First-trimester Doppler ultrasound examination

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ABSTRACT
First-trimester screening is focused on both markers of aneuploidies and structural abnormalities detection. In the past ten years, clinicians have been increasingly interested in using Doppler ultrasound in the first trimester of pregnancy. Doppler examination can help estimate the risk of aneuploidy and early diagnose severe fetal malformations. The purpose of this article is to highlight the importance of color Doppler ultrasound examination of the fetus in the first trimester. Color Doppler examination also has a great significance in studying maternal-fetal circulation. According to the ISUOG guidelines, several vascular territories should be covered: uterine arteries, umbilical artery, and ductus venosus. The nowadays first trimester Doppler examination not only identifies specific ultrasonographic markers for aneuploidy but also aids in the identification and analysis of many anatomical structures.

Keywords: first-trimester screening, Doppler examination, ultrasound, ductus venosus, cardiac screening, aneuploidy

INTRODUCTION
Over the past two decades, first-trimester ultrasound has had a continuous development and is currently used for assessing the fetal risk for aneuploidies and the maternal risk for preeclampsia, as well as for detecting major fetal structural abnormalities. The combination of the ultrasound examination and the biochemical analysis of the maternal serum led to the detection of up to 95% of cases of trisomy 21, with a false positive rate of 5% (1). The “combined test” includes the dosing of two maternal serum markers: beta-human chorionic gonadotropin (free beta-hCG) and pregnancy-associated plasma protein A (PAPP-A) (2).

First-trimester screening can detect both aneuploidies and structural abnormalities. The appropriate time for screening is usually at the end of the first trimester, between 11 and 13+6 weeks of gestation (3). Ultrasound markers, such as increased nuchal translucency, absent nasal bone, echogenic intestine, pyelectasia, shortened long bones, are not proper anomalies but rather signs of risk; they manifest in many affected fetuses but can also be sometimes identified in normal fetuses (4). The isolated presence of one of the ultrasound markers may be present in normal fetuses in 11% to 17% of cases. When multiple ultrasound markers are present, the risk of aneuploidy is significantly increased (5).
For the past ten years, clinicians have been increasingly interested in using Doppler ultrasound in the first trimester to estimate the risk of aneuploidy and to diagnose fetal malformations (6). Studies in the literature suggest a close link between the presence of aneuploidies and abnormal blood flow through the ductus venosus recorded using Doppler ultrasound (7). The flow through the ductus venosus is usually pulsating, with positive blood velocities throughout the cardiac cycle (8). Also, the wave corresponding to the inverted atrial contraction or the absence and insufficiency of the tricuspid may be associated with fetal abnormalities (8). Bilardo et al. noted an association between Down syndrome and increased flow into the hepatic arteries (9). Also, a decrease in umbilical artery flow may be associated with the development of intrauterine growth restriction (10). Doppler evaluation of the ductus venosus can lead to better results in screening for heart defects (11).

Minnella et al., in a retrospective study performed on 93,209 pregnancies without chromosomal abnormalities, at 11-13 weeks, diagnosed 60% of complex heart malformations, 30-40% of cases of tetralogy of Fallot, 25% of abnormalities of the tricuspid valve, 15% of cases of transposition of large vessels, all cases of tricuspid or pulmonary atresia, no aortic or pulmonary stenosis (12).

The purpose of this article is to highlight the importance of color Doppler ultrasound examination of the fetus in first-trimester screening.

**MATERIAL AND METHODS**

This paper aims to support the importance of Doppler examination in determining the risk of fetal abnormalities during the first-trimester screening. The research was done using special search engines, such as Google Scholar, PubMed, Medscape, UpToDate, and Cochrane, the variables being clear and included the field of interest of this study („first-trimester screening“, „ultrasound in the first-trimester“, „first-trimester Doppler ultrasound“, „first-trimester screening guidelines“).

The information used was based on existing studies in the literature, cohort studies, reviews, retrospective studies. We centralized the information and formulated correlations between current existing data in the literature according to the ISUOG guidelines.

All figures in the paper are included in the personal collection of Roxana Bohitea.

**SIGNIFICANCE OF THE COLOR DOPPLER EXAMINATION**

In the case of first-trimester ultrasound screening, the color Doppler examination has great significance in the study of maternal-fetal circulation. According to ISUOG guidelines for the use of Doppler examination at the 11-13+6 weeks of gestation, several factors should be analyzed given their known relevance, such as uterine arteries, umbilical artery, and ductus venosus. Other important key points to be analyzed may include the aorta, cord axis, subclavian artery, renal artery, tricuspid flow. These vessels can be important for certain individuals, but their examination is not considered to bring valid significance for all the fetuses (13).

**Cardiac examination**

The most common birth defect is a congenital heart disease which remains a major cause of stillbirths and neonatal death. In the first-trimester, the visualization of the heart structures has technical limitations, so the Doppler evaluation is greatly important. Color flow mapping improves the detection of blood vessels and chambers (Figures 1, 2, 3, 4) and shows the direction of blood flow. A conventional curvilinear transducer and MTI filtered color flow mapping can be used to improve ultrasound examination of the fetal heart compared to using a high frequency transducer. This resulted in a four-chamber image view in approximately 97.3% of fetuses than 84.0% (14). In a few cases, the diagnosis of fetal abnormalities is made in the last trimester, but a group of high-risk fetuses can be created who will benefit from close monitoring and additional evaluations, to make an early diagnosis and establish proper management (15).

**FIGURE 1. Ultrasound imaging of the cord axis at 11+5 weeks of gestation**

**Subclavian artery**

To visualize the subclavian arteries (Figure 5), a simple way is to find the thymus (figure 6) and move the transducer in a posterior plane. The right subclavian artery originates in the brachiocephalic trunk, along with the common right carotid artery. The aberrant right subclavian artery (ARSA) originates directly from
the aortic arch, distal to the left subclavian artery (16). The importance of Doppler evaluation of the subclavian artery stems from the fact that more than 20% of fetuses with ARSA had other abnormalities, and ARSA appears to be an independent marker of trisomy 21. In the study by Scala et al., the prevalence of ARSA in fetuses with Down syndrome was 23.6% and showed that Doppler ultrasound evaluation of the evolution and origin of the subclavian artery in the first trimester was feasible in 85% of cases (17).

Ductus venosus

To evaluate congenital cardiac defects in the first-trimester screening, the analysis of the ductus venosus represents an essential factor, given that its velocimetry flow reflects that of the central venous system of the fetus. The ductus venosus can be visualized in 2D imaging of the fetal trunk using a mid-sagittal longitudinal plane (13) (Figure 7). By including the Doppler evaluation in the first-trimester screening protocol, up to 60% of the congenital heart defects can be detected, with a false-positive rate of 5% (18).

Tricuspid flow

The importance of the Doppler evaluation of the tricuspid valve (Figure 8) emerges from the fact that tricuspid regurgitation appears to be a new ultrasound marker of trisomy 21 (19). Faiola et al. conducted a study on pregnancies between 11 + 0 and 13 + 6 weeks
of gestation and reported the incidence of tricuspid regurgitation of 8.5% of the 458 fetuses with normal karyotype and 65.1% of 126 with trisomy 21. They also demonstrated that the prevalence of tricuspid regurgitation is inversely proportional to fetal crown rump length (CRL) and directly proportional to NT thickness (20).

In the study by Minnella et al. in fetuses with major heart failure, fetal NT ≥ 95 or ≥ 99th percentile, tricuspid regurgitation or abnormal venous duct flow were observed in 36.5%, 21.3%, 28.9%, and 27.5%, respectively, while for those without heart failure the incidence was 6.1%, 0.9%, 1.2% and 1.8% (12).

Renal arteries

Doppler ultrasound provides easy identification of the fetal renal artery (Figure 9), in longitudinal view, from the origin as a branch of the abdominal aorta to the renal hilum. The pulsatility index decreases with increasing gestational age, decreasing flow impedance, and increasing renal perfusion. Thus, with the advancement of pregnancy, there is an increase in fetal urine production (21).

Umbilical arteries

Using color Doppler examination during the first-trimester screening, the cord vessels (the arteries and one vein) can be easily evaluated (Figure 10). In some cases, only one umbilical artery is present. The importance of establishing the number of cord vessels results from the association between the two vessels umbilical cord and congenital heart malformations. In addition, the single umbilical artery is also associated with intrauterine growth restriction and preterm delivery (22).

Uterine arteries

According to ISUOG guidelines, the uterine arteries evaluation can be performed by transabdominal or transvaginal approach, by identifying the cervical canal and then moving the para-cervical vascular plexus can be examined laterally. Measurements must be taken before the branching of the uterine arteries (13) (Figure 11).

For the prediction of early-onset pre-eclampsia, first trimester Doppler evaluation of the uterine arteries represents an important tool. According to the
study by Aguaiar et al., the measurement of both the sagittal and transverse pulsatility index in the uterine arteries does not change the final result of the pre-eclampsia screening (23).

The abnormal uterine artery flow in the case of low-risk patients justifies the use of aspirin prophylaxis according to a meta-analysis that involved over 50,000 women (24).

Uterine artery Doppler velocimetry can also be used to predict pre-eclampsia-related intrauterine growth restriction. However, Doppler evaluation better predicts pre-eclampsia than intrauterine growth restriction, having a greater diagnostic accuracy when the early Doppler evaluation presents more severe findings (18).

**CONCLUSIONS**

Given the small value of the crown to rump length in the first trimester, the Doppler examination adds an important aid for the identification and analysis of the anatomical structures. Another important feature of Doppler in the first-trimester ultrasound is that of a certified ultrasonographic marker for aneuploidy, and predicting subsequent pregnancy complications.

**REFERENCES**