Application of 3D-HyCoSy in the diagnosis of oviduct obstruction

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Abstract. The aim of the study was to analyze the application value of three-dimensional hysterosalpingo-contrast sonography (3D-HyCoSy) in the diagnosis of oviduct obstruction. Fifty-two patients with infertility and oviduct obstruction were continuously selected and treated with 3D-HyCoSy and CLP (CLP). It was found that according to CLP diagnosis, 40 oviducts were obstructed, 30 were partially obstructed, 12 were tortuous and 22 were completely obstructed. The 40 cases were unilaterally pathological, 24 were bilaterally pathological, 10 were diagnosed as congenital dysplasia, 35 were diagnosed as inflammation and 19 were diagnosed as tumor and cyst. Based on the diagnostic criteria of CLP, the diagnostic sensitivity, specificity, positive predictive values and negative predictive values of 3D-HyCoSy was 82.4, 88.3, 77.9 and 90.2%, respectively. The contrast agent flow time of oviduct obstruction (tortuosity and complete obstruction) as diagnosed by 3D-HyCoSy was significantly prolonged when compared with that of partial oviduct obstruction ($P<0.05$), and flow time of inflammation as diagnosed thereby was longer than that of congenital dysplasia, tumor and cyst. Following the diagnosis of inflammation, the shape of the contrast agent was tenuous, swollen, angled, rigid and distorted and the occurrence rate of inflammation was significantly higher ($P<0.05$). In conclusion, the diagnostic effect of 3D-HyCoSy on oviduct obstruction was more accurate and can show different features when diagnosing different types of inflammation, thus having a certain value for identifying the inflammation.

Introduction

The occurrence rate of female infertility is on the increase, and 30-60% of female infertility results from oviduct obstruction. Oviduct obstruction is mainly caused by congenital dysplasia, salpingitis, paramorphia, tumor or cyst (1).

At present, X-ray hysterosalpingography (HSG) is mainly applied in clinic, and the advantages include identification of the impact of uterine oviduct (2). Previous findings showed that X-ray HSG was more objective and accurate, and more safe and effective for patients. As such patients are likely to suffer little pain and accept the said treatment method more readily. Disadvantages of the method include that contrast agent sensitivity is more common, and lipiodol stimulation may result in chronic granuloma, exacerbating distal tubal obstruction and even leading to pulmonary artery embolism. Thus, the false-positive rate is higher and the radiation quantity of inspection ray is larger and patients receiving X-ray HSG should avoid getting pregnant within 3 months.

The laparoscopic (hysteroscopic) methylene blue hydrotubation is considered the 'golden standard' for diagnosing oviduct obstruction which can conduct examination and be used to provide therapy at the same time. However, it usually cannot be considered the conventional screening method because as a type of invasive inspection, it has greater surgical risks (3). With the clinical application of second-generation ultrasound contrast agent SonoVue, three-dimensional hysterosalpingo-contrast sonography (3D-HyCoSy) is widely applied for its non-invasion, repeatability, and high accuracy rate (4). The majority of previous studies have focused on the diagnostic accuracy of 3D-HyCoSy on oviduct obstruction (5,6). However, to the best of our knowledge, previous studies have paid less attention to the radiographic characteristics of 3D-HyCoSy, especially to the nature of obstruction.

The aim of the present study was to analyze the diagnostic value of 3D-HyCoSy in the identification of oviduct obstruction, thus providing a new reference for clinical diagnosis.

Patients and methods

Patients. In total, 52 patients were admitted to the Dongying People's Hospital (Shandong, China) and diagnosed with infertility and oviduct obstruction during the period January, 2015 to January, 2016. The patients had failed to become pregnant within 1 year without taking any contraceptive measures, and excluded any patients who were diagnosed with infertility and contrast medium sensitivity resulting from intrauterine operation, trauma history, being elderly, endocrine disease, male infertility, reproductive system disease and diseases occurring in other organs of the body. The age range of the patients was 22-35 years, with an average age of 26.4±5.3 years. The

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infertility time of patients was 1-5 years, and the average age was 2.7±1.3 years. Thirty patients were diagnosed with primary infertility and 22 patients were diagnosed with secondary infertility. The study was approved by the Ethics Committee of the Dongying People's Hospital. Written informed consent was obtained from patients and their family members. The patients with primary infertility and secondary infertility were treated with 3D-HyCoSy and CLP (CLP), respectively.

3D-HyCoSy method. The 3D-HyCoSy method was applied to patients within 3-5 days after menstruation, and the instruments used included MyLab 90 color ultrasound meter (Esaote, Italy) which was equipped with radiography function, contrast-tuned imaging (CnTI) technology and transvaginal intracavitary probe with a frequency of 5-9 MHz. The index of 2D and 3D ultrasound contrast instruments was 0.08. SonoVue (Bracco, Milan, Italy) and was chosen as the contrast agent, and the suspension used for the examination was prepared by nurses during the inspection.

The physicians informed the patients of the angiographic methods, process and objectives in detail prior to the radiography to reduce the patients' anxiety. Subsequently, 0.25 mg of intramuscular atropine was applied to the patients. Normal saline (5 ml) was added to the contrast agent, agitated and diluted, and the microbubble suspension containing 1 ml (5 mg/ml) + 20 ml of normal saline was extracted for standby application after the contrast agent was well mixed. The physician first conducted 2D transabdominal or transvaginal conventional ultrasound examination to primarily screen the qualified patients. The patients were allowed to urinate completely and lie in bed in lithotomy position, and the physician made the intracavitary probe colored with moderate amount of couplant and covered with condom, and hold the transvaginal probe in right hand to place it into the vagina to make it cling to the cervix. Subsequently, the examination was conducted in an ordered, comprehensive and all-around manner to observe the basic conditions of the patients' uterus and surrounding positions, to identify the position of uterus and bilateral ovary, to check whether there was hydrops in the pelvic cavity or not and to primarily seek and determine the position of bilateral cornua uteri. The physician placed the dual-lumen saccular duct into the uterine cavity after applying conventional disinfection to the vulva and vagina of patients, and then the physician injected 3-4 ml of normal saline into the sacculus to take out of the duct and block the intracervical mouth to finally drop the bivalve speculum out (Fig. 1). Following the beginning of radiography, the diluted contrast medium of 10-20 ml was slowly injected through the duct at a uniform speed to probe whether there was any adhesion or polyp and other occupying lesions in the uterine cavity and to seek the best section plane at the opening of oviducts of the cornua uteri. The contrast and 3D model was initiated to determine the region of interest, after which the volume sampling frame was placed and adjusted to completely wrap the lesion, and the physician kept the probe stable and asked the patient to lie on the examining couch. The static 3D ultrasound radiography model with free arm was chosen, and the probe was scanned from top to bottom after the injection of contrast medium to complete the sampling once and the sampling was conducted after every 10 sec. The sampling angle was adjusted to be 85-90˚ after 90 sec to collect the angiography

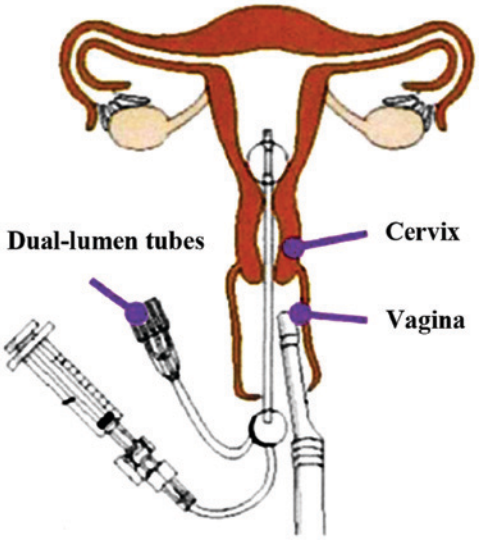

Figure 1. Schematic for angiography intubation.

images of bilateral oviducts, and the source materials were stored in the hard disk of the instrument for image analysis. The physician recorded and observed the distribution situation of the microbubble around the bilateral ovary and in intestine and womb rectum concave. Once the oviducts were found to be partially obstructive, they were appropriately pressurized. The images of radiography volume were captured after ending of the radiography to analyze and reconstruct the volume and to track the filling of contrast medium in proximal and umbrella end of uterine and bilateral oviducts. The results can be divided as follows:

i) Unobstruction: The operator did not feel any obvious resistance when injecting contrast medium, and the patients suffered no abdominal pain. Upon the injection of contrast medium into the uterine cavity, the physician observed that the strong echo of contrast medium rapidly moves towards the oviducts from bilateral cornua uteri and completely fills the oviducts. The stronger echo of contrast medium rapidly overflowed from the umbrella end and formed the shape of a ring or a half ring around the ovary, and free fluid sonolucent region was distributed in the uterus-rectum fossa or the scope of the original fluid sonolucent area expanded, and the dense strong echo of contrast medium floated in the free fluid sonolucent area. After 3D reconstruction, the uterine cavity was completely filled and in the shape of an inverted triangle, and the whole oviducts had the shape of a band with its development in the bilateral uterine cavity, and the terminal of oviducts had wrapped the ovary in the shape of a ring or a half ring.

ii) Partial obstruction: The resistance is stronger and a small amount of backflow appears when injecting contrast medium, and the patients may feel mild and moderate pain in the hypogastric region. The strong echo of contrast medium in the patients' uterine cavity slowly moves towards the oviducts, and physicians did not observe that the obvious jet-shaped strong echo overflowing from the umbrella end of oviducts, and the circular belt around the ovary and a small number of echo-free areas exist in uterus-rectum fossa or the expanded scope of the original echo-free area is not evident. After 3D reconstruction, the development of oviducts in the affected

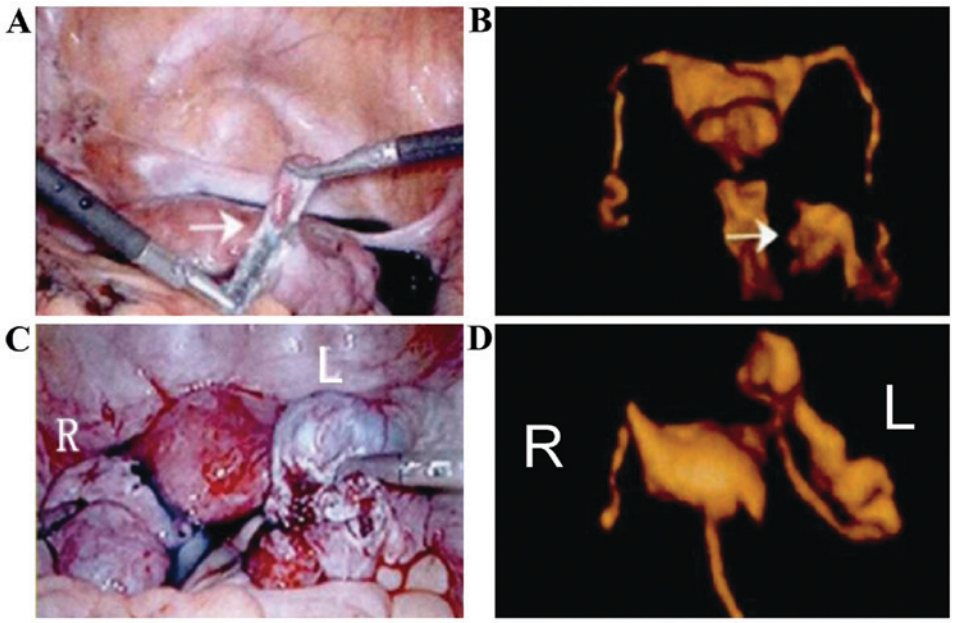

Figure 2. Contrast between 3D-HyCoSy and CLP. (A and B) Shows partial obstruction of the left oviduct, and arrow shows the adhesive umbrella end. (C and D) Shows the proximal obstruction of the left oviduct and proximal end of oviduct is obviously swelled). 3D-HyCoSy, three-dimensional hysterosalpingo-contrast sonography.

side was tenuous, distorted and reflexed, and the physicians identified interruption of partial echoes.

iii) Obstruction: The injection resistance was high, thus the injection was conducted by adding pressure, and the liquid was not injected when the injection volume reached 5-6 ml. The physicians observed that all or part of the contrast medium flowed in a reverse manner when they stopped adding pressure and injection. The contrast medium completely filled the uterine cavity, and the whole oviducts were not developed or partially developed, and the strong echo overflowed from the umbrella end of oviducts, and no ring-like substance wraps the ovary. There was no echo-free area in rectum fossa or the original echo-free area was not altered following reconstruction. The physicians observed that the stripped hyperecho appeared in the proximal end of the obstructive region but not in the distal end thereof.

CLP method. By determining whether methylene blue overflowed from the umbrella end, the results of the laparoscopic examination were divided as follows: i) Oviduct patency: No resistance occurred when methylene blue was injected into the patients' body, and the methylene blue completely filled the oviduct and overflowed from the umbrella end of the oviduct; ii) partial oviduct obstruction: The injection pressure was higher, and methylene blue completely filled the oviducts, and partial oviducts became swollen for >1 min or became adhesive to the umbrella end, and methylene blue slowly overflowed from the umbrella end in the shape of small beads; and iii) oviduct obstruction: The injection pressure of methylene blue was large, and methylene blue failed to completely fill the oviducts, or completely filled the swollen oviducts but failed to overflow from the umbrella end, and the tension of uterus was high.

The examination results were concluded and interpreted by two experienced senior physicians.

Observation target. The accuracy of 3D-HyCoSy was evaluated based on the diagnostic results of CLP. The physicians analyzed the features of different images of oviduct obstruction as diagnosed by 3D-HyCoSy as well as the pain degree, injection pressure of contrast medium and quantity of backflow of the patients. According to the pain standards suggested by the World Health Organization (WHO), pain can be classified as: The pain-free and quietness can be classified as grade 0, mild pain and tolerability were classified as grade I, moderate pain, tolerability, moaning and uneasiness were classified as grade II, and severe pain, intolerance, interruption of examination were classified as grade III.

Statistical methods. SPSS 19.0 statistical software (Chicago, IL, USA) was used to conduct data input and analysis. The quantitative data were expressed as mean ± standard deviation, and the comparison among groups was analyzed by ANOVA. Qualitative data were expressed by the number of cases or as a percentage (%), the inter-group comparison was tested by the χ^2 test (correction). Sensitivity was calculated as: true positive population/(true positive population + false negative population) x 100%, specificity as true negative population/(true negative population + false positive population) x 100%, positive predictive value as true positive population/(true positive population + false positive population) x 100%, and negative predictive value as true negative population/(true negative population + false negative population) x 100%. $P<0.05$ indicated that the difference was statistically significant.

Results

Comparison of diagnostic results of 3D-HyCoSy and CLP. According to CLP diagnosis, 40 oviducts were obstructed, 30 were partially obstructed, 12 were tortuous and 22 were completely obstructed. The 40 oviducts were unilaterally

Table I. Comparison of obstruction of different nature as diagnosed by 3D-HyCoSy.

Parameters	Flow time (sec)	Shape of contrast medium, n (%)	Pain degree	Injection pressure (kPa)	Quantity of backflow (ml)
Inflammation (n=35)	4.7±1.3	28 (80.0)	1.5±0.4	39.5±4.2	1.8±0.6
Congenital dysplasia (n=10)	2.5±1.2	5 (50.0)	0.7±0.2	34.2±4.3	0.5±0.2
Tumor and cyst lesion (n=19)	3.2±1.3	9 (47.4)	0.8±0.3	37.6±4.5	1.2±0.3
F (χ^2)	5.443	7.189	5.714	5.532	6.635
P-value	0.021	0.027	0.018	0.020	0.009

3D-HyCoSy, three-dimensional hysterosalpingo-contrast sonography.

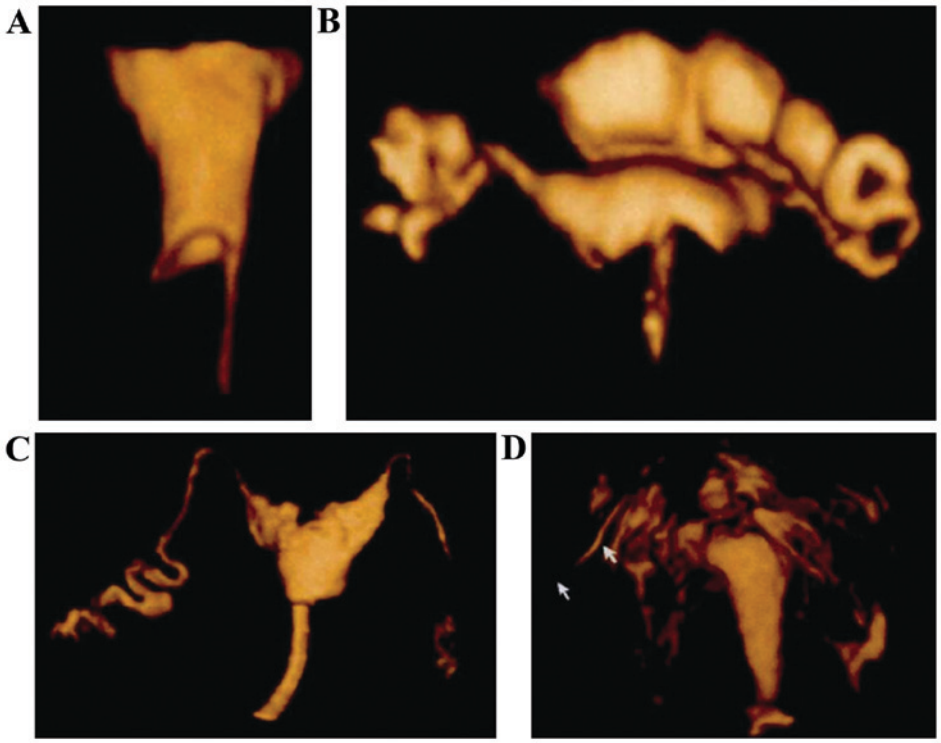

Figure 3. Shapes of inflammatory obstruction as diagnosed by 3D-HyCoSy. (A) Shows the proximal obstruction of bilateral oviducts. (B) Shows the distal obstruction, distortion and swelling of the left oviduct, (C) shows the angled right oviduct and (D) shows the backflow of the right oviduct. 3D-HyCoSy, three-dimensional hysterosalpingo-contrast sonography.

pathological, and 24 were bilaterally pathological. Among the 64 cases, 10 were diagnosed as congenital dysplasia, 35 as inflammation and 19 as tumor and cyst. Based on the diagnostic criteria of CLP, the diagnostic sensitivity, specificity, positive and negative predictive values of 3D-HyCoSy were 82.4, 88.3, 77.9 and 90.2%, respectively (Fig. 2).

Fig. 2 shows the contrast between 3D-HyCoSy and CLP Fig. 2A and B shows partial obstruction of the left oviduct, and the arrow shows the adhesive umbrella end. Fig. 2C and D shows the proximal obstruction of the left oviduct, and that the proximal end of the oviduct was obviously swollen.

Comparison of obstruction of different nature as diagnosed by 3D-HyCoSy. The contrast agent flow time of oviduct obstruction (tortuosity and complete obstruction) as diagnosed by 3D-HyCoSy was significantly prolonged when compared with that of partial oviduct obstruction (ratio between 4.2±1.3, 5.8±1.4 and 2.9±1.1 sec; F=5.624, P=0.015), and flow time of inflammation as diagnosed subsequently was longer than that of congenital dysplasia, tumor and cyst. Following the diagnosis of inflammation, the shape of the contrast agent was tenuous, swollen, angled, rigid and distorted and the occurrence rate of inflammation was higher, and the degree of pain suffered by patients, injection pressure of contrast medium and quantity of backflow was significantly increased following the diagnosis of inflammation (P<0.05) (Table I and Fig. 3).

Discussion

It has been shown that the 3D-HyCoSy can acquire 3D images of oviducts through the reconstruction of 3D surface modes, and can display three mutually perpendicular section

planes (coronal plane, sagittal section and cross section) at the same time, and can better acquire important information concerning the shape, way, patency degree and obstruction sites to evaluate the patency and oviducts as well as the spatial relationship between oviducts and ovary in a more comprehensive and accurate manner (7,8). Due to the application combining hysterosalpingo contrast sonography and 3D ultrasound, the diagnostic sensibility and specificity were obviously increased (9,10). Based on the diagnostic criteria of CLP, the diagnostic sensitivity, specificity, positive predictive and negative predictive values of 3D-HyCoSy were 82.4, 88.3, 77.9 and 90.2%, respectively. 3D-HyCoSy was easily operated and non-invasive and was important in diagnosing and identifying uterine cavity lesion and oviducts obstruction. We found that the contrast agent flow time of oviduct obstruction (tortuosity and complete obstruction) as diagnosed by 3D-HyCoSy was significantly prolonged when compared with that of partial oviduct obstruction, and flow time of inflammation as diagnosed subsequently was longer than that of congenital dysplasia, tumor and cyst. Following the diagnosis of inflammation, the shape of contrast agent was tenuous, swollen, angled, rigid and distorted and the occurrence rate of inflammation was higher. Additionally, the degree of pain suffered by patients, injection pressure of contrast medium and quantity of backflow obviously increased following the diagnosis of inflammation, and the difference was of statistical significance. This is where the innovation of the study was and it had better application value in judging the nature of oviducts obstruction in clinic, especially the inflammation.

Of course, although the advantages of 3D-HyCoSy has become more and more obvious in clinic, the observation range of 3D transvaginal ultrasonography is narrow and is not applicable to the patients with uterus augmentation and larger uterine fibroids, and it may influence the reconstruction of oviducts when the adnexal masses become larger or the structure becomes complicated (11,12). At the same time, 3D-HyCoSy did not display the inside oviducts clearly, especially the lesion occurring in the oviducts mucosa and pelvic cavity adhesion (12,13). In addition, research studies should continue to explore reduction in the pseudo obstruction resulting from oviducts spasm in examination (14). Additionally, 3D-HyCoSy was completed under the assistance of more advanced apparatus and instruments (radiography function) and better contrast medium, therefore the application of 3D-HyCoSy has a few limitations.

In conclusion, SonoVue 3D-HyCoSy has some significant advantages in diagnosing the patency of oviduts, and the application of SonoVue contrast medium combined with 3D volume imaging technology and codes contrast imaging technology greatly makes up the shortfall of 2D hysterosalpingo contrast sonography. Since the physicians can acquire the coronal plane of uterine cavity and the stereo images of the whole oviducts through 3D imaging, they can acquire more comprehensive and accurate information to conduct comprehensive analysis and evaluation towards the oviducts. Thus, 3D imaging can replace X-ray iodized oil imaging and even the laparoscopy to some extent, and can provide a more convenient, non-invasive and radiation-free examination method without any toxicity and side effects for the majority of patients with infertility. It can also play a certain role in treating infertility during the radiography, and has therefore become a new method to treat oviduct diseases, which is characteristic of high safety and high diagnostic accuracy. Therefore, 3D-HyCoSy is expected to become the most valuable and promising examination method in the field of gynecology.

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