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Ultrasound Doppler Evaluation of Uteroplacental and Fetoplacental Circulation in Pre-eclampsia

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Summary. Blood flow velocity waveforms (FVW) were recorded weekly from the umbilical and arcuate arteries in 58 hospitalised women with a pregnancy complicated by pre-eclampsia. The maximum velocity waveform was analysed for pulsatility index (PI) and the results from the final antenatal examination were related to the outcome of pregnancy. The umbilical artery FVW was abnormal in 36% of the pre-eclamptic pregnancies, as was the arcuate artery FVW in 42%. No difference in FVW was found between mild and severe pre-eclampsia. Abnormal FVW in the umbilical artery was associated significantly both with intra-uterine growth retardation (IUGR) ($P < 0.001$) and with signs of fetal distress (FD) ($P < 0.05$). Abnormal arcuate artery FVW was associated with FD ($P < 0.05$), but not with IUGR. The outcome of pregnancy was related to Placenta Waveform Class, which was derived from the blood velocity on both maternal and fetal sides of placenta. The results suggest that ultrasound Doppler examination of the umbilical artery is a useful aid in monitoring pregnancies complicated by pre-eclampsia, but that arcuate artery examination needs further evaluation.

Key words: Pre-eclampsia – Pulsed Doppler ultrasound – Umbilical artery – Arcuate artery – Blood flow velocity waveform

Introduction

A relationship exists between the occurrence of pre-eclampsia and increased maternal and perinatal mortality and morbidity. Placental infarcts, placental abruption or intra-uterine growth retardation (IUGR) are often found in cases of perinatal death in patients with pre-eclampsia [17]. The physiological dilation of sub-placental vessels seen in normal pregnancy [3] is halted in pre-eclampsia,

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the vessel lumen is narrowed [20], and the uteroplacental blood flow, as measured in radioisotope studies, has been found reduced in pre-eclampsia [18].

Radio-isotope placentography and nitrous oxide studies [15, 18] were the only ways of evaluating human placental blood flow until the introduction of the combined real-time and Doppler ultrasound technique [11]. This technique enables recording to be made of blood flow velocity waveforms (FVW) from the fetal aorta [7], umbilical arteries [10], fetal carotid arteries [25], and from the uteroplacental circulation [4].

A reduction in diastolic blood velocity in the arcuate artery with typical notching of the waveform pattern, has been reported in pregnancies complicated by pre-eclampsia and IUGR [4]. A relationship has been found between reduced blood flow diastolic velocities in the arcuate artery in early pregnancy and the subsequent development of pregnancy-induced hypertension and IUGR, and Doppler examination of the arcuate artery has been recommended for screening purposes with regard to such complications [5]. Abnormal FVW in the umbilical artery, with reduction or absence of diastolic velocity, has also been found in conjunction with abnormal outcome of pregnancy [23].

The aim of this study was to examine FVW in the arcuate and umbilical arteries in pregnancies complicated by pre-eclampsia, and to evaluate whether the FVW could be used to predict abnormal outcome of pregnancy.

Patients and Methods

The group studies comprised 58 hospitalised pregnant women with pre-eclampsia. Their mean age was 28 years (SD 5.5) and 39 women were multiparae, 16 primiparae and 3 multiparae. 31 of the pre-eclamptic women had mild signs; blood pressure between 140/90 and 160/110 mmHg and proteinuria less than 3+ (Redia-test, Boehringer Mannheim GmbH, Mannheim, W-Germany) and 27 had severe signs; blood pressure >160/110 mmHg and proteinuria exceeding 2+. The first examination was performed after at least 24 h of rest in hospital and than weekly until delivery. A total of 128 examination was performed (mean 2.2 per patient, range 1–4). The mean interval between the final antenatal examination and delivery was 6 days (range 0–19). Only the results of the final antenatal examination are reported here. All patients gave their informed consent, and the use of ultrasound Doppler on a human fetus had been approved by the Ethics Committée of the Medical Faculty, University of Lund.

A 3.5 MHz real-time linear array ultrasound scanner combined with a 2 MHz pulsed ultrasound Doppler [8], was used to record blood flow velocity waveforms (FVW) in the umbilical and arcuate arteries. A 100 Hz high-pass filter was used to remove signals from slow-moving tissue in the path of the Doppler ultrasound beam. The umbilical cord was located by means of the real-time transducer, and the characteristic signals of the umbilical artery recorded with the Doppler instrument. Characteristic sub-placental arcuate artery signals were traced at the periphery of the placenta and recorded. As the arcuate artery proved difficult to visualise on the screen of the ultrasound scanner, the signals frequently had to be recorded blindly from the placental bed.

The maximal velocity waveform was analysed for pulsatility index (PI) according to Gosling et al. [12], reference values for PI in the umbilical and arcuate arteries having previously been established [13]. Abnormal PI was defined as more than 2SD above the mean for the corresponding gestational age. As the arcuate artery PI is affected by heart rate [13], reference values corrected for maternal heart rate were used. Only umbilical artery signals recorded during periods of fetal quiescence (i.e., fetal apnoea, and without movements) were accepted for analysis. A recording was accepted for analysis if a steady state during at least 10 uniform cardiac cycles had been obtained.

The PI on either side (i.e., maternal and fetal) of the placenta was related to the pregnancy outcome variables; birthweight, birthweight deviation in per cent, placental weight and occurrence

of signs of fetal distress. Fetal distress was judged by the need for emergency caesarean section or instrumental vaginal delivery [22], five-minute Apgar score, umbilical artery pH and umbilical vein pH. The diagnosis of imminent asphyxia was based by the clinician in charge on cardiotocographic (CTG) changes or fetal scalp pH. The clinician was unaware of the Doppler blood flow results.

Fourteen elective caesarean section were performed, either because of deteriorating maternal condition ($n = 10$), suspicion of placental abruption ($n = 1$), breech presentation and/or fetopelvic disproportion ($n = 3$), and two fetuses died in utero; these 16 cases were excluded when relating the FVW to signs of fetal distress. Of the fetuses that died in utero, the first one had severely pathological blood velocity waveforms on both sides of the placenta at 35 and 37 weeks of gestation. An emergency caesarean section was performed three days after the last examination because of the abruption of placenta. Unfortunately, the fetus was dead at delivery. In the second case of stillbirth, there was a true knot of the umbilical cord. The blood velocity pattern was abnormal in all examined vessels 19 days before the intra-uterine death.

Operative delivery for fetal distress was performed in 15 cases; the Apgar score was less than 7 at 5 min in 3 newborns. Of 29 umbilical artery pH measurements performed, 6 were abnormal ($\leq$ 7.10). Umbilical vein pH was abnormal ($\leq$ 7.20) in 10 out of 50 measurements performed.

The outcome of pregnancy was correlated to Placenta Waveform Class (PWC), a classification based on the PI on the maternal and fetal side of the placenta. In *class 1* were those with a normal PI on both sides of the placenta, *class 2* had a normal umbilical artery PI and an abnormal arcuate artery PI, *class 3* a normal arcuate artery PI and an abnormal umbilical artery PI and *class 4* an abnormal umbilical and arcuate artery PI. This classification is a modification of the four classes proposed by Pearce et al. [19].

A newborn infant with a birthweight which was 2 standard deviations (SD) or more below the mean birthweight for gestational age of the Swedish population [21] was considered small-for-gestational age because of IUGR. The mean birthweight was 2695 g (SD: ±871), the mean birthweight deviation −11.3% (SD: ±18), the mean gestational age at delivery 258 days (SD: ±19) and the mean placenta weight was 493 g (SD: ±170).

The Chi-squared test, Fisher's test, Student's *t*-test and linear correlation analysis were used for statistical analysis of the results.

Results

Table 1 presents the outcome of pregnancy in the mild and severe pre-eclampsia groups. Table 2 gives the distribution of normal and abnormal PIs in the

Table 1. Pregnancy outcome variables in the two pre-eclampsia groups. Mean ± SD

		Pre-eclampsia		Significance of difference
		Mild	Severe	
No.		31	27	
Gestational age at birth (days)		266 ± 15	250 ± 19	$P < 0.001$
Birthweight (g)		2910 ± 834	2503 ± 895	$P < 0.05$
Birthweight deviation (%)		−11.1 ± 18	−11.4 ± 18	NS
Placental weight (g)		516 ± 161	466 ± 180	NS
IUGR:	absent	23	18	
	present	8	9	NS
FD:[a]	absent	15	5	
	present	12	10	NS

[a] 14 elective caesarean section (4 in mild and 10 in severe pre-eclampsia) and 2 intra-uterine deaths excluded; NS, non-significant; FD, fetal distress

Table 2. Pulsatility index (PI) in the umbilical artery (Ua), in the arcuate artery (Aa) and Placenta Waveform Classes (PWC) in the two pre-eclampsia groups

	Pre-eclampsia		Significance of difference
	Mild	Severe	
No.	31	27	
Umbilical artery PI:			
normal	18	20	
abnormal	13	7	NS
Arcuate artery PI:			
normal	17	16	
abnormal	14	11	NS
PWC: 1	11	12	
2	7	8	
3	6	4	
4	7	3	NS

Abnormal PI, > mean + 2 SD; NS, non-significant; PWC, *group 1;* normal PI in the Aa and Ua, *group 2;* abnormal PI in the Aa but normal PI in the Ua, *group 3;* normal PI in the Aa but abnormal PI in the Ua and *group 4;* abnormal PI in both vessels

Table 3. Outcome of pregnancy related to pulsatility index (PI) in the umbilical and arcuate arteries

	Umbilical artery PI			Arcuate artery PI		
	Normal	Abnormal	*P*-value	Normal	Abnormal	*P*-value
No.	38	20		33	24	
IUGR:						
absent	33	8		25	16	
present	5	12	$P < 0.01$	8	9	NS
FD:[a]						
absent	16	4		15	5	
present	9	13	$P < 0.05$	8	14	$P < 0.05$

[a] 14 elective caesarean sections and two intra-uterine fetal deaths are excluded; IUGR, intra-uterine growth retardation; FD, fetal distress; *P*-value, significance of difference

umbilical and arcuate arteries, and the Placental Waveform Classes (PWCs) in mild and severe pre-eclampsia. No difference was found between mild and severe pre-eclampsia with regard to outcome of pregnancy, abnormal PI or PWC.

The umbilical artery PI was abnormal in 20 cases or 35%, and the PI was abnormal in the arcuate artery in 25 cases or 43% (Table 3). A significant relationship was found between abnormal umbilical artery PI and IUGR and signs of fetal distress (Table 3). Abnormal arcuate artery PI showed no

Table 4. Outcome of pregnancy by Placenta Waveform Classes (PWC). Mean (± SD)

	Placenta Waveform Classes (PWC)						
	1	2	*P*	3	*P*	4	*P*
No.	23	15		10		10	
Gestational age at delivery (days)	262 ±14	264 ±14	NS	261 ±20	NS	240 ±27	< 0.05
Birthweight (g)	3091 ±773	2876 ±646	NS	2447 ±735	< 0.05	1767 ±864	< 0.001
Birthweight deviation (%)	−0.22 ±18	−9.7 ±13	NS	−21.1 ±11	< 0.001	−30.4 ±14	< 0.001
Placental weight (g)	583 ±180	508 ±108	NS	437 ±123	< 0.05	338 ±103	< 0.001
IUGR: absent	20	13		5		3	
present	3	2	NS	5	< 0.05	7	< 0.005
FD:[a] absent	12	4		3		1	
present	1	8	< 0.01	7	< 0.01	6	< 0.005

[a] 14 elective caesarean section and 2 intra-uterine fetal deaths excluded; IUGR, intra-uterine growth retardation; FD, fetal distress; *P*, significance of difference from the PWC1; PWC1, normal PI in the Aa and Ua; PWC2, abnormal PI in the Aa but normal PI in the Ua; PWC3, normal PI in the Aa but abnormal PI in the UA; PWC4, abnormal PI in both vessels

relationship with IUGR, but was related to signs of fetal distress (Table 3). The outcome of pregnancy by Placenta Waveform Class (PWC) is shown in Table 4.

No correlation was found between the umbilical artery PI and mean arterial pressure (MAP) or degree of proteinuria (coefficients of correlation 0.06 and 0.05, respectively). The same was true for the arcuate artery PI (corresponding coefficients of correlation 0.02 and 0.19).

Discussion

One of the major problems when evaluating Doppler fetal studies is common to all diagnostic tests applied in antenatal care – the difficulty of defining the standard, the yardstick, against which the test is to be validated. This is well recognized in perinatal clinical research, and usually, in absence of a better alternative, the tests are evaluated with reference to such characteristics of the pregnancy outcome as birthweight for gestational age, occurance of operative delivery because of imminent fetal asyphyxia, Apgar score etc.

As expected the mean gestational age of the newborn in the group with severe pre-eclampsia was significantly lower than in the group with mild pre-eclampsoa (Table 1). Consequently, the mean birthweight differed in a similar way. There were no other significant differences between the two groups.

The results suggest that a abnormal umbilical artery PI is a good predictor of IUGR in pregnancies complicated by pre-eclampsia, whereas an abnormal

arcuate artery PI is less predictive of IUGR (Table 3). When only the arcuate artery PI was abnormal (PWC 2), the likelihood of delivering a baby affected by IUGR was similar to that in PWC 1 (PI normal on both sides of the placenta, see Table 4).

In the present study, an abnormal umbilical and arcuate artery PI was associated with fetal distress (Table 3), and signs of fetal distress were significantly more frequent when the PI was abnormal on either one (PWC 2, 3) or both sides (PWC 4) of the placenta (Table 4).

Trudinger et al. [24] studied 172 complicated pregnancies and found a relationship between IUGR and an abnormal umbilical artery PI, but none between IUGR and an abnormal arcuate artery PI. Cohen-Overbeek et al. [6] examined the arcuate artery FVW in 53 IUGR pregnancies and also found no relationship between IUGR and an abnormal PI, whereas the incidence of emergency caesarean section and a low 5-minute Apgar score was significantly increased when arcuate artery PI was abnormal.

The subplacental vessels, in particular the spiral arteries, are known to dilate during pregnancy. This dilatation of the spiral arteries is due to invasion of the vessel wall by trophoblast, resulting in loss of the vascular contractile capacity due to loss of musculo-elastic tissue [3]. The blood pressure in the spiral arteries is reported to be very low in animals with haemochorial placentation [16]. The arcuate and radial arteries, though also dilated, retain their musculo-elastic wall; they are thus thought to control placental vascular resistance [20]. The normal dilatation of the sub-placental vessels is absent in pre-eclampsia, especially in the proximal part of the spiral artery which characteristically exhibits vessel wall thickening or atherosis [20]. The radial arteries are also narrowed and are similar in microscopic appearance [2].

The lack of relationship between abnormal arcuate artery PI and pre-eclampsia might be due to the fact that we frequently had to record signals blindly from sub-placental vessels. Such signals might in fact have originated from the spiral arteries with post-stenotic FVW, which might have a normal PI as has been shown in the carotid and peripheral circulation [1, 14]. This might explain, why only 42% of our pre-eclamptic patients had an abnormal arcuate artery PI. If this post-stenotic hypothesis is right (Fig. 1), then recording of FVW from the uterine artery would be preferable as the uterine artery would certainly not give rise to post-stenotic FVW. Besides, the uterine artery is representative of a greater part of the uteroplacental circulation.

Fleischer et al. [9] examined the uterine artery FVW in 71 hypertensive mothers, of whom 14 had pre-eclampsia. They used a fixed S/D ratio and reported a highly significant relationship between IUGR and abnormal uterine artery FVW. The uterine artery FVW was also abnormal in all five cases of intra-uterine fetal death. However, only 39% of their hypertensive mothers had an abnormal FVW in the uterine artery, which does not support the contention that the uterine artery is a better predictor of the outcome of pregnancy than the arcuate artery.

Although notching of the FVW in the uterine and arcuate arteries has been described in pregnancies complicated by IUGR or pre-eclampsia [4, 9], we have never seen this in sub-placental vessels.

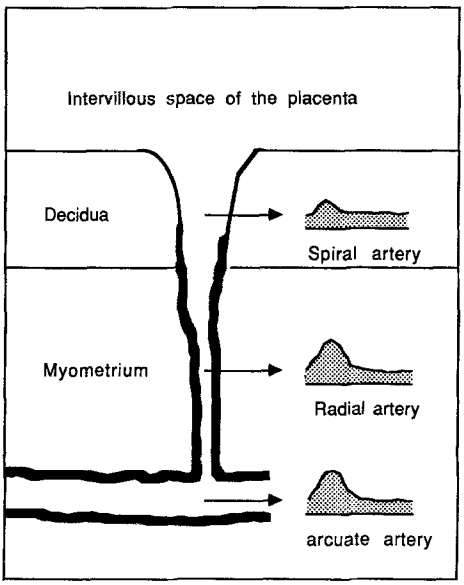

Fig. 1. Schematic illustration of blood flow velocity waveforms recorded from sub-placental vessels in pre-eclampsia. Waveforms from narrowed radial and arcuate arteries show increased pulsatility; velocity waveforms from the spiral arteries can, however, have a normal appearance ("post-stenotic hypothesis" – see text)

In conclusion, we have found an abnormal umbilical artery FVW to be a predictor of IUGR and fetal distress in pregnancies complicated by pre-eclampsia. An abnormal arcuate artery FVW was found to be associated with signs of fetal distress, but not with IUGR. Ultrasound Doppler-examination of the umbilical artery can be recommended for monitoring pre-eclamptic pregnancies, while arcuate artery examination needs further evaluation.

References

1. Atkinson P, Woodcock JP (1982) Doppler ultrasound and its use in clinical measurement. Academic Press, London, pp 178 and 182
2. Brosens I (1964) A study of the spiral arteries of the decidua basalis in normotensive and hypertensive pregnancies. J Obstet Gyn Br Cwlth 71:222–230
3. Brosens I, Robertson WB, Dixon HG (1967) The physiological response of the vessels of the placental bed in normal pregnancy. J Pathol Bact 93:569–579
4. Campbell S, Diaz-Recasens J, Griffin DR, Cohen-Overbeek T, Pearce JMF, Willson K, Teague MJ (1983) New Doppler technique for assessing uteroplacental blood flow. Lancet 1:675–677
5. Campbell S, Pearce JMF, Hackett G, Cohen-Overbeek T, Hernandes C (1986) Qualitative assessment of uteroplacental blood flow: early screening test for high-risk pregnancies. Obstet Gynecol 68:649–653
6. Cohen-Overbeek T, Pearce JM, Campbell S (1985) The antenatal assessment of utero-placental and feto-placental blood flow using Doppler ultrasound. Ultrasound Med Biol 11:329–339
7. Eik-Nes S, Brubakk AO, Ulstein M (1980) Measurement of human blood flow. Br Med J 1:283–284
8. Eik-Nes SH, Maršál K, Kristoffersen K (1984) Methodology and basic problems related to blood flow studies in the human fetus. Ultrasound Med Biol 10:329–337
9. Fleischer A, Schulman H, Farmakides G, Bracero L, Grunfeld L, Rochelson B, Koenigsberg M (1986) Uterine artery Doppler velocimetry in pregnant women with hypertension. Am J Obstet Gynecol 154:806–813

10. Giles WB, Trudinger BJ, Cook CM (1982) Umbilical artery velocity time waveforms in pregnancy. J Ultrasound Med 1 [Suppl] 98
11. Gill RW, Kossoff G (1979) Pulsed doppler combined with B-mode imaging for blood flow measurement. Contr Gynecol Obstet 6:139–141
12. Gosling RG, Dunbar G, King DH (1971) The quantitative analysis of occlusive peripheral arterial disease by a nonintrusive ultrasound technique. Angiology 22:52–55
13. Gudmundsson S, Maršál K (1988) Umbilical and uteroplacental blood flow velocity waveform in normal pregnancy – a cross-sectional study. Acta Obstet Gynaecol Scand 67 (in press)
14. Krissmann A, Bollinger A, Keller H (1982) Praxis der Doppler-Sonographie; periphere Arterien und Venen, hirnversorgende Arterien (Ger). Thieme, Stuttgart, S 206–207
15. Metcalfe J, Romney SL, Ramsy LH, Reid De, Burwell CS (1955) Estimation of uterine blood flow in normal human pregnancy at term. J Clin Invest 34:1632–1638
16. Moll W, Kunzel W, Herberger J (1975) Hemodynamic implications of hemochorial placentation. Eur J Obstet Gynaecol Repr Biol 5:67–74
17. Naeye R, Friedman EA (1979) Causes of perinatal death associated with gestational hypertension and proteinuria. Am J Obstet Gynecol 133:8–10
18. Nylund L, Lunell N-O, Lewander R, Sarby B (1983) Uteroplacental blood flow index in intrauterine growth retardation of fetal or maternal origin. Br J Obstet Gynaecol 90:16–20
19. Pearce JMF, Hernandez CE, Cohen-Overbeek T, Campbell S (1984) A classification of intrauterine growth retardation based upon flow velocity waveform obtained from the uteroplacental and fetoplacental circulation. XI. Annual Confrence of the Society for the Study of Fetal Physiology. Oxford 21–22 july, Abstract no. 15
20. Robertson WB, Brosens I, Dixon G (1975) Uteroplacental vascular pathology. Eur J Obstet Gynecol Reprod Biol 52:47–65
21. Sterky G (1970) Swedish standard curves for intra-uterine growth. Pediatrics 46:7–8
22. Sykes GS, Mollow PM, Johnson P (1983) Fetal distress and the condition newborn infant. Br Med J 287:943–945
23. Trudinger BJ, Giles WB, Cook CM, Bombardieri J (1985) Fetal umbilical artery flow velocity waveforms and placental resistance: clinical significance. Br J Obstet Gynecol 92:23–30
24. Trudinger BJ, Giles WB, Cook CM (1985) Flow velocity waveforms in the maternal uteroplacental and fetal umbilical placental circulations. Am J Obstet Gynecol 152:155–160
25. Wladimiroff J, Tonge HM, Stewart PA (1986) Doppler ultrasound assessment of cerebral blood flow in the human fetus. Br J Obstet Gynaecol 93:471–475