Doppler Velocimetry in the Umbilical and Middle Cerebral Arteries in Fetuses with Intrauterine Growth Retardation or Fetal Distress

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Summary : To clarify the usefulness of Doppler velocimetry in high-risk fetuses, i.e. with intrauterine growth retardation (IUGR) or with fetal distress, nomograms of the age-related changes in resistance and pulsatility indices in the fetal umbilical and middle cerebral arteries were made, and the best cut-off values for each parameter were determined. Included were 505 and 684 fetuses as the control and subject groups, respectively, between 22 and 41 weeks' gestation. Using the color-coded pulsed Doppler method, the resistance index in the umbilical and middle cerebral artery (RI_{UA}, RI_{MCA}), the pulsatility index in both these arteries (PI_{UA}, PI_{MCA}), and the RI and PI ratios between these arteries ($RI_{UA/MCA}$, $PI_{UA/MCA}$) were measured. In normal fetuses, RI_{UA} and PI_{UA} showed a gradual decrease with advance in gestational age. RI_{MCA} and PI_{MCA} showed a parabolic fashion with a peak around 30-31 weeks' gestation. $RI_{UA/MCA}$ and $PI_{UA/MCA}$ ratios decreased until 30-31 weeks' gestation and then increased to term. Analyses with receiver-operating-characteristic (ROC) curves revealed that PI_{UA} is the most appropriate parameter in identifying IUGR under the cut-off point of 1.5 S.D., with a sensitivity, specificity, positive and negative predictive value, and accuracy of 60.6%, 93.3%, 75.2%, 87.6%, and 85.0%, respectively. As for fetal distress, the $PI_{UA/MCA}$ ratio was the most efficacious parameter under the cut-off point of 2.0 S.D., with a sensitivity, specificity, positive and negative predictive value, and accuracy of 67.3%, 97.4%, 72.9%, 96.7% and 94.6%, respectively. The findings obtained indicate that the measurement of PI value in the umbilical artery is enough to detect IUGR per se, probably due to the reflection of the decrease in the placental vascular bed, and that the ratio of indices between the umbilical artery and middle cerebral artery is more accurate than independent evaluations in identifying fetuses developing fetal distress, reflecting a brain sparing effect as well as fetoplacental insufficiency.

Key words : Doppler velocimetry, Intrauterine growth retardation, Fetal distress, Resistance index, Pulsatility index, Receiver-operating-characteristics curve

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Introduction

Since Fitzgerald and Drumm in 1977[7] first described the use of Doppler ultrasound in the study of fetal umbilical arterial blood flow velocity as a new technique, the advent of color flow imaging and pulsed Doppler velocimetry

has enabled us to identify the deterioration of blood perfusion in the human fetus in utero. In the umbilical artery, diminishing end-diastolic flow shows a highly correlation with poor neonatal outcome[2)6)30)], especially if there is negative end-diastolic blood flow. On the other hand, it has been reported that Doppler examination of the middle cerebral artery in cases with intrauterine growth retardation (IUGR) may be of greater value in identifying hypoxic conditions[3)], and may prove to be a more sensitive screening or diagnostic test for determining flow redistribution to the brain[8)31)].

Several quantitative parameters for measuring placental vascular resistance distal to sampling vessels have been proposed, such as resistance index (RI), pulsatility index (PI), cerebral /aortic or cerebral/umbilical index ratio, to estimate changes in vascular resistance. However, there have been few investigations observing the comparative efficacy of different indices.

From this point of view, the aim of the present study was two-fold; 1) to make nomograms of the age-related changes in resistance and pulsatility indices in the fetal umbilical and middle cerebral arteries as well as the ratio between these vessels, and 2) to determine the best cut-off value for each parameter and to identify the most appropriate quantitative parameter in detecting the usefulness of Doppler velocimetry in high-risk pregnancies, that is, fetuses with IUGR or with fetal distress.

Materals and Methods

[1] *Population studied*

Retrospective analysis was performed on two groups of fetuses between 22 and 41 weeks' gestation. The gestational age was calculated from the first day of the last menstual period (LMP) and subsequently confirmed by the crown-rump length at 9-11 week' gestation.

1. Fetuses in the control group: The control group consisted of 505 fetuses from uncomplicated singleton pregnancies from 22 to 41 weeks' gestation. All fetuses fulfilled the following criteria: 1) The measurements of biparietal diameter, femur length and abdominal circumference were within the mean value±1.5 S.D. for the corresponding gestational week by Japanese standards[27)], 2) Fetuses were found to have no detectable anomaly in utero, 3) Their birth weights were within the appropriate range (mean±1.5 S.D.) for each gestational week by Japanese standards[19)], 4) Mothers were nonsmokers, with neither medical complications or drug administration, and 5) No sign of fetal distress, either in the prenatal period or in labor, with postnatal 1-min Apgar score of 8 or more.

2. Fetuses in the subject group : The subject group consisted of 684 high-risk fetuses given birth to at 24-41 weeks' gestation. All cases had maternal or fetal complications which demanded intensive care (Table 1). Among these, 170 cases resulted in IUGR, defined as birth

Table 1. Indications for Doppler examination.

Indication	Number of patients
Poor obstetric history	163
Threatened premature labor	121
Suspected intrauterine growth retardation	95
Known fetal abnormality	61
Toxemia	55
Anemia	42
Premature rupture of membrane	32
Diabetes mellitus	32
Oligohydramnios	26
Rhesus isoimmunization	14
Hydrops fetalis	12
Polyhydramnios	12
Myoma uteri	10
Idiopathic thrombocytopenic purpura	5
Thrombocytopenia	2
Placental tumor	2
total	684

weight below the mean-1.5 S.D. for the gestational week, according to Japanese Standards[19]. In all IUGR cases, baby-birth occurred within 2 weeks of the final observation of flow velocities. 52 out of 684 fetuses subsequently resulted in fetal distress diagnosed by antepartum cardiotocographic (CTG) findings. The CTG findings were categorized by the criteria of Rochard et al.[21]: A "*reactive fetal heart rate (FHR) pattern*" was defined as a heart rate between 120 and 160 beats per minute (bpm), a baseline FHR variability of 6 bpm or more, and FHR acceleration concurring with fetal movement. If the CTG appeared non-reactive, FHR monitoring was continued for a subsequent 120 minutes, eliminating FHR changes due to "*resting phase*" phenomenon[29]. Fetal distress was considered present when FHR patterns showed persistent loss of baseline variability, repeated late decelerations or severe variable decelerations[14].

All mothers were cared for at the Maternity and Perinatal Care Unit of Kyushu University Hospital and data acquisition was performed between 1992 and 1996.

[2] *Variable definition and data acquisition*

1. Flow velocity waveforms in the umbilical and middle cerebral arteries

The equipment used was a color-coded pulsed Doppler unit with a sector transducer of 3.75 MHz and a low-cut filter of 50 Hz (Model SSA-270 A, Toshiba, Tokyo). The methods for recording blood flow velocity waveforms from the umbilical and middle cerebral arteries were described in detail previously[11)24)]. The maximum flow velocity envelope was digitized using a digitizer (Graphtec Co. Ltd., KD-4030 A, Tokyo) and stored on a floppy disc in an online-microcomputer system (Macintosh 6260, Apple Computer Inc.).

2. Quantitative parameters for flow velocity waveforms

Selected were the following 6 parameters ; resistance index (RI) in the umbilical and middle cerebral arteries (RI_{UA}, RI_{MCA}), pulsatility index (PI) in these two arteries (PI_{UA}, PI_{MCA}), and RI and PI ratio between the umbilical and middle cerebral arteries ($RI_{UA/MCA}$, $PI_{UA/MCA}$).

RI and PI were measured according to the following formulae[24]:

RI=(maximum flow velocity−end-diastolic flow velocity)/maximum flow velocity

PI=(maximum flow velocity−end-diastolic flow velocity)/mean flow velocity

With the aid of a microcomputer system, all these values were calculated as the average of ten clearly traced consecutive cycles for each case.

[3] *Data processing and statistical analysis*

1. Construction of nomograms for the 6 parameters

Using the data obtained from the control-group fetuses, nomograms were made (mean and S.D.) of RI_{UA}, RI_{MCA}, PI_{UA}, PI_{MCA}, $PI_{UA/MCA}$ and $PI_{UA/MCA}$ for every 2-gestational week interval, from 22 to 41 weeks' gestation.

2. Determination of the best cut-off value and calculation of the sensitivity, specificity, positive predictive value, negative predictive value and accuracy in 6 parameters

The efficacy of fetal blood flow variables to indicate cases with IUGR or with fetal distress was evaluated in terms of sensitivity and specificity, as reflected in receiver-operating-characteristic (ROC) curves[20]. The ROC curve is a plot of the sensitivity on the false positive rate (1-specificity) for a test, at different cut-off points. Since the abnormal value for blood

flow variables changes in degree of abnormality as the cut-off level changes, the efficacy of the variables in predicting abnormal fetal outcome can be evaluated. Sensitivity and specificity were calculated for each cut-off level in 0.25 S.D. steps from the normal mean value towards abnormality. The best cut-off point for each parameter was determined, the validity of which in all 6 indices for detecting cases with IUGR or fetal distress were estimated by sensitivities, specificities, positive predictive values, negative predictive values and the accuracies calculated at those cut-off points.

3. Study on the interval between the observation of the abnormal wavefroms and subsequent fetal distress

Out of 52 cases with fetal distress, for cases having abnormal blood flow waveforms, the interval between the observation of the abnormal waveform and subsequent fetal distress was retrospectively investigated.

Results

1. Age-related nomograms of RI_{UA}, PI_{UA}, RI_{MCA}, PI_{MCA}, $RI_{UA/MCA}$ and $PI_{UA/MCA}$

RI_{UA} and PI_{UA} demonstrated a gradual decrease as gestational age advanced. RI_{MCA} and PI_{MCA} showed a rather parabolic fashion in value with a peak around 30-31 weeks, indicating a gradual increase until 30-31 weeks' gestation and then a gradual decrease to term. $RI_{UA/MCA}$ and $PI_{UA/MCA}$ ratios decreased until 30-31 weeks of gestation and then increased to term (Fig. 1, Table 2).

2. The best cut-off points of standard deviation for RI_{UA}, PI_{UA}, RI_{MCA}, PI_{MCA}, $RI_{UA/MCA}$ and $PI_{UA/MCA}$ ratio in detecting IUGR

The most efficacious cut-off values were 1.25, 1.5, 1.0, 1.0, 1.0 and 1.0 S.D. for RI_{UA}, PI_{UA}, RI_{MCA}, PI_{MCA}, $RI_{UA/MCA}$ and $PI_{UA/MCA}$, respectively. PI_{UA} was the most appropriate parameter compared with the others and it had the sensitivity, specificity, positive and negative predictive value, and accuracy of 60.6%, 93.3%, 75.2%, 87.6% and 85.0%, respectively (Fig. 2, Table 3).

3. The best cut-off points of standard deviation for RI_{UA}, PI_{UA}, RI_{MCA}, PI_{MCA}, $RI_{UA/MCA}$ and $PI_{UA/MCA}$ ratio in detecting fetal distress

The most efficacious cut-off values were 1.5, 1.75, 1.0, 1.0, 1.75 and 2.0 S.D. for RI_{UA}, PI_{UA}, RI_{MCA}, PI_{MCA}, $RI_{UA/MCA}$ and $PI_{UA/MCA}$, respectively. $PI_{UA/MCA}$ ratio was the most appropriate parameter compared with the others, and it had the sensitivity, specificity, positive and negative predictive value, and accuracy of 67.3%, 97.4%, 72.9%, 96.7% and 94.6%, respectively (Fig. 3, Table 4).

4. The interval between the observation of abnormal waveforms and subsequent fetal distress

In 52 cases with fetal distress, abnormal $PI_{UA/MCA}$ above 2.0 S.D. were recorded in 35 cases (67.3%). In all these cases, abnormal waveforms continued without recovery until delivery. The interval between the observation of abnormal waveforms and the detection of fetal distress resulting in emergent interventions ranged from 1 hour to 33 days, with a median value of 4 days (Fig. 4).

Discussion

In human Doppler studies on the fetal circulation, several investigators have reported that, in IUGR or fetal hypoxia, there is flow redistribution resulting from a decreased resistance to flow in vessels supplying the brain[4)12)24)]. In this study, I focused on both the placental and the cerebral circulation in the human fetus to assess which hemodynamic parameters, at

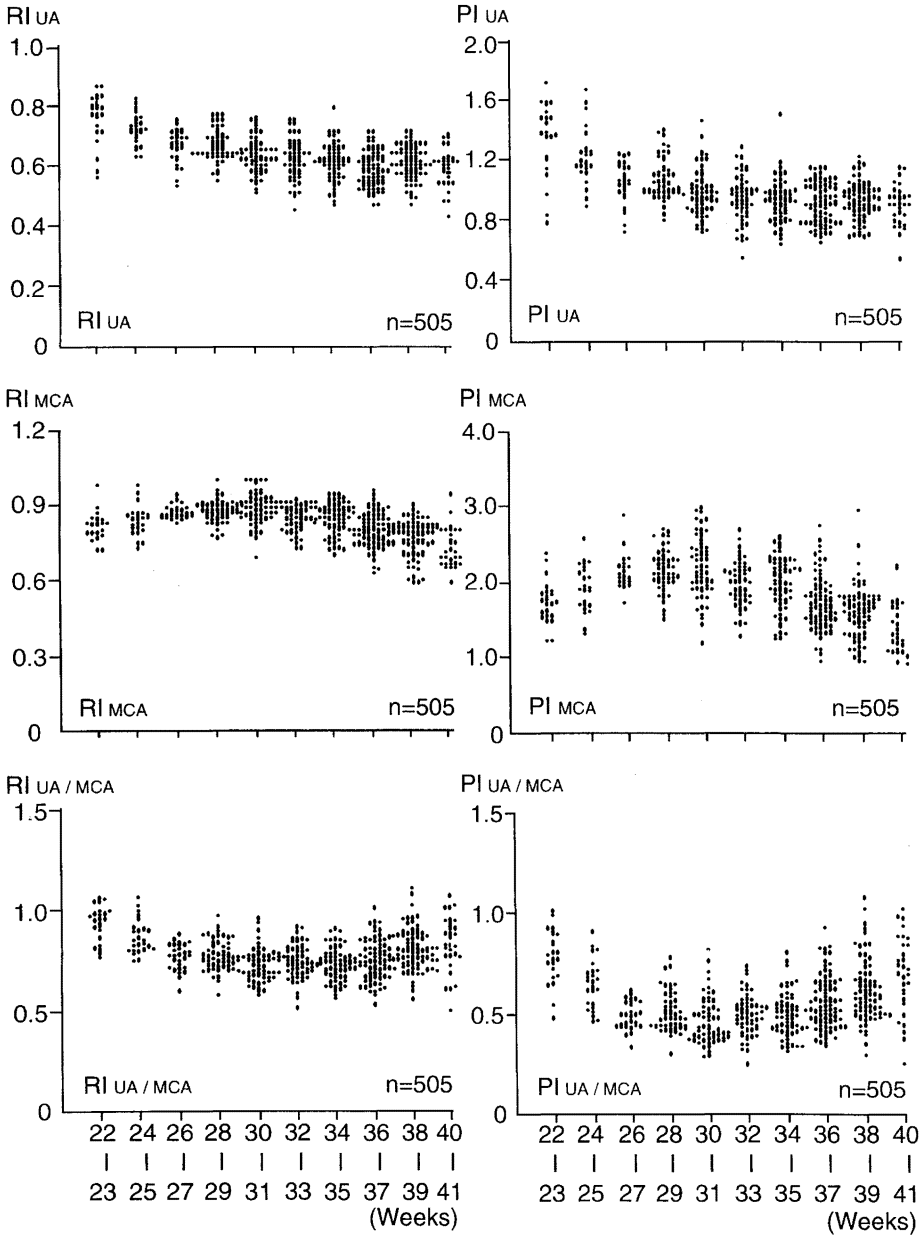

Fig. 1. Nomograms of RI_{UA}, PI_{UA}, RI_{MCA}, PI_{MCA}, $RI_{UA/MCA}$ and $PI_{UA/MCA}$ with advancing gestation.
RI: Resistance index, PI: Pulsatility index, UA: Umbilical artery, MCA: Middle cerebral artery, UA/MCA: Ratio between umbilical artery and middle cerebral artery, n: Number of cases

their best cut-off points, are most useful in detecting IUGR or fetal distress; major obstetric problems contributing significantly to perinatal morbidity and mortality.

Although many hemodynamic parameters have been proposed for quantifying blood flow waveforms[17)18)], I adopted 6 parameters; RI_{UA}, PI_{UA}, RI_{MCA}, PI_{MCA}, $RI_{UA/MCA}$ and $PI_{UA/MCA}$ ratios,

Table 2. Age-related changes of RI and PI values in the umbilical and middle cerebral arteries in normal fetuses.

Gestational weeks	Number of cases	RI_{UA} Mean (S.D.)	PI_{UA} Mean (S.D.)	RI_{MCA} Mean (S.D.)	PI_{MCA} Mean (S.D.)	$RI_{UA/MCA}$ Mean (S.D.)	$PI_{UA/MCA}$ Mean (S.D.)
22-23	27	0.749(0.081)	1.315(0.237)	0.820(0.052)	1.734(0.273)	0.914(0.089)	0.766(0.134)
24-25	22	0.725(0.051)	1.238(0.196)	0.841(0.060)	1.915(0.334)	0.866(0.087)	0.669(0.185)
26-27	29	0.664(0.055)	1.045(0.140)	0.872(0.026)	2.161(0.219)	0.761(0.065)	0.486(0.070)
28-29	54	0.665(0.052)	1.063(0.138)	0.873(0.043)	2.141(0.272)	0.764(0.075)	0.505(0.095)
30-31	60	0.633(0.058)	0.978(0.156)	0.886(0.063)	2.198(0.403)	0.717(0.081)	0.460(0.115)
32-33	55	0.622(0.064)	0.950(0.149)	0.843(0.048)	1.953(0.301)	0.740(0.079)	0.496(0.097)
34-35	65	0.607(0.056)	0.919(0.120)	0.845(0.061)	1.958(0.352)	0.721(0.076)	0.484(0.105)
36-37	85	0.590(0.057)	0.907(0.132)	0.805(0.079)	1.706(0.362)	0.739(0.096)	0.551(0.129)
38-39	78	0.606(0.055)	0.924(0.122)	0.769(0.072)	1.590(0.350)	0.795(0.103)	0.608(0.154)
40-41	30	0.597(0.057)	0.909(0.120)	0.720(0.074)	1.340(0.298)	0.838(0.122)	0.711(0.178)
Total	505						

RI: resistance index, PI: pulsatility index, UA: umbilical artery, MCA: middle cerebral artery, UA/MCA: ratio between the umbilical artery and middle cerebral artery, S.D.: standard deviation.

Table 3. The best cut-off values of standard deviations in 6 parameters and the sensitivity, specificity, PPV, NPV and accuracy for detecting intrauterine growth restriction.

	RI_{UA}	PI_{UA}	RI_{MCA}	PI_{MCA}	$RI_{UA/MCA}$	$PI_{UA/MCA}$
cut-off(S.D.)	1.25	1.5	1.0	1.0	1.0	1.0
sensitivity(%)	62.4	60.6	41.8	40.6	64.7	60.0
specificity(%)	91.5	93.3	89.1	87.3	85.7	88.3
PPV(%)	71.1	75.2	56.4	51.9	60.4	63.4
NPV(%)	87.8	87.6	82.0	81.4	87.8	86.8
accuracy	84.2	85.0	77.2	75.6	80.4	81.2

RI: resistance index, PI: pulsatility index, UA: umbilical artery, MCA: middle cerebral artery, UA/MCA: ratio between the umbilical artery and middle cerebral artery, S.D.: standard deviation, PPV: postive predictive value, NPV: negative predictive value.

all of which have Gaussian distributions and are postulated as not only reflecting each placental or cerebral vascular resistance or both, but also the degree of redistribution in compromised fetuses.

With respect to the umbilical blood flow, through the whole gestational period between 22 and 41 weeks, both the RI and PI showed a uniform decrease from 22 weeks' gestation with advancing age. This result coincides well with other reports[23], suggesting the gradual decrease in placental vascular resistance in normal fetuses with advance in gestation. On the other hand, both the RI_{MCA} and PI_{MCA} showed an increase from 22 weeks to 31 weeks and a gradual decrease from then on. Satoh et al. previously found such phenomenon and proposed that the change in based on the decrease in peripheral vascular resistance associated with a rapid increasing volume in the cerebral vascular bed near term[24]. Soothill et al. have established a reduction of pO_2 in the umbilical artery through cordocentesis during this period of gestation[26]. Referring these reports,

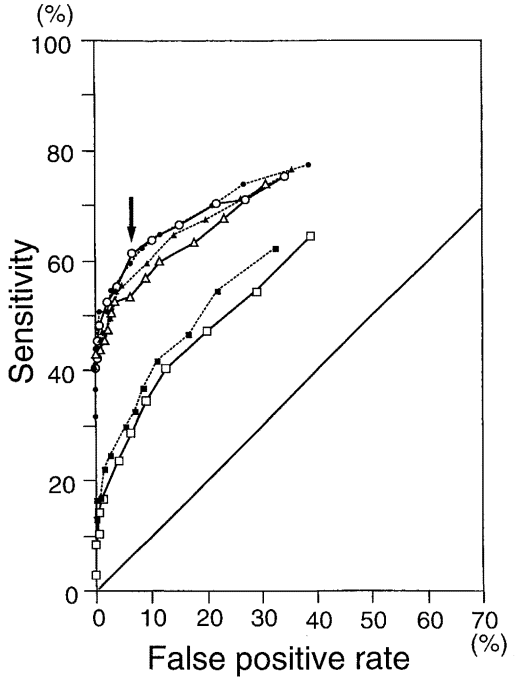

Fig. 2. Receiver-operating-characteristics (ROC) curves showing the sensitivity and false positive rate at every 0.25 standard deviation interval in 6 Doppler parameters to detect the best cut-off point in identifying intrauterine growth retardation.
●: Resistance index in the umbilical artery, ○: Pulsatility index in the umbilical artery, ■: Resistance index in the middle cerebral artery, □: Pulsatility index in the middle cerebral artery, ▲: Resistance index ratio between the umbilical and middle cerebral artery, △: Pulsatility index ratio between the umbilical and middle cerebral artery.
Arrow shows the best cut-off point with the highest accuracy (S.D.=1.5 for the pulsatility index value in the umbilical artery).

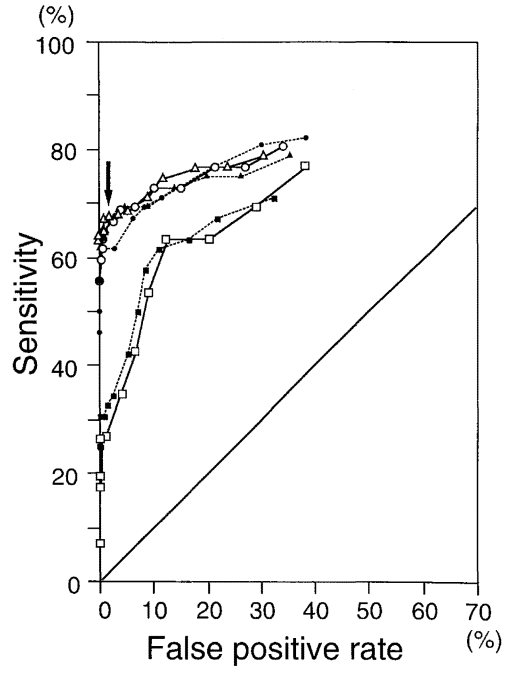

Fig. 3. Receiver-operating-characteristics (ROC) curves showing the sensitivity and false positive rate at every 0.25 standard deviation interval in 6 Doppler parameters to detect the best cut-off point in identifying fetal distress.
●: Resistance index in the umbilical artery, ○: Pulsatility index in the umbilical artery, ■: Resistance index in the middle cerebral artery, □: Pulsatility index in the middle cerebral artery, ▲: Resistance index ratio between the umbilical and middle cerebral artery, △: Pulsatility index ratio between the umbilical and middle cerebral artery.
Arrow shows the best cut-off point with the highest accuracy (S.D.=2.0 for the pulsatility index between the umbilical and middle cerebral artery).

the gradual decrease in PI values after 32 weeks' gestation appears to reflect a redistribution favoring blood supply to the brain, influenced by cerebral vascular change and physiological pO_2 reduction. As a consequence of these chronological changes, the ratio of indices between the umbilical and cerebral circulation has shown the nadir from 30 to 35 weeks' gestation.

In this study, the ROC curve was applied to determine the best cut-off value in the standard deviation for each parameter in IUGR or fetal distress. ROC curves were also used to identify statistically, the effects of changes in

Table 4. The best cut-off values of standard deviations in 6 parameters and the sensitivity, specificity, PPV, NPV and accuracy for detecting fetal distress.

	RI_{UA}	PI_{UA}	RI_{MCA}	PI_{MCA}	$RI_{UA/MCA}$	$PI_{UA/MCA}$
cut-off(S.D.)	1.5	1.75	1.0	1.0	1.75	2.0
sensitivity(%)	67.3	69.2	61.5	63.5	69.2	67.3
specificity(%)	93.7	96.2	89.1	87.3	96.8	97.4
PPV(%)	52.2	65.5	36.8	34.0	69.2	72.9
NPV(%)	96.5	96.8	95.7	95.9	96.8	96.7
accuracy	91.2	93.7	86.5	85.1	94.3	94.6

RI: resistance index, PI: pulsatility index, UA: umbilical artery, MCA: middle cerebral artery, UA/MCA: ratio between the umbilical artery and middle cerebral artery, S.D.: standard deviation, PPV: positive predictive value, NPV: negative predictive value.

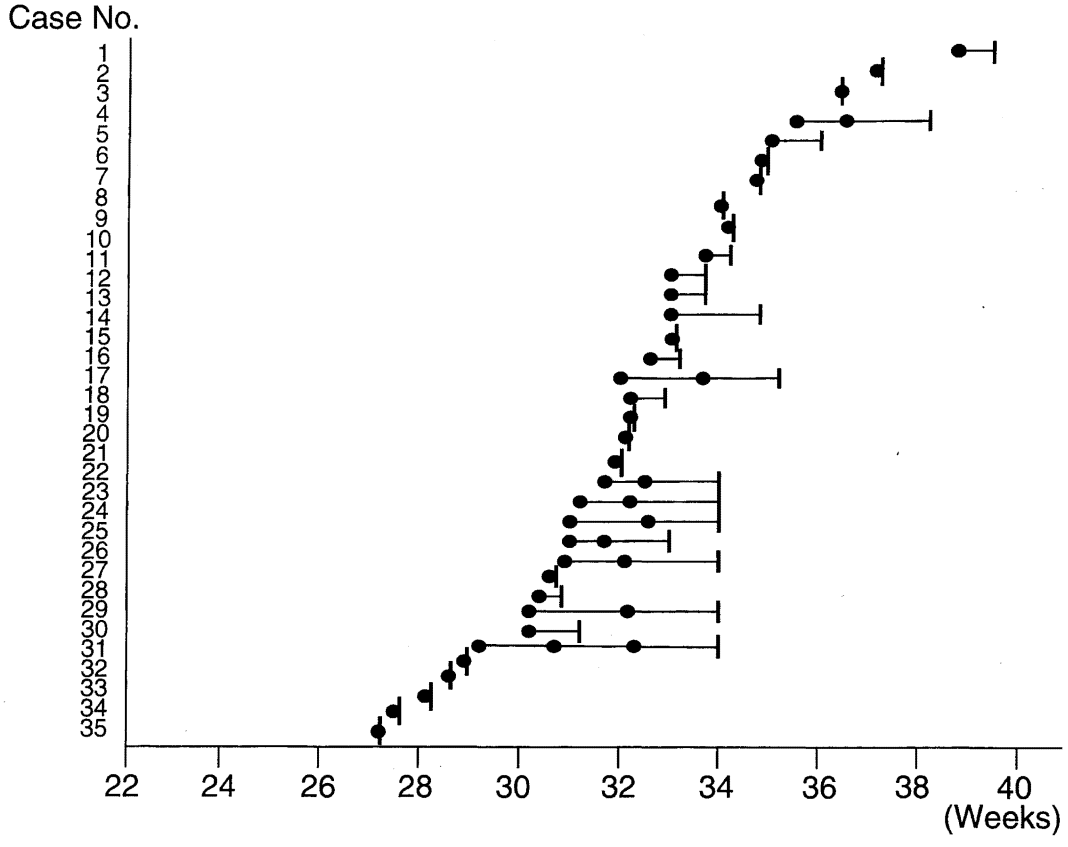

Fig. 4. The interval between the detection of abnormal $PI_{UA/MCA}$ and the time of delivery in 35 cases with fetal distress.
Each dot indicates the time of detection of abnormal blood flow. Vertical line indicates the time of delivery due to fetal distress.
No.: Number of cases with fetal distress.

the cut-off point, based on both the sensitivity and the false positive rate. The most distant point from the diagonal line is regarded as the best cut-off point of the standard deviation with the highest Doppler value accuracy in examining objective variables. This analytical technique provides a measure of diagnostic accuracy free of judgment bias having the inherent discriminatory power to separate the compromised from the healthy population[10)28)].

As for the detection of IUGR, this study demonstrated that the cut-off point of 1.5 S.D. for PI values in the umbilical artery has the highest efficacy, with the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 60.6%, 93.3%, 75.2 %, 87.6%, and 85.0%, respectively. Although it is well known that IUGR tends to have an increase in RI and PI values in the umbilical artery with a decrease in those in the intracranial artery[18)23)], the most efficacious parameter to correlate with fetal outcome is controversial. Wladimiroff et al. originally reported that the combination of PI values in both the umbilical and the internal carotid artery is useful to identify IUGR[32)]. Laurin et al., however, have claimed that velocimetry in the umbilical artery is enough to detect IUGR without flow measurements in the cerebral or other truncal vessels[15)]. Based on this study which includes fairly large case numbers, the measurement of PI values in the umbilical artery alone is thought to be enough to determine IUGR per se, probably due to the reflection of the decrease in the placental vascular bed, which frequently underlies the pathophysiology of growth retardation[9)] rather than additional hemodynamic parameters included in cerebral circulation.

Several studies describing the association of fetoplacental blood flow velocity with fetal distress in labor state that abnormal umbilical artery blood flow velocities are not effective as predictors with sensitivities ranging from 33% to 57% and positive predictive values ranging from 24% to 50%[1)16)22)]. In this study concerning the efficacy for detecting fetal distress, the best parameter was the ratio between PI values in the umbilical and the middle cerebral artery rather than other parameters obtained from a single vessel, with the sensitivity, specificity, positive and negative predictive values, and the accuracy of 67.3%, 97.4%, 72.9%, 96.7% and 94.6%, respectively, under the cut-off value of 2.0 S.D.. Doppler velocimetry of the umbilical artery detects only those hemodynamic abnormalities which are not in all cases associated with the deterioration of placental function that can produce fetal hypoxia[25)33)]. The oxygen exchange between the mother and the fetus could be altered even without any placental hemodynamic lesion. In this sence, the main advantage of comparing the placental and the cerebral vascular resistance is that I take into account, first, the possible existence of placental disease responsible for change in maternal to fetal oxygen transfer, and secondly, the cerebral hemodynamic consequences of these abnormalities. In addition, Hecher et al. have recently reported that the decrease in PI value in the middle cerebral artery directly correlates with the decrease in both venous blood pO_2 and pH[13)]. Therefore, the findings obtained in this study show that the ratio of indices between the umbilical artery and the middle cerebral artery has a better accuracy than independent evaluations in identifying the fetus developing fetal distress, in high-risk pregnancies.

I also retrospectively reviewed the interval between the observation of the aberration of

the flow waveform indices and subsequent fetal distress. 35 out of 52 cases with subsequent CTG findings of fetal distress had abnormal indices which lasted until delivery and revealed a wide range from 1 hour to 33 days between the first detection of abnormal flow pattern and fetal deterioration. This coincides well with the report by Arduini et al.[5], claiming that 37 fetuses with abnormal waveforms in the umbilical artery consequently resulted in fetal distress over an interval ranging between 1 to 26 days. Hence, the result obtained here indicates that the appearance of an abnormal $PI_{UA/MCA}$ ratio is an important alarming sign necessitating intensive monitoring of fetal well-being, but it is rather hard to accurately predict the most appropriate time of delivery. Further prospective studies are required to make this point clear.

In conclusion, PI values in the umbilical artery and the PI ratio between the umbilical and the middle cerebral arteries proved to have the highest efficacy in detecting IUGR or fetal distress, respectively.

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(和文抄録)

子宮内発育遅延胎児および胎児仮死症例における臍帯動脈・中大脳動脈血流計測の有用性に関する研究

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(目的)ドプラ法を用いてヒト胎児における血流速度波形の定量的な評価が可能になってきた．その結果，子宮内発育遅延症(IUGR)あるいは胎児仮死などの疾病状態においては，臍帯動脈の血管抵抗の上昇と脳血管抵抗の減少が生ずることが報告されており，定量的指標として諸種のindexが提唱されている．しかしながら，これらの血行動態の指標のいずれが最も有用であるかはいまだに明らかにされていない．このような背景から，本研究では，正常発育胎児における臍帯動脈および中大脳動脈の血管抵抗の指標の妊娠進行にともなう推移を明らかにすること，およびそれを基礎にしてIUGRおよび胎児仮死に対する胎内における血流評価の有用性を明らかにすることを目的とした．

(対象および方法)対象は妊娠22-41週の正常胎児505例および妊娠合併症を有し，intensive careを要したハイリスク胎児684例の，計1,189例である．方法は，カラードプラ法を用いて胎児の臍帯動脈(UA)および中大脳動脈(MCA)の血流原波形をコンピュータに入力して記録した．ついで，両動脈におけるResistance Index(RI)［(最高血流速度－拡張終期血流速度)/(最高血流速度)］(RI_{UA}, RI_{MCA})，Pulsatility Index(PI)［(最高血流速度－拡張終期血流速度)/(平均血流速度)］(PI_{UA}, PI_{MCA})，および両動脈のRI比($RI_{UA/MCA}$)ならびにPI比($PI_{UA/MCA}$)を求めた．正常胎児についてRI_{UA}, RI_{MCA}, PI_{UA}, PI_{MCA}, $RI_{UA/MCA}$および$PI_{UA/MCA}$の6つの指標に関して，2週毎の平均値および標準偏差(S.D.)を算出し，妊娠進行にともなうnomogramを作成した．出産体重が妊娠週数毎の標準体重分布の(平均値-1.5 S.D.)未満の値を示した症例をIUGR，また，胎児心拍数陣痛図で心拍数基線細変動の消失，反復する遅発一過性徐脈あるいは高度変動一過性徐脈が認められた症例を胎児仮死と判定した．Receiver-operating-characteristics (ROC) curveを用いて，IUGRおよび胎児仮死の存否に対する最もefficacyの高い指標ならびにS.D.のcut-off値を算出した．

(成績)1) 正常胎児では，妊娠進行に伴いRI_{UA}, PI_{UA}は単調に減少した．一方，RI_{MCA}, PI_{MCA}は妊娠30-31週まで増加し，以後は減少した．$RI_{UA/MCA}$および$PI_{UA/MCA}$は妊娠30-31週まで減少し，以後は増加した．2)ハイリスク胎児684例のなかで，IUGR例は170例(24.9%)であった．最もefficacyの高かった指標はPI_{UA}で，(平均値+1.5 S.D.)をcut-off値とした場合，sensiitivity, specificity, positive predictive value (PPV), negative predictive value (NPV)およびaccuracyは各々，60.6%, 93.3%, 75.2%, 87.6%および85.0%であった．3)684例のなかで，胎児仮死に至った症例は52例(7.6%)であった．最もefficacyの高かった指標は$PI_{UA/MCA}$で，(平均値+2.0 S.D.)をcut-off値とした場合，sensiitivity, specificity, PPV, NPVおよびaccuracyは各々，67.3%, 97.4%, 72.9%, 96.7%および94.6%であった．4) $PI_{UA/MCA}$が(平均値+2.0 S.D.)以上を示した胎児仮死例35例における$PI_{UA/MCA}$異常の出現から胎児仮死に至るまでの期間は1時間～33日(中央値：4日)であった．

(結語)本研究を通じて，1) IUGRの存否に対する最も有用な指標は臍帯動脈PI値(cut-off値：1.5 S.D.)であり，胎盤血管抵抗の上昇が存在していること，2)胎児仮死の存否に対する最も有用な指標は臍帯動脈PI/中大脳動脈PI比(cut-off値：2.0 S.D.)であり，本症では胎盤循環不全によって生じた胎児低酸素状態に起因した脳血管抵抗の減少により，脳循環を保持する血流再分配機構が発現されていることが明らかとなった．