensive, and there are certain risks of surgery and anesthesia, so its clinical application is limited [6]. Four-dimensional contrast-enhanced ultrasound (CEUS) of fallopian tube is non-invasive and

Table 1. Comparison of evaluation effect on fallopian tube patency between two diagnostic methods (n)

	Total case	Smooth and unobstructed fallopian tube	Smooth but obstructed fallopian tube	Hydrosalpinx	Fallopian tube obstruction
CEUS group	40	1	6	8	25
Laparoscope group	40	2	7	3	28

repeatable, and characterized by higher safety and accuracy, so it is more and more widely used in the examination and diagnosis of fallopian tube patency [7]. At the same time, the infertility in patients is mostly caused by chronic inflammation of reproductive system, so the inflammation-related factors in the body are often increased in such patients. At present, however, there has been no research on the correlations of four-dimensional CEUS time of fallopian tube with inflammatory factor levels in China [8]. In this study, we aimed to investigate the correlations of evaluation of fallopian tube patency via four-dimensional CEUS with serum inflammatory factors.

Materials and methods

General materials

A total of 40 patients with primary infertility treated in our hospital from March 2015 to September 2017 were selected. All patients were diagnosed based on clinical manifestations, physical examination and computed tomography (CT) examination, and the informed consent was obtained before enrollment. This study was approved by Ethics Committee of our hospital. All patients were aged 21-40 years old, and they had matrimonial cohabitation and normal sexual life for 2 years and above. Patients who used to receive abdominal surgery or pelvic surgery, or who suffered from chronic cervicitis, systemic infection, immune system diseases, malignant tumor or polycystic ovarian syndrome were excluded, and those who were allergic to contrast agents, receiving surgical treatment of reproductive system or immunosuppressive agents within 3 months before enrollment were also excluded. Patients enrolled were divided into CEUS group and laparoscope group according to the diagnosis and treatment methods. They were aged 21-40 years old with an average of (27.5 ± 1.1) years old, the duration of infertility was 1-15 years with an average of (6.0 ± 0.3) years, and the menarche age was 12-17 years old with an average of (14.1 ± 0.3) years old.

Methods

All patients were diagnosed with infertility due to fallopian tube obstruction. In CEUS group, four-dimensional CEUS was performed first using the Voluson E8 color Doppler instrument (provided by GE) equipped with transvaginal probe at a frequency of 5.0-9.0 MHz. During CEUS, the contrast agent was injected at a uniform speed, Contrast and 4D modes were selected, and the acquisition angle was adjusted within 85°-90°. The fallopian tube patency was evaluated under the surface mode. After CEUS, rotation and cutting observation was conducted for volume images, and the whole pictures of uterine cavity and fallopian tube were observed and diagnosed, followed by hysteroscopic hydrotubation and laparoscopic observation. In hydrotubation, diluted methylene blue was injected to observe and understand the patency of bilateral fallopian tubes.

Observation indexes

The evaluation effect on fallopian tube patency, diagnostic results for specific condition of fallopian tube obstruction, duration time and pain degree of patients were compared between the two diagnostic methods, and complications of the two diagnostic methods were recorded. The correlations of fallopian tube patency with serum inflammatory factors were analyzed and compared, and the correlations of passing time of contrast agent through the fallopian tube with serum high-sensitivity C-reactive protein (hs-CRP) and interleukin-1 (IL-1) were also analyzed.

Evaluation criteria

Evaluation criteria of fallopian tube patency were as follows. Smooth and unobstructed fallopian tube: CEUS showed natural and mild walking of fallopian tube, uniform diameter and size of fallopian tube, there were no resistance and reflux during the injection of contrast agent, and there was annular contrast agent shadow around the ovary within 2 s after injection of contrast agent, diffusing into pelvic cavity. Smooth but obstructed fallopian tube: The whole or part of the fallopian tube was distorted, the diameter and size of fallopian tube were

Table 2. Comparison of diagnostic results for fallopian tube obstruction between two diagnostic methods (n)

	Total case	Left obstruction	Right obstruction	Bilateral obstruction
CEUS group	26	3	4	18
Laparoscope group	28	4	6	18

Table 3. Comparisons of duration time and pain degree of patients between two diagnostic methods ($\bar{x} \pm s$)

	Examination duration time (min)	Pain degree (points)
CEUS group	26.8 ± 2.9	1.3 ± 0.2
Laparoscope group	38.9 ± 5.3	5.1 ± 0.6
t	12.667	38.000
p	0.000	0.000

non-uniform, and slender, spiral or angled fallopian tube could be seen; there was a certain resistance, but no or very little reflux, during the injection of contrast agent, semi-annular or a little contrast agent shadow could be seen around the ovary within 2 s after injection of contrast agent, and a little contrast agents in the pelvic cavity diffused. Hydrosalpinx: CEUS showed thickened fallopian tube or lesions in its end. Fallopian tube obstruction: Fallopian tube was partially or even not developed, there was large resistance or reflux during the injection of contrast agent, and there were no annular contrast agent shadow around the ovary and no diffusion of contrast agent in the pelvic cavity within 2 s after injection of contrast agent. Visual analogue scale (VAS) score ranging from 0 point (no pain) to 10 points (sharp pain) was used for the pain degree, and the score was positively correlated with the pain degree. Changes in levels of inflammatory factors, hs-CRP (< 10 mg/L) and IL-1 (130 ng/mL-250 ng/mL), were detected via enzyme-linked immunosorbent assay (ELISA).

Statistical processing

Statistical Product and Service Solutions (SPSS) 13.0 was used. Measurement data were presented as mean ± standard deviation (SD) student *t*-test was used for the comparison of means between two groups, and chi-square test was used for the intergroup comparison of rates. Pearson correlation was performed for correlation analysis. $P < 0.05$ suggested that the difference was statistically significant.

Results

No difference of the evaluation effect on fallopian tube patency between two diagnostic methods

The difference in diagnostic rate of fallopian tube obstruction between CEUS group (62.5%) and laparoscope group (70.0%) was not statistically significant ($\chi^2 = 0.503$, $P = 0.478 > 0.05$) (**Table 1**).

No difference of diagnostic results for fallopian tube obstruction between two diagnostic methods

The diagnostic results for specific condition of fallopian tube obstruction had no statistically significant differences between CEUS group and laparoscope group ($\chi^2 = 0.329$, $P = 0.848 > 0.05$) (**Table 2**).

Shorter duration time and lower pain degree of patients in CEUS group

The examination duration time in CEUS group was significantly shorter than that in laparoscope group ($P < 0.05$), and the pain degree of patients during diagnosis was significantly lower than that in laparoscope group ($P < 0.05$) (**Table 3**).

Lower relevant complications in patients from CEUS group

The total proportion of complications during diagnosis of fallopian tube obstruction in CEUS group was significantly lower than that in laparoscope group ($P < 0.05$) (**Table 4**).

Lower serum inflammatory factors in patients with fallopian tube patency

The levels of hs-CRP and IL-1 in patients with fallopian tube obstruction were significantly lower than those in patients without fallopian tube obstruction ($P < 0.05$) (**Table 5**).

Correlation of passing time of contrast agent through the fallopian tube with serum hs-CRP level

The passing time of contrast agent of four-dimensional CEUS through the fallopian tube

Table 4. Comparisons of relevant complications between two diagnostic methods (n)

	Pelvic inflammation	Severe pain	Wound infection	Total incidence rate
CEUS group	1	1	0	2 (5.0%)
Laparoscope group	3	11	1	15 (37.5%)
χ^2		-		10.756
p		-		0.001

Table 5. Correlations of fallopian tube patency with serum inflammatory factors ($\bar{x} \pm s$)

	hs-CRP (mg/L)	IL-1 (ng/mL)
Patients with fallopian tube obstruction	7.0 ± 0.3	118.0 ± 10.2
Patients without fallopian tube obstruction	12.3 ± 1.1	168.3 ± 12.6
t	29.399	19.624
p	0.000	0.000

was positively correlated with serum hs-CRP level ($r = 0.9208$, $P < 0.05$) (**Figure 1**).

Correlation of passing time of contrast agent through the fallopian tube with serum IL-1 level

The passing time of contrast agent of four-dimensional CEUS through the fallopian tube was positively correlated with serum IL-1 level ($r = 0.9087$, $P < 0.05$) (**Figure 2**).

Discussion

Fallopian tube obstruction is considered to be the leading cause of infertility, and infertility patients often suffer from fallopian tube obstruction due to the chronic inflammation of reproductive system [9]. With the development of medical technology, great progress has also been made in assisted reproductive technology, so the timely and accurate diagnosis of fallopian tube patency is critical to guide the assisted reproductive technology [10]. Although laparoscopic hydrotubation is a gold-standard index for the diagnosis of fallopian tube obstruction currently, it is not widely accepted in clinic due to high price and certain postoperative complications [11]. X-ray-guided hysterosalpingography, as an effective diagnostic method, has a certain diagnostic value, and can effectively assess the morphology and walking of fallopian tube, but it has high missed diagnosis and misdiagnosis rates, massive radioactive radiation contamination [12] and a certain risk of pulmonary artery embolism. Four-dimensional CEUS is a kind of non-invasive and repeatable diagnostic method [13], which has higher safety and accuracy, so it is more and more widely used in the examination of general conditions of fallopian tube [14].

All patients enrolled in this study received four-dimensional CEUS first, followed by laparoscopy. The evaluation effect on fallopian tube patency between the two diagnostic methods was compared, and found no difference in diagnostic rate or results of fallopian tube obstruction between CEUS group and laparoscope group, indicating that the diagnostic results of four-dimensional CEUS for fallopian tube obstruction and patency are similar to those of laparoscopic diagnosis. However, the examination duration time in CEUS group was significantly shorter than that in laparoscope group, and the pain degree of patients during diagnosis was significantly lower than that in laparoscope group, suggesting that four-dimensional CEUS is less time-consuming, and the pain degree of patients is low with a high level of comfort. Moreover, it was found that the total proportion of complications during diagnosis of fallopian tube obstruction in CEUS group was significantly lower than that in laparoscope group, indicating that there are fewer complications in four-dimensional CEUS with higher safety. Furthermore, the inflammatory factors in patients with fallopian tube obstruction were also investigated in this study and showed that the levels of hs-CRP and IL-1 in patients with fallopian tube obstruction were significantly lower than those in patients without fallopian tube obstruction, suggesting that the levels of inflammatory factors in patients with fallopian tube obstruction are significantly lower than normal levels. Meanwhile, The four-dimensional CEUS performed in this study visualized the harmonic imaging through changing the intensity of microbubble echo signal [15], and its ultrasound probe was only sensitive to the microbubble harmonic signal, effectively enhancing the contrast of fallopian tube and tissues in pelvic cavity [16]. The application of four-dimensional CEUS in the diagnosis of fallopian tube patency can clearly display the walking, shape

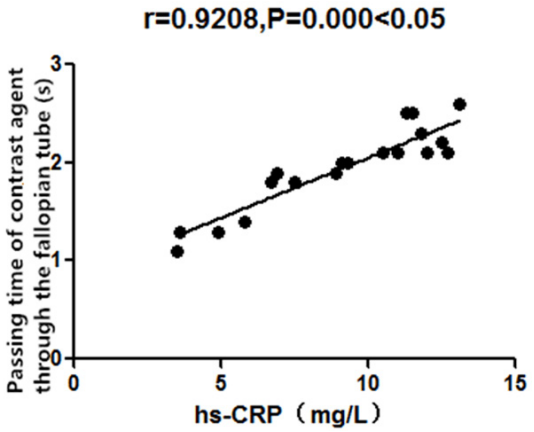

Figure 1. Correlation analysis of passing time of contrast agent through the fallopian tube with serum hs-CRP level. The passing time of contrast agent of four-dimensional CEUS through the fallopian tube is positively correlated with serum hs-CRP level ($P < 0.05$).

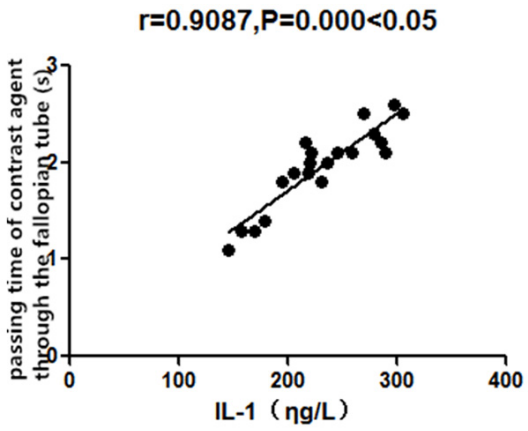

Figure 2. Correlation analysis of passing time of contrast agent through the fallopian tube with serum IL-1 level. The passing time of contrast agent of four-dimensional CEUS through the fallopian tube is positively correlated with serum IL-1 level ($P < 0.05$).

and size of fallopian tube [17]. At the same time, it can analyze the conditions of fallopian tube in dynamic and three-dimensional manners, and help understand the fallopian tube patency through comprehensive assessment of resistance during injection of contrast agent, and diffusion of contrast agent in fallopian tube and pelvic cavity [18]. Moreover, it reduces motion artifacts, thus forming the clear, continuous and dynamic CEUS images of fallopian tube, and better evaluating the spraying of contrast agent out of the fimbriated extremity of fallopian tube and its diffusion in pelvic cavity [19]. The shorter the passing time of contrast agent is, the more ideal the fallopian tube patency will be. The situation that the passing time of contrast agent is more than 2 s should attract clinical attention. Also, the more obvious the chronic inflammatory response in the body is, the higher the risk of fallopian tube obstruction will be [20]. In the present study, we found the passing time of contrast agent of four-dimensional CEUS through the fallopian tube was positively correlated with serum hs-CRP and IL-1 levels, indicating that inflammatory factor levels in patients with fallopian tube obstruction have certain correlations with the passing time of contrast agent of four-dimensional CEUS through the fallopian tube.

In conclusion, four-dimensional CEUS has the same effectiveness as laparoscopy in the diagnosis of fallopian tube obstruction, but it has higher safety and fewer complications and causes less pain in patients. At the same time, the longer the passing time of contrast agent through the fallopian tube is, and the more obvious the chronic inflammatory response in the body is, the higher the risk of fallopian tube obstruction will be.

Disclosure of conflict of interest

None.

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