# Analysis of Application of Four-dimensional Color Doppler Ultrasound in Prenatal Screening of Fetal Malformation

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**Abstract. Objective:** To investigate the clinical application value of four-dimensional color Doppler ultrasound in prenatal screening of fetal malformation. **Methods:** The comparative analysis was performed for 5033 pregnant women with 21-28 gestational weeks receiving two-dimensional ultrasound diagnosis and real-time four-dimensional color Doppler ultrasound in Nanning Eighth People's Hospital (hereinafter referred to as our hospital). Combined with the related data of pregnant women and four-dimensional color Doppler ultrasound results, the fetal malformation was judged. The review of the superior hospital, induced abortion results and imaging results of pregnant women after term delivery were used as the golden standard, and the relevant data were compared with the maternal abdominal examination. At the same time, the clinical specificity, sensitivity, negative detection rate and positive detection rate of the two diagnostic methods in the diagnosis of fetal malformation were compared. **Results:** The specificity, sensitivity, negative detection rate and positive detection rate of four-dimensional ultrasonic technique in the prenatal examination of fetal malformation were superior to those of two-dimensional ultrasound: There were (87+4897) cases consistent with the golden standard, 46 cases of missed diagnosis and 3 cases of misdiagnosis in two-dimensional ultrasound; there were (122+4900) cases consistent with the golden standard, 11 cases of missed diagnosis and no misdiagnosis in real-time four-dimensional ultrasound. And the differences between the two methods were statistically significant (P<0.05), and the real-time dynamic images could be obtained. **Conclusion:** Four-dimensional ultrasound applied in the prenatal analysis of fetal malformations can comprehensively observe the intrauterine fetal situation and improve the detection rate of fetal malformations, which can display the screening of fetal malformations most stereoscopically and intuitively and make up for the defects of two-dimensional ultrasound, so it is worthy of clinical application.

## Introduction

Fetal malformation mainly refers to the birth defect of fetus and the structural or chromosomal abnormalities of fetus in the womb, which can cause fetal or neonatal death. According to the existing data statistics, there is body deformity in about 3% of live neonates, which not only brings a heavy burden for their families, but also seriously reduces the life quality of newborns [1]. Therefore, improvement of the detection rate of fetal malformations,

early prenatal intervention and decrease of the birth rate of abnormal fetus using a suitable diagnostic method have been one of the urgent problems to be solved in the clinical medicine. Ultrasonic examination has been widely used in prenatal diagnosis because of its noninvasive, cheap and practical characteristics. With the development of perinatology, people's concept of fetal health has been greatly changed, and it is difficult for the conventional two-dimensional ultrasound to meet people's demands on examination. With the development of ultrasonic technique and deepening of clinical application, real-time four-dimensional color Doppler ultrasound, as a kind of new color ultrasonic examination technique, begins to be applied [2]. In this study, with the golden standard as the diagnosis results, the superiority and accuracy of two-dimensional ultrasound diagnosis and real-time four-dimensional color Doppler ultrasound examination in the judgment of fetal malformations were compared and analyzed, so as to clear the application value of real-time four-dimensional color Doppler ultrasound in the prenatal analysis of fetal malformations. Now it is reported as follows:

## Materials and Methods

### Clinical Data

5033 pregnant women receiving prenatal examination from September 2015 to January 2017 in our hospital were selected as objects of study. Pregnant women were aged 14-44 years old with an average of (29.2±4.5) years old, and the gestational age was 21-28 weeks with an average of (24.1±2.6) weeks; there were 2969 cases (59%) of first pregnancy and 2064 cases (41%) of multiple pregnancies; and there were 4973 cases of single birth and 60 cases of twins. All pregnant women signed the informed consent.

### Methods

GE Voluson E6 and GE Voluson 730 PRO V color Doppler ultrasound diagnostic instrument was selected for examination. Three-dimensional volume probe: 3.5-5.5MHz, convex array probe: 3.5-5.5MHz, transabdominal scan. In a supine position, or lateral position combined with the specific conditions of patients, the patients received the conventional two-dimensional ultrasound first, multi-section and all-dimensional two-dimensional scanning and routine measurement according to the regular order to judge whether there was fetal malformations; the fetal placenta and amniotic fluid were carefully observed. After that, the key sites were examined using the four-dimensional color Doppler ultrasound: The probe was placed in the region of interest, 4D program was started, and the three-dimensional sampling frame was reasonably adjusted to obtain and observe the four-dimensional dynamic images, followed by detailed analysis. The scopes of examination included the fetal chest and abdomen, limbs, spine, face and head, etc., and if there were suspected abnormal sites, they should be carefully observed and recorded, and the inspection images were effectively saved in the workstation. The pregnant women were followed up till the term delivery or induced labor, followed by confirmation of the results.

### Observational Indexes

All pregnant women were followed up for 0-3 months, and the golden standard was used as the final diagnosis results [3]. The relevant data were compared with the inspection result of the fetus in the abdomen, and the specificity, sensitivity, negative detection rate and positive

detection rate of the two diagnostic methods in the diagnosis of fetal malformations were compared with the final diagnostic results, and advantages and disadvantages of the two diagnostic methods in the diagnosis of fetal malformations were clarified based on it.

## Statistical Methods

SPSS22.0 statistical software was used for the analysis and treatment of recorded data of the above patients. $t/X^2$ test was used for detection. $P<0.05$ suggested that the difference was statistically significant.

## Judgment of Fetal Malformation

According to the relevant standard in international classification of disease (ICD) 10, the abnormal fetus was identified and classified [4]. If two kinds of malformation were found, it was donated as 1 systematic malformation and 2 disease malformations. Multi-position malformations often exist in congenital heart disease, and they should be donated as 1 disease malformation.

## Results

### Diagnostic Results

133 out of 5033 fetuses were finally diagnosed as fetal malformations through the review in superior hospital, induced labor or imaging examination after term delivery, accounting for 2.64%, including 18 cases of head deformity (14 cases of hydrocephalus, 3 cases of choroid plexus cyst and 1 case of corpus callosum dysplasia), accounting for 0.36%; 21 cases of facial deformity (16 cases of cleft lip and palate, 4 cases of nasal dysplasia or nasal bone loss, and 1 case of microtia), accounting for 0.42%; 3 cases of chest deformity (1 case of pleural effusion and 2 cases of congenital diaphragmatic hernia), accounting for 0.06%; 39 cases of abdominal deformity (22 cases of hydronephrosis, 3 cases of polycystic kidney, 3 cases of ectopical kidney with renal dysplasia, 5 cases of gallbladder dysplasia or loss, 1 case of duplex kidney, 2 cases of duodenal atresia, 1 case of intestinal atresia, 1 case of acromphalus and 1 case of megalocystis), accounting for 0.77%; 10 cases of limb deformity (5 cases of varus/ valgus deformity, 3 cases of limb flexion deformity and 2 cases of nanomelia), accounting for 0.2%; 3 cases of spinal deformity (1 case of rachischisis and 2 cases of scoliosis), accounting for 0.06%; 37 cases of cardiac deformity (3 cases of double outlet right ventricle, 1 case of transposition of conducting arteries, 4 cases of tetralogy of Fallot, 5 cases of ventricular septal defect, 1 case of pulmonary stenosis, 1 case of left ventricular dysplasia, 3 cases of oval foramen enlargement, 7 cases of persistent left superior vena cava, 2 cases of cardiac enlargement, 1 case of heart rhabdomyoma, 1 case of ascending aorta and aortic arch constriction and 8 cases of pericardial effusion), accounting for 0.74%; 1 case of neck cystic hygroma, accounting for 0.02%; and 1 case of sacral hemangioma, accounting for 0.02%.

### Comparison of Results

The golden standards of two-dimensional ultrasound and real-time four-dimensional ultrasound in the diagnosis of fetal malformations were compared and the results showed that there were (87+4897) cases consistent with the golden standard, 46 cases of missed diagnosis and 3 cases of misdiagnosis in two-dimensional ultrasound; there were (122+4900) cases

consistent with the golden standard, 11 cases of missed diagnosis and no misdiagnosis in real-time four-dimensional ultrasound (Table 1).

Table 1. Comparison of Diagnostic results of two-dimensional ultrasound and
real-time four-dimensional ultrasound (n).

| Diagnostic method | Diagnostic result | Two-dimensional ultrasound (n=5033) | Two-dimensional ultrasound (n=5033) | Real-time four-dimensional ultrasound (n=5033) | Real-time four-dimensional ultrasound (n=5033) |
|---|---|---|---|---|---|
| | | + | - | + | - |
| Through the review in superior hospital, induced labor or imaging examination after term delivery | +(n=133) | 87 | 46 | 122 | 11 |
| | -(n=4900) | 3 | 4897 | 0 | 4900 |

Each observational index of the two diagnostic methods was compared. The specificity, sensitivity, negative detection rate and positive detection rate of four-dimensional ultrasound in the prenatal examination of fetal malformation were superior to those of two-dimensional ultrasound. And the differences between the two methods were statistically significant (P<0.05, Table 2).

Table 2. Comparison of diagnostic value of two-dimensional ultrasound and real-time
four-dimensional ultrasound in the inspection of fetal malformation (n).

| Group | Sensitivity | Specificity | Positive detection rate | Negative detection rate |
|---|---|---|---|---|
| Two-dimensional ultrasound | 65.41 (87/133) | 99.94 (4897/4900) | 96.67 (87/90) | 99.07 (4897/4943) |
| Real-time four-dimensional ultrasound | 91.72 (122/133) | 100.00 (4900/4900) | 100.00 (122/122) | 99.78 (4989/5000) |
| $X^2$ | 48.1637 | 6.0013 | 8.1205 | 37.7521 |
| P | 0.0000 | 0.0141 | 0.0045 | 0.0000 |

Fetal malformation is a kind of common clinical disease, and its incidence in China is 2%-5% [5]. Prenatal screening of fetal malformation is of great significance in reducing the incidence of fetal malformations and improving the quality of life of newborns, which is also an important means to control the birth rate of abnormal fetus [6]. In the past, two-dimensional ultrasound is characterized by simple operation, low price and strong function, so it is widely affirmed in the primary hospital. But the missed diagnosis and misdiagnosis rates of two-dimensional ultrasound are large, and it cannot effectively and accurately reflect the actual situation of fetus, so its clinical application is limited [7]. Other detection methods, such as amniotic fluid cast-off cell chromosome karyotype X-ray examination, have not yet been

recognized and accepted by the majority of pregnant women [8]. In recent years, four-dimensional color Doppler ultrasound can help observe the three-dimensional structure, and provide the necessary one-dimensional vision, as well as dynamic images, so it has become a new diagnostic method for fetal congenital malformations. The observer can observe the fetal movement by imaging, observe the fetal malformation images and anatomical structure, and timely position the deformed site and severity, and obtain the disease information [9-10], which greatly improves the diagnosis of fetal malformations and avoids the missed diagnosis and misdiagnosis. However, in practice, there are still many deformed newborns, and one of the reasons is that the effects of two-dimensional ultrasound and real-time four-dimensional color Doppler ultrasound in prenatal analysis of fetal malformations are different and different ultrasound examination methods lead to missed diagnosis and misdiagnosis. Based on the background of this study, this paper mainly discusses the effects of two-dimensional ultrasound and real-time four-dimensional color Doppler ultrasound in prenatal analysis of fetal malformations, in order to clarify the advantages and disadvantages of them in the clinical diagnosis and provide reference for the prenatal examination of fetal malformations.

Morphological changes are the basis of ultrasound imaging diagnosis. Four-dimensional color Doppler ultrasound can track the morphological changes in fetal structure in real time, and its dynamic images are timely and continuous, which can observe the fetus in different positions and stages. The imaging can help track the fetal movement and development, providing a strong reference for doctor's diagnosis, and avoiding missed diagnosis and misdiagnosis as far as possible [11]. The clinical study on four-dimensional color Doppler ultrasound shows that the pregnant week of 23-27 weeks is the best time to observe the fetal face, pregnant week of 22-28 weeks is the best time to check the heart structure, and pregnant week of 20-26 weeks is the best time to observe the fetal limbs. There is more amniotic fluid in the above pregnant week, intrauterine activity space for fetus is large and its activities are more frequent, so the four-dimensional imaging effect is more ideal. And two-dimensional ultrasound cannot achieve the three-dimensional observation and real-time continuous tracking of fetal morphology. Thus, four-dimensional ultrasound diagnostic technique is widely used in the prenatal screening of fetal malformations to observe the fetal limb deformity and movement disorders, which can also effectively assess the degrees of fetal malformations and defects.

Four-dimensional color Doppler ultrasound can realize the all-round examination of fetus in a intuitive and three-dimensional mode, clear on the for, and its diagnosis rate of early fetal malformation is high. And ultrasound diagnosis is more sensitive to the complex structure and overlapping parts, which can show the body movement more intuitively, and get the coronal plane and other information that cannot be obtained by two-dimensional ultrasound diagnosis. At the same time, four-dimensional ultrasound combined with color Doppler flow imaging is a new imaging technique, which has a higher reliability in the detection of fetal malformations and can diagnose the organ development of fetus and plays an important role in the placenta and cardiovascular system malformation diagnosis [12]. Four-dimensional color Doppler ultrasound imaging makes up for the defects of two-dimensional imaging, and can analyze the fetal development comprehensively and observe the fetus in parent from multi angles, whose main advantages are as follows compared with two-dimensional ultrasound: (1) Head and face: Ultrasonic testing can observe the fetal intracranial structure from three directions: thalamus horizontal section, lateral ventricle horizontal section and cerebellar cross-section, and more than 95% of neurological malformations can be accurately observed; (2) Organ deformity: Two-dimensional ultrasound cannot clearly observe the fetal heart structure, but the

four-dimensional color Doppler ultrasound can make up for its shortcomings, effectively reducing the interference in clinical observation of fetal position; (3) Spinal deformity: Conventional two-dimensional ultrasound cannot correctly show the curved structure in the spine, but four-dimensional ultrasound can directly observe various structures in the fetal spine, which can also accurately display the curvature of spine; (4) Limb deformity: In the human skeleton, limbs, especially the hand, is more complex. Two-dimensional ultrasound cannot fully reflect the development of fetal bones, but only from a single side, resulting in low diagnostic accuracy and lack of science; four-dimensional color Doppler ultrasound can not only clearly understand the limb structure of fetus, but also observe the hands and feet under the fetal movement. In addition, the study found that four-dimensional color Doppler ultrasound has a low rate of missed diagnosis in the detection of facial and spine deformity compared to ordinary two-dimensional color Doppler ultrasound. Therefore, the four-dimensional color Doppler ultrasound has a higher accuracy in the diagnosis of head, organs, spine and limbs, which can greatly reduce the rates of missed diagnosis and misdiagnosis. It can be seen that the real-time four-dimensional ultrasound in the clinical diagnosis of fetal malformations has obvious advantages compared with the two-dimensional ultrasound.

The results of this study also verified the above results. The results show that the specificity, sensitivity, negative detection rate and positive detection rate of real-time four-dimensional ultrasound in the prenatal examination of fetal malformations are better than those of two-dimensional ultrasound, which has a higher detection rate and very low misdiagnosis rate. There were (87+4897) cases consistent with the golden standard, 46 cases of missed diagnosis and 3 cases of misdiagnosis in two-dimensional ultrasound; there were (122+4900) cases consistent with the golden standard, 11 cases of missed diagnosis and no misdiagnosis in real-time four-dimensional ultrasound. The sensitivity, specificity, negative detection rate and positive detection rate of two-dimensional ultrasound were 87/133, 4897/4900, 4897/4943 and 87/90, while the sensitivity, specificity, negative detection rate and positive detection rate of four-dimensional color Doppler ultrasound were 122/133, 4900/4900, 4989/5000 and 122/122; and the differences were statistically significant (P<0.05). In this study, 7 out of 11 missed patients in real-time four-dimensional ultrasound were complex malformation, but only one deformity was found in inspection process, and the other one was artificially ignored. It can be seen that the order of four-dimensional ultrasound examination should be strictly followed in the prenatal examination of pregnant women, so as to avoid the missed diagnosis and improve the accuracy.

At present, the screening of fetal structure using ultrasound in the second trimester of pregnancy has become an important part of the prenatal diagnosis, but there are large risks in ultrasound examination. If the inspection results show the false negative, defect infants may be born, and the false positive may lead to the induced labor of normal fetus. Therefore, using the four-dimensional ultrasound with higher accuracy, intuition and definition in the screening of fetal malformation has significance in reducing the missed diagnosis and misdiagnosis rates and decreasing the neonatal malformations.

**Summary**

In conclusion, the real-time four-dimensional color Doppler ultrasound has great advantages in the screening of fetal malformation in pregnant metaphase, compared with the more widely-used two-dimensional ultrasound. The application of four-dimensional color Doppler ultrasound in prenatal analysis of fetal malformation can accurately diagnose whether there is congenital malformation and significantly improve the diagnostic accuracy with higher prenatal diagnostic values, which also provides a scientific basis for the diagnosis of clinicians. These are very beneficial for child-bearing and child-rearing and can effectively reduce the defect rate of the newborn, so four-dimensional color Doppler ultrasound is the main method of prenatal screening of fetal malformations. Four-dimensional color Doppler ultrasound has broad prospects, and it is worthy of popularization and promotion in clinical prenatal screening.

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