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PROFOUND IMPACT OF UNCOMPLICATED PREGNANCY ON DIASTOLIC, BUT NOT SYSTOLIC PULSE CONTOUR OF AORTIC PRESSURE

THESE

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RESUME

L'objectif de cette étude était de déterminer l'impact de la grossesse non compliquée sur l'onde de pouls de la pression aortique centrale.

Méthode :

66 femmes au total avec une grossesse simple ont été réparties en trois groupes selon le stade de leur gestation : premier trimestre (T1, n=22), deuxième trimestre (T2, n=20) et troisième trimestre (T3, n=24). Le groupe contrôle (C, n=21) était constitué de femmes non enceintes, en bonne santé habituelle, prenant une contraception oestroprogestative.

La tonométrie d'aplanation a été utilisée pour l'acquisition des ondes de pouls centrale : un appareil disponible dans le commerce (SphygmoCor) permet l'enregistrement de l'onde de pouls périphérique avec un tonomètre d'aplanation de l'artère radiale au niveau du poignet, puis effectue sa transformation en sa forme centrale, grâce à une analyse de Fourrier et une fonction de transfert.

L'influence des ondes réfléchies sur l'onde de pouls a été déterminée non seulement pendant la systole (augmentation systolique), comme on procède habituellement dans l'analyse de l'onde de pouls, mais aussi pendant la diastole (augmentation diastolique).

Résultats :

Au cours de la grossesse, les pressions centrales systolique et diastolique sont restées inchangées et comparables aux valeurs mesurées chez les femmes qui ne sont pas enceintes. Dans le groupe contrôle, l'augmentation systolique s'élevait à $8.1\pm7.5\%$ de la pression de pouls ; il n'y avait pas de différence statistiquement significative avec les valeurs obtenues chez les femmes enceintes, et ce, à n'importe quel stade de la grossesse (T1 : $4.6\pm11.4\%$, T2 : $5.0\pm9.3\%$, T3 : $4.7\pm8.1\%$). Par contre, l'amplitude de l'augmentation diastolique diminuait avec la progression de la grossesse (C $6.5\pm2.4\%$, T1 : $5.2\pm3.1\%$, T2 : $3.8\pm2.6\%$; $P=0.002$ versus C; T3 : $2.3\pm2.0\%$; $P<0.0001$ versus C et $P=0.004$ versus T1).

Conclusion :

La grossesse ne modifie pas la forme de l'onde de pouls systolique centrale, ce qui implique de la part du système cardiovasculaire une adaptation fine à la demande croissante de flux sanguin, et ce, à tous les stades de la grossesse. Par contre, l'amplitude de l'onde de réflexion atteignant l'aorte pendant la diastole diminue progressivement au cours de la grossesse.

Perspectives :

De récentes études montrent qu'une valeur anormalement haute de l'augmentation systolique de la pression centrale, comme on peut la déterminer avec la tonométrie d'aplanation, pourrait être un indice de trouble hypertensif de la grossesse débutant. Cette technique simple pourrait être d'autant plus facile à mettre en œuvre si les valeurs normales pour l'augmentation systolique étaient indépendantes du stade de la grossesse, comme le suggèrent nos résultats, du moins pour les mesures prises en position assise.

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Profound impact of uncomplicated pregnancy on diastolic, but not systolic pulse contour of aortic pressure

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Objective To evaluate the impact of uncomplicated pregnancy on the pulse contour of central aortic pressure.

Methods A total of 66 women with singleton pregnancy were grouped according to pregnancy duration: first trimester (T1, $n = 22$), second trimester (T2, $n = 20$), and third trimester (T3, $n = 24$). Non-pregnant healthy women, who took combined oral contraception, were included as controls (C, $n = 21$). The pulse contour of aortic pressure was obtained with radial applanation tonometry, using a commercial device (SphygmoCor). The influence of reflected waves on the contour was evaluated not only in systole, as usual with pulse contour analysis (systolic augmentation), but also in diastole (diastolic augmentation).

Results Throughout pregnancy, central systolic and diastolic blood pressure remained unchanged and comparable to values in the non-pregnant state. Systolic augmentation amounted to $8.1 \pm 7.5\%$ of pulse pressure in the control group (mean $\pm$ SD), and there was no statistically significant deviation from this value at any stage of pregnancy (T1, $4.6 \pm 11.4\%$; T2, $5.0 \pm 9.3\%$; T3, $4.7 \pm 8.1\%$). In contrast, the amplitude of the diastolic augmentation wave progressively declined with advancing

pregnancy (C, $6.5 \pm 2.4\%$; T1, $5.2 \pm 3.1\%$; T2, $3.8 \pm 2.6\%$; $P = 0.002$ versus C, T3, $2.3 \pm 2.0\%$; $P < 0.0001$ versus C and $P = 0.0004$ versus T1).

Conclusion The systolic shape of the central aortic pressure contour is left unaltered by pregnancy, implying a finely tuned adaptation of the cardiovascular system to the increased demand for blood flow at all stages of the gravid state. In contrast, the amplitude of reflection waves reaching the aortic root in diastole progressively decreases with advancing pregnancy. *J Hypertens* 24:1641–1648 © 2006 Lippincott Williams & Wilkins.

Introduction

Normal pregnancy induces a variety of cardiovascular adaptations. Observed changes include a rise in heart rate, stroke volume and cardiac output, concomitant with a decrease in total peripheral vascular resistance [1–3]. It was previously admitted that systolic blood pressure decreases in the first and the second trimester to return to near the non-pregnant level at the end of the third trimester [4]. In contrast, more recent studies did not reveal significant changes in systolic blood pressure [2,5,6]. Whether pregnancy affects diastolic blood pressure or mean arterial pressure is controversial, with either a decrease in the first trimester [3,7,8] or no change [2,5,6] being reported. With regard to pulse pressure, two studies have reported either no or only minimal variation [6,9].

During pregnancy, the relative stability of blood pressure in the face of substantially increased stroke volume and cardiac output is explained, not only by the aforementioned reduction in peripheral vascular resistance, but also by an increase in the compliance of conduit arteries,

essentially the aorta [2,3,5,6]. Such a change acts to limit the amplitude of the forward pressure wave generated in this vessel by left ventricular ejection. In addition, it diminishes the propagation velocity along the arterial tree of both the forward and the reflected pressure waves. The latter, which travels back from the peripheral sites of reflection towards the heart, will then tend to reach the ascending aorta relatively late in systole, or even in diastole. In such conditions, one would expect little or no augmentation of proximal aortic pressure by the reflected wave.

There are only limited human data concerning the actual impact of normal pregnancy on the central aortic pressure waveform. For obvious reasons, invasive measurements are not ethically acceptable in this setting. One study provided serial non-invasive recordings of pulse pressure in the subclavian artery of healthy women in the first, second and third trimester of pregnancy, together with Doppler ultrasound measurements of blood flow velocity in the ascending aorta. Inference was made that

pregnancy indeed delayed the occurrence of reflected waves, but systolic augmentation of aortic pressure *per se* was not reported [2].

Applanation tonometry is an easily applicable non-invasive method for the assessment of the pressure waveform in the ascending aorta [10]. The peripheral pulse is recorded by means of a piezoelectric high-fidelity pressure sensor applied on the skin overlaying a peripheral, superficial artery. The acquired peripheral pulse waveform is then mathematically transformed into its central version, using Fourier analysis and a generalized transfer function (GTF) [11]. The best site to record the peripheral pulse wave is at the wrist, where the radial artery is easily accessible in the majority of individuals. The radial artery recording is calibrated with blood pressure measured at the level of the brachial artery, because blood pressure is practically identical in both vessels. The mathematical derivation to transform peripheral recordings into the central pressure waveform has been validated against invasive measurements [12,13], and has reasonable reproducibility [14,15]. With this method, it has been shown that pre-eclampsia in the third trimester of pregnancy is associated with an abnormally high augmentation of the central systolic pressure by reflected waves [16]. To our knowledge, applanation tonometry of the radial artery has been used only once to characterize the effects of a normal pregnancy on the central arterial pressure waveform [17,18]. In that report, analysis was limited to systolic events.

In the present study, we examined the impact of uncomplicated pregnancy on the shape of the ascending aortic pressure pulse, as reconstructed with radial applanation tonometry. Equal attention was paid to the systolic and diastolic parts of the reconstructed waveforms.

Methods

Subjects

Sixty-six women with singleton pregnancy were recruited from the outpatient obstetrics clinic in our hospital and grouped according to pregnancy duration. The first trimester group (T1) included women with gestational age from the beginning of pregnancy until 13 weeks, the second trimester group (T2) from 14 until 26 weeks, and the third trimester group (T3) from 27 weeks until delivery. Demographic data are shown in Table 1. All subjects were in good health, except one who had multiple sclerosis, in the remission phase and without sequellae at the time of study. In particular, none of the study participants had any history of cardiovascular disease. Women with known or suspected complications during pregnancy, such as pregnancy-induced hypertension, gestational diabetes or pre-eclampsia, were excluded. Isolated proteinuria was also an exclusion criterion. There was no intake of any antihypertensive or cardiovascular drug. Medication at the time of the study was: antiemetica (six women in the first trimester), magnesium (one woman in the second trimester and eight women in the third trimester), vitamins and folic acid (15 women of all trimesters), antacid (aluminii oxidii hydricum: three women), paracetamol (four women) and mefenamic acid (one woman).

In addition, 21 non-pregnant women, who had been taking combined oral contraceptives for at least 2 months, were included in a control group (C). They were healthy, without any cardiovascular or gynaecological disease and did not take any other medication. The examination was performed outside the period of interruption of contraceptive medication.

All women were fully informed on the study protocol and gave their written consent. The investigation conformed with the principles outlined in the declaration of Helsinki, and was approved by the Institutional Review Board of our hospital.

Experimental design

As required in a cross-sectional study, each woman, whether pregnant or not, was examined only once.

Table 1 Characteristic of the subjects

	Non-pregnant	Pregnant		
	Controls	1st Trimester (T1)	2nd Trimester (T2)	3rd Trimester (T3)
No. of subjects	21	22	20	24
Duration of pregancy (weeks)	–	10.4 ± 1.9	19.4 ± 4.1	34.6 ± 3.7
Age (years)	27.0 ± 4.1	27.0 ± 4.7	28.8 ± 5.0	28.6 ± 4.2
Height (cm)	167 ± 7	164 ± 6	164 ± 6	167 ± 8
Weight (kg)	56.8 ± 7.0	62.3 ± 12.0	60.7 ± 12.4	63.7 ± 12.4
BMI (kg/m^2)	20.4 ± 2.3	23.3 ± 4.6	22.8 ± 3.6	22.7 ± 3.7
Parity	20 nulliparous	14 primiparous	15 primiparous	15 primiparous
Ethnic group				
Caucasian	20	13	18	18
Black	0	2	0	2
Asian	1	1	0	1
Others	0	6	2	1
Smoker or ex-smoker	8	7	9	7

BMI, Body mass index (in pregnant women, refers to value just before pregnancy). Data are means ± SD. No significant differences between groups.

After 15 min of resting in the seated position, the right brachial blood pressure was assessed once using a mercury sphygmomanometer (Mercuro 300; Riester, Germany), and then the pulse wave was recorded three times on the right radial artery. Finally, three new measurements of blood pressure were made and averaged for calibration of the radial pulse. Individual parameter values derived from the pulse wave analysis were means obtained from the three aforementioned tonometric recordings.

All measurements were taken by the first author, in her fourth year of specialty training (general medicine), with subjects in the seated position and forearms supported by armrests.

Pulse wave analysis

The measurement of the radial pulse wave with applanation tonometry and the subsequent derivation of the aortic pulse wave were made using the SphygmoCor system (AtCor Medical, Sydney, Australia). In this method, a pen-shaped high-fidelity solid-state pressure transducer is used to flatten the radial artery at the wrist using gentle pressure. Data are collected directly into a portable computer using the SphygmoCor software, with an online display of waveforms in order to allow the best possible recording. Pulse waves acquired over a period of 10 s are converted to a central waveform, using the GTF, as described [11].

All pulse wave recordings made in the present study met the quality criteria defined by the manufacturer, namely a mean pulsatile amplitude of the raw tonometric signal higher than 80 mV, as well as a beat-to-beat variability of pulse pressure and of diastolic pressure less than 5% of average pulse pressure.

From the recorded waveforms, the SphygmoCor software calculates various indices, including the duration of the cardiac cycle, the duration of ventricular ejection, and the systolic augmentation index. Ejection duration is calculated from the radial pulse as the time from the foot of the pressure wave to the incisura. Systolic augmentation of aortic pressure caused by reflection (sometimes termed 'augmentation index') is defined as the pressure difference between the first and the second peaks of the aortic waveform, expressed as a percentage of the aortic pulse pressure.

Further processing of the aortic pulse wave

To estimate the mean aortic pressure profile of each group, the relevant individual waveforms were ensemble-averaged in each group of women using the following procedure, which took into account the variations of ejection duration and total length of cardiac cycle between subjects. Each individual waveform was broken down into a systolic and a diastolic part, as determined from the ejection duration provided by the SphygmoCor analysis software. The time abscissas of each part were linearly mapped to new time axes, in such a manner that, within a group of women, the durations of both systole and diastole became uniformly equal to the respective mean values for this group. The mapped waveforms were resampled at 128 Hz (i.e. the original sampling rate), using linear interpolation, and normalized relative to aortic pulse pressure. In this last step, which was taken to facilitate comparisons of waveform shapes between groups, diastolic pressure became 0% and peak systolic pressure became 100% of aortic pulse pressure.

Because a prominent diastolic wave was clearly visible on the raw inspection of many tracings, its amplitude was quantified on each individual dataset, as follows (see Fig. 2, inset). A straight line was drawn through the first data point in diastole, so as to have tangent contact with the later, upward concave part of the diastolic pressure decay. The amplitude of the superimposed diastolic wave was then read as the maximum positive vertical distance going from this line to the actual aortic pressure, within the time interval from the beginning of diastole to the time abscissa of the contact point. This amplitude was defined as the diastolic augmentation and expressed as a percentage of the aortic pulse pressure.

Statistical analysis

The mean values of each variable were compared between groups with simple analysis of variance. When the F value was significant, pairwise comparisons were made using Fisher's least significant difference. The potential influence of heart rate, body height and weight on systolic augmentation and on the diastolic wave was tested with analysis of covariance (i.e. a linear model incorporating as independent predictors all aforementioned variables in addition to group membership). Computations related to statistical analysis were carried out using the JMP software (version 3.1; SAS Institute, Cary, North Carolina, USA). The alpha level of all tests was set at 0.05. All data were summarized as the mean ± SD.

Results

As shown in Table 1, the four groups of subjects were well matched for age, body height, and smoking habits, three variables of potential impact on the shape of the arterial pulse [10]. Body weight tended to be lower in non-pregnant than in pregnant women, although this difference was not statistically significant.

Haemodynamic variables in the four groups of women are shown in Table 2. These data indicate that pregnancy had no influence on the systolic and diastolic values of either brachial or aortic pressure. Whether compared with non-pregnant conditions or early pregnancy (first and second trimester), late pregnancy (third trimester) was characterized by a 12% increase in heart rate ($P < 0.001$),

Table 2 Haemodynamic data and pulse contour analysis

| | Non-pregnant | Pregnant | | |
	Controls	1st Trimester (T1)	2nd Trimester (T2)	3rd Trimester (T3)
No. of subjects	21	22	20	24
Heart rate (beats/min)	76 ± 11	80 ± 10	79 ± 8	89 ± 8**,§,#
Peripheral blood pressure[a]				
Systolic (mmHg)	105 ± 7	107 ± 11	105 ± 9	110 ± 10
Diastolic (mmHg)	68 ± 7	65 ± 9	63 ± 7	64 ± 8
Central blood pressure[b]				
Systolic (mmHg)	92 ± 6	92 ± 10	91 ± 9	93 ± 8
Diastolic (mmHg)	69 ± 7	66 ± 9	65 ± 7	66 ± 8
Ejection duration[b]				
In milliseconds	288 ± 25	288 ± 23	298 ± 17	278 ± 20#
In % of cardiac cycle	36.3 ± 3.6	38.2 ± 4.0*	39.2 ± 3.0*	41.6 ± 3.2**,§,#
Central dp/dt max (mmHg/s)[b]	642 ± 176	691 ± 155	703 ± 206	708 ± 146
Central systolic augmentation (%)				
Uncorrected[b]	8.1 ± 7.5	4.6 ± 8.1	5 ± 9.3	4.7 ± 8.1
Corrected[b,c]	8.7 ± 6.6	7.0 ± 11	7.0 ± 8.0	11 ± 7.6

dp/dt max, Maximal slope of the ascending central pressure pulse. [a]Measured by sphygmomanometry. [b]Calculated by the SphymoCor software. [c]Value of systolic augmentation adjusted to a fixed heart rate of 75 beats. Data are means ± SD. *$P < 0.05$; **$P < 0.01$: T1, T2 or T3 versus C. §$P < 0.05$, T2 or T3 versus T1. #$P < 0.05$ T3 versus T2.

with ejection duration correspondingly shortened when expressed in milliseconds ($P = 0.03$) but occupying a somewhat greater proportion of the total cardiac cycle ($P < 0.001$). The systolic aortic augmentation index ranged from −15 to +31% of pulse pressure. Being negative or zero in a quarter of subjects, it was of high apparent variability within groups (coefficient of variation close to or above 100%), and did not significantly differ between groups ($P = 0.55$). This index could not be calculated in one subject because of the lack of a clearly defined inflection point on the ascending limb of the aortic pressure waveform, and was disregarded in two others because the calculated values were tagged as unreliable by the SphygmoCor software.

Systolic augmentation is clearly visible on the averaged aortic pressure waveforms in the shape of a peak occurring in the second half of the ejection period, separated from the first half by an inflection point (Fig. 1). In keeping with the aforementioned calculations, this feature appears unchanged by pregnancy. In contrast, the first half of diastole contains an upward convexity (diastolic wave), which is most noticeable in non-pregnant women and progressively wanes with advancing pregnancy. Consistent with the visual impression conveyed by Fig. 1, the amplitude of the diastolic wave, calculated from each individual data set as shown on the inset to Fig. 2, was highest in control subjects (6.5 ± 2.4% of pulse pressure), with a monotonous decrease from the first (5.2 ± 3.1%), to the second (3.8 ± 2.6%, $P = 0.002$ versus controls) and third trimester of pregnancy (2.3 ± 2.0%, $P < 0.0001$ versus controls, $P = 0.0004$ versus first trimester).

It is known that systolic augmentation decreases with increasing heart rate [19], although the effect of this variable on the diastolic wave is unknown. Because of the slight heart rate acceleration noted in the third trimester of pregnancy (Table 2), two attempts were

made to control for the influence of this variable. First, we tabulated the value of systolic augmentation corrected for heart rate, an adjustment offered by the SphygmoCor software (i.e. the AI@75 parameter listed in the program's output). As shown in the last line of Table 2, the conclusion of an essentially unaltered systolic augmentation

Fig. 1
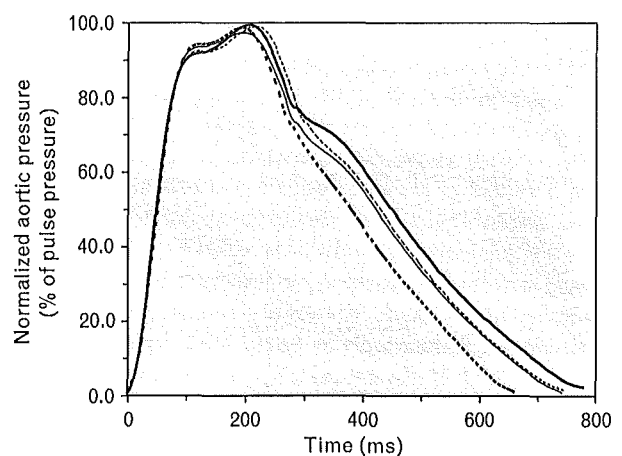
Average aortic pressure waveforms in the four groups of women. Aortic pressure waveforms were ensemble-averaged in each group using the following procedure, which took into account the variations in ejection duration and total length of cardiac cycle between subjects. Each individual waveform was broken down into a systolic and a diastolic part, as determined by the pulse wave analysis software provided with the SphygmoCor device. The time axes of each part were linearly mapped to new time axes, in such a manner that, within a group, the durations of systole and diastole became uniformly equal to the respective mean values for this group. The mapped waveforms were re-sampled at 128 Hz, using linear interpolation, and normalized relative to aortic pulse pressure. In this last step, which was taken to facilitate comparisons between groups, diastolic pressure became 0% and peak systolic pressure became 100% or aortic pulse pressure. ——— Controls ($n = 21$); ——— pregnant 1st trimester ($n = 22$); - - - - - pregnant 2nd trimester ($n = 20$); ●●●●● pregnant 3rd trimester ($n = 24$).

Fig. 2
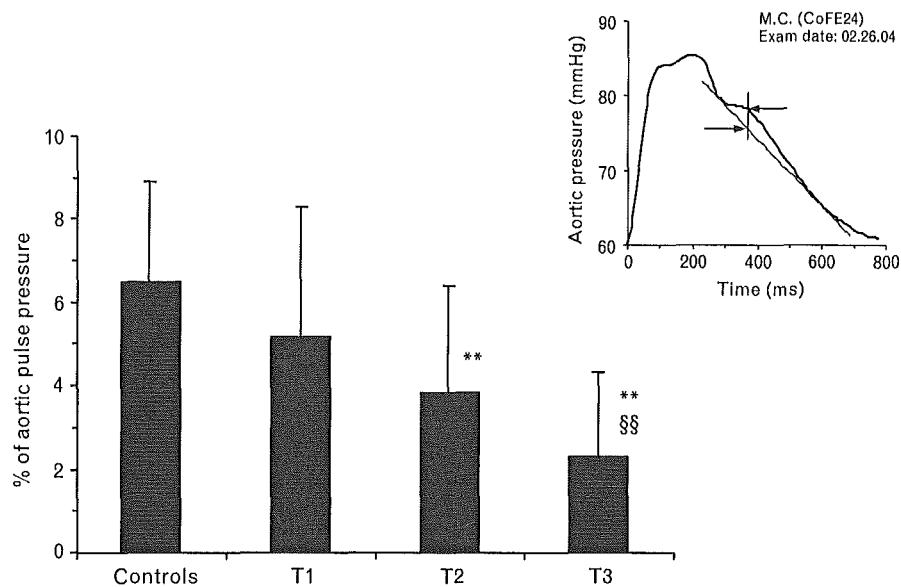
Amplitude of diastolic wave superimposed on the diastolic decay of aortic pressure. This amplitude was quantified on each individual dataset, as shown in the inset. A straight line was drawn through the first data point in diastole, so as to have tangent contact with the later, upward concave part of the diastolic pressure decay. Amplitude of the superimposed diastolic wave was then read as the maximum positive vertical distance going from this line to the actual aortic pressure, within the time interval from the beginning of diastole to the time abscissa of the contact point. T1, T2, and T3, respectively, designate the first, second, and third trimester of pregnancy. Data are means ± SD. **$P < 0.01$: T1, T2 or T3 versus controls. §§$P < 0.01$, T2 or T3 versus T1.

throughout pregnancy was not modified. Second, we introduced heart rate as a covariate in the comparisons between study groups, using a model that included a heart rate by group interaction term. When adjusted in this fashion rather than by the SphygmoCor software, systolic augmentation remained unaffected by pregnancy ($P = 0.52$) and decreased by 3.4% of pulse pressure for each 10 beat/min increase in heart rate ($P = 0.0003$). The interaction term was clearly non-significant ($P = 0.84$), indicating that this dependence of systolic augmentation on heart rate was the same irrespective of pregnancy status. In contrast, the amplitude of the diastolic wave remained strongly associated with the stage of pregnancy ($P = 0.0001$), but showed no relationship whatsoever with heart rate ($P = 0.92$). Further adjustments for age, body height and body weight had negligible influence on any of the above results. Interestingly, these last analyses disclosed an independent influence of age on the systolic and diastolic augmentations, without any interaction with pregnancy status ($P = 0.31$). For each additional age year, systolic augmentation increased by 0.6% ($P = 0.003$), whereas diastolic augmentation decreased by 0.2% ($P = 0.001$).

Discussion

In the present study, we characterized the impact of pregnancy on central aortic pressure, with particular consideration given to the shape of the central arterial

pressure waveform. We anticipated a progressive modification of this waveform with advancing pregnancy, because of the profound effects of the gravid state on the dynamics of ventricular ejection as well as on the mechanics of conduit arteries and on peripheral resistance, all of which co-determine the shape of the central pressure pulse. The new findings are twofold. First, the systolic part of the central pressure waveform remains unaltered throughout pregnancy. Second, the pattern of diastolic decay undergoes a progressive modification, most marked in the third trimester.

An invasive measurement of aortic pressure was ethically not feasible in these healthy women. To achieve our goal, we therefore resorted to an indirect, non-invasive technique, which consisted of recording the radial pulse with applanation tonometry, and then using it to reconstruct aortic pressure mathematically using a GTF, the term 'generalized' referring to an assumption of constancy across subjects and conditions [10]. A clear limitation to the present study is the fact that the GTF has never been validated in pregnancy, as was done by direct invasive measurements in non-pregnant subjects [11,13,20]. Supporting the validity of aortic pressure waveform reconstruction in the pregnant women, the dependence of systolic augmentation on heart rate was similar in all four study groups (i.e. an average decrease by 3.4% of pulse pressure for each 10 beats/min increase in beating frequency) and

remarkably close to the value of 3.9% observed in a study of non-pregnant subjects in whom controlled changes of heart rate were induced by pacing [19].

The central aortic pulse results from the additive superposition of a forward traveling pressure wave generated by ventricular contraction and of a reflection wave that travels backwards from the peripheral sites of reflection towards the heart [21]. The particular contour of central pulse pressure depends on the particular shape of either wave, as well as on the timing of one with respect to the other. The shape of the forward wave is related to the dynamics of ventricular ejection and to the mechanical properties of conducting arteries, notably their stiffness [22]. In addition to these factors, the shape of the backward wave depends on the spatial dispersion of the reflection sites, which current understanding predominantly locates in resistance arterioles [23,24], although some reflection also takes place in larger vessels, as a result of impedance non-uniformities introduced by branching or by longitudinal changes in elastic wall properties (elastic tapering). Finally, the time delay between the reflected and the forward wave depends on the velocity of pressure pulse propagation (pulse wave velocity), which in turn is a decreasing function of arterial stiffness [25]. These considerations explain the age-dependent changes in the aortic pulse morphology of healthy humans [26]. At one extreme, children have very compliant arteries and thus a low pulse wave velocity, such that aortic pressure augmentation caused by reflections essentially occurs in diastole. In the elderly by contrast, arteries are stiffer, pulse wave velocity is higher, and reflected waves reach the aorta predominantly in the second half of ventricular ejection, thus augmenting systolic central pressure. The pattern of central aortic pressure observed in the non-pregnant women who took part in the present study is an intermediate one, compatible with augmentation straddling end-systole and the first half of diastole (Fig. 1). This pattern is consistent with observations made by others in healthy young adults, using either non-invasive means similar to those employed in the present study [26] or invasive high-fidelity recordings of pressure in the ascending aorta [27]. Based on the above discussion, not only should systolic augmentation increase, but diastolic augmentation should also decrease with advancing age, as was indeed revealed by the statistical analysis of our data (see end of Results section). This latter observation comes in further support to the applicability of the GTF in normal pregnancy.

Pregnancy potentially affects all determinants of the contour of aortic pressure pulse. Because of the accompanying increase in stroke volume, and thus flow in the course of ejection, the forward wave might alter its shape, but such a change seems minimized by the associated decrease in aortic characteristic impedance, which reflects a lower stiffness of the great vessels [2]. Consistent with the relative stability of the forward wave shape in the course of pregnancy, the maximal dp/dt calculated from the upstroke of reconstructed aortic pressure was similar in the four groups of women included in the present study (Table 2). With respect to the non-pregnant state, the general peripheral vasodilation associated with pregnancy [1,3] should reduce the amplitude of the reflected waves, and the latter should also reach the aorta later because of the lower propagation velocity along the more compliant conduction vessels [2]. Accordingly, the contour of aortic pressure in pregnancy should be characterized by a reduction in amplitude and a shift from systole to diastole of the augmentation caused by reflected wave. Consistent with this expectation, Smith et al. [17] recently found that uncomplicated pregnancy was associated with a statistically significant decline of systolic augmentation (mean $\pm$ SD unpregnant controls 21 $\pm$ 9.0% $n = 10$, first trimester pregnancy 14 $\pm$ 7.6% $n = 20$, second trimester 10 $\pm$ 9.8% $n = 20$, third trimester 10 $\pm$ 8.8% $n = 20$), but limited their analysis to the systolic part of the central aortic pressure waveform. Here, we provide additional information by demonstrating a stepwise amplitude reduction of the diastolic wave with progressing pregnancy (Figs 1 and 2). In our study, systolic augmentation was relatively unaltered (Table 2 and Fig. 1), which, taken at face value, would seem to contradict the report by Smith et al. [17]. This discrepancy can be explained, at least partly, by noting the more marked difference in heart rate between pregnant and control women in that report (third trimester 93 $\pm$ 8 beats/min, non-pregnant 69 $\pm$ 11 beats/min, $P < 0.001$), when compared with ours (Table 2), taking into consideration the known decline of systolic augmentation with beating frequency [19], a relationship quite apparent in our data as already mentioned. In contrast, the impact of pregnancy on diastolic augmentation, shown for the first time in the present study, had no independent association with (and therefore was presumably not mediated by) changes in heart rate.

With only reconstructed central aortic pressure available, any explanation of the discordant behaviour of systolic and diastolic augmentation observed in the course of pregnancy must remain speculative. There is general agreement on the presence in humans and many other mammals of two distinct groups of reflection sites, one in the upper part of the body (i.e. head and upper extremities), and one in the lower part (abdomen and legs) [22,28,29]. As compared with reflected waves from the lower body, those from the upper body travel a shorter length and thus reach the aortic root sooner. Computer simulations with models of the arterial system that incorporate this concept have generated aortic pressure waveforms, which, under the proper set of realistic assumptions, mimic very closely those of non-pregnant women shown in Fig. 1 [30], suggesting that the systolic and diastolic augmentations observed in the present

study might correspond to reflections generated from the upper and lower parts of the body, respectively. In this configuration, systolic augmentation might be conserved thoughout pregnancy in spite of reduced peripheral resistance in the upper limb, as a result of the appearance of new cephalad reflection sites, not an unreasonable possibility in view of data indicating that, contrary to other vessels, the carotid arteries stiffen [31,32], and contrary to other vascular bed blood flow in the major cerebral arteries slightly decreases [33] in the course of pregnancy. On the other hand, general vasodilation in the lower part of the body would contribute to attenuate diastolic augmentation.

The progressive time-course of diastolic wave attenuation (Fig. 2) is intriguing when considering that the global hemodynamic pattern of pregnancy, namely the augmentation of cardiac output and diminution of peripheral vascular resistance, is already well established in the first trimester, with relatively few further changes thereafter [1,2,7]. A possible, although highly speculative, explanation for these contrasting behaviours could be that the growing presence of the gravid uterus, in spite of its modest contribution to global peripheral conductance [34] might nevertheless progressively increase the spatial dispersion of reflection sites in the lower part of the body, resulting in a spread-out backward wave of diminished amplitude reaching the aortic root in diastole.

In summary, we found that pregnancy had no effect on the systolic and diastolic values of central aortic pressure. In addition, we characterized the impact of pregnancy on the shape of the central aortic pressure pulse in systole, and for the first time in diastole. We found an unaltered systolic shape, contrasting with a progressive modification of the diastolic waveform.

Conclusion
Our results indicate for the first time a differential impact of uncomplicated pregnancy on the diastolic and systolic shapes of the central aortic pulse. Considering that the time-course of aortic pressure in systole is an essential determinant of left-ventricular afterload, the marked invariance of the systolic shape and peak pressure implies a finely tuned adaptation of the cardiovascular system to the increased demand for blood flow at all stages of the gravid state. Recent data indicate that an abnormally high systolic augmentation of the central aortic pulse, as determined from applanation tonometry of the radial artery, might be an indicator of incipient hypertensive disorders in pregnancy [16,18]. The use of this simple technique would be greatly facilitated if the normal range for systolic augmentation was independent of pregnancy stage, as our results imply at least for measurements taken in the seated position.

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