## Fetomaternal Doppler sonography nomograms

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#### Summary

*Purpose:* To constitute Doppler flow velocity nomograms for use in obstetric clinics and to analyse the technical infrastructure of constructing Doppler sonography nomograms for clinical use.

*Methods:* On a cross-sectional study plan basis 602 flow results of 370 pregnant women were used. Pregnancy gestational ages were confirmed with an early sonogram prior to the 14<sup>th</sup> gestational week. Patients in whom primary section for placental insufficiency had to be done, who had pathological fetal heart rate monitoring, signs of intrauterine asphyxia, multiple pregnancy or a fetal anomaly were excluded. Every two gestational weeks patients were grouped and for these groups the 5<sup>th</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 95<sup>th</sup> percentiles were calculated to represent the umbilical artery, fetal aorta, middle cerebral artery (MCA) and uterine artery S/D ratio, resistence index (RI) and pulsatility index (PI) Doppler flow velocity nomograms.

*Results:* In normal pregnancies, after the 22<sup>nd</sup>-24<sup>th</sup> gestational week, the uteroplacental flow velocities were constant, but at the fetal vessels there were changes in velocity waveforms after this period. With advancing gestation in the third trimester, umbilical artery and middle cerebral artery impedance was lower and the resistance in the descending fetal aorta remained nearly constant.

*Conclusion:* With growing gestational age the Doppler velocity forms change. In fact because of this, for Doppler velocity studies and to differentiate between normal and abnormal pregnancy status, nomograms adapted to gestational age should be used. For practical use in different obstetrics clinics, we are presenting our Doppler velocity norm-curves.

Key words: Obstetric doppler sonography; Fetomaternal Doppler nomograms; Norm values.

#### Introduction

#### Constituting nomograms

The importance of constituting fetomaternal Doppler ultrasound nomograms is to differentiate normal pregnancies from abnormal ones. To achieve this aim physiologic reference values for blood flow velocities must be known [1].

In an "ideal" pregnancy, many parameters of Doppler sonographic velocimetry are within physiologic ranges. Values obtained from such pregnancies would define a variable in a very narrow range; it would qualify an ideal pregnancy, but would oppose biologic distribution of values [2].

#### Dependency of values on gestational age

The quantity of perfusion in trophoblastic tissue is related to gestational age. For this reason, in interpreting the Doppler sonographic findings, gestational age should be taken into account as well. That is, nomograms for Doppler sonographic measurements should be standardized according to gestational age. In general, the accepted time for starting Doppler measurements is the beginning of the second trimester because of their clinical relevance. This is the right time that allows modifications in antenatal care in a high-risk pregnancy. For specific conditions, earlier timing of measurements may be considered [3].

In cross-sectional studies, it is a general principal that an adequate number of measurements for each gestational week should be performed (>15 measurements for each gestational week) [4]. Making more than one measurement in each pregnancy should be avoided to prevent narrowing of the biologic distribution, which would shrink tolerance zones [5].

The main objective in constituting fetomaternal Doppler sonographic nomograms is to improve prognosis in high risk pregnancies, especially if there are no abnormal values in Doppler examination. Therefore, Doppler sonographic values of high-risk pregnancies must be gathered too [6]. Curves presented below depict normal fetal and maternal Doppler sonograpic values, and can be used in routine practice.

#### Material and Methods

#### Definition of the control group

This group consisted of pregnancies whose gestational ages were accurately measured before 14 weeks' gestation. The exclusion criteria were previous cesarean section for placental insufficiency, abnormal fetal heart rate (FHR) monitoring, tendency to intrauterine hypoxia, multiple gestations and fetal abnormalities. The following criteria were fulfilled by the included patients: Birth weight of newborns within the range of 10-90<sup>th</sup> percentiles according to Roemer *et al.* [7], APGAR scores  $\geq$  7 at 5 and 10 minutes, postpartum umbilical cord pH values  $\geq$  7.2.

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#### Constituting the curves

Indices: Analysis of Doppler sonographic flow values quantitatively is more problematic than analysing qualitatively. Quantitative analysis also overcomes erroneous measurements in small vessels. There are plenty of indices for qualitative analysis [8].

Following are the most frequently used indices (Figure 1):

- Systolic/diastolic ratio (S/D, Stuart 1980);
- Resistance index (RI, Pourcelot 1974);
- Pulsatility index (PI, Gosling and King 1977).

In analyzing sonographic results and calculating indices, the following characters have been used:

- S = Temporal peak of maximum frequency;
- D = End-diastolic maximum frequency;
- C = Temporal average of maximum frequency, F mean;
- I = Instantaneous spatial average frequency;
- E = Temporal average of spatial average frequency.
- Calculation of formulas are as follows (Figure 1):

SD-ratio - S/D;

RI - (S-D)/S;

PI - (S-D)/C.

While calculating PI values, in some sonographic devices, E values are used instead of C values. As a result PI values increase slightly.

In search of literature, we did not encounter any information about the superiority of any one of these indices over the other [5, 9-12]. Although S/D ratio is easily calculated, RI is the easiest to interpret. RI values approach zero if the resistance decreases and approach one if resistance increases. If end-diastolic flow is absent, PI is the only index making evaluation of blood flow possible, because in this situation S/D will be equal to infinite and RI to one.

#### Percentiles

The control group consisted of 370 pregnant women: 602 measurements (1.62 measurements/pregnancy) were performed by PW-Doppler and nomograms were constituted. Nomograms were constituted according to gestational age because the values could not be assigned to the normal distribution. Measurements performed in two consecutive gestational weeks were allocated as one group. Graphics were established by calculating values for the 5<sup>th</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup>, and 95<sup>th</sup> percentiles. Curves were smoothened by cubic regression. In Figures 2 and 3, the original and the curve smoothened by cubic regression are presented. As seen in these figures, smoothening of curves does not affect the values of the variable considerably.



Figure 1. — Scheme of the Doppler curve.

S = systolic, D = diastolic, C = Temporal average of maximum frequency. Calculation of formulas of the main Doppler sono-graphic indices.

#### Results

Curves established from 370 patients (602 measurements) are depicted in Figures 2-14. Measurements were performed on the umbilical artery, fetal aorta, middle cerebral artery and uterine artery. In each vessel S/D ratio, RI and PI indices were obtained and nomograms were set up. Curves presented in Figures 3 to 14 are smoothened curves by cubic regression.









Figure 3. — Umbilical artery systolic/diastolic (S/D) ratio nomogram obtained from normal pregnancies; curves were straightened by cubic regression.

#### Discussion

Doppler sonography in obstetrics is a widely accepted functional method of examining the utero-fetoplacental unit. It is a noninvasive method and has become almost a standard technique in antenatal care. This method is an important tool to define high-risk pregnancies.

Doppler sonographic nomograms are used for differentiation between normal and abnormal blood flow results, which helps to determine high-risk pregnancies. By taking threshold values of pathologic pregnancies into consideration, nomograms are capable of differentiating



Figure 4. — Umbilical artery resistance index (RI) nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 5. — Umbilical artery pulsatility index (PI) nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 6. — Descending fetal aorta S/D ratio nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 7. — Descending fetal aorta RI nomogram obtained from normal pregnancies; curves were straightened by cubic regression.

between normal and abnormal. The presented nomograms (Figures 3-14) were constituted to meet this target. While confronting these nomograms, it must always kept in mind that these curves were corrected by cubic regression, that the values on these nomograms should not be taken as mathematical equations, and that limitations of sensitivity and specifity exist.

The data were collected cross-sectional instead of as longitudinal data collections, and therefore the potential problems concerning repeat examinations could not be evaluated. This point may cause problems in interpretation of the Doppler sonographic results. To estimate, if a doppler sonographic result is a deviation within normal ranges or a predictor of a high risk pregnancy, repeated measurements should be considered.

#### Using nomograms in practice

Just like the defense mechanism of peripheral vasoconstriction in an adult in the face of hemorrhagic shock, the "brain sparing" mechanism ("brain sparing effect") becomes active in a fetus with asphyxia or chronic placental insufficiency. As a result of the brain sparing mechanism, resistance both in the umbilical artery and fetal aorta increases. Doppler indices related to these vessels increase as a consequence. The end-diastolic blood flow increases in the middle cerebral artery (MCA) by the same effect. Doppler indices for this vessel decrease consequently.

Some points should be considered while using the nomograms:

1) Among the measurements performed on the fetal aorta and umbilical arteries, values between the  $90^{\text{th}}$  and  $95^{\text{th}}$  percentiles should be considered as borderline and repeat follow-ups should be planned. Values exceeding the  $95^{\text{th}}$  percentile are considered abnormal.

2) Doppler values between the 5<sup>th</sup> and 10<sup>th</sup> percentiles in MCA should be considered as borderline and repeat follow-ups should be planned. Values below the 5th percentile are considered abnormal.



Figure 8. — Descending fetal aorta PI nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 9. — Middle cerebral artery S/D ratio nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 10. — Middle cerebral artery RI nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 11. — Middle cerebral artery PI nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 12. — Uterine artery S/D ratio nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 13. — Uterine artery RI nomogram obtained from normal pregnancies; curves were straightened by cubic regression.



Figure 14. — Uterine artery PI nomogram obtained from normal pregnancies; curves were straightened by cubic regression.

3) Measurements taken after 24 weeks' of gestation from uterine arteries are more valuable. The early diastolic notching seen in this vessel, and values exceeding the  $95^{\text{th}}$  percentile are considered abnormal. One point to remember is notching by itself predicts elevated risk of preeclampsia.

# Changes in Doppler sonographic measurements during the course of pregnancy:

During the course of pregnancy, Doppler sonographic measurements of fetomaternal vessels display changing values.

#### Umbilical artery

Blood flow velocity in the umbilical artery increases with progressing gestational age. As a result the S/D ratio continuously decreases due to increasing arterial blood flow. With progressing gestational age end-diastolic blood flow becomes evident during the whole heart cycle, matching with previous longitudinal studies of Fogarty *et al.* [10] and Hünecke *et al.* [15], as with many cross-sectional studies [16-19].

Trudinger *et al.* [20] explained these changes with the following mechanisms:

- Continuous maturation in placental villi

- Continuous widening of placental vessels cause a continuous decrease in vascular resistance

- Continuous increase in fetal cardiac output
- Continuous changes in the vessel compliance
- Continuous increase in fetal blood pressure.

Especially in the third trimester of pregnancy, depending on these factors normal values become scattered on nomograms. This scattering is more prominent in the S/D ratio than the PI. The resistance index is not affected by these factors after 28 weeks' gestation.

#### Fetal descending aorta

Besides the umbilical artery, routine Doppler sonographic velocimetry on the descending fetal aorta is possible. As gestation advances, the S/D ratio of the fetal aorta decreases insignificantly [21]. The flow velocity waveform of the fetal aorta shows a continuous forward stream during the whole heart cycle, but when compared to the flow velocity waveform of the umbilical artery, the end-diastolic flow is less than the systolic component. Due to this reason the S/D ratio in the fetal aorta goes farther than the S/D ratio in the umbilical artery. As pregnancy advances, vessel diameters get wider and peripheral resistance decreases, and diastolic flow increases. Nevertheless, this does not cause a significant S/D ratio decrease in the fetal aorta. Resistance and pulsatility indices are not affected significantly, and show a similar course as in the umbilical artery.

#### Middle cerebral artery (MCA)

The most favourably positioned vessel for Doppler sonographic examination of fetal brain perfusion is the middle cerebral artery. Biologic variability of vessels perfusing the fetal brain is excessive due to the fetal activity status. As the pregnancy advances vascular resistance decreases [22]. During the early stages of pregnancy, end-diastolic flow velocities in cerebral vessels are weak, but velocities increase towards the end of gestation. Hyperactivity of the fetus, increase of intrauterine pressure (e.g. polyhydramnios), and external pressure to the fetal head (e.g. by the probe) might erroneously increase end-diastolic flow velocities [23]. Different investigators have undertaken studies - utilizing data obtained from the umbilical artery and MCA - to develop indices for evaluation of intrauterine risk. The results of our study group are on the way to publication.

#### Uterine arteries

In order to evaluate uteroplacental perfusion, measurements taken from the uterine artery give more accurate information than measurements taken from arcuate arteries [10]. Velocities obtained from uterine arteries are higher than from arcuate vessels. This is important in interpreting nomograms, and attention should always be paid to the vessel in which measurements were performed.

Blood flow velocities in the uterine artery depends on the localisation of placenta and gestational age [6]. If the placenta is laterally located, blood flow velocities in the ipsilateral uterine artery is more important than the flow velocities of the contralateral vessel. Differences between flow velocities of the right and left uterine arteries are evident at early stages of pregnancy. However in the third trimester, the difference between the S/D ratio of the vessels decreases up to 0.3-0.4 [10]. If an abnormal flow pattern is observed in the uterine arteries, this most probably indicates insufficient perfusion of the fetoplacental unit, which predicts a high probability for developing preeclampsia, resulting in intrauterine growth retardation [24]. At early stages of pregnancy end-diastolic flow velocities in placental arteries are low, but systolic flow is evident [10]. With trophoblastic invasion and maturation of the uteroplacental vessels, beyond the second trimester the high pressure system is converted to a low pressure system, and vascular resistance declines [25]. The biologic variability after the middle of the second trimester becomes almost stable.

Before 24 weeks' gestation early diastolic notching, due to the immature uteroplacental vascular system, is normally observed. Beyond this gestational age, persistant early diastolic notching is associated with preeclampsia [26-28].

In normal pregnancies, uteroplacental flow velocities become almost stable after the middle of the second trimester, meanwhile fetal blood flow velocities are also altered. With progressing pregnancy, resistance in the umbilical arteries and MCA decreases. Although the impedance to blood flow in the descending aorta is almost stable during pregnancy, advancing gestational age narrrows the biologic variability of the flow spectrum.

According to all these findings, gestational agematched nomograms are recommended to define threshold values, and to differentiate and predict pathologic pregnancies earlier.

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