Ginekol Pol. 2014, 85, 26-30

Fetal pulmonary and cerebral artery Doppler velocimetry in normal and high risk pregnancy

Tętniczy przepływ krwi w płucach i OUN płodu w ciąży o przebiegu prawidłowym i w ciąży wysokiego ryzyka

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Abstract

Studies on fetal lung/brain circulation by means of power Doppler technique have suggested a marked reduction in lung perfusion in high-risk pregnancies as a sign of circulation redistribution. The ratio between lung/brain perfusion might therefore give a new method to predict fetal circulation centralization.

Objective: *The aim of the present study was to obtain fetal lung and cerebral artery ratio in normal and high-risk pregnancies.*

Study design: *Doppler samples from proximal right pulmonary artery blood velocities and middle cerebral artery (MCA) were recorded cross-sectionally in 228 normal singleton pregnancies at gestational age 22 to 40 weeks. MCA / right pulmonary artery pulsatility index (PI) ratio was calculated. Doppler samples from proximal right pulmonary artery and MCA were also recorded in 89 high-risk singleton pregnancies and the results related to perinatal outcome.*

Results: *In the normal controls, right pulmonary artery PI remained stable until 30 weeks of gestation with slight increase thereafter until term. The MCA to right pulmonary artery PI ratio increased between 22 and 28 weeks of gestation with the rapid fall towards term. In the high-risk pregnancies group, right pulmonary artery PI showed no significant correlation to perinatal outcome, but signs of brain-sparing in the MCA were correlated to all adverse outcome parameters.*

Conclusion: *Velocimetry of the middle cerebral artery is better than velocimetry of right pulmonary artery in predicting adverse outcome of pregnancy. The brain/lung PI ratio does not improve the prediction of adverse outcome of pregnancy.*

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Otrzymano: **18.08.2013**
Zaakceptowano do druku: **30.10.2013**

Key words: **pulmonary artery** / **middle cerebral artery** / **brain-sparing** / **fetus** / / **Doppler** / **pregnancy** /

Streszczenie

Wstęp: *Ocena przepływu krwi przy pomocy metod ddopplerowskich w krążeniu płucnym I mózgowym sugerowała istotny spadek perfuzji płuc w ciążach wysokiego ryzyka jako wykładnik zmienionej redystrybucji krwi w ustroju płodu. Stworzyło to koncepcję z której wynika, że stosunek perfuzji krwi w płucach i mózgu może być nową metodą oceniającą centralizację krążenia.*

Cel pracy: *Celem badań było określenie współczynnika określającego stosunek przepływów krwi w płucach i mózgu w ciąży o przebiegu prawidłowym i w ciąży wysokiego ryzyka.*

Materiał i metody: *Przepływ krwi oceniano metodą dopplerowska w proksymalnej części prawej tętnicy płucnej oraz w tętnicy środkowej mózgu w dwóch grupach pacjentek: u 228 ciężarnych z ciążą pojedynczą o przebiegu prawidłowym między 22 a 40 tygodniem ciąży oraz u 89 ciężarnych z ciążą wysokiego ryzyka. W oparciu o uzyskane wyniki obliczano stosunek wartości PI w naczyniach płucnych i mózgowych. Uzyskane wyniki odnoszono do stanu noworodka po porodzie.*

Wyniki: *W grupie kontrolnej wartości PI tętnicy płucnej są stabilne aż do 30. tygodnia ciąży z następowym nieznacznym wzrostem aż do terminu porodu. Wartości stosunku PI w tętnicy środkowej mózgu do PI prawej tętnicy płucnej wzrastają między 22. a 28. tygodniem ciąży z następowym spadkiem do terminu porodu. W grupie ciąż wysokiego ryzyka, nie stwierdzono istotnej zależności między wartościami PI prawej tętnicy płucnej a stanem noworodka po porodzie. W tej grupie ciąż wykładniki centralizacji krążenia wykazywały zależność w odniesieniu do parametrów charakteryzujących zły stan noworodka po porodzie.*

Wnioski: *Ocena przepływu krwi w tętnicy środkowej mózgu, w porównaniu z oceną przepływu w tętnicy płucnej, ma większą wartość predykcyjną w prognozowaniu stanu płodu. Analiza współczynnika – PI mózgu/PI płuc – nie poprawia tej oceny.*

Słowa kluczowe: **tętnica płucna** / **tętnica środkowa mózgu** / **centralizacja krążenia** / / **płód** / **Doppler** / **ciąża** /

Introduction

The development of two-dimensional and Doppler ultrasound made possible non-invasive investigation of fetal circulation and has given knowledge about maternal and fetal circulation. Doppler examinations have been found useful in the evaluation of high-risk pregnancies, particulary complicated by intra-uterine growth restriction (IUGR) and pregnancy induced hypertension (PIH) [1-3].

Signs of fetal brain-sparing during chronic hypoxia are well established [4,5]. Studies on fetal sheep during hypoxia have revealed redistribution of circulation favoring the vital organs brain, heart and adrenals [6]. In experimental lamb studies, fetal lung blood flow decreased most of all organs studied during hypoxia [7]. Attempts have been made to use the Doppler technique in the prediction human fetal circulation redistribution during chronic hypoxia. Research on signs of decreased flow to less important fetal organs during centralization of circulation such as gut, kidney, liver, and peripheral arteries have been disappointing [8-11]. However, studies on fetal lung/brain circulation using digital analysis of power Doppler signal intensity in the two organs have suggested a marked reduction in lung perfusion in high-risk pregnancies [2]. Brain flow signals were increased at the same time. The ratio between lung/brain perfusion might therefore give a new method to predict fetal circulation centralization [2].

The aims of the present study were therefore to obtain fetal right pulmonary artery pulsatility index (RPA PI) and middle cerebral artery (MCA PI) in the course of normal pregnancy. Secondary, to calculate middle cerebral artery PI to right pulmonary artery PI ratio (MCA/RPA-ratio) during the course of normal pregnancy. Finally, to evaluate signs of circulation redistribution in these vessels in fetuses at risk for intrauterine hypoxia.

Materials and methods

Doppler samples from proximal right pulmonary artery blood velocities and middle cerebral artery were recorded in a cross-sectional study in 228 normal singleton pregnancies at gestational age 22 to 40 weeks. All pregnancies had an uneventful course of pregnancy, labour and delivery. All patients gave their informed consent and the study protocol has been approved by the Hospital Ethics Committee Malmo-Sweden). Gestational age had been established in each pregnancy by ultrasound examination performed in the first trimester of pregnancy.

Doppler samples from the proximal right pulmonary artery and middle cerebral artery were also recorded in 89 high-risk singleton pregnancies referred for antenatal blood flow examination indicated by intra-uterine growth retardation (IUGR) (n=54) and pregnancy induced hypertension (PIH) (n=35). The definition used as pregnancy-induced hypertension was: values of blood

pressure 140/90 mmHg, an increase of systolic blood pressure of 30 mmHg and diastolic blood pressure of 15 mmHg above the basic values. Examinations were repeated in some cases, but results from the last examination before delivery were only correlated to outcome of pregnancy. Median gestational age at the last examination was 34 weeks (range 26-40 weeks). The median interval between the examination and labour was 3,5 days (range 0-7 days). The clinicians were only informed of the umbilical (UA) and uterine artery (Ut.A) blood velocimetry, but not of fetal cerebral and pulmonary blood flow recording, which were performed at the same time as.

Acuson XP and Sequoia ultrasound units (Siemens Medical Co) with pulsed, color and power Doppler possibilities was used during the study. Conventional B-mode sonography was used to visualize the fetal chest at it's transverse, cross-sectional plane at the level of the pulmonary artery. The main pulmonary artery was located and then the right pulmonary artery just beyond bifurcation of the main pulmonary artery [12]. The blood velocity waveform was obtained by positioning the Doppler sample volume into proximal part of right pulmonary artery just beyond bifurcation of main pulmonary artery. The right branch was chosen for the measurements as there is no difference between waveforms obtained from right and left pulmonary artery [12,13]. Characteristic of right pulmonary arterial blood velocity waveform is illustrated in Figure 1.

The middle cerebral artery was visualized at the level of circle of Willis by the use of color Doppler. The pulsed Doppler sample volume was placed in the middle cerebral artery at near 0^0 angles to the ultrasound beam and the blood velocity waveforms were obtained and stored. Care was taken not to push on the fetal head, while examining middle cerebral artery as that might increase pressure and, consequently reduce cerebral perfusion [2]. Fetal brain sparing effect was defined as PI < mean - 2SD.

Umbilical artery velocimetry was recorded from a free floating loop of the cord. The blood velocity waveform was analysed for PI and compared with normal reference values [14]. All Doppler examinations were made during absence of fetal breathing movements.

Uterine artery blood velocity was located bilaterally by color flow mapping in an oblique scan, with the sample volume placed in the artery just cranial to the apparent crossing of the external iliac blood vessels. Three subsequent blood velocity waveforms for each vessel were analyzed for PI according to Gosling et al., which is an acknowledged measure of downward vascular impedance [15]. The mean of both uterine arteries PI were calculated, PI exceeding 1.20 was deemed abnormal [14]. Middle cerebral artery over right pulmonary artery PI ratio (MCA/RPA PI ratio) was calculated. All examinations of normal controls were performed by one operator (MD).

In the high-risk pregnancies, the Doppler results were attributed to perinatal outcome, including gestational age at delivery, birthweight, Apgar score at 5 minute of life, umbilical arterial and venous pH, the need for operative delivery for fetal distress (ODFD), the needs for admission to neonatal intensive care unit (NICU), artificial ventilation and perinatal mortality. A small-for-gestational-age (SGA) infant was defined as birthweight below the tenth percentile for corresponding gestational age [16].

The computer software Statistica version 5.0 (StatSoft, Inc.) was used for statistical analysis. Normal reference charts

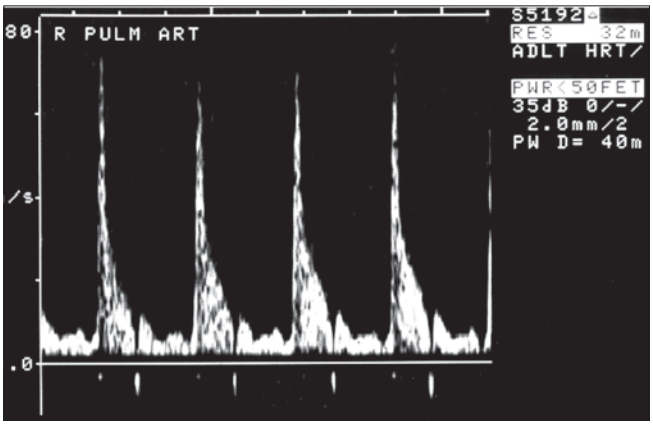

Figure 1. Typical spectrum of blood velocity waveforms of proximal branch right fetal pulmonary artery in normal pregnancy.

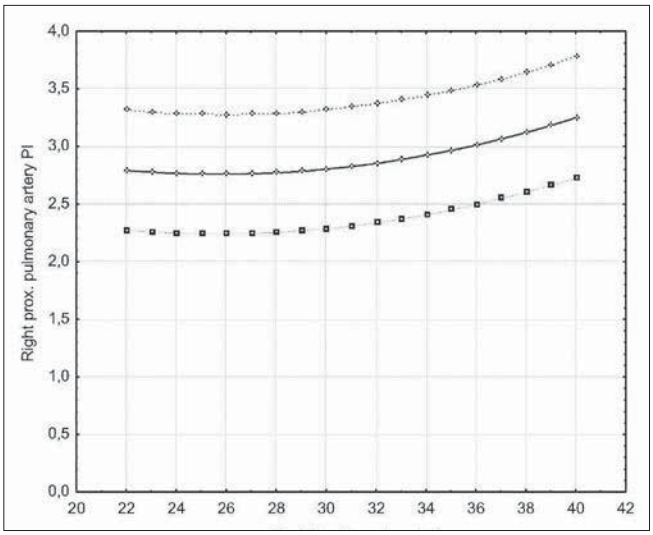

Figure 2. Mean and 95% CI of right proximal pulmonary artery pulsatility index (PI) in in the second half of pregnancy.

for MCA PI, RPA PI and MCA/RPA ratios were constructed by polynomial regression analysis by the quadratic method giving mean, 2.5 and 97.5 percentiles cut-off's. Fisher's exact test was used to determine numeric differences between groups with normal and abnormal blood flow velocity. The Mann-Whitney non-parametric test was used to compare continuing variables in the two groups.

Results

Right pulmonary artery PI in the normal controls remained stable until 30 weeks of gestation with slight increase thereafter until term (Figure 2). In the course of normal pregnancy the middle cerebral artery curve is quite similar to the curve presented by Mari and Deter [17] (Figure 3).

The middle cerebral artery to right pulmonary artery (MCA/RPA) PI ratio increased between 22 and 28 weeks of gestation with the rapid fall towards term (Figure 4).

In the high-risk pregnancy group, the median gestational age at delivery was 34 weeks (range 27-41 weeks).

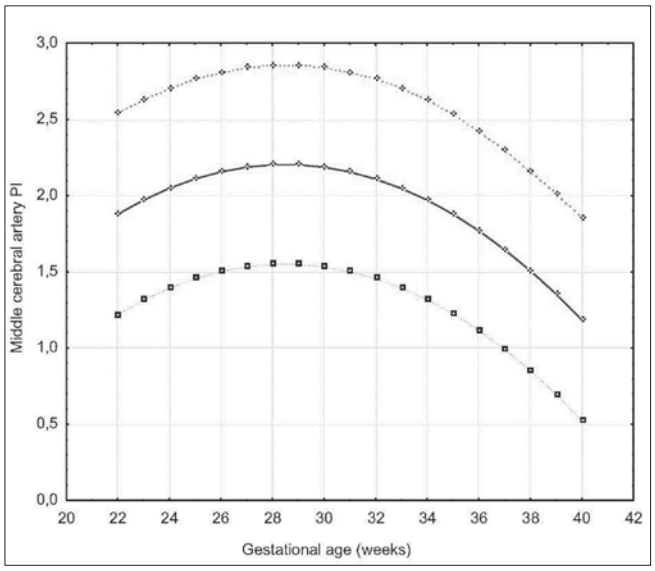

Figure 3. Mean and 95%CI of middle cerebral artery pulsatility index (PI) in in the second half of pregnancy.

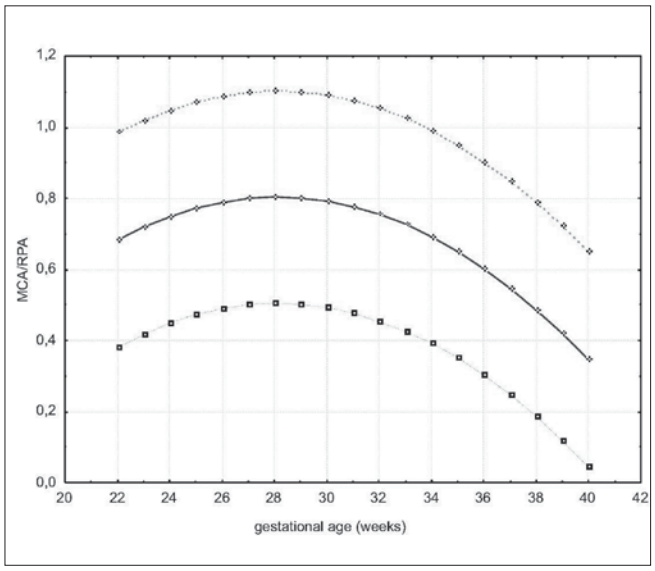

Figure 4. Mean and 95%CI of middle cerebral artery pulsatility index (PI) over right pulmonary artery PI ratio (MCA/RPA) in the second half of pregnancy.

The mean birthweight of infants was 1908±787 g and 54 (61%) newborns were small-for-gestational age at birth. The needs for ODFD were in 42 cases and 47 neonates were admitted to NICU, where 36 of them were ventilated. Apgar score <7 at 5 min was found in 19. Arterial pH <7.15 and venous pH <7.20 was found in 24 and 26 cases, respectively. There were seven perinatal deaths – all after delivery due to severe IUGR and prematurity (29 weeks of gestational age – 810g; 27 weeks of gestational age – 720g; 27 weeks of gestational age – 650g; 27 weeks of gestational age – 680g; 28 weeks of gestational age – 780g; 32 weeks – 990g; 32 weeks – 980g).

In the high-risk pregnancies, 40 (45%) had a normal proximal right pulmonary artery PI. There were no significant differences in perinatal outcome between cases with normal and abnormal pulmonary artery PI. Signs of brain-sparing in MCA were found in 39 (44%) fetuses and was highly correlated in all adverse outcome parameters except SGA newborns. The group of high-risk pregnancies consists of 31 (35%) fetuses with abnormal MCA/RPA PI ratio. Significance of differences was found in all parameters studied except SGA newborns, ventilation in NICU and ODFD.

Discussion

The results demonstrate a change in fetal RPA and MCA blood flow with advancing gestation in second half of pregnancy. MCA / RPA PI ratio was also demonstrated from 22nd to 40th week of pregnancy. The analysis of blood flow in high-risk pregnancies showed that right pulmonary artery PI seems to be a poor marker in predicting perinatal outcome. There were no differences in perinatal outcome between fetus with normal and abnormal right pulmonary artery PI . However, an abnormal MCA/RPA ratio was related to adverse outcome, but this was mainly due to changes in MCA PI. This study revealed that middle cerebral artery PI better correspond with changes in fetal redistribution and adverse outcome of pregnancy than does the RPA.

Although 31 fetuses manifested abnormal values of MCA/RPA-ratio, MCA-PI seemed to be a better predictor of adverse perinatal outcome than was MCA/RPA-PI-ratio. Furthermore, the group of fetuses with abnormal right pulmonary artery PI consisted of 40 fetuses – only 44,9% of the high-risk pregnancy group. This suggests that right pulmonary artery blood flow might change during fetal circulation redistribution, but this reaction is probably not constant during this period and might occur in the beginning of this process. Results by Jensen et al. suggests that lung perfusion might be improved after repeated hypoxic insult [17].

Rasanen et al. described decrease of pulsatility index (PI) of proximal pulmonary artery with advanced gestational age until 35th week of gestation [12]. The conflicting results between the present study on normal controls and the previous study by Rasanen et al. may be explained by the difference in number of investigated patients, as their population group consisted of only 100 patients [12].

Ren-Ing Liang et al. in their study analyzed differences between multigate spectral Doppler scanning with the power Doppler imaging option and traditional spectral Doppler ultrasonography with color flow mapping [18]. Their study revealed a significant difference between main pulmonary artery and peripheral blood flow. This may explain previous results in studies on fetal brain/ lung circulation using digital analysis of power Doppler signal intensity, where a marked reduction in lung perfusion was seen in high-risk pregnancies. The Power Doppler might thus reflect tissue perfusion, while spectral Doppler reflects vascular impedance in the vessel. This might explain the conflicting results of present study and a previous results [2].

Studies on animal and the human fetus have shown that fetal cardiac output is redistributed during hypoxia, favoring vital organs such as the brain, heart and adrenals [4]. By reducing blood flow to less important organs the need for oxygen and nutrients is reduced and the fetus is able to maintain oxygen and blood

gas status within normal limits. Blood pH may remain stable due this phenomenon. The centralization of fetal circulation results in reduced flow in the kidneys and gut, which may cause oligohydramnios and necrotizing enterocolitis in the newborn. Circulation redistribution might also lead to asymmetrical growth of the fetal body.

Studies focused on fetal superior mesenteric and hepatic arteries revealed that signs of redistribution in the mesenteric artery might be a late sign of fetal compromise [9]. The vascular sparing of the fetal liver can be seen at an early stage of fetal compromise. This sparing effect seems to disappear in severely compromised fetuses[19]. The velocimetry of splenic artery and PI values in the course of high-risk remained within normal values [20]. Arudini et al. revealed in their studies on the renal artery, that blood flow in this vessel is decreased during long term fetal hypoxia [21]. Stigter et al. studied influence of changes in fetal renal artery on fetal condition in the growth-restricted preterm fetus [22]. They revealed that redistribution is reflected by changes of peak-systolic velocities rather than by changes in pulsatility index. Spectrum of both the renal and pulmonary blood velocity has low flow velocities in diastole. Changes during reduction might be difficult to interpret by Doppler, especially in the severely affected fetus where reversal of venous flow during atrial contraction might be superimposed in the diastolic flow pattern.

The evaluation of placental and fetal liver, adrenals, kidney, and lung blood flow by power-Doppler ultrasound has improved our knowledge on fetal circulation. In normal pregnancy, the power-Doppler computer analyzed signal intensity seems to increase in all organs with gestation up to 36 weeks, after which a decline in intensity is noted [11]. The change in the other organs might be explained by centralization of fetal circulation secondary to failing placental function. In high-risk pregnancies the decrease in organ blood flow is even more pronounced, suggesting further development of fetal circulatory centralization [9]. Fetal cerebral power-Doppler signal intensity and the brain/lung-ratio increases towards the end of normal pregnancy. The data from the previous study shows that power Doppler represents centralization of fetal circulation during chronic hypoxia by evaluation of fetal organ tissue perfusion, rather than vascular impedance.

Conclusion

The main conclusion of this study is that velocimetry of the middle cerebral artery is better than velocimetry of right pulmonary artery in predicting outcome in high-risk pregnancy. MCA/RPA PI ratio was of limited value in predicting redistribution of fetal circulation in high-risk pregnancies.

Acknowledgements:

The medical faculty, University of Lund, research funds at the University hospital in Malmö and Region Skåne supported the study.

Oświadczenie autorów

1. Andrzej Bręborowicz – autor koncepcji i założeń pracy, zebranie materiału, przygotowanie manuskryptu, analiza wyników, zebranie piśmiennictwa.
2. Mariusz Dubiel – zebranie materiału, analiza statystyczna wyników, przygotowanie manuskryptu.
3. Marek Pietryga – współautor tekstu pracy, współautor protokołu i aktualizacja literatury.
4. Grzegorz H. Bręborowicz – autor założeń pracy, analizy i interpretacji wyników, przygotowanie, korekta i akceptacja ostatecznego kształtu pracy – autor zgłaszający i odpowiedzialny za manuskrypt.
5. Saemundur Gudmundsson – udział w przygotowaniu koncepcji badań, korekta oraz ostateczne zatwierdzenie manuskryptu.

Źródło finansowania:

Praca nie była finansowana przez żadną instytucję naukowo-badawczą, stowarzyszenie ani inny podmiot, autorzy nie otrzymali żadnego grantu.

Konflikt interesów:

Autorzy nie zgłaszają konfliktu interesów oraz nie otrzymali żadnego wynagrodzenia związanego z powstawaniem pracy.

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