

Detection of uterine artery hemodynamic changes in patients with gestational hypertension based on Doppler ultrasonography

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Summary

Doppler ultrasonography has great value in detecting the changes in uterine artery hemodynamics in patients with pregnancy-induced hypertension. In the present study, 50 women with gestational hypertension and 50 normal pregnant women were selected. The comparison of the general data and laboratory examination revealed that the pre-pregnancy body mass index (BMI) and mean arterial pressure were significantly higher in the gestational hypertension group, when compared to the normal group ($P < 0.05$), while the serum albumin value was significantly lower in the gestational hypertension group, when compared to the normal group ($P < 0.05$). The Doppler ultrasonography revealed that the S/D, PI and RI values were significantly higher in the gestational hypertension group, when compared to the normal group ($P < 0.05$). In comparing the pregnancy outcome, the gestational hypertension group had shorter pregnancy termination time, lower birth weight, and more adverse outcomes, such as premature delivery, fetal distress and fetal growth restriction (FGR) ($P < 0.05$). The multi-variate regression analysis suggested that only the hemodynamic changes of the uterine artery can be used for predicting the outcome of pregnancy. These results revealed that the uterine artery hemodynamics of patients with gestational hypertension present with significant changes, when compared to normal women, which can be used in predicting adverse pregnancy outcomes. Targeted intervention can be provided to women with gestational hypertension to reduce the adverse pregnancy outcomes, according to the ultrasonography results.

Key words: Gestation period; Hypertension; Uterine artery; Doppler ultrasonography; Hemodynamics.

Introduction

Gestational hypertension is a common disease during pregnancy [1], which can seriously affect the health of mothers and infants [2]. It is an important cause of maternal, fetal and neonatal deaths, and can increase the probability of adverse pregnancy outcomes. It was found that patients with gestational hypertension are three times more likely to give birth to low-birth-weight infants, when compared to normal pregnant women, and the likelihood of low neonatal score is higher [3]. Finding effective methods to monitor the condition of patients with gestational hypertension and predict the adverse outcome of pregnancy are of great significance to reduce the possibility of adverse outcomes. Doppler ultrasound is a good modality to detect hemodynamic changes. Yakasai *et al.* [4] performed ultrasound examinations on the middle cerebral artery, umbilical artery and uterine artery of 34 patients with gestational hypertension, and found that the maximum systolic flow velocity of the uterine artery was normal in only six patients. This indicates that the detection of abnormalities based on the Doppler ultrasound plays an important role in the management and treatment of gestational hypertension. Goswami [5] reported that pregnant women with an abnormal uterine artery waveform detected by Doppler ul-

trasound were likely to suffer from gestational hypertension and preeclampsia. Furthermore, among these women, 3% of these women might have abrupt placental abruption, and 8% of these women might have premature delivery. The changes in the uterine artery are closely correlated to pregnancy outcomes, and treatment can be timely performed after the ultrasound examination. Mitsui *et al.* [6] monitored the uterine artery blood flow of 76 patients with gestational hypertension, and found that patients with early gestational hypertension had a high frequency of early diastolic gap, and a higher average umbilical artery pulsatility index (UAPI). They also found significant differences in UA resistance between the FGR group and non-FGR group, indicating that early gestational hypertension can be prevented by monitoring the UA resistance and UA blood flow. Through ultrasonic detection, Arakaki *et al.* [7] found that the uterine artery and placenta volume of patients with early gestational hypertension were significantly different, when compared to those of patients with late gestational hypertension and normal pregnant women, and that low pulsatility index (PI) and small placenta volume can be used to predict early gestational hypertension. In the present study, uterine artery Doppler ultrasonography was performed on 50 patients with gestational hypertension and normal pregnant

Table 1. — Comparison of the general data of pregnant women.

General data	Gestational hypertension group	Normal group	<i>t</i> value	<i>P</i> value
Age (years)	27.68 ± 3.45	26.84 ± 3.68	-1.732	0.087
Gestational weeks (week)	32.13 ± 2.22	31.67 ± 1.31	-1.256	0.668
Gravidity (time)	1.92 ± 0.71	1.81 ± 1.23	-1.948	0.059
Pre-pregnancy BMI (kg/m ²)	24.56 ± 4.12	20.97 ± 3.68	-4.268	< 0.001
Heart rate (bpm)	84.62 ± 11.34	85.67 ± 10.67	1.214	0.264
Mean arterial pressure (mmHg)	116.43 ± 10.67	84.51 ± 9.21	-23.648	< 0.001

Table 2. — The comparison of laboratory examinations of pregnant women.

Laboratory examination	Gestational hypertension group	Normal group	<i>t</i> value	<i>P</i> value
Fasting blood glucose (mmol/L)	4.63 ± 0.82	4.62 ± 0.76	-0.362	0.763
Blood urea nitrogen (mmol/L)	3.51 ± 1.28	3.48 ± 0.97	-2.286	0.026
Blood albumin (g/L)	31.29 ± 5.62	38.74 ± 5.73	7.626	< 0.001
Hemoglobin (g/L)	118.78 ± 15.61	118.62 ± 16.24	-0.152	0.861

Table 3. — Comparison of hemodynamic indicators.

Index	Gestational hypertension group	Normal group	<i>t</i> value	<i>P</i> value
AT (s)	0.12 ± 0.02	0.11 ± 0.03	0.964	0.347
S/D	2.46 ± 0.79	1.86 ± 0.51	5.637	< 0.001
PI	0.98 ± 0.42	0.63 ± 0.27	6.412	< 0.001
RI	0.55 ± 0.13	0.42 ± 0.07	6.814	< 0.001

women, and the relevant hemodynamic indexes were analyzed and compared to determine its values in monitoring the disease condition and predicting the adverse pregnancy outcome.

Gestational Hypertension

Gestational hypertension is one of the special diseases in the gestation period, which manifests as hypertension, edema and proteinuria. Patients with mild symptoms may present with mild headache and hypertension, while patients with severe symptoms may present with headache, nausea, significantly increased blood pressure, coma, convulsion, and liver or kidney function failure. Magnesium sulfate is the main drug for treating gestational hypertension, and diazepam and amyltal sodium can also be used for sedation. Induced labor or caesarean section is advocated, according to the disease condition.

The hemodynamics would change in early pregnancy [8] to maintain the normal growth of the fetus. Furthermore, the blood volume, systemic vascular resistance and arterial blood pressure of the parent body would all change. The uterine artery is the main supplying artery of the uterus. During normal pregnancy, blood volume and velocity would increase [9, 10]. The exchange of nutrients between maternal blood and fetal blood is of great significance to the normal growth of the fetus. When the resistance of the uterine artery decreases, the elevated blood volume is transported to the placenta to improve the ability to transmit oxygen and nutrition to the fetus. When uterine artery resistance increases, placental circulatory ischemia

may cause gestational hypertension. The changes in uterine artery hemodynamics can be detected by Doppler ultrasonography, in order to understand the fetal status and predict the pregnancy outcome.

Research Methods

Research subjects

Fifty pregnant women with gestational hypertension, who were admitted to the First People's Hospital of Nantong, Jiangsu, China, were selected. The age of these patients ranged within 22-36 years old (mean age: 27.68 ± 3.45 years old), and the mean number of gestational weeks was 32.13 ± 2.2 weeks. Furthermore, 50 normal pregnant women were also selected. The age of these subjects ranged within 23-37 years old (mean: 26.84 ± 3.68 years old), and the mean number of gestational weeks was 31.67 ± 1.3 weeks. All research subjects were informed with the aim and procedures of the experiment, and provided a signed informed consent.

The inclusive criteria included single pregnancy, without hypertension, diabetes, and other cardiovascular and cerebrovascular diseases before pregnancy, but without cognitive disorders.

Experimental procedures

The general data of the 100 pregnant women were collected, and conventional laboratory examinations were performed.

The ultrasound examination was performed using a GE V730 color Doppler ultrasonic diagnosis apparatus, and the frequency of the probe was 2-6 MHz. Pregnant woman took

Table 4. — Comparison of pregnancy outcomes.

	The gestational hypertension group	The normal group	<i>t</i> value	<i>P</i> value
Termination time of gestation (week)	37.46 ± 2.67	39.61 ± 2.53	4.658	< 0.001
Birth weight of newborns (g)	2505.67 ± 542.36	3368.92 ± 543.67	5.621	< 0.001

Table 5. — The multivariate regression analysis results.

Variable	Odd ratio	95% confidence interval	Value of <i>P</i>
General data (X1)	0.246	0.026-2.125	0.486
Laboratory examination (X2)	0.314	0.045-2.085	0.321
Uterine arterial hemodynamics (X3)	10.698	2.896-41.325	0

a supine position, and maintained stable breathing. Amniotic fluid, fetal movement and fetal heart were examined. The uterine artery was identified, and the blood flow was detected using the ultrasound diagnosis apparatus. Color Doppler flow imaging was used for sampling at the site, which was 1 cm behind the external iliac artery, at an angle smaller than 30°. The maximum uterine artery systolic velocity (Vs) and end diastolic velocity (Vd), acceleration time (AT), Vs-to-Vd ratio (S/D), PI and resistance index (RI) were observed.

All pregnant women who participated in the experiment were followed-up to determine the pregnancy outcome, number of gestational weeks, and weight of the newborns. Pregnancy outcome was classified as normal or adverse. Adverse pregnancy outcomes include abnormal phenomena, such as premature delivery, fetal distress and fetal growth restriction (FGR).

Statistical method

The statistical analysis was performed using SPSS 13.0. The measurement data were expressed as $\bar{x} \pm s$, and processed using *t*-test, while the enumeration data were expressed as *n*, and processed using Chi-square test. A *P*-value of < 0.05 was considered statistically significant.

Results

Comparison of the general data

The gestational hypertension group and normal group had no significant difference in terms of age, gestational week and gravidity. The pre-pregnancy BMI in the gestational hypertension group was significantly higher than that in the normal group ($P < 0.001$), which reached $24.56 \pm 4.12 \text{ kg/m}^2$. However, there was no significant difference in heart rate. The mean arterial pressure in the gestational hypertension group was also significantly higher than that in the normal group ($P < 0.001$), which reached $116.43 \pm 10.67 \text{ mmHg}$.

Comparison of laboratory examination

The laboratory examination results revealed that there was a significant difference in serum albumin between the two groups ($P < 0.001$). The serum albumin value in the gestational hypertension group was $31.29 \pm 5.62 \text{ g/L}$, while the value in the normal group was $38.74 \pm 5.73 \text{ g/L}$. The

hemoglobin value in the gestational hypertension group was significantly lower than that in the normal group.

Comparison of uterine arterial hemodynamics

The spectrogram of the uterine artery is presented in Figures 1 and 2. Table 3 and Figure 3 shows the comparison of hemodynamic indicators. It was found that the difference in AT in the gestational hypertension group and normal group was not statistically significant. The S/D in the gestational hypertension group was 2.46 ± 0.79 , while the value in the normal group was 1.86 ± 0.51 . The S/D value was significantly higher in the gestational hypertension group than in the normal group, and the difference was statistically significant ($P < 0.001$). Furthermore, the gestational hypertension group had significantly higher PI and RI, when compared to the normal group ($P < 0.001$).

Comparison of pregnancy outcomes

Table 4 and Figure 4 shows the comparison of pregnancy outcomes between the two groups. The termination time of pregnancy in the gestational pregnancy group was significantly shorter than that in the normal group ($P < 0.001$). The difference in birth weights of newborns were also statistically significant ($P < 0.001$), and the birth weights of newborns was significantly lower in the gestational hypertension group. In the gestational hypertension group, there were 27 cases of premature birth, nine cases of fetal distress and 24 cases of FGR, while in the normal group, there were only four cases of premature birth, two cases of fetal distress and three cases of FGR.

Prediction of adverse pregnancy outcomes

The multivariate regression analysis was performed on factors that might cause adverse pregnancy outcomes according to the above results. The analysis results are presented in Table 5.

General examination, laboratory examination and uterine artery blood flow were used as variables to predict the adverse pregnancy outcomes. According to the regression results, merely the results of the uterine artery hemodynamics can be used to predict the pregnancy outcomes ($P < 0.001$). Pregnancy outcomes can be predicted by Doppler ultrasound of the uterine artery.

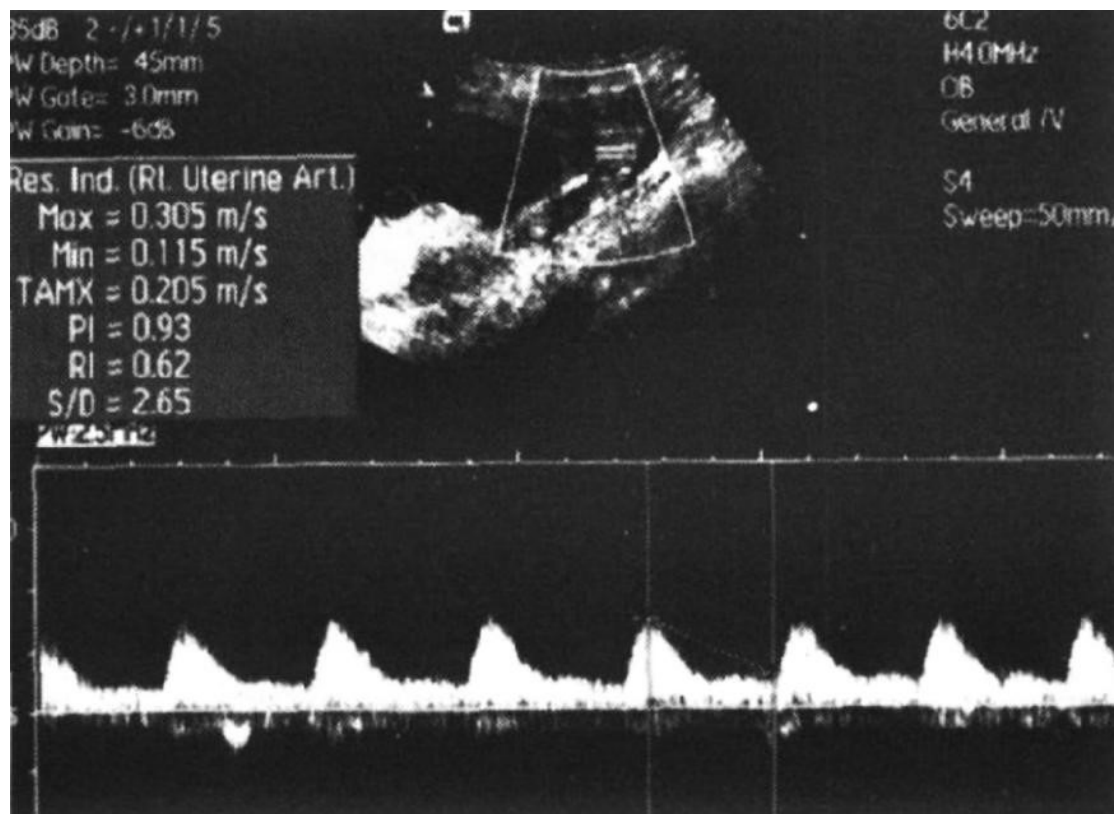


Figure 1. — The spectrogram of the uterine artery in the gestational hypertension group.

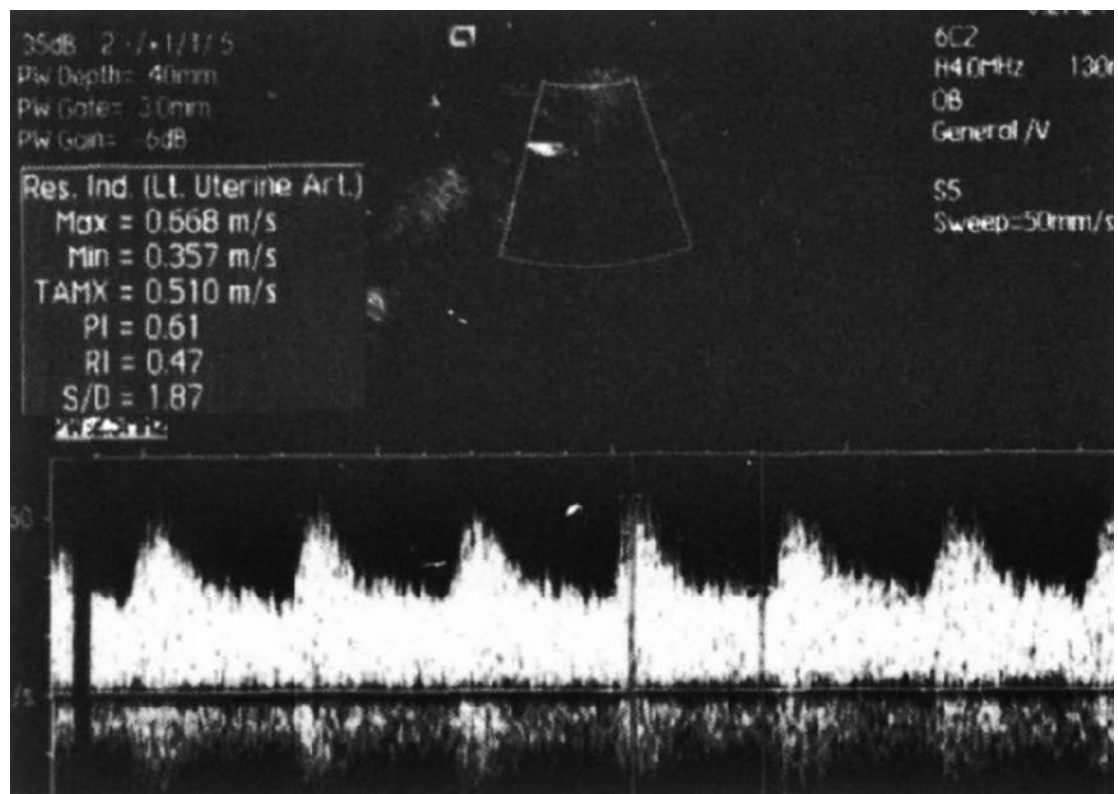


Figure 2. — The spectrogram of the uterine artery in the normal group.

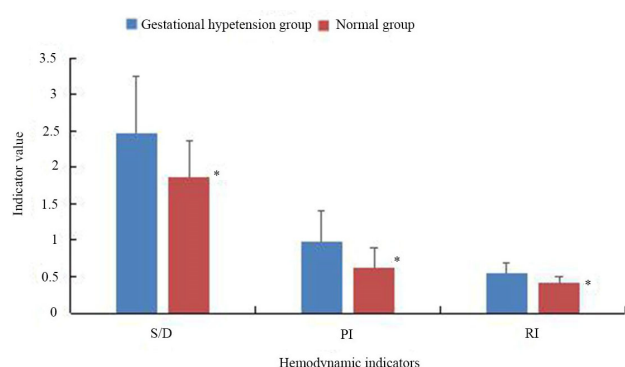


Figure 3. — The comparison of hemodynamic indicators. *, indicates that $P < 0.05$, and the difference was statistically significant.

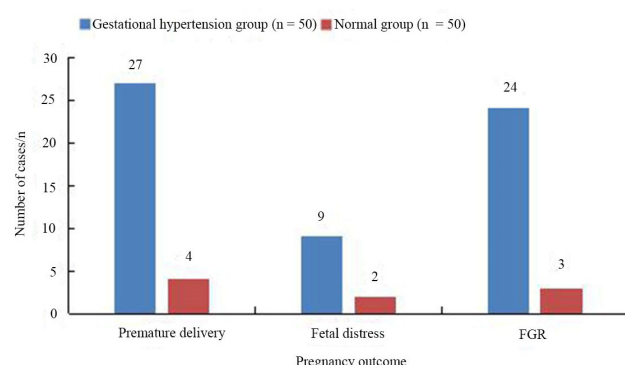


Figure 4. — Comparison of pregnancy outcomes.

Conclusion and Discussion

Gestational hypertension is one of the unique and influential diseases in the gestation period, and its incidence ranges within 5-10% [11]. Monitoring the development of gestational hypertension in real time is of great significance for the maintenance of maternal and infant health. It was found that the changes in hemodynamics are closely correlated to the status of pregnant women, and have a significant impact on pregnancy outcomes.

In the present study, 50 pregnant women with gestational hypertension and 50 normal pregnant women were selected as the research subjects. The general data and laboratory examination results revealed that there were significant differences in individual indicators between the two groups. The pre-pregnancy BMI and mean arterial pressure were significantly higher in the gestational hypertension group than in the normal group ($P < 0.05$). However, the serum albumin value was significantly lower in the gestational hypertension group than in the normal group ($P < 0.05$). Ehrenthal *et al.* [12] reported that the risk of gestational hypertension increased with the increase in pre-pregnancy BMI, and this was not associated with other obesity-related complications.

The uterine artery can provide blood supply and nutrition for the fetus, in order to meet the needs of fetal growth and

development during pregnancy. During normal pregnancy, the uterine artery PI would decrease, resistance would gradually decrease, and these would return to the pre-pregnancy level at six weeks after delivery [13]. The hemodynamic parameters of the uterine artery can be obtained by Doppler ultrasonography, and the blood supply of the uterine placenta can be directly understood. The results of the present study revealed that the S/D, PI and RI were significantly higher in the gestational hypertension group than in the normal group ($P < 0.05$), indicating that abnormal uterine artery hemodynamics is correlated to the symptoms of gestational hypertension. With the aggravation of gestational hypertension, edema appears in the placenta, the RI of the uterine artery would increase, and the survival of the fetus would be greatly affected, resulting in adverse outcomes.

The changes in uterine artery hemodynamics in patients with gestational hypertension causes the blood supply of oxygen exchange between the mother and fetus to be insufficient. This prevents the fetus from receiving the nutrients needed for normal development, which can easily lead to fetal distress, FGR and other adverse outcomes. When abnormal waveforms of the uterine artery were detected by ultrasonography, the probability of occurrence of placental ischemia and placental infarction was higher [14]. The follow-up results of pregnancy outcomes of the two groups of pregnant women revealed that the gestational hypertension group had significantly shorter pregnancy termination time and lower birth weight of newborns, when compared to the normal group ($P < 0.05$). However, the number of adverse outcomes in the gestational hypertension group was larger as the number of cases of premature birth, fetal distress and FGR in the gestational hypertension group became significantly larger than those in the normal group. These findings suggest that gestational hypertension can produce a large impact on pregnancy outcome. The multivariate regression analysis of the general data, laboratory examination and uterine artery hemodynamics suggested that the change in uterine artery hemodynamics is the only index that can predict the adverse outcome of pregnancy.

In summary, Doppler ultrasonography can monitor the development of uterine artery hemodynamics in patients with gestational hypertension, and provides a more timely and accurate understanding of the changes in placental function, in order to make a reliable prediction of the trend of the disease and pregnancy outcomes, and take measures to reduce the occurrence of adverse pregnancy outcomes.

Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the First People's Hospital of Nantong, Jiangsu, China (approval number: 2019-22).

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Conflict of Interest

The authors have no conflicts of interest.

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References

- [1] Clark S.M., Dunn H.E., Hankins G.D.: "A review of oral labetalol and nifedipine in mild to moderate hypertension in pregnancy". *Semin Perinatol*, 2015, 39, 548-555.
- [2] Kintiraki E., Papakatsika S., Kotronis G., Goulis D.G., Kotsis V.: "Pregnancy-Induced hypertension". *Hormones (Athens)*, 2015, 14, 211-223.
- [3] Muti M., Tshimanga M., Notion G.T., Bangure D., Chonzi P.: "Prevalence of pregnancy induced hypertension and pregnancy outcomes among women seeking maternity services in Harare., Zimbabwe". *BMC Cardiovasc Disord*, 2015, 15, 111.
- [4] Yakasai I., Tabari M., Rabi A.: "Pattern of fetal arterial blood flow in selected vessels in patients with pregnancy induced hypertension in Aminu Kano Teaching Hospital Kano., Nigeria". *West African Journal of Radiology*, 2013, 20, 9.
- [5] Goswami G.: "Uterine artery doppler study for prediction of adverse outcome in high risk pregnancy". 2015, 4, 9735-9742.
- [6] Mitsui T., Masuyama H., Maki J., Tamada S., Hirano Y., Eto E., *et al.*: "Differences in uterine artery blood flow and fetal growth between the early and late onset of pregnancy-induced hypertension". *J Med Ultrason (2001)*, 2016, 43, 509-517.
- [7] Arakaki T., Hasegawa J., Nakamura M., Hamada S., Muramoto M., Takita H., *et al.*: "Prediction of early- and late-onset pregnancy-induced hypertension using placental volume on three-dimensional ultrasound and uterine artery Doppler". *Ultrasound Obstet Gynecol*, 2015, 45, 539-543.
- [8] Aprile F.T., Luca G.D., Bruno M.G.: "Arterial hypertension during pregnancy, An appraisal on risk factors". *Italian Journal of Gynaecology & Obstetrics*, 2010, 22, 202-226.
- [9] Hu X.Q., Xiao D., Zhu R., Huang X., Yang S., Wilson S., *et al.*: "Pregnancy upregulates large-conductance Ca(2+)-activated K(+) channel activity and attenuates myogenic tone in uterine arteries". *Hypertension*, 2011, 58, 1132-1139.
- [10] Ampey B.C., Morschauser T.J., Ramadoss J., Magness R.R.: "Domain-Specific Partitioning of Uterine Artery Endothelial Connexin43 and Caveolin-1". *Hypertension*. 2016, 68, 982-988.
- [11] Foo L., Tay J., Lees C.C., McEniery C.M., Wilkinson I.B.: "Hypertension in pregnancy, natural history and treatment options". *Curr Hypertens Rep.*, 2015, 17, 36.
- [12] Ehrental D.B., Jurkovic C., Hoffman M., Jiang X., Weintraub W.S.: "Prepregnancy body mass index as an independent risk factor for pregnancy-induced hypertension". *J Womens Health (Larchmt)*, 2011, 20, 67-72.
- [13] Ogueh O., Clough A., Hancock M., Johnson M.R.: "A longitudinal study of the control of renal and uterine hemodynamic changes of pregnancy". *Hypertens Pregnancy*, 2011, 30, 243-259.
- [14] Thuring A., Marsal K., Laurini R.: "Placental ischemia and changes in umbilical and uteroplacental arterial and venous hemodynamics". *J Matern Fetal Neonatal Med.*, 2012, 25, 750-755.

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