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The Role of Ductus Venosus Doppler Flow in the Diagnosis of Chromosomal Abnormalities During the First Trimester of Pregnancy*

Znaczenie oceny przepływu krwi w przewodzie żylnym w diagnostyce wad chromosomowych u płodu w I trymestrze ciąży

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Background. The ductus venosus (DV) is an intrahepatic end-part of the umbilical vein. Inappropriate first trimester DV Doppler blood flow patterns correspond to a higher risk of chromosomal abnormalities.
Objectives. The aim of the study was to assess the usefulness of ductus venosus Doppler flow in a first trimester screening for aneuploidies.
Material and Methods. A prospective study included 1526 singleton pregnancies with increased risk of chromosomal abnormalities who underwent prenatal first trimester screening between the years 2006–2009. All ultrasound scans were performed by experienced sonographers and included an assessment of fetal growth, nuchal translucency (NT), nasal bone assessment (NB) and ductus venosus (DV) blood flow. Reversed a-wave (atrial diastole) in the ductus venosus flow pattern was recognized as abnormal. In addition to DV blood flow, the levels of pregnancy-associated plasma protein-A (PAPP-A) and free β – human chorionic gonadotropin (β-hCG) in maternal serum were measured. The risk of chromosomal abnormalities was calculated using the Fetal Medicine Foundation software. The following risk levels were assumed: high risk results – 1:100 or lower, intermediate risk 1:100–1:1000, and low risk above 1:1000. In 523 pregnancies, patients underwent amniocentesis and karyotyping.
Results. The authors diagnosed 46 cases with chromosomal abnormalities (using amniocentesis and karyotyping). 29 patients had spontaneous miscarriage, in 21 cases they reported fetuses with congenital malformations (mostly heart defects). Abnormal DV blood flow was recognized in 113 pregnant women (7.4%). The majority of cases affected by abnormal DV blood flow were classified as intermediate and high disorder risk groups – 100 (6.5%). The comparison between a combined test with and without DV assessment revealed that the addition of DV flow pattern results increased sensitivity from 84% to 92% in screening for aneuploidies. The false-positive ratio was between 0.4% and 2.4%.
Conclusions. Ductus venosus Doppler blood flow examination is useful in the first trimester prenatal diagnostic since it increases the sensitivity of the combined test in the assessment of risk for chromosomal abnormalities. The authors recommend assessing DV blood flow during the first trimester screening in all pregnancies, irrespectively of the chromosomal abnormalities background risk. This procedure in clinical practice seems to be favorable and less complicated (**Adv Clin Exp Med 2013, 22, 3, 395–401**).

Key words: ductus venosus, Doppler, chromosomal abnormalities.

Streszczenie

Wprowadzenie. Przewód żylny (DV) jest naczyniem stanowiącym zakończenie części wewnątrzwątrobowej żyły pępowinowej. Nieprawidłowy przepływ dopplerowski w DV w I trymestrze ciąży wiąże się ze zwiększonym ryzykiem wystąpienia wad u płodu.

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Cel pracy. Ocena przydatności badań dopplerowskich przepływu krwi w DV płodu w I trymestrze ciąży w ocenie ryzyka wystąpienia aneuploidii.
Materiał i metody. U 1526 ciężarnych w ciążach jednopłodowych w latach 2006–2009 wykonano badania przesiewowe w ramach diagnostyki prenatalnej w I trymestrze ciąży. Badania obejmowały pomiary wielkości płodów, przezierności karkowej (NT – *nuchal translucency*), kości nosowej (NB – *nasal bone*) i przepływu krwi w DV. Za nieprawidłowy przepływ krwi w DV uznawano falę wsteczną w fazie skurczu przedsionków. W surowicy krwi ciężarnych oznaczano wolną podjednostkę β gonadotropiny kosmówkowej (hCG) oraz specyficzne białko ciążowe A (PAPP-A). Ryzyko wystąpienia zaburzeń chromosomowych obliczano za pomocą programu Fetal Medicine Foundation. Za wysokie ryzyko wad chromosomowych uznawano wartości poniżej 1:100, średnie ryzyko 1:100––1:1000, a niskie – powyżej 1:1000. U 523 ciężarnych wykonano amniopunkcje z następową oceną cytogenetyczną.
Wyniki. Na podstawie badań genetycznych wykryto 46 ciężarnych z aberracjami chromosomowymi u płodów. U 29 ciężarnych doszło do poronienia samoistnego, u 21 – stwierdzono wady strukturalne u płodu (głównie wady serca). Nieprawidłowy przepływ w DV wykazano u 113 ciężarnych (7,4%), w większości w grupie średniego i wysokiego ryzyka wad – 100 ciężarnych (6,5%). Testy przesiewowe z wykorzystaniem badań przepływu krwi w DV, w porównaniu do testów bez badań w DV, wykazały wzrost czułości z 84 do 92% w ocenie ryzyka wystąpienia aneuploidii u płodów. Odsetek wyników fałszywie dodatnich wynosił (0,4–2,4%).
Wnioski. Badania dopplerowskiego przepływu krwi w DV są przydatne w diagnostyce prenatalnej w I trymestrze ciąży, ponieważ zwiększają czułość testu zintegrowanego w ocenie ryzyka wystąpienia wad chromosomowych u płodów. Podczas badań przesiewowych w I trymestrze ciąży autorzy proponują ocenę przepływu krwi w DV u wszystkich ciężarnych, niezależnie od ryzyka wad chromosomowych. Takie postępowanie w praktyce wydaje się prostsze i korzystniejsze (**Adv Clin Exp Med 2013, 22, 3, 395–401**).

Słowa kluczowe: przewód żylny, Doppler, wady chromosomowe.

Ductus venosus (DV) is an intrahepatic end part of the umbilical vein. In an ultrasound examination, the ductus venosus may be presented using either B-mode or color Doppler [1]. The best results for the Doppler spectrum can be achieved in a dorso-anterior fetus position. Routinely, the Doppler sample should be about 0.5–1.0 mm wide and the scan should be performed on the initial part of the vessel [2]. The proper assessment of the ductus venosus wave requires it to be performed in fetus quiescence. In order to achieve a better assessment of the examined ductus venosus, the A-wave insonation angle should be less than 30 degrees [3]. The capacity filter should be set on the lowest possible frequency (50–70 Hz) [4].

Appropriate DV Doppler flow during every stage of fetal development demonstrates progressive flow ("forward") and consists of three components: systolic wave considered with ventricular systole (S-wave), diastolic wave considered with ventricular diastole (D-wave), and systolic wave considered with atrial systole (A-wave) [1–4]. The ductus venosus Doppler spectrum phases strictly correspond to gradient pressure between the umbilical vein and the right atrium.

There are some parameters which are used to perform quantitative assessment of the ductus venosus flow spectrum to assess preload [5]. These parameters are calculated using the following formulas: (S-A)/S, (S-A)/V_{mean}, (S-A)/D, A/S and S/A, where S is maximal blood flow velocity during ventricular systole, D is maximal blood flow velocity during early diastole, A is blood flow velocity during atrial systole (and afterwards during ventricular diastole) and V_{mean} is mean blood flow velocity [1, 6]. Besides the quantitative assessment of the DV Doppler spectrum, a qualitative assessment is also used in clinical practice. Reversed A-wave (during atrial systole) is acknowledged as an anomalous DV spectrum [6, 7, 8].

The aim of the study was to assess the relevance of ductus venosus Doppler flow in first semester screening for aneuploidies.

Material and Methods

A three-year (2006–2009), prospective study of pregnant women in singleton pregnancies with increased risk of chromosomal abnormalities who have undergone prenatal first trimester screening was performed. 1526 cases were enrolled in the study. In all cases, pregnant women were above 35 years of age and had delivered newborns with chromosomal abnormalities or severe malformations in prior pregnancies, or were translocation carriers, or had abnormal first trimester ultrasound scan. All the patients delivered in authors' Department, so the authors were able to examine their newborns as well.

All ultrasound scans were performed by experienced sonographers and included assessment of fetal growth, nuchal translucency (NT), nasal bone (NB) and ductus venosus (DV) blood flow.

The ductus venosus Doppler spectrum was assessed qualitatively to recognize a reversed A-wave (during atrial diastole) as an abnormal flow.

In addition to the quantitative method, a qualitative assessment of the ductus venosus Doppler spectrum was also done to help properly recognize a reversed A-wave (during atrial diastole) as an abnormal flow. After ultrasound

examination, first trimester screening tests were performed for the level of pregnancy-associated plasma protein-A (PAPP-A) and free β-human chorionic gonadotropin (β-hCG) in the maternal serum. A Kryptor™ system was used for laboratory tests. The risk of chromosomal abnormalities was calculated using the Fetal Medicine Foundation software. The following risk levels were assumed: high risk results 1:100 or lower, intermediate risk 1:100–1:1000, and low risk above 1:1000. In 523 cases where the pregnancies were in their 15th week (or later), after providing genetic counseling, the authors obtained the patients' written consent and performed amniocentesis with karyotyping.

In the statistical analysis, the authors included a set of variables obtained from the ultrasound examinations and the laboratory test results as well as a chromosomal abnormalities risk assessment using the combined test in their clinical database. Statistical analysis was performed using Statistica 6.0 (Statsoft Polska).

Results

Table 1 provides characteristics of the study population. Table 2 provides indications for the invasive diagnostic – amniocentesis. In the study population, regardless of whether the results of the ultrasonographic and laboratory screening tests were negative or not, the most frequent recommendation for amniocentesis was the age of the patients (46%). All patients from this group underwent genetic counseling to estimate the risk of the amniocentesis procedure and the chromosomal abnormalities as well. The authors found that apprehension about the potential abnormalities was greater than about the risks of amniocentesis and the couples, having discussed the matter with the doctors, eventually decided to undergo the invasive test.

The results of the karyotyping revealed chromosomal abnormalities in 46 cases: 21 cases of Down Syndrome, 10 cases of Edwards Syndrome, 9 cases of Patau Syndrome and 6 cases of Turner Syndrome.

29 pregnant women (1.9%) had spontaneous miscarriage. Only one of the miscarriages was a result of genetic amniocentesis. In that particular case, the patient was of an intermediate risk of chromosomal abnormalities according to the combined test and decided to undergo the invasive diagnostic. Amniocentesis revealed normal fetal karyotype.

Table 1. Characteristics of the study group

Tabela 1. Charakterystyka badanej grupy ciężarnych

Feature (Cecha)	Median (ranges) or number of (Mediana (zakres wartości) lub liczba i %)
Age of pregnant women (years) (Wiek ciężarnych – lata)	36.7 (25.0–42.0)
Weight (kg) (Masa ciała – kg)	66.0 (44.0–110.0)
Spontaneous pregnancies (Ciąże powstałe samoistnie)	1512 (99.1)
Smoking during pregnancy (Ciężarne palące)	72 (4.7)
Crown-Rump-Length (mm) (Wymiar siedzeniowo-ciemieniowy – mm)	76 (48 – 82)
Euploid fetuses (Prawidłowy kariotyp płodu)	1480 (96.9)
Trisomy 21	21 (1.4)
Trisomy 18	10 (0.6)
Trisomy 13	9 (0.5)
Monosomy X	6 (0.4)

Table 2. Indications for genetic amniocentesis in the study group (n = 523)

Tabela 2. Wskazania do amniopunkcji genetycznej u badanych ciężarnych (n = 523)

Indication for amniocentesis (Wskazanie do amniopunkcji)	Numbers (Liczba)	%
Age above 35 years of age (Wiek powyżej 35. roku życia)	244	46.7
Intermediate risk in combined test (1:100–1:1000) (Średnie ryzyko wad w teście zintegrowanym – 1:100–1:1000)	162	31.0
High risk in combined test (below 1:100) (Duże ryzyko wad w teście zintegrowanym – poniżej 1:100)	67	12.7
Malformations in present pregnancy (Wady rozwojowe u płodu w aktualnej ciąży)	21	4.0
Chromosomal abnormalities in prior pregnancy (Urodzenie w poprzedniej ciąży dziecka z wadami chromosomowymi)	20	3.8
Parents translocations carriers (Nosicielstwo translokacji u rodziców)	9	1.8

Table 3. Prenatal screening test results using combined test without DV assessment and pregnancy outcome (n = 1526)

Tabela 3. Wyniki przesiewowych badań prenatalnych za pomocą testu zintegrowanego, bez uwzględnienia badań dopplerowskiego przepływu krwi w DV w odniesieniu do losów ciąży (n = 1526)

Risk level in combined test (Ryzyko w teście zintegrowanym)	Healthy newborns (Zdrowe noworodki) N (%)	Miscarriages (Poronienia) N (%)	Chromosomal disorders (Wady chromosomowe) N (%)	Heart and other malformations (Wady serca i inne wady) N (%)
Low risk (Małe ryzyko)	1277 (83.75)	3 (0.2)	5 (0.3)	4 (0.3)
Intermediate risk (Średnie ryzyko)	154 (10.1)	10 (0.6)	9 (0.6)	9 (0.6)
High risk (Duże ryzyko)	6 (0.4)	16 (1.0)	28 (1.8)	5 (0.3)
Cumulatively (Łącznie)	1437 (94.2)	29 (1.9)	42 (2.7)	18 (1.2)

In 21 cases, the ultrasound examination revealed fetal congenital malformations: 9 heart defects, 4 urinary tract anomalies, 3 gastrointestinal anomalies, 2 generalized fetal oedema, 2 central nervous system malformations and 1 omphalocele.

Heart anomalies were not diagnosed until the 22nd week of gestation. Diagnosis was confirmed by an experienced fetal cardiologist *in utero* and reconfirmed after delivery. Other abnormalities were identified in the first trimester ultrasound screening (11–13+6 weeks).

Table 3 provides screening results of the first trimester screening without the assessment of ductus venosus blood flow.

It is remarkable that in 5 cases (0.3%), in spite of a low risk of chromosomal abnormalities in the combined test, the authors found chromosomal abnormalities: 4 cases of trisomy 21 and one case of trisomy 18. Two fetuses with Down Syndrome were diagnosed prenatally (in these cases, genetic amniocentesis was performed because of the women's age above 35 years) and the remaining two cases were diagnosed after delivery.

In the intermediate risk level group, the chromosomal abnormalities appeared in 9 cases while in the high risk group in 28 cases. In the group of 9 pregnant women with intermediate risk, there were only 2 patients who decided to undergo amniocentesis, the remaining subjects decided against it. All abnormalities from the high risk group were diagnosed prenatally (amniocentesis & karyotyping).

Cumulatively, chromosomal abnormalities were observed in 42 pregnant women (2.7%).

Table 4 provides the results of the first trimester screening including the assessment of ductus venosus blood flow. Improper DV flow was observed in 113 pregnant women (7.4%), mainly in the intermediate and high risk groups, which consisted of 100 cases (6.5%).

Table 5 provides a comparison between the results of the screening test with and without ductus venosus blood flow assessment. The results confirm that a combined test connected with the assessment of ductus venosus blood flow is characterized by a higher sensitivity rate (92%) than a separate combined test (84%) with similar specificity rate. The false-positive ratio was satisfactory (2.4%).

Discussion

Prenatal first trimester screening, performed between 11 and 14 weeks of gestation, has great importance for modern obstetrics because it makes it possible to assess the risk of chromosomal abnormalities, fetal malformations and the risk of pregnancy induced hypertension [9–11].

An abnormal DV Doppler blood flow in the first trimester corresponds to a higher risk of fetal genetic disorders, malformations, arrhythmias, intrauterine growth restriction (IUGR), twin to twin transfusion syndrome (TTTS) in multiple pregnancies and unfavorable pregnancy outcome [15–19].

Recently many researchers report the high sensitivity of ductus venosus blood flow assessment in the prediction of fetal aneuploidies [20–22]. In the present study population, abnormal DV blood flow was found among healthy fetuses in 7.4% of cases. Other studies reported lower rates: Borrell [20] – 5.0%, Toyama [23] – 6.4%, Prefumo [24] – 5.2% and Maiz [18] – 3.2%, and yet for some, the rates could be as high as 13.0% in Zoppi [25]. In the present group of aneuploid

Table 4. Prenatal screening test result using combined test including DV assessment and pregnancy outcome (n = 1526)

Tabela 4. Wyniki przesiewowych badań prenatalnych za pomocą testu zintegrowanego z uwzględnieniem badań dopplerowskiego przepływu krwi w DV w odniesieniu do losów ciąży (n = 1526)

DV blood flow + combined test disorders risk (Przepływ w DV + ryzyko wad w teście zintegrowanym)	Healthy newborns (Zdrowe noworodki) N (%)	Miscarriages (Poronienia) N (%)	Chromosomal abnormalities (Wady chromosomowe) N (%)	Heart and other malformations (Wady serca i inne wady) N (%)
ADVF + LDR (PPWDV + MRW)	1273 (83.4)	1 (0.06)	1 (0.06)	1 (0.06)
IDVF + LDR (NPWDV + MRW)	4 (0.3)	2 (0.1)	2 (0.1)	3 (0.2)
ADVF + IDR (PPWDV + ŚRW)	122 (7.9)	2 (0.1)	1 (0.06)	1 (0.06)
IDVF + IDR (NPWDV + ŚRW)	32 (2.1)	8 (0.5)	10 (0.6)	8 (0.5)
ADVF + HDR (PPWDV + DRW)	5 (0.3)	4 (0.3)	1 (0.06)	1 (0.06)
IDVF + HDR (NPWDV + DRW)	1 (0.06)	12 (0.8)	27 (1.8)	4 (0.3)

ADVF – appropriate DV flow.
PPWDV – prawidłowy przepływ w DV.
LDR – low disorder risk.
MRW – małe ryzyko wad.
IDVF – inappropriate DV flow.
NPWDV – nieprawidłowy przepływ w DV.
IDR – intermediate disorder risk.
śrw – średnie ryzyko wad.
HDR – high disorder risk.
DRW – duże ryzyko wad.

fetuses, abnormal DV blood flow was found in 29 cases (69%). In similar studies, authors reported comparable rates: Zoppi [25] – 70%, Borrell [20] – 75%, Toyama [23] – 71% and Maiz [18] – 66%.

Currently two fundamental strategies are considered to be useful in clinical practice [19]. In the first approach – which the authors recommend – ductus venosus blood flow should be assessed in all cases simultaneously with combined test screening. The second strategy recommends the assessment of ductus venosus blood flow only in pregnancies with an intermediate risk of chromosomal abnormalities (1:51–1:1000) or with a nuchal translucency above 95th percentile for a given gestation week.

The authors recommend the first approach as less complicated and of a higher utility, because it makes it possible to comprehensively assess the risk of chromosomal abnormalities without the need to wait for laboratory test results and secondary ultrasound examinations, which also entails a new risk calculation. The Maiza [18] and Borrella [26] studies confirmed that both clinical strategies characterize similar sensitivity in aneuploid risk assessment (93–95%) with a 3–5% rate of false-positive results.

In the present study group, the authors classify as intermediate risk of chromosomal abnormality in combined test results between 1:100 and 1:1000. Currently, the first trimester screening is qualified as positive with a risk above 1:50 without the DV assessment, and above 1:100 with DV spectrum blood flow examination in the group of intermediate risk (between 1:51–1:1000) [18, 19].

Maiz's [18] findings confirmed that the sensitivity of the combined test in the assessment of first trimester screening for aneuploidies increased from 80–88% to 94–97% when including the DV examination. The Borrell [26] study's conclusions were quite similar to Maiz's. In his study, the addition of DV diagnostics to the combined test increased the sensitivity in detecting genetic disorders from 88 to 92% and decreased the false-positive ratio from 5 to 1%. The present study results were similar to those authors. They achieved an increase of the method's sensitivity by the addition of DV assessment from 85% to 92% with a 2.4% false-positive ratio.

Table 5. Combined test with and without DV assessment specificity, sensitivity and false-positive ratio in aneuploidies screening

Tabela 5. Czułość, swoistość oraz odsetek wyników fałszywie dodatnich testów zintegrowanych z uwzględnieniem i bez uwzględnienia przepływów w DV w wykrywaniu aneuploidii u płodu

Type of test (Rodzaj testu)	Sensitivity (Czułość) %	Specificity (Swoistość) %	False-positive ratio (Odsetek wyników fałszywie dodatnich)
Combined test without DV flow (Test zintegrowany, bez przepływu w DV)	84.8	99.5	0.4
Combined test + DV flow (Test zintegrowany + przepływ w DV)	92.8	97.4	2.4

While in cases of the low and high risk level of chromosomal abnormalities groups the decision about further procedure does not seem to be difficult, the women classified as belonging to the intermediate risk level group might especially benefit from including the DV procedure. For the first group, a follow-up ultrasound examination between the 18th and 22nd week of gestation is recommended. In the second group, invasive procedures are required. Intermediate risk pregnancies proceedings appear to be questionable: in these cases, the authors suggest the assessment of DV blood flows and performing a "triple test" between 15 and 18 weeks of gestation (a test consisting of α-fetoprotein, free β-human chorionic gonadotropin and unconjugated estriol) or eventually the serum level of inhibin A. Using these findings, it may be easier to decide about further diagnostic procedures.

The authors concluded that ductus venosus Doppler blood flow examination is useful in the first trimester prenatal diagnostic since it increases the sensitivity of the combined test in the assessment of risk for chromosomal abnormalities. The authors recommend assessing DV blood flow during the first trimester screening in all pregnancies, irrespectively of the chromosomal abnormalities basic risk. This procedure in clinical practice seems to be favorable and less complicated.

References

[1] **Merz E:** Ultrasound diagnostic in the obstetrics and gynecology – ed. pol. Zalewski J, Florjański J. Urban & Partner, Wrocław 2004, 477–499.

[2] **Węgrzyn P, Fiegler P, Kamiński K:** Doppler measurements of blood flow velocity and waveforms in fetal venous circulation. Ginekol Pol 2004, 75, 153–159.

[3] **Teixeira LS, Leite J, Vegas MJBC, Faria MML, Chaves AS, Teixera RC, Pires MC, Pettersen H:** Ductus venosus Doppler velocimetry in the first trimester: a new finding. Ultrasound Obstet Gynecol 2008, 31, 261–265.

[4] **Maiz N, Kagan KO, Milovanovic Z, Celik E, Nicolaides KH:** Learning curve for Doppler assessment of ductus venosus flow at 11+0 to 13+6 weeks' gestation. Ultrasound Obstet Gynecol 2008, 31, 503–506.

[5] **Bahlmann F, Wellek S, Reinhardt I, Merz E, Steiner E, Welter E:** Reference values of ductus venosus flow velocity waveforms and various calculated waveform indices. Prenat Diagn 2000, 20, 623–634.

[6] **Tchirikov M, Schraeder HJ, Hecher K:** Ductus venosus shunting in the fetal venous circulation: regulatory mechanisms, diagnostic methods and importance. Ultrasound Obstet Gynecol 2006, 27, 452–461.

[7] **Carvalho FH, Moron AF, Mattar R, Santana RM, Murta CG, Barbosa MM, Torloni MR, Vasques FA:** Ductus venosus Doppler velocimetry in the prediction of acidemia at birth: which is the best parameter? Prenat Diagn 2005, 25, 1212–1216.

[8] **Jakobovits A:** Sonographic evaluation of the circulation in the ductus venosus Arantii. Orv Hetil 2005, 146, 1301–1304.

[9] **Becker R, Wegner RD:** Detailed screening for fetal anomalies and cardiac defects at the 11–13 week scan. Ultrasound Obstet Gynecol 2006, 27, 613–618.

[10] **Kagan KO, Wright D, Valencia C, Maiz N, Nicolaides KH:** Screening for trisomies 21, 18 and 13 by maternal age, fetal nuchal translucency, fetal heart rate, free β-hCG and pregnancy-associated plasma protein-A. Hum Reprod 2008, 23, 1968–1975.

[11] **Poon LC, Kametas NA, Maiz N, Akolekar R, Nicolaides KH:** First-trimester prediction of hypertensive disorders in pregnancy. Hypertension 2009, 53, 812–818.

[12] **Oh C, Harman C, Baschat AA:** Abnormal first-trimester ductus venosus blood flow: a risk factor for adverse outcome in fetuses with normal nuchal translucency. Ultrasound Obstet Gynecol 2007, 30, 192–196.

[13] **Maiz N, Valencia C, Emmanuel EE, Staboulidou I, Nicolaides KH:** Screening for adverse pregnancy outcome by ductus venosus Doppler at 11–13+6 weeks of gestation. Obstet Gynecol 2008, 112, 598–605.

[14] **Maiz N, Staboulidou I, Leal AM, Minekawa R, Nicolaides KH:** Ductus venosus Doppler at 11 to 13 weeks of gestation in the prediction of outcome in twin pregnancies. Obstet Gynecol 2009, 113, 860–865.
[15] **Baś-Budecka E, Perenc M, Sieroszewski P:** The role of fetal nuchal translucency (NT) and ductus venosus blood flow (DV) in the detection of congenital heart defects. Ginekol Pol 2010, 4, 272–276.
[16] **Papatheodorou SI, Evangelou E, Makrydimas G, Ioannidis JPA:** First-trimester ductus venosus screening for cardiac defects: a meta-analysis. BJOG 2011, 181, 1438–1445.
[17] **Martinez JM, Comas M, Borrell A, Bennasar M, Gomez O, Puerto B, Gratacos E:** Abnormal first-trimester ductus venosus blood flow: a marker of cardiac defects in fetuses with normal karyotype and nuchal translucency. Ultrasound Obstet Gynecol 2010, 35, 267–272.
[18] **Maiz N, Valencia C, Kagan KO, Wright D, Nicolaides KH:** Ductus venosus Doppler in screening for trisomies 21, 18 and 13 and Turner syndrome at 11–13 weeks of gestation. Ultrasound Obstet Gynecol 2009, 33, 512–517.
[19] **Maiz N, Nicolaides KH:** Ductus venosus in the first trimester: contribution to screening of chromosomal, cardiac defects and monochorionic twin complications. Fetal Diagn Ther 2010, 28, 65–71.
[20] **Borrell A, Gonce A, Martinez JM, Borobio V, Fortuny A, Coll O, Cuckle H**: First-trimester screening for Down syndrome with ductus venosus Doppler studies in addition to nuchal translucency and serum markers. Prenat Diagn 2005, 25, 901–905.
[21] **Florjański J, Zalewski J, Barwiński I, Heimrath J, Nowak M, Blok D**: Usefulness of some ultrasonographic markers in the assessment of risk of aneuploidy in fetuses in the first trimester of pregnancy. Adv Clin Exp Med 2004, 13, 11–14.
[22] **Nicolaides KH, Spencer K, Avgidou K, Faiola S, Falcon O:** Multicenter study of first-trimester screening for trisomy 21 in 75821 pregnancies: results and estimation of the potential impact of individual risk-orientated two-stage first-trimester screening. Ultrasound Obstet Gynecol 2005, 25, 221–226.
[23] **Toyama JM, Brizol ML, Liao AW, Lopes LM, Nomura RM, Saldanha FA, Zugaib M:** Ductus venosus blond flow assessment At 11 to 14 weeks of gestation and fetal outcome. Ultrasound Obstet Gynecol 2004, 23, 341–345.
[24] **Prefumo F, Sethna F, Sairam S, Bhide A, Thilaganathan B:** First-trimester ductus venosus, nasal bones, and Down Syndrome in high-risk population. Obstet Gynecol 2005, 105, 1348–1354.
[25] **Zoppi MA, Putzolu M, Ibba RM, Floris M, Monni G:** First-trimester ductus venosus velocimetry in relation to nuchal translucency thickness and fetal karyotype. Fetal Diagn Ther 2002, 17, 52–57.
[26] **Borrell A, Borobio V, Bestwick JP, Wald NJ:** Ductus venosus pulsatility index as an antenatal screening marker for Down's syndrome use with the combined and integrated tests. J Med Screen 2009, 16, 12–118.

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