Abstract. Clinical value of color Doppler ultrasound and two-dimensional ultrasound in the diagnosis of ovarian sex cord-stromal tumors (OSCSTs) were explored. A total of 91 patients with positive OSCSTs admitted to Sichuan Provincial Hospital for Women and Children from May 2014 to June 2018 were selected as research objects. There were 48 patients diagnosed by color Doppler ultrasound technology as the color Doppler group and 43 patients diagnosed by two-dimensional ultrasound technology as the two-dimensional ultrasound group. Results of ultrasound images in the two groups were compared, and the diagnostic value of two ultrasound techniques combined with detection of CA125 and CA199 for OSCSTs was compared. The real internal echo of color Doppler ultrasound was significantly higher than that of two-dimensional ultrasound (P<0.05). The blood flow signal of color Doppler ultrasound was significantly higher than that of two-dimensional ultrasound (P<0.05). The diagnostic sensitivity and diagnostic coincidence rate of color Doppler ultrasound for lymph node metastasis of OSCSTs were significantly higher than those of two-dimensional ultrasound (P<0.05). Color Doppler ultrasound combined with CA125 and CA199 detection has higher accuracy than two-dimensional ultrasound combination. In conclusion, both color Doppler ultrasound and two-dimensional ultrasound are used to observe OSCSTs for early diagnosis, but the sensitivity and diagnostic coincidence rate of color Doppler ultrasound for clinical diagnosis of OSCSTs are higher than those of two-dimensional ultrasound, so color Doppler ultrasound has higher diagnostic value in OSCSTs.

Introduction

Ovarian sex cord-stromal tumors (OSCSTs) are rare mixed ovarian tumors. OSCSTs are composed of stromal elements of gonads, sex cord-like cells or a plurality of luteinized cells in different differentiation stages in a single or mixed manner (1,2). However, due to the non-significant specificity of its histological features, clinicopathological manifestations, physical examination and imaging features, it is difficult to differentiate OSCSTs from similar gynecologic tumors. Therefore, clinical diagnosis and differentiation are difficult, especially when judging the benign and malignant nature of tumors, and patients could miss the best treatment time (3,4). Clinically, ovarian tumors are usually diagnosed by histopathological examination and surgery, and treated by surgical resection (5,6). However, due to the relatively few clinical records and confirmed cases of OSCSTs, and insufficient cognition, no definite diagnosis can be made before surgery (7,8).

Imaging examination plays an important role in the quantitative, and qualitative detection and diagnosis of ovarian tumors, of which ultrasound has the advantages of less radiation damage, simple operation and high resolution to soft tissue (9,10). The existing two-dimensional ultrasound technology is relatively mature with widespread clinical application. It is the main method to examine ovarian tumors. The diagnostic accuracy has been improved in recent years through the use of high-frequency probes. However, it still has shortcomings, for example, poor diagnostic efficiency, obvious misdiagnosis rate, and low accuracy in judging pathological types or disease development degree, leading to an increase in the possibility of misdiagnosis and missed diagnosis (11,12). Two-dimensional ultrasound is a section imaging technology, and color Doppler ultrasound provides real-time stereoscopic imaging on this basis. Color Doppler ultrasound has the advantages of short distance between probe and ovary, high resolution between blood vessel and ovary. When monitoring blood flow, it can make judgment according to the difference of blood flow distribution in ovarian masses (13,14). It has been reported in literature (15) that color Doppler ultrasound is effective in detecting the success rate of blood flow signals of
ovarian malignant tumors, providing more valuable information for the diagnosis and differentiation of lesions. This study compared the diagnostic value of two-dimensional ultrasound and color Doppler ultrasound for OSCSTs.

Patients and methods

General materials. A total of 91 patients with positive OSCSTs admitted to Sichuan Provincial Hospital for Women and Children (Chengdu, China) from May 2014 to June 2018 were selected as research objects, of whom 48 patients diagnosed by color Doppler ultrasound technology were the color Doppler group and 43 patients diagnosed by two-dimensional ultrasound technology were the two-dimensional ultrasound group. All the subjects were aged between 18 and 78 years, with an average age of 41.2±11.7 years and BMI of 21.1±3.3 kg/m². Among them, there were 29 cases of granulosa cell tumors, 5 cases of thecoma, 20 cases of mixed tumors, 13 cases of supportive stromal cell tumors, 16 cases of sclerosing stromal tumors and 8 cases of fibrosarcoma. There were no significant differences in age, BMI, abdominal pain and ascites of patients between the two groups (P>0.05) (Table I).

Inclusion and exclusion criteria. Inclusion criteria: Patients diagnosed as OSCSTs by pathological diagnosis. Exclusion criteria: Patients previously treated for OSCST diseases; women with other malignant tumors; patients who were breast-feeding or pregnant; patients with cognitive impairment or communication impairment; patients with poor compliance. All patients and their families agreed to participate in the experiment and signed an informed consent. The study was approved by the Medical Ethics Committee of Sichuan Provincial Hospital for Women and Children.

Experimental reagents and materials. The color Doppler diagnostic apparatus was purchased from Siemens (S2000) and LOGIQ (E9).

Ultrasound experimental methods. During the examination, the probe frequency is 4-8 MHz in abdomen and 4-9 MHz in vagina. Stone amputation was performed when the bladder was empty. Internal echo and boundary of the two groups were observed and recorded by travaginal two-dimensional ultrasound, and color Doppler ultrasound was used to examine the section of the highest possibility at highest definition. The blood flow condition inside and around the tumor was observed and recorded, the location and size of ovarian tumor combined with abdominal two-dimensional ultrasound images were observed, the relationship between morphology and viscera and organs was summarized, and ascites was detected.

Detection method. Venous blood (3 ml) was taken from fasting patients in the morning as examination specimen. After centrifugation at 1,500 x g for 5 min at normal temperature, the serum was taken and stored at -20°C. Electrochemiluminescence was used to detect serum CA125 and CA199. The steps were as follows: the serum sample was pre-treated with reducing reagents; CA125 and CA199 were placed at constant temperature for antigen-antibody complex; ruthenium-labeled and biotin-labeled antibodies were added, and after binding, magnetic beads were added to generate a solid phase complex. The magnetic beads are adsorbed and cleaned by the electrode. After the light-emitting reaction occurs, the sample to be tested and the light signal were examined. The weaker the light signal, the larger the amount of the sample to be tested. The normal value of serum CA125 is 0-35 U/ml, and it is positive when >35 U/ml. The normal value of serum CA199 was 0-37 U/ml, and it is positive when >37 U/ml. Any positive result of the index will be judged as positive.

Observation indicators. Color Doppler ultrasound and two-dimensional ultrasound were used to measure size, form, boundary and location of tumors. The results of two ultrasound images for patients with OSCSTs were compared. The sensitivity, specificity and diagnostic accuracy of the two kinds of ultrasound in the detection of pathological signs of OSCSTs were compared.

Statistical methods. In this experiment, SPSS 19.0 statistical (Beijing ND Times Science and Technology Co., Ltd.) was
Chi-square test was used for counting data, measuring data were expressed by mean ± standard deviation and t-test was used for comparison between the two groups. Graphpad Prism8 was used to present the illustrations. P<0.05 was considered to indicate a statistically significant difference.

### Table I. General data of patients.

| Factors                           | Color Doppler ultrasound group n=48 | Two-dimensional ultrasound group n=43 | t/χ² value | P-value |
|-----------------------------------|-------------------------------------|--------------------------------------|------------|---------|
| Age (years)                       |                                     |                                      | 0.002      | 0.967   |
| ≤41                               | 27 (56.25)                          | 24 (55.81)                           |            |         |
| >41                               | 21 (43.75)                          | 19 (44.19)                           |            |         |
| BMI (kg/m²)                       |                                     |                                      | 0.008      | 0.930   |
| ≤21                               | 23 (47.92)                          | 21 (48.84)                           |            |         |
| <21                               | 25 (52.08)                          | 22 (51.16)                           |            |         |
| Irregular vaginal bleeding        |                                     |                                      | 0.402      | 0.526   |
| Yes                               | 21 (43.75)                          | 16 (37.21)                           |            |         |
| No                                | 27 (56.25)                          | 27 (62.79)                           |            |         |
| Abdominal pain                    |                                     |                                      | 2.227      | 0.996   |
| Yes                               | 29 (60.42)                          | 26 (60.47)                           |            |         |
| No                                | 19 (39.58)                          | 17 (39.53)                           |            |         |
| Ascites                           |                                     |                                      | 0.096      | 0.757   |
| Yes                               | 9 (18.75)                           | 7 (16.28)                            |            |         |
| No                                | 39 (81.25)                          | 36 (83.72)                           |            |         |
| Typing                            |                                     |                                      | 0.488      | 0.993   |
| Granulosa cell tumors             | 15 (31.25)                          | 14 (32.56)                           |            |         |
| Thecoma                           | 2 (4.17)                            | 3 (6.98)                             |            |         |
| Mixed tumors                      | 11 (22.92)                          | 9 (20.93)                            |            |         |
| Supportive stromal cell tumors    | 7 (14.58)                           | 6 (13.95)                            |            |         |
| Sclerosing stromal tumors         | 9 (18.75)                           | 7 (16.28)                            |            |         |
| Fibrosarcoma                      | 4 (8.33)                            | 4 (9.30)                             |            |         |
| C125 (U/ml)                       | 95.62±14.52                         | 98.63±15.45                          | 0.958      | 0.341   |
| C199 (U/ml)                       | 97.46±15.73                         | 98.72±15.82                          | 0.381      | 0.705   |
| AFP (µg/l)                        | 75.63±9.62                          | 76.36±9.93                           | 0.356      | 0.723   |

### Table II. Comparison of size, form, boundary and location of tumors under color Doppler ultrasound and two-dimensional ultrasound.

| Features of tumors | Color Doppler ultrasound group n=48 | Two-dimensional ultrasound group n=43 | t/χ² value | P-value |
|--------------------|-------------------------------------|--------------------------------------|------------|---------|
| Tumor size         | 7.34±4.53                           | 7.51±4.46                           | 0.180      | 0.858   |
| Form               |                                     |                                      | 0.112      | 0.738   |
| Irregular          | 3 (6.25)                            | 2 (4.65)                            |            |         |
| Regular            | 45 (93.75)                          | 41 (95.35)                          |            |         |
| Boundary           |                                     |                                      | 0.267      | 0.605   |
| Clear              | 43 (89.58)                          | 37 (86.05)                          |            |         |
| Not clear          | 5 (10.42)                           | 6 (13.95)                           |            |         |
| Location           |                                     |                                      | 0.024      | 0.876   |
| Unilateral         | 32 (66.67)                          | 28 (65.12)                          |            |         |
| Multilaterality    | 16 (33.33)                          | 15 (34.88)                          |            |         |
Results

Comparison of size, form, boundary and location of patients with positive OSCSTs under color Doppler ultrasound and two-dimensional ultrasound. The size, form, boundary and location detected by color Doppler ultrasound in patients with OSCSTs were not significantly different from those detected by two-dimensional ultrasound (P>0.05), more details are shown in Table II.

Comparison of results of two kinds of ultrasound images in patients with positive OSCSTs. The real internal echo of color Doppler ultrasound was significantly higher than that of two-dimensional ultrasound, with significant statistical differences (P<0.05). The blood flow signal of color Doppler ultrasound was significantly higher than that of two-dimensional ultrasound, with significant statistical differences (P<0.05). There was no statistically significant difference in posterior echo and calcified lesion (P>0.05) (Table III, Figs. 1 and 2).

Comparison of the sensitivity, specificity and diagnostic accuracy of two kinds of ultrasound in detecting OSCST metastasis. The diagnostic sensitivity and the coincidence rate of color Doppler ultrasound for lymph node metastasis of OSCSTs were significantly higher than those of two-dimensional ultrasound (P<0.05). Differences were statistically significant (P<0.05) (Tables IV and V).

Discussion

OSCSTs can occur in women of any age group, and its manifestations of abdominal pain and abdominal distension become more and more obvious as the tumor grows larger, and even cause pedicle torsion and rupture in severe cases (16). Most of the OSCSTs can release steroid hormones and frequently cause corresponding clinical symptoms, such as menstrual disorder and hemorrhage of women caused by the increase of estrogen level, and masculinization characteristics of a few patients caused by the increase of androgen expression (17,18). Ultrasound is generally used to assist the diagnosis of OSCSTs. Two-dimensional ultrasound provides early diagnosis for patients suspected of malignant tumors by presenting single-angle cross-sectional images of the human body. It has the advantages of non-invasiveness, repeatability, economy and high safety. At the same time, it is difficult to clearly express the three-dimensional morphological structure of ovary, which affects the accuracy of clinical differentiation of benign and malignant ovarian tumors (19,20). Color Doppler ultrasound spatial stereogram vascular parameters can be used to observe neovascularization and blood cells in tumors, so as to judge the development of the disease (21). At present, there are few reports on the diagnosis of OSCSTs by color Doppler ultrasound and two-dimensional ultrasound. Therefore, we use pathological examination results as the gold standard to explore the diagnostic value of ultrasound imaging in OSCSTs, so as to provide a more accurate scheme for the diagnosis of OSCSTs patients.

In our study, the application value of color Doppler ultrasound and two-dimensional ultrasound in the diagnosis of OSCSTs was explored. First, we investigated the differences in size, form, boundary and location of tumors between color Doppler ultrasound and two-dimensional ultrasound. Our results showed that there were no significant differences in size, form, boundary and location of tumors between patients with positive OSCSTs and those of under two-dimensional ultrasound (P>0.05). Then we analyzed the diagnostic efficiency of color Doppler ultrasound and two-dimensional ultrasound for OSCSTs. The results showed that the diagnostic sensitivity and diagnostic coincidence rate of color Doppler ultrasound for lymph node metastasis of OSCSTs were significantly higher than those of two-dimensional ultrasound (P<0.05). The accuracy of color Doppler ultrasound combined with CA125 and CA199 detection was higher than that of two-dimensional ultrasound (P<0.05). Previous studies (22-24) have suggested that the sensitivity and

Table III. Comparison of results of two kinds of ultrasound images in patients with positive ovarian sex cord-stromal tumors.

| Features of imaging | Color Doppler ultrasound group n=48 | Two-dimensional ultrasound group n=43 | t/χ² value | P-value |
|---------------------|-------------------------------------|-------------------------------------|------------|--------|
| Internal echo       |                                      |                                    | 4.135      | 0.042  |
| Solid type          | 31 (64.58)                          | 19 (44.19)                         |            |        |
| Cystic-solid type   | 17 (35.42)                          | 24 (55.81)                         |            |        |
| Posterior echo      |                                      |                                    | 1.128      | 0.569  |
| Uniformity          | 10 (20.83)                          | 7 (16.28)                          |            |        |
| Weak                | 27 (56.25)                          | 22 (51.16)                         |            |        |
| Enhanced            | 11 (22.92)                          | 14 (32.56)                         |            |        |
| Blood flow signal   |                                      |                                    | 5.093      | 0.024  |
| Obvious             | 33 (68.75)                          | 38 (88.37)                         |            |        |
| Not obvious         | 15 (31.25)                          | 5 (11.63)                          |            |        |
| Calcified lesions   |                                      |                                    | 1.129      | 0.288  |
| Yes                 | 16 (33.33)                          | 19 (44.19)                         |            |        |
| No                  | 32 (66.67)                          | 24 (55.81)                         |            |        |
diagnostic specificity of color Doppler ultrasound for ovarian malignant tumors are higher than those of two-dimensional ultrasound. Color Doppler ultrasound is more accurate than two-dimensional ultrasound in displaying abnormal spots of lesions and color blood signals. This proves our conclusion to some extent. Then we studied the relationship between features of OSCSTs imaging and pathological examination results of two kinds of ultrasound examinations. The results showed that the real internal echo of color Doppler ultrasound was significantly higher than that of two-dimensional ultrasound, with significant statistical difference (P<0.05). The blood flow signal of color Doppler ultrasound was significantly higher than that of two-dimensional ultrasound, with significant statistical difference (P<0.05). There is no significant statistical significance in posterior echo and calcified lesions (P>0.05), suggesting that the internal echo of OSCSTs tumor is related to pathological type. It is often dominated by solid hypoecho, and color Doppler has relatively high expression of color blood flow signals. Previous studies have shown that (25), ovarian sarcoma fibroma, as an uncommon OSCST, has been detected by ultrasound as a solid tumor with typical characteristics of well-defined hypoechoic masses. However, there are few specific research documents on OSCSTs ultrasound imaging. From this study, color Doppler ultrasound shows more solid mass and blood flow signals than two-dimensional ultrasound. There are no significant differences in general clinical pathological data and tumor characteristics between patients in the two groups. It is speculated that differences in internal echo and blood flow signals give color Doppler ultrasound higher diagnostic value for OSCSTs than two-dimensional ultrasound, and the diagnostic reliability is high. From our research, it seems that color Doppler ultrasound has more obvious diagnostic sensitivity for internal echo and blood flow signals in features of OSCST imaging.

In conclusion, this study shows that color Doppler ultrasound has high diagnostic value for OSCSTs, and its diagnostic results can be used as an important reference for diagnosis and treatment of OSCSTs in clinical practice.

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Authors' contributions
GH, JZ and WX conceived and designed the study. GH, JZ, ZY, ZZ and YB were responsible for the collection, analysis and interpretation of the data. GH drafted the manuscript. JZ and WX revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The study was approved by the Medical Ethics Committee of Sichuan Provincial Hospital for Women and Children (Chengdu, China). Signed informed consents were obtained from the patients and/or the guardians.

Patient consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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