GENERAL OBSTETRICS AND GYNECOLOGY: OBSTETRICS

Change in pulse wave velocity throughout normal pregnancy and its value in predicting pregnancy-induced hypertension: A longitudinal study

Mizuho Oyama-Kato, MD, Masahide Ohmichi, MD, PhD,* Kazuhiro Takahashi, MD, PhD, Sachiko Suzuki, Noriko Henmi, MD, Yukio Yokoyama, MD, PhD, Hirohisa Kurachi, MD, PhD

Department of Obstetrics and Gynecology, Yamagata University School of Medicine, Iidanishi, Yamagata, Japan

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Objective: We longitudinally examined the changes of brachial to ankle distensibility using pulse wave velocity (PWV) throughout pregnancy and its difference between normal pregnancy and pregnancy-induced hypertension (PIH) groups.

Study design: One hundred and eighty-three pregnant women were included in this study. The PWV examinations were performed in a longitudinal way during the first, second, and third trimesters of pregnancy, and immediately and 1 month after delivery.

Results: In normal pregnancies, the PWV significantly decreased at the second trimester, increased from the third trimester through immediately after delivery, and decreased again at 1 month after delivery. In PIH patients, it increased in proportion to the progression of gestation.

Conclusion: We monitored the longitudinal changes in PWV and constructed a PWV normogram during pregnancy. The predictive value of PWV and blood pressure for PIH was higher than that of blood pressure alone, suggesting the usefulness of measuring PWV to predict PIH.

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During normal pregnancy, both the maternal total blood volume and the cardiac output increase markedly. The increase in maternal total blood volume begins during the first trimester, and reaches a plateau at the beginning of the third trimester. Cardiac output rises by 40% to 50% above nonpregnant values. Because of hemodynamic adaptations, however, arterial blood pressure decreases during the first and middle trimesters of pregnancy.1 On the other hand, because of a lack of appropriate adaptation of hemodynamics, arterial blood pressure increases in pregnancy-induced hypertension...
(PIH). However, the precise mechanisms of these phenomena remain unknown.

Recent advances in ultrasonography have made possible the detection of atherosclerotic events. Flow-mediated dilatation (FMD) is an established index for evaluating endothelial function. FMD tends to increase during normal pregnancy, suggesting that the enhancement of nitric oxide production in normal pregnancy may contribute to the decrease in peripheral resistance. FMD decreased in PIH, indicating that endothelial dysfunction plays a role in the pathophysiology of PIH. However, there are several pathological features of PIH in addition to endothelial dysfunction. It was reported that PIH is associated with increased cerebral arterial wall stiffness. Although FMD is not affected by arterial structure (elastic fibers or collagen), pulse wave velocity (PWV) reflects tunicamedia function and is affected by pathohistological changes of arterial structure. For measuring PWV, estimating the aortic PWV by measuring the carotid and femoral distensibility has been used. However, this is an invasive procedure, complex and time consuming, and it requires a specially qualified operator. Recently, a new automatic device has been developed for measuring brachial-to-ankle PWV (baPWV), which was shown to have a good correlation with aortic PWV, by measuring the brachial and tibial distensibility. This method is noninvasive and rapid, and the repeatability is good. In addition, the simplicity of this method is well-suited for use in screening large populations.

There have been only a few reports which examined PWV during pregnancy cross-sectionally. There also have been only a few longitudinal reports about PWV throughout pregnancy, but the number of subjects was so small. It was reported that the value of PWV significantly decreased throughout pregnancy compared to that in the nonpregnant state. However, neither the longitudinal changes in PWV throughout pregnancy in this large number of subjects nor the comparison of the value of PWV between normal pregnancy and PIH has been reported so far. These considerations led us to examine the baPWV value noninvasively during pregnancy and to evaluate the potential utility of this measuring PWV as a predictor of PIH. To our knowledge, this is the first longitudinal study of PWV during pregnancy in a large population.

**Material and methods**

**Subjects**

One hundred eighty-three pregnant women aged between 18 and 39 years were recruited from the patients visiting the obstetric outpatient clinic of Yamagata University Hospital and Yokoyama Hospital between October 2002 and December 2003. All procedures were approved by the local ethics committee, and written informed consent was obtained from all patients. Clinical characteristics of this study population are summarized in Table I. We excluded subjects with chronic hypertension, hyperlipemia, diabetes mellitus, or bicornal pregnancy. All subjects were nonsmokers. These 183 pregnant women were assessed for baPWV and other studied parameters longitudinally in the first trimester (gestational weeks 9-14, mean ± SD 10.50 ± 1.60 weeks), in the second trimester (gestational weeks 21-29, mean ± SD 25.03 ± 1.75 weeks), in the third trimester (gestational weeks 32-39, mean ± SD 33.94 ± 1.12 weeks), after their delivery (3-5 days after delivery, median 4 days), and at 1 month after their delivery. The gestational ages at delivery were 38.90 ± 1.28 weeks in normal group and 38.81 ± 1.42 weeks in PIH group.

We also studied blood pressure, body weight, urinary protein, urinary sugar, and edema. All newborns were studied with respect to their birth weight, Apgar score, and complications. PIH was diagnosed according to the definition of the American College of Obstetrics and Gynecology. PIH was defined as hypertension or proteinuria after 20 weeks of gestation in previously normotensive women with no proteinuria. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg. Proteinuria was defined as 2+ or more on urinalysis or proteinuria greater than 300 mg in a 24-hour collection. Five severe cases of PIH were observed.

**Methods**

Brachial-to-ankle PWV was determined using an automatic device (the model BP-203PRE, Colin, Inc, Komaki, Japan), which allows pulse wave recording and automatic calculation of baPWV as previously described and validated. This device records PWV, blood pressure, electrocardiogram, and heart sounds simultaneously. After 5 minutes’ rest in the supine position, pressure wave forms of the brachial and tibial arteries were recorded with cuffs wrapped on both brachia and
ankles, the electrocardiogram was recorded using electrodes placed on both wrists, and a microphone for detecting heart sounds was placed on the left edge of the sternum. The pressure waveforms obtained by the cuff were derived from a plethysmographic sensor that determines volume pulse form and an oscillometric sensor that measures blood pressure. Volume waveforms at the brachia and ankles were stored for a sampling time of 10 seconds with automatic gain analysis and quality adjustment. Sufficient waveform data were obtained in this stored sample. The characteristic points of waveforms were determined automatically according to the phase velocity theory. The components over 5 Hz were stored and the initial rise of wave form was determined. The time interval between the brachium and ankle (ΔT_{ba}) was the time interval between the initial rise in the brachial and tibial pressure waveforms. The distance between sampling points of baPWV was calculated automatically based on body height. The length from aortic valve to ankle (L_a) was estimated using the following equation: L_a = 0.8129 \times \text{height} + 12.328 (all values for length and height are in centimeters). The length from the aortic valve to the brachium (L_b) was estimated using the following equation: L_b = 0.2195 \times \text{height} - 2.074. BaPWV was estimated using the following equation: baPWV = (L_a - L_b)/ΔT_{ba}. Bilateral baPWV and brachial and ankle blood pressures were measured automatically and simultaneously using this device, and we used only left brachial blood pressure in our analyses. PWV values were measured in the first, second, and third trimesters, and soon after delivery and 1 month after delivery in this study.

Statistics

Data are expressed throughout as the mean ± SD. Statistical analysis was performed using one-way analysis of variance (ANOVA) for repeated measures (Statview). If the ANOVA indicated a significant difference, then a Scheffe’s post hoc test was performed. The unpaired t test was used for comparisons between 2 groups. Values of P < .05 were considered to indicate statistical significance.

Results

Changes in PWV in normal pregnancy group

We first examined the longitudinal changes in PWV value from the first trimester through 1 month after delivery in the normal pregnancy group (n = 167) (Figure 1). In comparison with the value of PWV in the first trimester, PWV significantly (P < .01) decreased in the second trimester. In comparison with PWV in the second trimester, the PWV value tended to slightly increase in the third trimester, and significantly (P < .01) increased immediately after delivery followed by a slight decrease at 1 month after delivery.

Changes in PWV in PIH group

We next examined the changes in the blood pressure and PWV value from the first trimester through 1 month after delivery in the PIH group. In contrast to the results in the normal pregnancy group, PWV did not decrease between the first and second trimesters in the PIH group.
group. PWV significantly \((P < .01)\) and markedly increased after delivery, followed by a decrease 1 month after delivery (Figure 2). PIH was diagnosed on the basis of the criteria described above.

**Comparison of the value of PWV between normal pregnancy and PIH groups**

We also compared the changes in the PWV value between the normal pregnancy and PIH groups. Figure 3A shows the changes in the PWV value in the 2 groups from the first trimester through 1 month after delivery. The PWV value in the PIH group was significantly \((P < .01)\) higher than that in the normal pregnancy group in the second and third trimesters, and after delivery.

The most striking difference in the changes in the PWV value between the 2 groups was that PWV decreased in the second trimester compared with that in the first trimester in the normal pregnancy group, whereas such a decrease was not observed in the PIH pregnancy group. The percent change in the PWV value in the second trimester relative to that in the first trimester was compared between the 2 groups (Figure 3B). The difference in the percent change in the PWV value between the groups was statistically significant \((P < .01)\).

We next assessed the value of measuring PWV in addition to BP by calculating the predictive value for PIH with the use of either PWV or BP, or both. When using either only PWV value or systolic blood pressure \((sBP)\) increase in the second trimester compared with those in the first trimester as an index, the positive predictive value for PIH was \(41.1\%\) or \(29.6\%\), respectively. However, the positive predictive value increased to \(60.0\%\) when both PWV value and sBP were used as an index (Table II). We used 50 cm/sec (PWV) and 10 mmHg (sBP) cut-off values because the standard deviations in each case were under these values. The negative predictive value was \(94.6\%\) (PWV only), \(94.9\%\) (sBP only), \(97.2\%\) (PWV and sBP), respectively. In other words, PIH occurred in \(29.6\%\) of patients in whom blood pressure increased between the first and second trimesters, and in \(60.0\%\) of patients in whom both blood pressure and PWV increased over this interval.

**Comment**

PWV measurement is a simple, reproducible, and non-invasive method for the evaluation of arterial stiffness and seems to be useful for assessing the vasculature both during pregnancy and postpartum. We constructed the normogram of changes in the PWV value by using this method and longitudinally investigating a large number of subjects. The PWV value in the normal pregnancy group significantly decreased in the second trimester, suggesting that vascular stiffness is changed during pregnancy, as reported previously.\(^{18,19}\) In contrast, the PWV value in the PIH group increased throughout pregnancy, suggesting that vascular stiffness in the

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**Table II Predictive value for PIH**

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<td>41.1%</td>
<td>29.6%</td>
<td>60.0%</td>
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The positive predictive value for PIH was obtained using the fact that either PWV value or systolic blood pressure was increased \(\geq 50\) cm/sec or \(\geq 10\) mmHg, respectively, in the second trimester compared with those in the first trimester.
PIH group was significantly increased compared with that in normal pregnancy. Moreover, increased vascular stiffness in the PIH group was sustained for at least 1 month after delivery, suggesting that patients with PIH could be candidates for atherosclerotic events at later times, as reported previously.20

Recently, several new methods have been developed for the assessment of arterial compliance, but most are complex and time consuming, and need a specially qualified operator. To evaluate the arterial compliance in the outpatient, the use of simple and reproducible methods is needed. The automatic device used in this study may be suitable for this purpose. It was reported that noninvasive baPWV showed a good correlation with the aortic PWV obtained by an invasive recording,11,13 indicating the validity of the noninvasive baPWV measurement. Moreover, the method we used to measure baPWV does not require any specialized technique, and the examiner has only to wrap cuffs on the brachium and ankle. After these simple preparations, baPWV is measured automatically. The simplicity of this method makes it suitable for screening large populations. Thus, the validity, reproducibility, and clinical usefulness of the automatic device we used for baPWV measurement are known.11 We observed large standard deviations for our estimates of PWV (Figures 1 and 2), but this was caused by actual variation between individuals within our sample populations. Variability between repeated trials in the same individual was small, with standard deviations typically less than 50 cm/sec (data not shown). The statistical analysis indicated that there were significant differences between some groups. Therefore, we believe that PWV might be useful as information about the cardiovascular function in clinical practice.

This study has some limitations. One of them is that the gestational age used to assess the parameters under investigation was not the same in all subjects. Although the window of each group was not very wide, it is possible that differences in the gestational age within in the same group may have affected the results. We are continuing to investigate the effect of gestational age on the PWV in subjects adjusted regarding the gestational age. Another limitation of this study was that the blood pressures were not available before the pregnancy. Because we excluded subjects with chronic hypertension, the possibility that some women enrolled in the study had chronic hypertension is not so high. Another limitation of this study was that the PWV is influenced not only by the vascular stiffness but also by blood pressure. Although blood pressure is physiologically changed during pregnancy, the changes in blood pressure were not significantly different between the groups. Thus, the difference of the change of PWV during pregnancy between the groups may have been mainly caused by differences in vascular stiffness. Another limitation of this study was that the number of subjects in the PIH group might not have been sufficient to assess the effect of PIH on vascular stiffness. We are currently investigating this issue in a larger number of subjects.

There have not been many reports in which PWV was examined during pregnancy. Especially pertaining to longitudinal study, there were only a few reports and the numbers of subjects of those were so small. To our knowledge, this is the first study showing the longitudinal changes of PWV during pregnancy in a large population. We measured the PWV values in 183 subjects longitudinally using this method and constructed the normogram of PWV throughout pregnancy.

There are some reports that FMD tends to decrease before onset of PIH.6,7 We found that the PWV value increased in PIH. Considering the fact that PWV is affected not only by endothelial function but also by pathologic changes of the contraction of blood vessels,12,21,22 this result suggests that the pathology of hypertensive disorder during pregnancy involves dysfunction of the tunicamedia in addition to that of the endothelium.

It was reported that FMD decreased before the onset of PIH.20,23 The predictive value of PWV and blood pressure for PIH was higher than that of blood pressure alone, suggesting the usefulness of measuring PWV to predict PIH.

The predictive value of PWV for PIH was not very high in this study, whereas high predictive value of FMD for PIH was reported.25 Because endothelial dysfunction is considered to be associated with PIH,24 FMD may be an earlier predictor, considering the pathology of this hypertensive disorder. However, arterial wall stiffness is also involved in the pathologic features of PIH. Because measuring baPWV is easier than measuring FMD, the former is more suitable for screening large populations. This is one of the advantages of PWV over FMD. There have been no reports comparing FMD and PWV as predictors of PIH. The predictive value for PIH using both FMD and PWV might be higher than that using either of them used alone. More detailed examinations will be necessary to test this.

Although there have been no reports examining the change of FMD during the postpartum period, the results of this study showed that the PWV value tended to be higher 1 month following delivery in the PIH group than in the normal pregnancy group. PIH has a high rate of recurrence, and women with a history of PIH have a higher incidence of chronic hypertension in later life than do normotensive pregnant women.25 These facts may be related to our finding that the postpartum PWV value tended to be higher in the PIH group.

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References


