Ductus venosus pulsatility index in the screening protocol for trisomy 21 at 11-13 weeks


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Objective
Anomalies of the blood flow in the ductus venosus (DV) can be associated with fetal aneuploidies. Assessment of DV flow can be qualitative – analysis of the shape of the A wave (positive or negative) or quantitative - measure of the pulsatility index for veins (DV PI). We aimed to investigate the value of the addition of qualitative and quantitative assessment of DV flow to the basic protocol for screening for Down's syndrome at 11 to 13+6 weeks.

Methods
Ultrasound (US) examinations with the assessment of DV were performed by Fetal Medicine Foundation certified doctors in 8230 fetuses, as a part of the routine screening for chromosomal defects at 11-13+6 weeks of pregnancy. In all patients CRL, nuchal translucency (NT) and fetal heart rate were measured and a first trimester anomaly scan was performed. The shape of the DV A-wave was assessed (positive or negative) and the PI was calculated. Blood samples were taken for first trimester biochemistry analysis (Delfia Express, Perkin–Elmer). Free β-hCG and PAPP-A levels were expressed as MoMs. Risk for chromosomal defects was calculated with Astraia software. The cut-off value for the high risk was 1/300. High-risk patients were offered an invasive test (amniocentesis) for karyotyping. In those not consenting, the karyotype was determined after birth if there was a suspicion of trisomy 21.

Results
We excluded 676 because they had either a major structural defect with normal karyotype or other chromosomal defects (not trisomy 21), or were lost to follow-up. Among 7554 patients that qualified for the final analysis, trisomy 21 was found in 80 fetuses (1.1%). The remaining 7474 fetuses presented a normal phenotype (98.9%). An abnormal wave A was observed in 258 (3.5%) of fetuses with a normal karyotype and in 38 (47.5%) with trisomy 21 (p<0.0001). Basic screening with following combination of markers: maternal age, NT, fetal heart rate, free β-hCG and PAPP-A provided the lowest detection rate (DR) 87.50% for FPR=6.94%. After adding qualitative A-wave assessment, DR increased to 88.75% for FPR=5.65%. The best DR=93.75% for FPR=5.55% was achieved when quantitative DV PI was added. For the latter increasing cut-off for high risk to 1/200 resulted in the same DR=93.75% for decreased FPR=3.72%. The application of the ROC (Receiver Operating Curves) curve for the analysis confirmed the validity of addition of the qualitative and quantitative DV marker. The diagnostic power of the test was the highest with added DV PI, with the ROC AUC of 0.974.

Conclusion
The assessment of the DV flow performed at 11-13+6 weeks results in increased detection rate of trisomy 21 and reduced false positive rate. The screening model based on the quantitative DV flow analysis (DV PI) gives better results compared to the qualitative flow assessment.