Opposite changes in carotid versus aortic stiffness during healthy human pregnancy

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ABSTRACT

Systemic arterial compliance has been known to increase during healthy pregnancy, whereas, recently, the carotid artery has been reported to stiffen. To clarify this controversy, we simultaneously measured aortic PWV (pulse wave velocity) and carotid artery elastic parameters in a cohort of pregnant women. Twelve normotensive pregnant women were studied longitudinally during the three trimesters of pregnancy (T1, T2 and T3 respectively) and 12 weeks PP (postpartum). Carotid artery diastolic diameter and pulsatile distension was measured by an echo-wall tracking method and carotid pulse pressure by applanation tonometry. Carotid strain, compliance, distensibility coefficient, stiffness index \( \beta \), \( E_{inc} \) (incremental elastic modulus) and augmentation index were calculated. Aortic PWV was determined to estimate aortic distensibility. All carotid artery elastic parameters indicated significant stiffening from T1 to T3 (1.8 ± 0.2 versus 2.9 ± 0.3 mmHg for \( E_{inc} \)), which was reversed after delivery (2.3 ± 0.2 mmHg). Aortic PWV decreased during pregnancy (6.2 ± 0.2 versus 5.4 ± 0.2 m/s) and increased in the PP period (6.7 ± 0.2 m/s). No correlation was found between changes in carotid artery elastic parameters and changes in aortic PWV either from T1 to T3 or from T3 to PP. The carotid artery exhibits regionally specific stiffening during pregnancy, which appears to represent a qualitatively different change in arterial elastic behaviour.

INTRODUCTION

Pregnancy is associated with characteristic changes in central haemodynamics: blood volume, heart rate and cardiac output increase, whereas total peripheral resistance and cardiac afterload decrease. The reduction in cardiac afterload is explained partly by increased systemic arterial compliance [1–4]. Indeed, distensibility of the aorta and the femoral artery was shown to increase during pregnancy [1–4]. In contrast, we have shown recently that the carotid artery became stiffer during healthy human pregnancy [5], which implies directionally opposite changes in the elastic behaviour of carotid versus other arterial segments.

Therefore, the aim of the present study was to test the hypothesis that normal pregnancy is associated with reduced carotid, but increased aortic, compliance. To this end we related carotid artery elastic parameters measured locally by an echo-wall track technique to aortic distensibility assessed by PWV (pulse wave velocity) in healthy pregnant women during the three trimesters and PP (postpartum).

Key words: aorta, carotid artery, elasticity, pregnancy, stiffness.

Abbreviations: AI, augmentation index; D, end-diastolic diameter; \( \Delta D \), change in diameter from end diastole to peak systole; DBP, diastolic carotid pressure; DC, distensibility coefficient; \( E_{inc} \), incremental elastic modulus; IMCSA, intima-media cross-sectional area; IMT, intima-media thickness; LCSA, lumen cross-sectional area; \( \Delta P \), carotid pulse pressure; PP, postpartum; PWV, pulse wave velocity; SBP, systolic carotid pressure; T1, T2 and T3, first, second and third trimesters of pregnancy respectively.

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EXPERIMENTAL

Subjects and general procedure
Twelve healthy pregnant women (age, 31 ± 5 years) were studied longitudinally at each trimester of pregnancy (T1 = 12 ± 0.9, T2 = 20 ± 1.0 and T3 = 33 ± 0.6 weeks respectively) and 13 ± 0.3 weeks PP. All subjects were normotensives, non-smokers and were not taking regular medication. All participants gave written informed consent, and the study was approved by the Ethical Committee of Semmelweis University. Subjects were studied in the early afternoon under standardized conditions, in a quiet room at a comfortable temperature. All the participants fasted for at least 2 h before the testing was carried out, and were asked to refrain from strenuous exercise or drinking alcohol or caffeine-containing beverages for 24 h before the study. Upon arrival at the investigation unit, the subjects were equipped with measurement devices, and then rested in the left lateral position for about 15 min until the absence of evident heart rate and mean blood pressure trends demonstrated that satisfactory baseline conditions had been achieved.

Carotid ultrasonography
The diameter of the right common carotid artery, its pulsatile distension and the IMT (intima-media thickness) of the posterior wall were measured by ultrasonography. The scanner was positioned 1.5 cm proximal to the bifurcation. The ultrasound device comprised a vessel-wall echo-tracking system (Wall Track System; Pie Medical, Maastricht, The Netherlands) combined with a conventional ultrasound scanner (Scanner 200; Pie Medical) and has been described in detail previously [6,7]. Carotid artery diameter was recorded in 5 epochs, each containing 4–8 distension pulses.

Carotid artery pulse pressure
Common carotid artery pressure was measured by applanation tonometry (SPT-301; Millar Instruments, Houston, TX, U.S.A.). Systolic and diastolic blood pressure values, measured on the brachial artery by an automatic microphonic sphygmomanometer built into the Colin device (Colin CBM-7000; ADinstruments Ltd, Hastings, U.K.), were used to calibrate the carotid pressure pulse. The carotid pulse wave recording was calibrated by using brachial diastolic and electronically determined mean brachial pressure values. Diastolic brachial pressure was assigned to the minimum value of the carotid pressure pulse wave and mean pressure to its electrically averaged value. This calibration of the tonometric signal was based on the assumption that mean pressure did not change in large conduit arteries and that diastolic pressure was not substantially different in the brachial and carotid arteries [8]. The cut-off frequency of the recording devices was above 25 kHz, therefore no distortion was induced into the frequency content of pulsatile signals.

The carotid tonometric pulse waveform was used to calculate the AI (augmentation index). The carotid pulse waveform is known to manifest an inflection point that divides the waveform into early and late systolic peaks, produced by the forward and reflected waves. The ratio of the difference between the two peaks to the carotid pulse amplitude was taken as AI [5]. In young, healthy subjects the retrograde pressure wave fuses late with the antegrade wave, which results in negative augmentation.

Carotid artery elastic variables
Strain was calculated as the relative change in end-diastolic diameter during pulsatile distension as 100 × ΔD/D, where D is end-diastolic diameter and ΔD is the change in diameter from end diastole to peak systole. The baseline carotid compliance was calculated as ΔD/ΔP, where ΔP is carotid pulse pressure. The distensibility coefficient (DC) was calculated as DC = 2 × ΔD/(D × ΔP) [9]. Stiffness index β was expressed as ln (SBP/DBP) × D/ΔD, where SBP and DBP are systolic and diastolic carotid pressure respectively [10]. Carotid artery LCSA (lumen cross-sectional area) and IMCSA (intima-media cross-sectional area) were calculated as LCSA = π × D^2/4 and IMCSA = π × (D/2 + IMT)^2 − π × (D/2)^2. Incremental elastic modulus was determined as E_{inc} = [3 × (1 + LCSA/IMCSA)]/DC [11].

PWV
Aortic PWV was determined from carotid and femoral pressure waveforms obtained non-invasively by applanation tonometry (SPT-301, Millar Instruments) using the SphygmoCor® system (SCOR; PWV Medical, Sydney, Australia). Waveforms were referenced to a concurrently recorded ECG, and the carotid-to-femoral transit time (ΔT) was calculated from the foot-to-foot time difference between carotid and femoral waveforms. This methodology is widely used and has good reproducibility [12]. After the waveform collection, distance measurements between the carotid and femoral sampling sites were taken with a standard tape measure. This required the following three measurements: (i) from the midpoint of the jugulum to the lower edge of the umbilicus, (ii) from the edge of the umbilicus to the femoral artery sampling site, and (iii) from the midpoint of the sternal notch to the sampling site on the carotid. The third distance listed above was subtracted from the sum of the first two distances. PWV was calculated by dividing the time component by the distance component.

Statistical analysis
The results are expressed as the means ± S.E.M. One-way repeated measure of ANOVA with the Duncan post hoc test for multiple comparisons was used to test for differences between groups. Differences were considered
Table 1 Haemodynamic variables, carotid artery elastic parameters, augmentation index and PWV values in the three trimesters of pregnancy (T1, T2 and T3) and PP

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>91 ± 3.2</td>
<td>96 ± 2.1</td>
<td>100 ± 3.9*</td>
<td>104 ± 2.6</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>77 ± 1.5</td>
<td>79 ± 2.9</td>
<td>84 ± 2.2</td>
<td>80 ± 1.5</td>
</tr>
<tr>
<td>ΔP (mmHg)</td>
<td>32 ± 1.7</td>
<td>34 ± 1.9</td>
<td>35 ± 1.8</td>
<td>36 ± 2.3</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>79 ± 2.3</td>
<td>85 ± 2.6</td>
<td>92 ± 2.0*</td>
<td>77 ± 2.0*</td>
</tr>
<tr>
<td>D (μm)</td>
<td>5849 ± 97</td>
<td>6146 ± 118</td>
<td>6326 ± 126*</td>
<td>6041 ± 100†</td>
</tr>
<tr>
<td>ΔD (μm)</td>
<td>601 ± 42</td>
<td>561 ± 47</td>
<td>462 ± 37*</td>
<td>557 ± 41†</td>
</tr>
<tr>
<td>IMT (μm)</td>
<td>514 ± 16</td>
<td>523 ± 19</td>
<td>538 ± 17</td>
<td>507 ± 25</td>
</tr>
<tr>
<td>Strain (%)</td>
<td>10.31 ± 0.76</td>
<td>9.17 ± 0.77</td>
<td>7.39 ± 0.67*</td>
<td>9.25 ± 0.68†</td>
</tr>
<tr>
<td>Compliance (μm/mmHg)</td>
<td>19.46 ± 1.73</td>
<td>16.03 ± 1.00</td>
<td>13.42 ± 1.02*</td>
<td>15.98 ± 1.04‡</td>
</tr>
<tr>
<td>DC (10⁻¹/mmHg)</td>
<td>6.71 ± 0.66</td>
<td>5.40 ± 0.39</td>
<td>4.29 ± 0.36*</td>
<td>5.30 ± 0.33‡</td>
</tr>
<tr>
<td>Stiffness index β</td>
<td>4.56 ± 0.41</td>
<td>5.39 ± 0.70</td>
<td>6.30 ± 0.53*</td>
<td>4.73 ± 0.36‡</td>
</tr>
<tr>
<td>Einc (mmHg)</td>
<td>1.79 ± 0.16</td>
<td>2.20 ± 0.16</td>
<td>2.85 ± 0.28*</td>
<td>2.25 ± 0.15‡</td>
</tr>
<tr>
<td>AI (%)</td>
<td>7 ± 5</td>
<td>15 ± 6</td>
<td>20 ± 7*</td>
<td>6 ± 6†</td>
</tr>
<tr>
<td>PWVave (m/s)</td>
<td>6.2 ± 0.2</td>
<td>5.9 ± 0.2</td>
<td>5.4 ± 0.2*</td>
<td>6.7 ± 0.2†</td>
</tr>
</tbody>
</table>

The results are expressed as the means ± S.E.M. Groups were compared for differences by one-way repeated measure of ANOVA and the post-hoc Duncan test. *T3 significantly different from T1, P < 0.05; †PP significantly different from T3, P < 0.05. MAP, mean brachial arterial pressure. HR, heart rate. Significant at P < 0.05. Statistical analyses were performed using the SigmaStat for Windows, version 2.03, program (SPSS, Chicago, IL, U.S.A.).

RESULTS

Haemodynamic data, carotid artery dimensions and elastic parameters, AI and PWV values for the three trimesters of pregnancy (T1, T2 and T3 respectively) and the PP period are shown in Table 1. Carotid systolic pressure increased from T1 to T3, with no further change at PP, whereas mean brachial pressure and ΔP did not change for the observation period. Heart rate increased during pregnancy and declined after delivery.

Carotid artery D increased during pregnancy and decreased after delivery. Concurrently, pulsatile distension decreased during pregnancy and increased in the PP period. Carotid IMT did not change throughout the observation period. With pulse pressure remaining unaltered, the changes in carotid dimensions resulted in reduced strain, compliance and DC from T1 to T3, which was reversed after delivery. The stiffness index β and Einc, which characterizes the stiffness of wall material, also increased from T1 to T3 and decreased at PP (Table 1 and Figure 1).

In contrast, aortic PWV was gradually reduced during pregnancy from 6.2 ± 0.2 m/s at T1 to 5.4 ± 0.2 m/s at T3, then increased in the PP period to 6.7 ± 0.2 m/s (Figure 1 and Table 1). Carotid AI obtained more negative values at T3 compared with T1, due to reduced PWV and to the delayed return of the reflected pulse wave, and increased again at PP (Table 1). Increases in carotid Einc from T1 to T3 were not related to concurrent reductions in aortic PWV across subjects. Similarly, no relationships were found between reductions in Einc from T3 to PP and concurrent increases in PWV (Figure 2).
Lack of relationship between changes in carotid pressure fall. The actual systolic pressure value, which were not available, but we assume that the moderate obvious limitations, preconception blood pressure values appear to be a contradiction. It is generally thought that blood pressure falls in early pregnancy \[14\], i.e. heart rate increased from 79 $\pm$ 2 beats/min at T1, to 92 $\pm$ 2 beats/min at T2; comparable changes in heart rate, which were induced in patients with low risk of atherosclerosis by atrial pacing, produced moderate changes in aortic PWV from 6.8 $\pm$ 1.0 m/s at 80 beats/min to 7.0 $\pm$ 0.9 m/s at 90 beats/min \[22\]. An additional confounding factor may be gender, as in one study heart rate was found to influence PWV in men, but not in women \[26\].

The observation that carotid artery stiffens during pregnancy supports our previous findings \[5\]. In the present study all carotid artery elastic parameters were adversely affected during pregnancy. It may be argued that the increase in D of the carotid artery should have a favourable effect on the compliance characteristics of the vessel. But compliance was reduced, because the increase in heart rate, although significant, was moderate. In the present study heart rate increased from 79 $\pm$ 2 beats/min at T1, to 92 $\pm$ 2 beats/min at T2; comparable changes in heart rate, which were induced in patients with low risk of atherosclerosis by atrial pacing, produced moderate changes in aortic PWV from 6.8 $\pm$ 1.0 m/s at 80 beats/min to 7.0 $\pm$ 0.9 m/s at 90 beats/min \[22\]. An additional confounding factor may be gender, as in one study heart rate was found to influence PWV in men, but not in women \[26\].

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biomechanics during pregnancy is an exciting area that requires further study.

Limitations

Carotid artery elastic parameters were measured locally at a specific site, therefore stiffening of the carotid arterial wall can be attributed to an anatomically defined segment of the arterial tree. On the other hand PWV was determined over a length of the arterial tree, which included the common carotid artery, the thoracic and the abdominal aorta, the iliac artery and part of the femoral artery. The elastic behaviour of these segments is quantitatively differentiated, exhibiting increasing stiffness towards the periphery, and showing differential changes during pregnancy [27]. It is conceivable that comparing carotid versus femoral elastic parameters during pregnancy might have produced more accentuated changes.

Measurement of ΔP was performed indirectly, using calibrated tonometry, which is likely to introduce some error. The effect of this error, however, was minimized by the longitudinal study design, as far as the main conclusion of the study is concerned.

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