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Original Research Article

Quantitative assessment of placental vasculature and placental volume in normal pregnancies with the use of 3D Power Doppler

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ABSTRACT

Purpose: The aim of the study was to determine reference values for placental vascular indices and placental volume according to gestational age.
Material/methods: The assessment of placental vascular indices and placental volume using 3D Power Doppler and the Virtual Organ Computer-aided Analysis (VOCAL) technique was performed on 100 normal fetuses between 22 and 41 weeks of gestation. In this study the method of the individual setting of the power Doppler gain value was used. Only patients with entirely visualized placenta were included in the study.
Results: No statistically relevant difference in the values of placental vascular indices and placental volume between different localizations of the placenta was detected. No statistically significant changes to placental vascular indices depending on gestational age were found. It enabled to determine the 10th, 50th and 90th percentile values for the vascularization index (VI), flow index (FI), vascularization-flow index (VFI), which are independent of gestational age. No correlation was found between placental volume and placental vascular indices.
Conclusions: The values of placental vascular indices are constant between the 22nd and 41st week of a normal pregnancy. Placental volume measured with the use of the VOCAL program increases between 22nd and 41st week of a normal pregnancy. In a normal pregnancy the placental vasculature increases adequately to the increase of its volume. The method of the individual setting of the power Doppler gain value makes it possible to achieve comparable values of placental vascular indices regardless of the distance between the probe and the placenta.

1. Introduction

The latest technological progress has enabled the quantitative evaluation of placental vascular indices and placental volume with the use of three-dimensional (3D) Power Doppler and Virtual Organ Computer-aided Analysis (VOCAL) technique. It is necessary to introduce reference values for placental vascular indices and placental volume in order for this method to be useful in predicting and diagnosing pregnancy complications related to the insufficient development of the placenta.

However, to this date there have been few studies concerning the evaluation of placental vasculature with the use of the 3D Power Doppler technique, including only two in which placental vasculature has been assessed for the whole placental volume [1–6].

The aim of the study was to determine the reference values for placental vascular indices: vascularization index (VI), flow index (FI) and vascularization flow index (VFI) and placental volume according to gestational age.

2. Materials and methods

The prospective study included 100 patients in normal pregnancy (gestational age of between 22nd and 41st week), who underwent ultrasound examination in the Department of Gynecology and Obstetrics of the Wroclaw Medical University. All patients gave their informed consent prior to their inclusion in the

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study and the protocol of the study was approved by the Local Ethics Committee.

The Voluson E8 Expert (GE Medical Systems) device with a volumetric abdominal probe RAB 4-8D (4–8 MHz) was used for ultrasound scanning.

The following inclusion criteria were applied: singleton pregnancy, lack of maternal systemic disease, normal fetal anatomy, normal fetal growth, the ability to visualize the entire placenta and gestational age above 22nd week. The exclusion criteria were as follows: multiple pregnancy, maternal systemic disease, fetal malformation, fetal chromosomal abnormality, estimated fetal weight of under the 10th percentile for a given gestational age, unknown date of delivery, abnormal placental localization, inability to visualize the entire placenta, as well as nicotine, alcohol and drug abuse.

The studied group included primarily 148 patients, but the following patients did not meet the criteria of inclusion:

- patients that developed preeclampsia in the course of pregnancy,
- 2 patients with fetal malformations,
- 20 patients with fetal intrauterine growth retardation,
- 24 patients were the visualization of the entire placenta was not possible.

Among this group, irrespective of gestational age, the inability to achieve the 3D sample of the whole placenta was observed in:

- (16.6%) patients with placenta located on the anterior uterine wall,
- 11 (45.8%) patients with placenta located on the posterior uterine wall,
- 1 (4.1%) patient with placenta located in the fundus,
- 8 (33.3%) patients with placenta located laterally.

The visualization of the whole placenta was not possible in 8 (33.3%) patients in the gestational age between 30 and 35 weeks and 16 (66.7%) patients with gestational age in the range between 36 and 40 weeks.

The protocol of ultrasound examination included:

- evaluation of fetal biometry according to Hadlock et al. [7],
- evaluation of fetal anatomy,
- evaluation of the localization of the placenta,
- the use of 3D Power Doppler and the VOCAL technique for the evaluation of placental vascular indices – the vascularization index (VI), flow index (FI) and vascularization-flow index (VFI) for the whole placental volume (PV).

The same pre-established power Doppler signal settings were used during the examination of the placental vasculature: Pulse Repetition Frequency: 0.9 kHz, Frequency: low, Quality: norm, Smooth: 4/5, Artifact: On, Wall Motion Filter: low 1. A gain value was set individually depending on the thickness of maternal adipose tissue and the localization of the placenta. To obtain a good visualization of placental vessels, the gain value was set at maximum and then reduced to eliminate any artifacts. To avoid the shadowing that comes from fetal tissues in cases of localization of placenta on the posterior uterine wall we placed the transducer on the lateral sides of the uterus.

The scanning of the placental vascular tree was performed with the use of 3D static power Doppler (scanning angle 85°, Quality: high, Speckle Reduction Imaging II 3) in the absence of fetal and maternal movements. Only entire scanned placentas were included in the study. The following settings of the VOCAL II (Virtual Organ Computer-aided Analysis) program were used to measure the volume of the placenta: manual trace and rotation angle 30°. Finally the 3D Power Doppler Volume Histogram program automatically calculated the values of VI, FI and VFI within the obtained volume.

2.1. Statistical analysis

The statistical analysis was performed using the STATISTICA 9.0 software (StatSoft Inc., Poland). Two-tailed *t* tests were used to compare the normally distributed variables with homoscedastic variances. The Mann–Whitney *U* test was performed to compare the numeric, non-normal or heteroscedastic variances or ordinal type variables, whereas for the categorical variables the chi-square tests were used.

Histograms plotting, Shapiro–Wilk and Kolmogorov–Smirnov tests enabled the assessment of the distribution of variables within groups.

The Kruskal–Wallis test was used to analyze the correlation between placental vascular indices and the localization of the placenta.

For the analysis of correlation between placental volume and placental vascular indices, the Pearson's correlation analysis was used.

p-Value less than 0.05 was considered statistically significant.

3. Results

3.1. Analysis of correlation between the localization of the placenta and the values of placental vascular indices

In the group of 100 pregnant patients who took part in the study the following localizations of placenta were diagnosed:

- anterior uterine wall: 48 cases (48%)
- posterior uterine wall: 29 cases (29%)
- uterine fundus: 18 cases (18%)
- lateral uterine wall: 5 cases (5%)

The comparison of VI, FI, VFI values depending on the localization of the placenta in normal pregnancies has been presented in Table 1.

No statistically relevant difference was detected in the VI, FI, VFI and PV values between different placental localizations. We present the distribution of VI, FI, VFI values depending on the localization of the placenta in Figs. 1–3.

Table 1
Comparison of VI, FI, VFI values depending on localization of the placenta.

	Localization of the placenta				Value *p**
	Anterior wall (n = 48)	Posterior wall (n = 29)	Fundus (n = 18)	Lateral wall (n = 5)	
VI median (range)	12.00 (3.80–26.00)	11.00 (4.30–33.00)	14.20 (5.80–23.60)	7.00 (5.50–17.00)	0.26
FI median (range)	48.20 (34.00–61.00)	45.00 (28.00–57.00)	47.00 (33.00–58.00)	43.00 (37.00–52.00)	0.08
VFI median (range)	6.00 (1.30–15.00)	4.60 (1.80–15.00)	6.45 (2.60–10.00)	3.00 (2.60–9.00)	0.18

VI, vascularization index; FI, flow index; VFI, vascularization-flow index.
* *p* value calculated by means of the Kruskal–Wallis test.

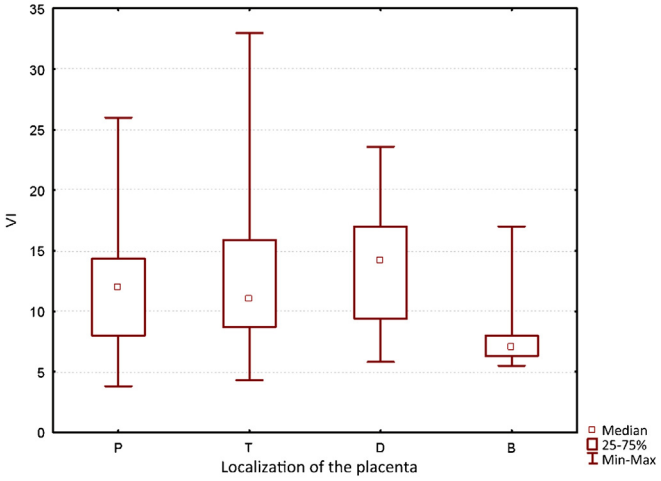

Fig. 1. Distribution of VI values depending on localization of the placenta. P, anterior wall; T, posterior wall; D, uterine fundus; B, lateral wall. Median, median value of the vascularization index (VI); 25–75%, 25–75% interquartile range; Min–Max, minimal and maximal VI values interval.

3.2. Analysis of correlation between placental vascular indices and gestational age

The Pearson correlation analysis was performed in order to evaluate the correlation between placental vascular indices (VI, FI, VFI) and gestational age. Values of the Pearson's correlation coefficient (r) for the VI, FI and VFI were, respectively, as follows: $r = 0.17$ ($p = 0.08$), $r = -0.03$ ($p = 0.76$), $r = 0.12$ ($p = 0.22$). No statistically significant changes to the VI, FI and VFI depending on gestational age were found.

Table 2 presents collectively the values of the 10th, 50th and 90th percentile for the VI, FI and VFI.

3.3. Analysis of correlation between placental volume and gestational age in normal pregnancies

A strong positive correlation between the placental volume and gestational age was revealed by means of the Pearson correlation analysis ($r = 0.84$; $p < 0.001$). This correlation is presented in Fig. 4.

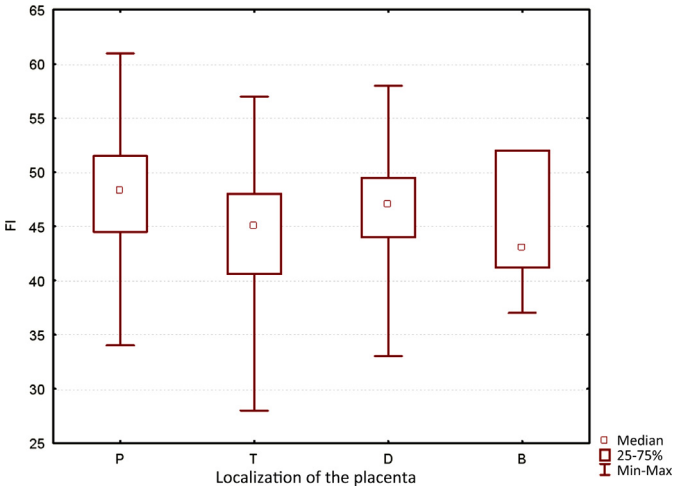

Fig. 2. Distribution of FI values depending on localization of the placenta. P, anterior wall; T, posterior wall; D, uterine fundus; B, lateral wall; Median, median value of the flow index (FI); 25–75%, 25–75% interquartile range; Min-Max, minimal and maximal FI values interval.

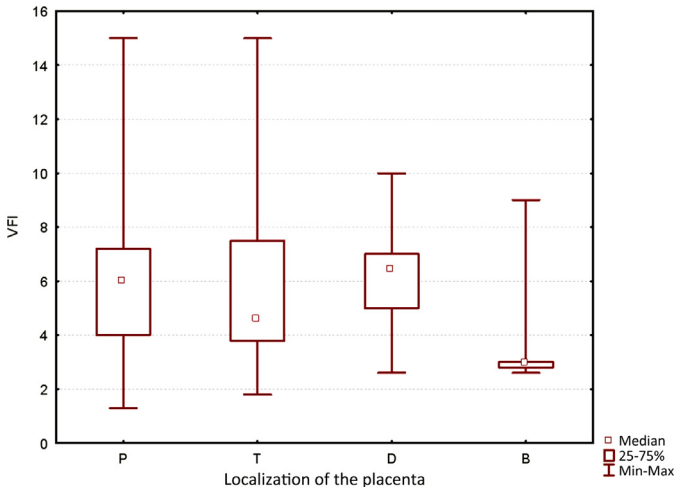

Fig. 3. Distribution of VFI values depending on localization of the placenta. P, anterior wall; T, posterior wall; D, uterine fundus; B, lateral wall; Median, median value of the vascularization-flow index (VFI); 25–75%, 25–75% interquartile range; Min-Max, minimal and maximal VFI values interval.

The use of the linear regression function made it possible to create a formula for calculation of the expected placental volume between the 22nd and 41st week of pregnancy:

$$\text{Expected placental volume}\,(\text{cm}^3) = -116.4 + 12.985 \times \text{gest. week}\,(r = 0.84;\ p < 0.001)$$

3.4. Analysis of correlation between placental vascular indices and placental volume

The Pearson correlation analysis was performed to evaluate correlation between placental vascular indices and placental volume in normal pregnancies. Table 3 presents calculated values of coefficient r and significance level p.

No correlation was found between placental volume and placental vascular indices (VI, FI, VFI).

Table 2
Values of the 10th, 50th and 90th percentile for vascularization index VI, flow index FI and vascularization flow index VFI.

Index	10th percentile	50th percentile	90th percentile
VI	6.1	11.6	21.0
FI	38.5	47.0	53.5
VFI	2.9	5.7	9.0

VI, vascularization index; FI, flow index; VFI, vascularization-flow index.

Table 3
Correlation coefficient r and significance levels p for placental vascular indices VI, FI and VFI.

	Placental volume
VI	$r = 0.17$ $p = 0.08$
FI	$r = 0.05$ $p = 0.6$
VFI	$r = 0.15$ $p = 0.13$

r, correlation coefficient; p, significance levels; VI, vascularization index; FI, flow index; VFI, vascularization-flow index.

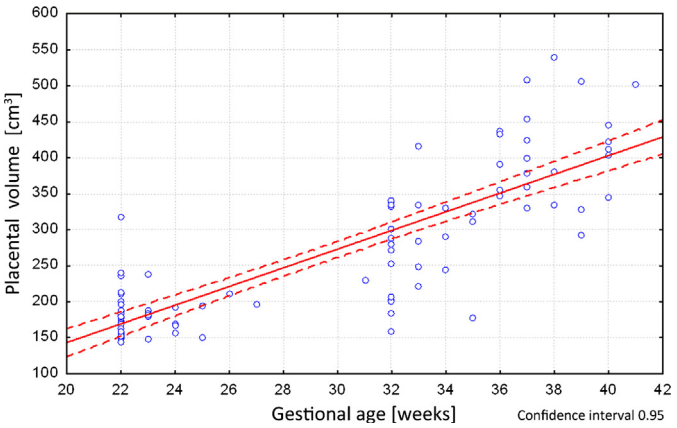

Fig. 4. Analysis of correlation between placental volume and gestational age.

4. Discussion

4.1. Methods used for evaluation of placental vascular indices

In this study the same pre-established power Doppler signal settings were used in order to standardize the assessment of the placental vasculature. The only parameter that was set individually for each patient was the gain value, as the power Doppler signal is dependent on depth. The use of fixed gain value provides an image of a rich vascular tree in cases of placentas located near the probe (i.e. on the anterior uterine wall) and an insufficient image of the vascular tree of placentas located at a distance from the probe (i.e. on posterior uterine wall or in the case of overweight patients). Therefore, the use of the fixed gain value requires maintaining a fixed distance between the probe and the placenta to obtain comparable results. Thus, in studies where the placenta vasculature was assessed using the fixed gain value, the vasculature of the placentas located on the posterior and anterior uterine wall was analyzed separately or only pregnancies with anterior placenta were included [1,8]. Overweight patients were also not included in the study [1]. The above-mentioned difficulties considerably limit the possibility of employing this method in practice.

In this study, as recommended by Martins et al. [9] the lowest gain settings that allow the detection of blood flow and adequate visualization of placental vessels were used.

The study by Raine-Fenning et al. [10] revealed that the gain value has a significant effect on the power Doppler signal and therefore on the VI, FI and VFI values. With the aim of assessing whether the method of the individual setting of power Doppler gain value enables a comparable assessment of placental vascular indices regardless of the distance between the probe and the placenta, a comparison of VI, FI and VFI values depending on the placental localization was performed. No statistically important difference was found regarding the values of VI, FI and VFI between different placental localizations. Thus, it has been demonstrated that an individual set of the power Doppler gain value enables an adequate and comparable assessment of the placental vasculature, without the need to maintain a constant distance between the probe and the placenta, which is impossible in practice.

Another difference regarding the method of ultrasound examination between most of the studies that have been carried out so far and this study is the volume in which placental vascular indices have been measured.

In the first study related to the issue under discussion, performed by Yu et al. [4] in 2003, the values of placental vascular indices were calculated for a fixed, small placental volume. In 2005, Mercé et al. [3] introduced a technique called the "vascular biopsy". The main disadvantage of this method is the assessment of placental vascular indices in only one part of the placenta with the highest density of vessels.

The study by Guiot et al. [1] determined the values of placental vascular indices VI, FI and VFI for different parts of the placenta. In order to standardize the procedure five constant places of measurement were chosen on the cross-section of the placenta. A significant changeability of VI and FI values depending on the place of measurement was revealed using the above-mentioned method. The main disadvantage of the method introduced by Guiot et al. [1] is that it is time-consuming because of the necessity of measuring vasculature in five different places. Furthermore, the obtained results still do not reflect the vasculature of the whole placenta.

In this study the method of measuring the VI, FI and VFI placental vascular indices for the whole placental volume was used. This method makes it possible to gain full information on placental vasculature. It is especially important because, as shown in the recent studies of Lai et al. [11] and Negrini et al. [12], in normal pregnancies there are significant differences in the values of the vascularization index, flow index and vascularization-flow index between different parts of the placenta due to a high regional variability of placental perfusion. The technique of measuring placental vascular indices for the whole placental volume was used also by de Paula et al. [5]. The main disadvantage of this technique is the need to exclude all patients in whose case the placenta cannot be entirely visualized.

4.2. Assessment of placental vasculature in normal pregnancies

Reference data connected with the relationship between the placental vascular indices and gestational age are contradictory. In the study by Yu et al. [4], which included 100 patients who were 20–40 weeks pregnant, the increase of VI, FI and VFI values was revealed during the pregnancy. Mercé et al. [3] stated in their study including 99 patients who were 15–40 weeks pregnant that there is a correlation between the values of placental vascular indices and gestational age. The most significant correlation was observed in the case of the flow index – its value increases steadily with gestational age. Vascularization index shows a high spread of its values before the 30th week of pregnancy, then it stabilizes and after the 37th week it gradually decreases until the date of delivery. The change of the vascularization flow index VFI with gestational age reflects the changes of the FI and VI values [3]. Giuot et al. [1] revealed in a group of normal pregnancies between the 23rd and 37th week that the values of placental vascular indices are independent of gestational age.

The analysis of the results of the study has demonstrated that in normal pregnancies the values of placental vascular indices are constant between the 22nd and 41st week of pregnancy. It enabled to determine the 10th, 50th and 90th percentile values for the VI, FI and VFI indices, which are independent of gestational age. It might be useful for an easy discrimination between the normal and abnormal placental vasculature [5,6].

Taking into consideration the methodology of the studies described above, it can be concluded that only in studies assessing placental vasculature in small part of the placenta [1,3] a change of placental vascular indices according to gestational age was revealed. In the studies where vasculature was assessed in five different places of the placenta [4], as well as for the whole placental volume [4,5] values of placental vasculature indices remain constant during the whole pregnancy.

4.3. Assessment of placental volume in normal pregnancies

Reference data for placental volume in the first part of normal pregnancy were presented in the study of Boito et al. [13]. It was demonstrated that the average placental volume measured with

the use of VOCAL technique in the 10th week of pregnancy was 15.8 ml, whereas in the 23rd week of pregnancy it was 198.4 ml. de Paula et al. [5] in 2008 provided reference values for placental volume between the 12th and 40th week of pregnancy. The average placental volume was: 83 ml in 12th week, 181.5 ml in the 20th week, 304.6 ml in the 30th week and 427.7 ml in the 40th week of pregnancy respectively [14]. In this study the mean placental volume in 22nd week of pregnancy was 182.6 ± 35.4 ml, in the 32nd week 274.4 ± 65.1 ml and in the 39th/40th week 406.6 ± 73.9 ml. As shown our results are in agreement with above-mentioned studies.

In this study, a strong positive correlation was demonstrated between placental volume and gestational age. The use of the linear regression function enables to create a formula for calculation of the expected placental volume between the 22nd and 41st week of pregnancy.

In numerous studies, a relation was revealed between a decreased placental volume and the intrauterine growth restriction (IUGR), preeclampsia and chromosomal abnormalities [6,15–18]. Therefore, the introduction of the reference values, which was attempted in the study by Boito et al. [13], de Paula et al. [5] and in this study, seems to be of clinical use for diagnosis of these complications.

In this study a correlation between placental vasculature, evaluated with the use of the VI, FI and VFI indices and its volume was assessed. No correlation, neither positive nor negative, was showed between placental vasculature indices and its volume. Knowing that placental vascular indices are constant, while placental volume increases during pregnancy it can be concluded that in normal pregnancy placental vasculature increases adequately to the increase in placental volume.

5. Conclusions

The values of placental vascular indices measured by 3D Power Doppler are constant between the 22nd and 41st week of a normal pregnancy. Placental volume measured with the use of the VOCAL program increases between 22nd and 41st week of a normal pregnancy.

The fact of maintaining the constant values of placental vascular indices with the increasing placental volume leads to the conclusion that in normal pregnancy placental vasculature increases adequately to the increase of its volume.

The method of individual setting of power Doppler gain value enables to achieve comparable values of placental vascular indices regardless of the distance between the probe and the placenta.

Conflict of interests

The authors declare no conflict of interest.

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