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## **MIDDLE CEREBRAL ARTERY FLOW VELOCITY WAVEFORMS IN PREDICTION OF ADVERSE OUTCOME IN INTRAUTERINE GROWTH RETARDED FETUSES**

### **KRVNI OPTOK SREDNJE MOŽDANE ARTERIJE U PRETKAZIVANJU NEPOVOLJNA ISHODA U FETUSA S USPORENIM RASTOM**

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*Professional paper*

*Key words:* perinatal outcome, IUGR, a. cerebri media flow

**SUMMARY.** The development of a Doppler ultrasound technique offers new opportunities in the follow-up of the maternal and fetal circulation in the normal and in the high-risk pregnancies. Analysis of sonograms (Doppler velocity waveform) on the a.cerebri media (ACM) gives important information about the status and the condition of the fetus. The resistance index (RI) has a significant application in the clinical practice for the detection and follow-up of the fetal growth and the perinatal outcome at the IUGR fetus. **Material and methods.** The Doppler ultrasound (US) follow-up was performed in 86 normal pregnancies and 78 pregnancies with an IUGR of the fetus within the third trimester, divided in seven groups of gestational weeks (g.w.) With the Doppler machine TOSHIBA SONOLAYER SSA 120A and the application of an 3.75 MHz transabdominal probe, RI was determined at the a.cerebri media (RIACM). **Results.** The analysis of the RIACM in normal pregnancies showed that the distribution was regular in the followed-up gestational weeks which manifested as a permanent decrease of the values for RIACM (of 0.83 in the 28–29 g.w.; 0.77 in the 34–35 g.w., up to 0.725 at the term). In the pregnancies with an IUGR of the fetus, the RIACM was measured, which for any group of a g.w. statistically was significantly different from the findings in the normal pregnancies ( $p < 0.05$ ). Abnormal Doppler findings had a strong association with Apgar score 5min  $< 7$ ; SC-FD; NICU  $> 48$  h ( $p < 0.001$ ). In the prediction of the generally bad perinatal outcome, which includes all the previously analyzed parameters, RIACM predicted bad perinatal outcome with sensitivity (68.9%), specificity (77%), PPV (79%) and NPV (69.4%). **Conclusion.** The RIACM represents an important Doppler parameter for prediction of perinatal outcome in the clinical practice. Apart from the numerous results which promote Doppler ultrasound as the earliest predictor of the fetal suffering than the CTG, the best results could be obtained by application of these two and several other antepartal methods and analyses. Doppler US analysis points out to chronic changes which do not mean that the pregnancy has to be terminated at once until acute changes are detected by CTG. These two methods do not exclude each other, but on the contrary they complement each other.

*Stručni članak*

*Ključne riječi:* perinatalni ishod, IUGR, a. cerebri media optok krvi

**SAŽETAK.** Razvitek Doppler ultrazvučne tehnike pruža nove mogućnosti u praćenju maternalne i fetalne cirkulacije u normalnim i visoko rizičnim trudnoćama. Analizom sonograma (Doppler velocity waveform) urađenim na arteriji cerebri medii (ACM) dobije se važna informacija o statusu i stanju fetusa. Indeks rezistencije (RI) ima važnu primjenu u kliničkoj praksi za određivanje i praćenje fetalnog rasta i perinatalnog ishoda u IUGR fetusa. **Materijal i metode.** Dopler ultrazvukom praćene su 86 normalne trudnoće i 78 trudnoća s IUGR fetusa tijekom trećeg trimestra, podijeljene u sedam grupa prema gestacijskim tjednima (g.t.). Za određivanje RI a. cerebri medije korišten je Doppler aparat TOSHIBA SONOLAYER SSA 120A, s primjenom transabdominalne sonde od 3.75 MHz. **Rezultati.** Analiza RI a. cerebri medije u normalnim trudnoćama je pokazala pravilnu distribuciju u praćenim gestacijskim tjednima s permanentnim padom vrijednosti RI (od 0,83 u 28–29 g.t., 0,77 u 34–35 g.t. do 0,725 u terminu). Kod trudnoća s IUGR fetusa izmjereni se RI a. cerebri medije za sve grupe g.t. statistički signifikantno razlikovao od nalaza normalnih trudnoća ( $p < 0.05$ ). Abnormalni dopler nalazi su jako povezani s Apgar skorom 5 min  $< 7$ ; SC-FD; NICU  $> 48$ h; perinatalnim mortalitetom ( $p < 0.001$ ). U predviđanju lošeg perinatalnog ishoda, u kojemu su uključeni svi prije analizirani parametri, RI a. cerebri medije je predviđao loš perinatalni ishod sa senzitivnošću od 68,9%, specifičnošću od 77%, PPV od 79% i NPV od 69,4%. **Zaključak.** RI a.cerebri medije je važan parametar za predviđanje perinatalnog ishoda u kliničkoj praksi. Usprkos brojnim rezultatima koji promiču dopler ultrazvuk za najranije predviđanje fetalne patnje od CTG-a, najbolji rezultati se dobivaju zajedničkom primjenom ove dvije kao i nekoliko drugih antepartalnih metoda i analiza. Dopler ultrazvučna analiza pokazuje kronične promjene koje same po sebi ne ukazuju na potrebu momentalnog prekida trudnoće, sve dok se CTG-om ne utvrde akutne promjene. Ove dvije metode ne isključuju jedna drugu već se dopunjuju.

In 1987 Wladimiroff<sup>1</sup> measured the blood flow through the internal carotid artery for the first time. It is since then that more extensive investigations of the fetus cere-

bral circulation have started, including the efforts to present such in other blood vessels: a.cerebri anterior, a.cerebri media and a.cerebri posterior. The flow through the

brain blood vessels increases as the pregnancy progresses, especially after the 32-nd gestational week. It is assumed that this is the way metabolic requirements of the brain are met under the condition of progressive decrease in oxygen partial pressure and increase in carbon dioxide partial pressure.<sup>2,3</sup> Analyses of sonograms indicate that blood flow in brain blood vessels increases primarily at the expense of the increase in blood flow in the course of diastole. As the time passes, the most relevant data are those about the flow in a.cerebri media, which is a better indicator of brain perfusion than the remaining brain blood vessels, especially the carotid artery which, in addition to the brain, also supplies other parts of the head and neck, in contrast to a.cerebri media that supplies only the brain.<sup>4-6</sup>

Namely, intrauterine growth retardation, particularly the asymmetric type is often associated with abnormal blood flow in uteroplacental or fetoplacental circulation.<sup>7,8</sup> Increased values of peripheral vascular resistance at the level of uteroplacental circulation and a.umbilicalis as its indicator are present in a high percentage in cases of fetal growth retardation.<sup>9,10</sup> The result of this is reduction in transport of oxygen, glucose and other essential nutrients.<sup>11,12</sup> In a state of hypoxia of retarded growth fetus, a typical hemodynamic modification known as »brain-sparing effect« is manifested. In fact, it is a protective reaction of fetus against hypoxia that manifests itself in redistribution of the circulation in the brain, liver and heart at the expense of the flow reduction in the periphery.<sup>13,14</sup>

Identification of the above stated condition by means of Doppler investigation of peripheral blood vessels (a. umbilicalis) and cerebral blood vessels (a. cerebri media) is highly associated with the presence of fetal hypoxia.<sup>15,16</sup> Some authors point out that in relation to cardio-tocographic record and NST, Doppler's measurement of flow is of higher sensitivity but lower specificity in diagnosing unfavorable perinatal outcome at fetuses with high risk. According to these authors, retarded growth fetuses, but with a regular flow, are not more endangered by development of fetal distress than the eutrophic children.<sup>17,18</sup> Fetuses of normal NST and pathological sonograms have a more unfavorable prognosis than those with normal sonograms and pathological NST. On the other hand, in cases of abnormal NST the prognosis is valid if pathological sonograms are also added to.<sup>19-21</sup> These two methods should supplement rather than exclude each other and so combined increase reliability in identifying suffering fetus.

## Material and method

The paper represents a prospective study of Doppler ultrasound investigation of pregnant women in the third trimester that was carried out in the three years-period. RIACM was determined in the third quarter with pulsed Doppler ultrasound.

Gestation age was determined according to the last period date, confirmed by means of ultrasound biometry

of crown-rump length (CRL) of 7–12 gestation week and/or fetal BPD, FL and AC at 16–22 gestation week.

Normal pregnancies were considered the ones meeting the following criteria: ultrasound determined gestation age that is  $\pm 1$  week of the determined age according to the date of the last period, term spontaneous vaginal birth (with full 37 gestation weeks), birth weight exceeding 10 percentiles, absence of congenital abnormalities. Exclusion of high risk pregnancies: multiple pregnancy, pre-term birth, pregnancy induced hypertension, cesarean section, IUGR, diabetes mellitus, RH sensitization, fetus malformations, present fetal distress.

The group of pregnancies with fetal IUGR included all those with newborns birth weight less than 10 percentiles for the determined gestation age according to Lubchenco's graph.<sup>22</sup>

Cardiotocograph criteria for fetal distress were determined according to standard indicators: fetal bradycardia ( $< 90$ ) or prolonged deceleration with decreased beat-to-beat variability, recurring late decelerations, periodical serious variable decelerations, unexplained sinusoidal sample (excluded drug effect and Rh alloimmunization).

Doppler examination was conducted applying pulsating Doppler scanner-Toshiba, Sonolayer SSA-250 A with 3,75 MHz transabdominal probe. The peak of the systolic and minimal diastolic flow was measured at 3–5 successive heart cycles. Resistance index was determined according to the standard formula of Pourcelot.<sup>23</sup>

Flow through a.cerebri media was determined in the following way: after the transverse section of the thalamus and cavum septi pelucidi had been displayed, by moving the probe and cursor parallel to the previous section, a.cerebri media was identified.<sup>24,25</sup> Abnormal values were considered to be those where the deviation from the normal values was  $\pm 2SD$ . With normal findings, examination was repeated in 10–14 day intervals, while with abnormal findings this was conducted in shorter time intervals ( $< 7$  days).

The results of the study were statistically processed on Pentium personal computer using the programs Statistics, Excel, EPI-6, determining: mean value  $\pm 2SD$ ,  $\chi^2$  test, Student t-test, Specificity, Sensitivity, Positive predictive value, Negative predictive value.

## Results

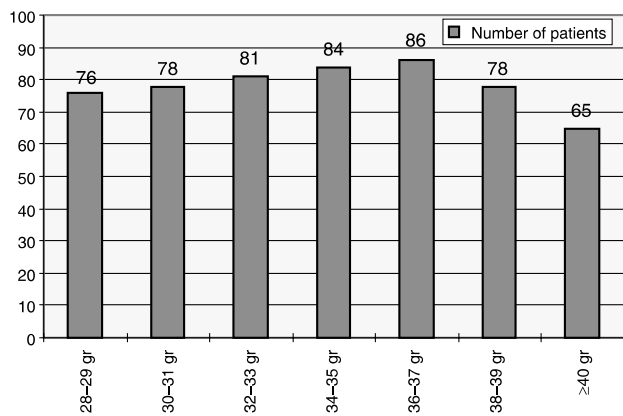
### Determination of RIAU and RIACM in the third trimester of normal pregnancies

Out of a hundred investigated pregnancies, 86 fulfilled the set criteria for normal pregnancy (Table 1). They were investigated in the course of the third quarter in two-week intervals, up to the completion of the pregnancy.

Normal pregnancies were divided in seven groups according to gestation week. For each of these groups there were statistically determined mean value, standard deviation, standard error (Graph 1 and 2).

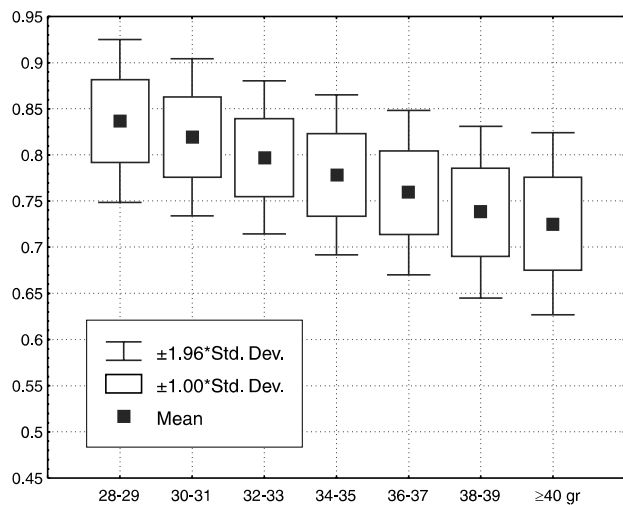
Table 1. General characteristics of normal pregnant patients (N=86)  
 Tablica 1. Opće karakteristike zdravih trudnica

	Med.	SD	min-max
Age – Dob	25.41	2.24	18–35
Delivery – Porod	39.4	0.18	38–42
Birth weight (grams) Porodna težina	3491	328	2900–4650



Graph 1. Number of examined patients with normal pregnancy according to weeks of gestation

Grafikon 1. Broj istraženih normalnih trudnoća po tjednima



Graph 2. Distribution of RIACM in normal pregnancies  
 Grafikon 2. Distribucija RIACM u normalnim trudnoćama

Distribution of RIACM and the mean values  $\pm 1.96$  SD are graphically presented for each individual group of gestation week. Finally, the values for RIACM in-

cluding the presentation of distribution of mean values are summarized through summary tables and graphs. Results of the analysis of a.cerebri media sonograms are showed on graphs, separately for each group of gestation week (Table 2, Graph 2).

Statistic analysis of RIACM shows normal distribution for each individual group of gestation week, and decrease in RIACM as the pregnancy developed.

### RIACM in the third trimester in pregnancies with IUGR

Out of the investigated pregnancies 78 pregnancies met the set criteria for IUGR (birth weight <10 percentile of the normal value according to Lubscenco table). Such pregnancies were investigated in the course of their hospitalization or as outpatients up to the completion of their pregnancy (Table 3).

Pregnancies with IUGR were divided in seven groups according to gestation week in which birth occurred.

In order to determine the character of distribution of values for RIACM in pregnancies with IUGR in relation to those of normal pregnancy, statistical correlation was made by means of »t-test«.

In addition to the presentation of the trend of value decreasing as the pregnancy progresses, which was also characteristic of normal pregnancies, apparent are obvious deviations (37.1%) presented as  $\pm 2SD$  in relation to the values with normal pregnancies.

At the same time, statistical analysis of RIACM proves that the values in relation to those with normal pregnancies statistically deviate significantly ( $p < 0.05$ ) for each individual gestation week group.

In order to indicate the value of Doppler investigation of RIACM in predicting the fetal suffering and consequently the perinatal outcome, which in fact was the primary goal of this study, the study proceeded with the analysis of the group of pregnancies with IUGR.

The value of Doppler indices was statistically analyzed in predicting: Apgar score in 5 min <7, cesarean section because of fetal distress (SC-FD) according to cardiocographic criteria, stay of the newborn in Neonatal Intensive Care Unit (NICU) for more than 48 hours, together with perinatal mortality, as common criteria for »bad perinatal outcome«.

Apgar score in 5 min <7 (Table 4) was present at 32 (41%) pregnancies. In relation to it, the Doppler of RIACM showed a statistically significant association ( $p < 0.001$ ).

Table – Tablica 2. RIACM in normal pregnancies / RIACM u normalnim trudnoćama

GW	Valid N	Mean	Median	Minimum	Maximum	Variance	Std. Dev.	Std. Error
28–29	76	0.836842	0.835	0.76	0.94	0.00203	0.045054	0.005168
30–31	78	0.819103	0.82	0.74	0.92	0.001889	0.04346	0.004921
32–33	81	0.797407	0.79	0.73	0.9	0.001789	0.042302	0.0047
34–35	84	0.778452	0.77	0.7	0.89	0.001955	0.04422	0.004825
36–37	86	0.759302	0.755	0.68	0.88	0.002068	0.045472	0.004903
38–39	78	0.738077	0.73	0.66	0.86	0.002252	0.047456	0.005373
≥40	65	0.725538	0.71	0.65	0.85	0.002541	0.050406	0.006252

Table 3. General characteristics of patients with IUGR (N=78)  
 Tablica 3. Opće karakteristike trudnica s IUGR

	Med.	SD	min-max
Age – Dob	26.36	4.05	18–37
Delivery (g.w.) – Porod	37.4	2.385	29–41
Birth weight (grams) Porodna težina	2056.9	460.4	770–2600

Table 4. Comparison of Apgar score with RIACM  
 Tablica 4. Usporedba Apgar zbroja s RIACM

	Doppler RIACM Normal	Doppler RIACM Abnormal	Total	$\chi^2$ test
Apgar score (5 min >7)	38 (83%)	8 (17%)	46	
Apgar score (5 min <7)	11 (34%)	21 (66%)	32	p<0.001
Total	49	29	78	

Table 5. Comparison of SC and cardiotocographic findings with RIACM  
 Tablica 5. Usporedba carskih rezova i kardiokotografskog nalaza  
 s RIACM

	Doppler RIACM Normal	Doppler RIACM Abnormal	Total	$\chi^2$ test
CTG Normal	36 (73%)	13 (27%)	49	
CTG Abnormal (SC-FD)	7 (24%)	22 (76%)	29	p<0.001
Total	43	35	78	

Table 6. Comparison of NICU >48 h and RIACM  
 Tablica 6. Usporedba boravka u JINT >48 sati i RIACM

	Doppler RIACM Normal	Doppler RIACM Abnormal	Total	$\chi^2$ test
NICU >48 h ne – no	44 (88%)	6 (12%)	50	
NICU >48 h da – yes	5 (18%)	23 (82%)	28	p<0.001
Total	49	29	78	

Table – Tablica 7. Perinatal mortality / Perinatalni mortalitet

GW	Risk f-r	Birth weight (g)	Apgar score	Delivery	ACM Doppler
33	EPH, IUGR	1100	0	FM in utero	ACM abnormal
36	EPH, IUGR	1900	4/6	SC-FD	ACM abnormal
35	EPH, IUGR	1250	2/3	SC-FD	ACM abnormal
	Oligo- hydramnion				
33	EPH, IUGR	1800	4/4	SC-FD	ACM abnormal
32	EPH, IUGR	1000	4/6	Par vias vaginalis	ACM abnormal
39	EPH, IUGR	2100	2/3	SC-FD	ACM abnormal
30	EPH, IUGR	920	1/2	SC-FD	ACM abnormal
34	EPH, IUGR	1180	4/5	SC-FD	ACM abnormal
	Oligo- hydramnion				

Table 8. Sensitivity, specificity, PPV, NPV of  
 RIACM in prediction of bad perinatal out-  
 come

Tablica 8. Osjetljivost, specifičnost, pozitiv-  
 na prediktivna vrijednost i negativna predik-  
 tivna vrijednost RIACM u pretkazivanju lošeg  
 perinatalnog ishoda

Sensitivity	26/38 – 68.9%
Specificity	31/40 – 77%
PPV	23/29 – 79%
NPV	34/49 – 69.4%

Cesarean section fetal distress according to cardio-to-  
 graphic criteria was realized in 29 (37.2%) pregnan-  
 cies (Table 5). In relation to it, the Doppler of RIACM  
 showed a statistically significant association (p<0.001).

NICU >48 h (Table 6) was necessary for 27 (34.6%)  
 newborns. In relation to this parameter, the Doppler of  
 RIACM showed a statistically significant association  
 (p<0.001) as well.

Perinatal mortality was registered in 8 cases. Doppler  
 of ACM showed statistically very strong association and  
 100% sensitivity in its predicting (Table 7).

In the prediction of the generally bad perinatal out-  
 come, which includes all the previously analyzed param-  
 eters, RIACM predicted bad perinatal outcome with sensi-  
 tivity 68.9%, specificity 77%, PPV 79% and NPV 69.4%  
 (Table 8).

## Discussion

Circulation in the fetal brain circulation anatomically  
 corresponds to the circulation in adults. Blood flow through  
 brain is increased in the course of pregnancy following  
 the growth of the brain tissue. Flow in the a.cerebri me-  
 dia increases from 23 ml/min in 19 g.w. to 133 ml/min  
 in term fetuses.<sup>4,5,26</sup> The percentage of combined systolic  
 volume circulating in a.cerebri media is between 3–7%,  
 constantly, with no changes in the course of pregnancy.  
 Already in the course of the first three-month-period  
 when the diastolic flow is absent in a.umbilicalis and  
 aorta, at the level of intracranial circulation, it was regis-  
 tered in a high percentage. Such characteristic low re-  
 sistance is explained with the necessity of ensuring nor-  
 mal supply with oxygen and glucose to the embryonal  
 brain. Measurements of indices showed parabolic appear-  
 ance with increase in the second quarter and evident drop  
 in the third quarter.<sup>25</sup>

Analyses of sonograms and RIACM values in the stud-  
 ied group of normal pregnancies showed reduction as  
 the pregnancy progressed, which was manifested by a  
 gradual increase of diastolic flow (from RI=28 g.w.=0.84,  
 up to RI=0.72 at term), thereby maintaining the state of  
 physiological fetal condition of hypoxia, and through  
 decrease in resistance, enabling physiological redistri-  
 bution of the brain circulation, aiming at maintaining the  
 required brain oxygenation. Similar findings for Doppler  
 indices for ACM were also presented by a number of  
 other authors.<sup>6,25,27</sup>

Normal distribution that was registered at all gestation  
 week groups just confirms the representativeness of the

group and offers the results obtained ( $\pm 2SD$ ) as a valid comparative indicator (standard) for the future investigations (Table 2).

Obtained results for RIACM with fetuses with IUGR indicate the maintained tendency of insufficient increase in flows as the pregnancy progresses. Namely, the statistical analysis (t-test) in relation to the values with normal pregnancies showed a significantly increased resistance and increase peripheral resistance of flows ( $p < 0.05$ ) in pregnancies with IUGR.

Occurrence of abnormal flows in this group of patients was 37% for RIACM. The remaining group of fetuses with IUGR and normal flows can be commented through the character of the definition of IUGR. Indeed a part of the fetuses with IUGR are constitutionally small children, resulting from the genetic potential or because of the simple reason that they are not representatives of the population whose curves of birth weight (<10 percentiles) are taken as standard ones for the requirements of this study. With such children, usually noted to be with »symmetric retardation«, the blood flow usually do not deviate from the normal value, there is no increased peripheral resistance in the circulation, so that the indices for analysis of sonograms are within the limits of normal ones.<sup>28,29</sup>

The other group has growth retardation known as asymmetric IUGR with whom the fetus does not succeed in reaching its genetically set weight. No matter what are the reasons for such a type of growth retardation, circulatory changes are almost identical and mainly the result of the achieved hypoxic condition.<sup>14,16,30</sup> The answer to the hypoxic condition is progressive and protective for the fetus. The fetal minute volume is redistributed with vasodilatation and increased flow through vital organs (brain, heart and adrenal glands) at the expense of vasoconstriction and decrease in flow through peripheral tissues, the so called brain sparing effect.<sup>31,32</sup> In this way an effort is made to maintain normal oxygenation of the brain tissue.<sup>33,34</sup> Among the more important goals set by the current perinatology is a right time prediction of hypoxic condition and fetus suffering, for the purpose of a timely completion of birth and decrease in morbidity and mortality.

Of the various indices, the systolic/diastolic (S/D) ratio, RI and PI have been used most extensively in obstetric practice. S/D ratio is used extensively in obstetrics, particularly in the United States. The RI values, on the other hand, have defined limits with a minimum value of 0 and a maximum value of 1.0. Unlike the S/D, the RI shows Gaussian distribution and is therefore amenable to parametric statistical analyses. At the beginning of fetal danger diastolic flow of ACM is increasing. In the fetus with IUGR there is expressively increased speed of flow and the low PI in ACM in relation to health fetuses of the same gestational age; the maximum speed of peak systolic flow velocity and PI of ACM should be better indices of fetal suffering regarding RI ACM. Theoretically, the PI provides more hemodynamic information than the RI and S/D ratio, since it includes data on the whole cardiac cycle in the form of its denominator, which

is the time-averaged value of the maximum frequency shift envelope over one cardiac cycle.

In practice, however, computation of the time-averaged value is not as precise as determination of the peak systolic or end-diastolic frequency shifts. There has been a paucity of data regarding the relative diagnostic merits of these indices. In a prospective blinded study Maulik and al.<sup>35</sup> showed that the RI had the best and PI the worst discriminatory performance.

One of the goals of this investigation was the appraisal of the values of RIACM in predicting perinatal outcome (Apgar 5 min <7; SC-FD; NICU >48 h; perinatal mortality). All investigated parameters of the bad perinatal outcome both individually and summarily were significantly more frequent in the group with abnormal values of RIACM ( $p < 0.001$ ).

Comparisons between cerebral Doppler indices and measurements of  $pO_2$ ,  $pCO_2$  and pH on a blood sample taken by cordocentesis showed a good correlation between  $pO_2$  and Doppler indices already in the early phase of hypoxia.<sup>13,14,34</sup> Vasomotor answer to the hypoxic condition will be vasodilatation with manifested increase of the diastolic sonogram component. Several published studies determine the value of flow measurements through a. cerebri media in predicting perinatal outcome with sensitivity of 58–87%. In our study, the value of RIACM ( $p < 0.001$ ) was 68.9% sensitivity, 77% specificity, 79% PPV and 69.4% NPV.

Hence, the level of deviation (from normal values) of Doppler ultrasound findings in IUGR pregnancies imposes as a good predictor of the pregnancy outcome. According to a series of comparative results published in the literature, Doppler measurements in relation to the standard method fetus monitoring (non-stress test, biophysical profile), showed the same or better results in predicting fetal hypoxia and perinatal outcome.

Chronic fetal hypoxemia leads to a decreased preload, decreased cardiac compliance, and elevated end-diastolic pressure in the right ventricle. These changes raise central venous pressure in the chronically hypoxemic fetus, which shows up as an increased reverse flow in Doppler waveforms of the IVC and the ductus venosus during late diastole. Changes in the fetal central venous circulation are associated with an advanced stage of fetal hypoxemia. At this late stage of fetal adaptation to hypoxemia, cardiac decompensation is often noted with myocardial dysfunction. Indeed, fetal metabolic acidemia is often present in association with Doppler waveform abnormalities of the IVC and ductus venosus. The literature suggests that venous Doppler abnormalities in the IVC and ductus venosus and abnormal results from FHR monitoring (even computerized FHR) may indicate a more advanced stage of fetal compromise because they occur after the arterial Doppler abnormalities appear.<sup>36–39</sup>

DV Doppler effectively identifies preterm IUGR fetuses who are at the highest risk for adverse outcome at least one week before delivery independent of the UA waveform. Progressive escalation of the DV Doppler index is associated with a high stillbirth rate. The rate

and degree of Doppler deterioration and risks for adverse perinatal outcome are strongly related and in part determined by gestational age.

DV PIV measurement is the best predictor of perinatal outcome. This measurement may be useful in timing the delivery of early IUGR fetuses and in improving perinatal outcome, even when delivery may be indicated at an earlier GA. However, as GA was also an important factor influencing outcome, with poorer outcome at earlier gestation at delivery, this hypothesis needs to be tested in a multicenter, prospective, randomized trial.<sup>40</sup> DV changes in fetuses delivered before 32 weeks' gestation started to occur on the average two weeks before the clinician decided to deliver the fetus.

DV PIV  $\geq 3$  SD within 24 h of delivery was the best predictor for neonatal mortality and severe morbidity.

The only other significant prognostic factor for perinatal outcome was GA, showing a 50% reduction in the incidence of adverse outcome for every additional week of gestation at delivery. This emphasizes the important influence of fetal maturity upon the outcome in IUGR.<sup>41</sup>

Of the fetal cerebral veins studied, the presence of pulsations in the fetal vein of Galen (GV) seems to be the best predictor of adverse outcome of high-risk pregnancy.<sup>42</sup>

Abnormal Doppler findings of fetal circulation precede the development of fetal distress according to cardiocytographic criteria.<sup>20–23,43,44</sup> The application of Doppler method showed not only significant reduction in SC-FD and NICU > 48h but also reduction in perinatal mortality by 38%.<sup>45,46</sup> Association of abnormal Doppler findings with pathologic CTG is high. As a result of the gradual development of a chronic hypoxic condition, abnormal Doppler findings precede 10–17 days the pathological CTG findings.<sup>34</sup> Though the results show that the analysis of flows is a more sensitive method in detection of fetal hypoxia than CTG, the fact that they differ essentially should not be neglected. In contrast to pathologic Doppler findings that show chronic changes, CTG changes point more to acute impairments of homeostasis.<sup>47–49</sup>

Nevertheless, detection of hypoxia and fetal distress is most successful when both or more diagnostic methods are applied. This is why they should supplement rather than exclude each other, thus increasing the certainty in predicting fetal suffering, and through a timely completion of birth will lead to a significant decrease in perinatal mortality and morbidity.

## Conclusions

Doppler ultrasound examination enables a noninvasive, quick and relatively simple checkup of uteroplacental and fetal circulation. RIACM in the third quarter of normal pregnancies has normal distribution and gradually decreases as the pregnancy progresses. There is a significant difference in RIACM values between normal pregnancies and those with IUGR. Abnormal RIACM values in pregnancies with IUGR significantly associate with bad perinatal outcome (Apgar 5 min < 7; SC-FD; NICU > 48 h; perinatal mortality).

Doppler examination of a cerebri media flow is a method of high importance in the examination of fetal IUGR in clinical practice. Along with the standard antepartum methods (US, CTG, biophysical profile) it contributes to the predicting and monitoring of hypoxia and fetal suffering. It enables timely completion of birth and decrease of perinatal mortality and morbidity.

Clearly, IUGR is a complex disorder involving several fetal organ systems. While fetal biometry and arterial Doppler yield the best information on the early compensatory phase of this disorder, venous Doppler, CTG analysis, and the biophysical profile score provide data on the later stages (commonly associated with fetal acidosis and impending cardiovascular collapse). It's my hope that future studies will shed more light on the pathophysiology of this disease and on the various interactions of diagnostic tools in fetal surveillance.

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