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Major impact of body position on arterial stiffness indices derived from radial applanation tonometry in pregnant and non pregnant woman

THESE

préparée sous la direction du Professeur associé François Feihl
(avec la collaboration du Professeur Patrick Hohlfeld)
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par

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Rapport de synthèse

Pendant la grossesse, la pression artérielle reste stable malgré une nette augmentation du volume d'éjection systolique et du débit cardiaque. Cette stabilité vient d'un côté d'une vasodilatation périphérique entraînant une diminution des résistances périphériques et d'un autre côté d'une moindre rigidité des principales artères notamment l'aorte. En conséquence, l'amplitude des ondes de pouls est atténuée, de même que leur vitesse de propagation dans le sens tant antérogade que rétrograde (ondes réfléchies). Les ondes réfléchies tendent ainsi à atteindre l'aorte ascendante plus tard durant la systole, voire durant la diastole, ce qui peut contribuer à diminuer la pression pulsée.

La prééclampsie perturbe massivement ce processus d'adaptation. Il s'agit d'une maladie hypertensive de la grossesse engendrant une importante morbidité et mortalité néonatale et maternelle. Il est à remarquer que la diminution de la rigidité artérielle n'est pas observée chez les patientes atteintes avec pour conséquence une forte augmentation de la pression systolique centrale (aortique) par les ondes réfléchies. Ce fait a été établi grâce à l'existence de la tonométrie d'aplanation, une méthode permettant l'évaluation non invasive de l'onde de pouls centrale.

Dans cette méthode, un senseur de pression piézo-électrique permet de capter l'onde de pouls périphérique, le plus souvent sur l'artère radiale. Par la suite, un algorithme validé permet d'en déduire la forme de l'onde de pouls centrale et de visualiser à quel moment du cycle cardiaque s'y ajoutent les ondes réfléchies. Plusieurs études font état d'une forte augmentation de la pression systolique centrale par les ondes réfléchies chez les patientes atteintes de prééclampsie, suggérant l'utilisation de cette méthode pour le diagnostic et le monitoring voire pour le dépistage de ces patientes.

Pour atteindre ce but, il est nécessaire d'établir des normes en rapport notamment avec l'âge gestationnel. Dans la littérature, les données pertinentes actuellement disponibles sont variables, voire contradictoires. Par exemple, les ondes réfléchies proéminentes dans la partie diastolique de l'onde de pouls centrale disparaissaient chez des patientes enceintes au 3ème trimestre comparées à des contrôles non enceintes dans une étude lausannoise, alors que deux autres études présentent l'observation contraire. Autre exemple, certains auteurs décrivent une diminution progressive de l'augmentation systolique jusqu'à l'accouchement alors que d'autres rapportent un nadir aux environs du 6ème mois, suivi d'un retour à des valeurs plus élevées en fin de grossesse. Les mesures effectuées dans toutes ces études différaient dans leur exécution, les patientes étant notamment dans des postions corporelles différentes (couchées, semi-couchées, assises, en décubitus latéral). Or nous savons que le status hémodynamique est très sensible aux changements de position, particulièrement durant la grossesse où l'utérus gravide est susceptible d'avoir des interactions mécaniques avec les veines et possiblement les artères abdominales. Ces différences méthodologiques pourraient donc expliquer, au moins en partie, l'hétérogénéité des résultats concernant l'onde de pouls chez la femme enceinte, ce qui à notre connaissance n'a jamais été exploré.

Nous avons mesuré l'onde de pouls dans les positions assise et couchée chez des femmes enceintes, au 3ème trimestre d'une grossesse non compliquée, et nous avons effectué une comparaison avec des données similaire obtenues chez des femmes non enceintes en bonne santé habituelle.

Les résultats montrent que la position du corps a un impact majeur sur la forme de l'onde de pouls centrale. Comparée à la position assise, la position couchée se caractérise par une moindre augmentation systolique et, par contraste, une augmentation diastolique plus marquée. De manière inattendue, cet effet s'observe aussi bien en présence qu'en l'absence de grossesse, suggérant que la cause première n'en réside pas dans les interactions mécaniques de l'utérus gravide avec les vaisseaux sanguins abdominaux. Nos observations pourraient par contre être expliquées par l'influence de la position du corps, via un phénomène hydrostatique simple, sur la pression transmurale des artères éloignées du cœur, tout particulièrement celles des membres inférieurs et de l'étage abdominal. En position verticale, ces vaisseaux augmenteraient leur rigidité pour résister à la distension de leur paroi, ce qui y accroîtrait la vitesse de propagation des ondes de pression.

En l'état, cette explication reste hypothétique. Mais quoi qu'il en soit, nos résultats expliquent certaines discordances entre les études conduites à ce jour pour caractériser l'influence de la grossesse physiologique sur la forme de l'onde de pouls central. De plus, ils indiquent que la position du corps doit être prise en compte lors de toute investigation utilisant la tonométrie d'applanation pour déterminer la rigidité des artères chez les jeunes femmes enceintes ou non.

Il sera aussi nécessaire d'en tenir compte pour établir des normes en vue d'une utilisation de la tonométrie d'aplanation pour dépister ou suivre les patientes atteintes de prééclampsie. Il serait enfin intéressant d'évaluer si l'effet de la position sur la forme de l'onde de pouls central existe également dans l'autre sexe et chez des personnes plus âgées.

Original Article

Major impact of body position on arterial stiffness indices derived from radial applanation tonometry in pregnant and nonpregnant women

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Objective: To evaluate the impact of body position on the arterial stiffness indices provided by radial applanation tonometry in pregnant and nonpregnant women.

Methods: Twenty-four young women (18–30 years) in the third trimester of a normal pregnancy and 20 healthy nonpregnant women of the same age were enrolled. In each, applanation tonometry was carried out in the sitting and supine position. The following stiffness indices were analyzed: systolic augmentation index (sAix), sAix adjusted for heart rate (sAix@75) and diastolic augmentation index (dAix), all expressed in % of central aortic pulse pressure.

Results: The sAix was apparently not influenced by body position, but the transition from seated to supine was associated with a substantial decrease in heart rate. When correcting for this confounder by calculating the sAix@75, systolic augmentation was substantially lower when individuals were supine (mean ± SD: nonpregnant 3.0 ± 14.4%, pregnant 8.8 ± 9.7%) than when they were sitting (nonpregnant 5.7 ± 13.0%, pregnant 11.1 ± 83%, $P = 0.005$ supine vs. seated in both study groups, $P > 0.2$ for pregnant vs. nonpregnant). The influence of body position on the dAix went in the opposite direction (supine: nonpregnant 9.7 ± 6.6%, pregnant 4.4 ± 3.5%; seated: nonpregnant 7.7 ± 5.8%, pregnant 3.3 ± 2.4%, $P < 0.00001$ supine vs. seated in both study groups, $P = 0.001$ for pregnant vs. nonpregnant).

Conclusion: Body position has a major impact on the pattern of central aortic pressure augmentation by reflected waves in healthy young women examined either during third trimester pregnancy or in the nonpregnant state.

Keywords: aorta/ph (physiology), blood pressure/ph (physiology), brachial artery/ph (physiology), diastole/ph (physiology), female, heart rate/ph (physiology), humans, pregnancy/ph (physiology), systole/ph (physiology)

Abbreviations: dAix, diastolic augmentation index; dMTT, mean transit time of diastolic reflection wave; dT1r, onset time of diastolic reflected wave; PPA, pulse pressure amplification; sAix, systolic augmentation index; sAix@75, sAix corrected for the influence of heart rate; sT1r, onset time of systolic reflected wave

INTRODUCTION

During normal pregnancy, blood pressure (BP) remains relatively stable, despite marked increased in stroke volume and cardiac output. This stability is explained in large part by a state of peripheral vasodilation leading to substantial reduction in peripheral vascular resistance. As another factor, there is also a decrease in the stiffness of major conduit arteries, including the aorta [1–4], acting first to limit the amplitude of the forward pressure wave generated in these vessels by left ventricular ejection, and second to diminish 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 toward the heart, then tend to reach the ascending aorta relatively late in systole, or even in diastole. Such conditions minimize the augmentation of proximal aortic pressure by reflected waves.

These processes of cardiovascular adaptation are massively perturbed in preeclampsia, a hypertensive disorder of pregnancy that importantly contributes to maternal and neonatal morbidity and mortality [5]. Particularly, there is now substantial evidence that the aforementioned decrease in the stiffness of conduit arteries does not occur in preeclampsia, with the consequence that central aortic pressure becomes markedly augmented in systole by reflected waves [6–10]. The recognition of this fact has been made possible by the advent of noninvasive means for the clinical exploration of arterial hemodynamics, notably applanation tonometry.

Applanation tonometry is an easily applicable noninvasive method for the assessment of the pressure waveform in the ascending aorta [11,12], based on the recording of the

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peripheral pulse by means of a piezoelectric high-fidelity pressure sensor applied on the skin overlaying a peripheral vessel, usually the radial artery. From the raw radial pulse, a well validated algorithm [13,14] estimates the detailed shape of the pressure wave within the ascending aorta, allowing to recognize if, and in which phase of the cardiac cycle (systole, diastole or both), aortic pressure is augmented by reflected waves. A string of studies carried out with applanation tonometry have now shown that systolic augmentation is markedly enhanced in third trimester preeclamptic, in comparison with normal, pregnancies [6–10], suggesting that this noninvasive method could acquire clinical usefulness as a diagnostic and monitoring tool. For such a hope to materialize, it is necessary to define the expected range of normal results as a function of gestational age. In that respect, the available data are somewhat variable. For example, some [7,15], but not all studies [16], have found a lower systolic augmentation in normal third trimester pregnancies, when comparison was made with healthy nonpregnant, age-matched controls. In addition, two groups have recently reported a time course of systolic augmentation characterized by a nadir in the middle and a re-increase at the end of normal pregnancies [8,17], whereas earlier work suggested a monotonous decrease with advancing gestation [15]. Finally, in third trimester normal pregnancies, we have described a quasidisappearance of the prominent reflected waves characteristically found on the diastolic part of the central aortic pressure waveform in young healthy nonpregnant individuals [16], a finding contradicted by data presented in two other reports [1,7].

In pregnancy, hemodynamic status is particularly sensitive to changes in body position, because the mechanical interactions of the gravid uterus with large intra-abdominal veins and possibly arteries are susceptible to gravitational effects [18]. This sensitivity to body position could conceivably extend to the dynamics of arterial pressure wave propagation. In that respect, it is striking that, in the aforementioned reports of pulse wave analysis in pregnant women, applanation tonometry was carried out with the individuals either fully recumbent (supine) [7,8], semirecumbent [10], in lateral decubitus [6,17], or sitting [16]. This factor might explain, at least in part, the inhomogeneous descriptions of central aortic pressure behavior during normal pregnancy, an hypothesis that, to our knowledge, has never been tested.

Here, we have examined healthy women in the third trimester of an uncomplicated pregnancy, as well as healthy nonpregnant age-matched controls. In each individual, applanation tonometry of the radial artery was carried out in the supine and the sitting position.

METHODS

Participants

Twenty pregnant women were chosen from the outpatient obstetrics clinic in our hospital. The inclusion criteria were a noncomplicated singleton pregnancy with cephalic presentation over 35 weeks of amenorrhea, maternal age between 20 and 40 years and a BP under 130/85 mmHg. The exclusion criteria were past or actual history of diabetes, hypertension, vascular disease, hypercholesterolemia, any kind of medication other than pregnancy vitamins and folic acid and nicotine addiction. We excluded the women with declared intolerance for the supine position.

Twenty-four nonpregnant healthy women were recruited by advertisement. The exclusion criteria were the same as above. The only medication authorized was combined oral contraceptives.

All women gave free and informed written consent. The study protocol was approved by the Institutional Review Board of our hospital and fulfilled the principles outlined in the Declaration of Helsinki.

Pulse wave analysis

Pulse wave analysis was carried out based on applanation tonometry of the radial artery, using the SphygmoCor device (AtCor Medical, West Ryde, Australia), as previously described [16,19]. In short, the central element in this system is a pen-shaped piezoelectric pressure transducer, with which the radial artery is flattened against the radial bone, thus allowing recording of the radial pulse. Pulse waves recorded during 10 s are then processed in order to reconstruct a central waveform using a generalized transfer function, as abundantly described elsewhere [11,14].

The SphygmoCor software, provided by the manufacturer, implements a range of criteria to determine whether the quality of the recorded waveform is sufficient for subsequent analysis. These criteria include a mean pulsatile amplitude of the raw tonometric signal higher than 80 mV and a beat-to-beat variability of pulse pressure (PP) and diastolic pressure lower than 5% of average PP. We rejected any recording which did not fulfill these criteria.

Experimental design

Each woman was examined only once. After 10-min resting in a sitting position (sitting 1 position), the systolic and diastolic arterial BP were taken three times on each arm with an oscillometric device (StabiloGraph; IEM, Stolberg, Germany) and averaged. As the difference between sides was always less than 20 mmHg for systolic pressure and less than 10 mmHg for diastolic pressure, we only considered BP on the chosen side for the subsequent measurements. The average values for SBP and DBP were entered into the SphygmoCor program as calibration. The radial arterial pulse wave was then recorded three times on the chosen side.

The participant had then to lie down on her back (supine position). After 5 min in that position, brachial BPs were again taken in triplicate, followed by three recordings of the radial pulse wave.

Finally, the women resumed the sitting position (sitting 2 position) for another 10 min before repetition of the whole process.

Data analysis

To obtain a graphical overview of the influence of experimental conditions, the central arterial pulse waveforms were ensemble-averaged across individuals and expressed in percentage of the corresponding PP, as previously described [16,19,20].

From the radial pressure waveform, the Sphygmocor software estimates ejection duration as the time from the foot of the pressure wave to the incisura. On the reconstructed central pressure waveforms, it then positions the systolic points P1 (the peak of the forward pressure wave) and P2 (the peak of the reflected systolic wave) as shown in Fig. 1. The time lag sT1r (onset time of systolic reflected wave) from the initial systolic upstroke to point P1 gives an estimate of twice the travel time of the systolic reflected wave. The relative importance of the forward and reflected pressure waves is expressed as a systolic augmentation index (sAix) according to the formula:

$$\text{sAix} = 100 \times (\text{P2} - \text{P1})/\text{pulse pressure}$$

The AIx may be positive or negative, with a positive value indicating augmentation of peak systolic pressure by reflections. Because the sAix is dependent on heart rate (HR), the software also corrects for this influence by estimating the value that would be observed with a beating frequency of 75 beats/min (sAix@75).

Central to peripheral PP amplification (PPA) was defined as the ratio of radial-to-central PP, expressed in percentage. PPA is negatively correlated to the sAix [21], whereas its computation is more robust because it is not influenced by errors in the determination of P1.

We complemented the above calculations by computing the amplitude of diastolic reflection waves (dAix), as previously described [16,19,20]. Briefly, to delineate the portion of the central diastolic pressure profile containing superimposed reflected waves, we assumed that such reflections would translate into deviation from the monoexponential decay profile predicted by the Windkessel model. In addition, this latter prediction was approximated as linear for practical purposes. Thus, we determined a straight line in tangent contact with the diastolic profile as shown in Fig. 1. The time abscissas of the contact points on the left (dT1r, onset time of diastolic reflected wave) and on the right (dTf) were, respectively, considered as indicating the onset and termination of diastolic reflections. The amplitude of diastolic reflections was quantified using the maximal positive vertical distance between the actual pressure profile (point P3) and the tangent (point P4), taking into account only data from dT1r to dTf. As in the case of the sAix, the dAix is expressed in percentage of aortic PP, that is,

$$\text{dAix} = 100 \times (\text{P3} - \text{P4})/\text{pulse pressure}.$$

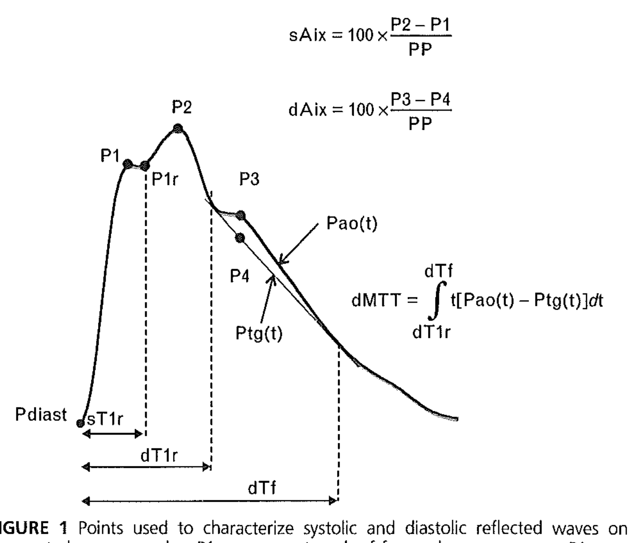

FIGURE 1 Points used to characterize systolic and diastolic reflected waves on the central pressure pulse. P1, pressure at peak of forward pressure wave. P1r, pressure at the inflection point marking the onset of the systolic reflected wave. sT1r, time elapsed from begin of systolic upstroke to P1r. P2, peak of reflected wave in systole. dT1r, time to onset of reflected wave in diastole. P3, pressure at peak of reflected wave in diastole. Td_final, time at end of reflected wave in diastole. dT1r and dTf defined by the contact points of a straight line tangent to the diastolic part of the waveform as shown. P4 approximates the pressure that would exist at the time of P3 in absence of reflection. Indices of wave reflection are calculated according to the formulas shown in which PP represents pulse pressure. Pao(t) and Ptg(t) are two functions of time describing the actual pressure waveform and the aforementioned tangent, respectively. See Methods section.

Statistical analysis

Statistical analysis was carried out with repeated measures analysis of variance (ANOVA). The fixed factors included in the model were group (pregnant/nonpregnant), position (seated 1, supine, seated 2) and their interaction, with participants included as a random factor nested under group. When the relevant *F*-value was significant, the following contrasts of means were tested: seated 1 vs. seated 2, and supine vs. average of seated 1 and 2. The nominal α was uniformly set at 0.05. The data were summarized as mean ± SD in text and tables, and mean ± SEM in figures. The calculations were made with the JMP software (version 5.0; SAS Institute, Cary, North Carolina, USA).

RESULTS

Demographic data, as well as the values of peripheral and central BP recorded in the course of the protocol in the two groups of women, are shown in Table 1. The two groups of women were well matched for age, body size and body weight in the nonpregnant state. As expected, HR was substantially augmented in third trimester pregnancy. Brachial as well as derived central arterial BP was marginally higher in pregnant compared with nonpregnant women.

HR, ejection duration and BP were essentially identical at the seated 1 and 2 times of the protocol. Compared to its value recorded in the seated position, the supine HR was lower by approximately 10% in both study groups, an effect with high statistical significance ($P < 0.0001$). Concomitant to slowing HR, the transition from sitting to supine also increased ejection duration, but this effect was less marked in the pregnant group ($P < 0.001$ for interaction of group and position). The changes in body position had no impact of any practical importance on either peripheral or central BP. Figure 2 shows the central aortic pressure waveforms, ensemble-averaged for each body position in nonpregnant and pregnant women. The two profiles obtained in the seated position were essentially superimposable, with an inflection point corresponding to the onset of systolic augmentation (i.e. point P1 in Fig. 1) that was well recognizable in both study groups and, in keeping with our previous study [16], a diastolic reflection wave much more marked in nonpregnant than in pregnant women. In the latter, the profile's shorter duration directly reflects their higher HR.

TABLE 1. Demographic and hemodynamic data in the two groups of women

	Nonpregnant			Pregnant		
Number of women		20			24	
Age (years)		28.2 ± 4.4			28.4 ± 4.1	
Height (cm)		167 ± 6			166 ± 7	
Weight (kg)						
Before pregnancy		58 ± 6.3			60.1 ± 9.8	
Third trimester pregnancy		–			80 ± 11.0	
Weeks of pregnancy		–			37 ± 2	
Position	Seated 1	Supine	Seated 2	Seated 1	Supine	Seated 2
Heart rate (beats/min)	72 ± 7	66 ± 7**	70 ± 7	86 ± 10††	79 ± 12**,††	85 ± 12††
Ejection duration (ms)	296 ± 17	332 ± 16**	299 ± 19	281 ± 22†	297 ± 24**,††	285 ± 22†
Peripheral BP (mmHg)						
Systolic	116 ± 10	112 ± 9*	113 ± 10	122 ± 13†	120 ± 11†,*	122 ± 11†
Diastolic	73 ± 9	67 ± 6**	71 ± 6	76 ± 10	76 ± 8††	76 ± 10
Mean	87 ± 8	81 ± 6**	85 ± 6	91 ± 11	90 ± 9††	92 ± 10††
Central BP (mmHg)						
Systolic	101 ± 9	97 ± 7*	99 ± 8	106 ± 12†	105 ± 10*,†	106 ± 11†
Diastolic	74 ± 9	68 ± 6**	72 ± 6	77 ± 10	77 ± 8††	78 ± 10†
Mean	87 ± 8	81 ± 6**	85 ± 6	91 ± 11	90 ± 9††	92 ± 10†
PPA (%)	158 ± 17	156 ± 18	160 ± 17	165 ± 16	163 ± 15	165 ± 18

Hemodynamic measurements carried out first in the seated position (Seated 1); then after 10 min of lying supine; and, finally, after 10 min of coming back to the seated position (Seated 2). BP, blood pressure; PPA, pulse pressure amplification, radial pulse pressure in percentage of aortic pulse pressure.
*$P < 0.05$.
**$P < 0.01$ Supine vs. mean of Seated 1 and 2.
†$P < 0.05$.
††$P < 0.01$ Pregant vs. Nonpregnant.

The transition from seated to supine was not associated with any marked modifications in the systolic part of the ensemble averaged waveforms. In contrast, and in both study groups, this change in body position had a clear impact on the diastolic augmentation wave, making it more prominent. The longer duration of the waveform recorded in the supine position directly reflects the lower HR in this condition.

Consistent with the qualitative information conveyed by Fig. 2, there were no statistically significant effects of either pregnancy status or body position on the sAix, at least in absence of adjustment for HR (Fig. 3, sAix, upper panel), nor on PP amplification (PPA, last line of Table 1). In both study groups and body positions, sAix and PPA were strongly and negatively correlated ($r^2 \geq 0.8$, $P < 0.001$), which is in accord with expectations [21]. After adjustment for a constant HR of 75 beats/min, the differences in systolic augmentation between pregnant and nonpregnant women remained nonsignificant ($P = 0.1$) (Fig. 3, sAix@75, middle panel). However, this adjusted index was significantly and markedly lower in the supine (nonpregnant 3.0 ± 14.4%, pregnant 8.8 ± 9.7%) than in the seated position (average of seated 1 and seated 2: nonpregnant 5.7 ± 13.0%, pregnant 11.1 ± 8.3%, $P = 0.005$ vs. supine in both study groups, position by group interaction $P > 0.8$). Consistent with Fig. 2 and our previous study [16], the dAix was lower in pregnant than in nonpregnant women ($P = 0.001$, Fig. 3, dAix, lower panel). In both study groups, and in contrast with the sAix@75, the dAix was markedly higher in the supine (nonpregnant 9.7 ± 6.6%, pregnant 4.4 ± 3.5%) than in the seated position (average of seated 1 and 2: nonpregnant 7.7 ± 5.8%, pregnant: 3.3 ± 2.4%, $P < 0.00001$ vs.

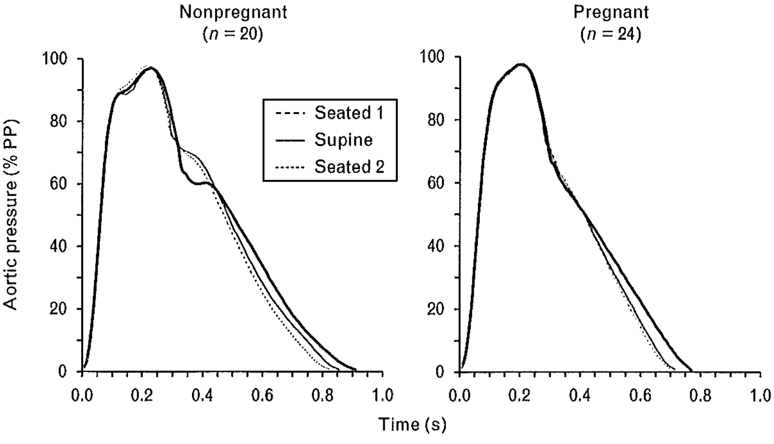

FIGURE 2 Ensemble-averaged central aortic pressure waveforms in the different age-groups. Waveforms reconstructed from the radial pulse recorded with the individual in either the sitting or the supine position. Number of individuals comprised in ensemble-averaging indicated in parentheses.

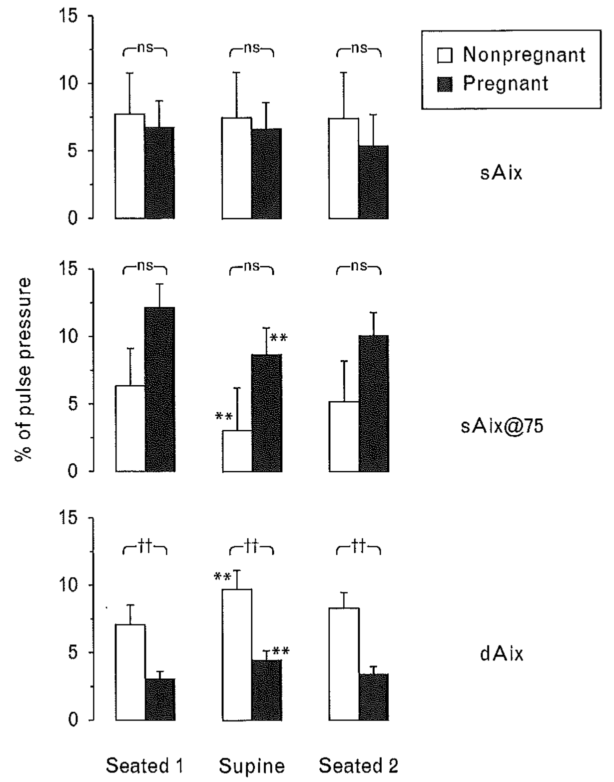

FIGURE 3 Augmentation of central aortic pressure by reflected waves as a function of body position in nonpregnant and pregnant women. sAix, systolic augmentation index. sAix@75, systolic augmentation index corrected for heart rate. dAix, diastolic augmentation index. $**P < 0.01$ supine vs. average of Seated 1 and 2. There were no statistically significance differences between Seated 1 and 2.

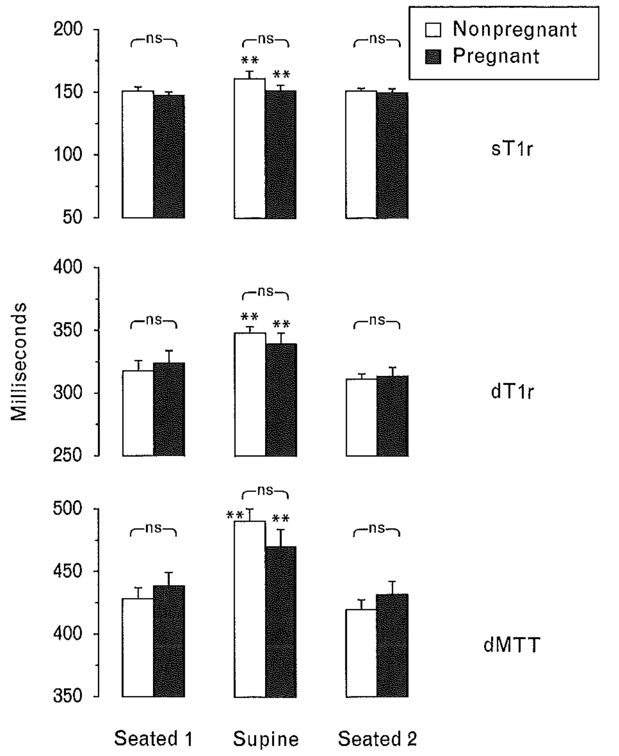

FIGURE 4 Timing of reflected waves on central aortic pressure pulse, as a function of body position in nonpregnant and pregnant women. sT1r, time to onset of systolic reflected wave dT1r time to onset of diastolic reflected wave. dMTT, mean transit time of diastolic reflected wave. $**P < 0.01$ supine vs. average of Seated 1 and 2. There were no statistically significance differences between Seated 1 and 2.

supine in both study groups, position by group interaction $P > 0.2$).

As reflected by the parameter sT1r, the timing of systolic augmentation was independent of pregnancy status and appeared slightly delayed in the supine compared with the sitting position (Fig. 4, upper panel). The timing of the diastolic wave could not be analyzed in six pregnant women in whom – at least in the seated position – there was no recognizable upper convexity of the central waveform in this phase of the cardiac cycle. In the 18 other pregnant women, this timing, as reflected by the parameters dT1r (onset of diastolic augmentation, Fig. 4, middle panel) and dMTT (mean transit time, Fig. 4, lower panel) was the same as in the 20 nonpregnant controls. In both study groups, the transition from seated to supine induced a marked and statistically significant increase in dT1r and dMTT. In Fig. 2, this effect of position on diastolic wave timing is also visible in the nonpregnant group, although not clearly discerned in the pregnant group due to the rather low amplitude of the ensemble-averaged diastolic waves.

There was no differences between the seated 1 and 2 phases of the protocol in any of the indices shown in Figs 3 and 4 ($P > 0.3$ in all cases).

Because BP and HR have a known influence on wave reflections [22,23] and varied somewhat between experimental conditions (Table 1), all statistical analyses were repeated, adding mean BP and HR as a covariates into the ANOVA model. With this analysis, the sAix and sAix@75 were strongly and positively correlated to mean BP ($P < 0.001$) and strongly and negatively correlated to HR ($P < 0.001$), whereas effects of pregnancy status, body position and their interaction remained nonsignificant. Application of the adjusted model disclosed no relationship of either mean BP or HR with the dAix and did not modify results regarding the influence of pregnancy and position on this index.

DISCUSSION

The present study was designed to test, in third trimester normal pregnancy, the impact of body position on the pattern of reflected pressure waves within the central aorta. Such an impact was expected on the basis that reflections are generated in part in large intra-abdominal arteries [24,25], whose geometry and mechanical properties, thus ability to produce reflections, could undergo substantial changes as contact forces exerted by the gravid uterus on these vessels are modified. The main new findings are two-fold. First, in pregnant women, the transition from sitting to supine indeed substantially altered the augmentation of central aortic pressure by reflected waves. Second, and more surprisingly, a qualitatively and quantitatively similar impact of body position was also observed in nonpregnant conditions.

An originality of the present study lies in the analysis, not only of the systolic, but also of the diastolic part of the central pulse waveform, in which we detected reflected waves based on deviation from the mono-exponential decay predicted by the Windkessel model. This approach is in accord with views expressed in standard texts [24]. Clearly, another source of deviation would be the incisura, which reflects the transient increase in pressure dictated by the Bernouilli equation in the presence of the flow deceleration at the time of aortic valve closure. However, this hydrodynamic phenomenon is largely insufficient to account for the non-Windkessel behavior of the aortic pressure pulse, the largest part being explained by the existence of reflected waves [26]. Figure 1 conveys the impression that end-ejection is being used to determine the start of the diastolic wave, but in fact its delineation makes no such assumption. Indeed, dTr1 was always longer than the end-ejection time calculated by the SphygmoCor software (10th percentile, median and 90th percentile of dT1r – ejection time differences: 5, 17 and 61 ms). It must be remembered that the Sphygmocor determines ejection time from the radial waveform [27], whereas we use the reconstructed central waveform to delineate the diastolic wave.

Whether in pregnant or nonpregnant women, the sAix appeared uninfluenced by body position. In both groups, however, HR was conspicuously lower when individuals were lying supine as opposed to sitting (Table 1), consistent with a lesser activation of the sympathetic system, as expected. It is well established that, with decreasing HR, and consequently increasing ejection duration, the reflected pressure waves have more opportunity to reach the ascending aorta in systole, leading to a higher sAix if all other factors remain constant [22]. When applying the standard correction for this confounding influence of HR, that is, the computation of the sAix@75, systolic augmentation of central aortic pressure appeared to be lower in the supine, compared with the sitting position. Strikingly, and in both study groups, the respective impacts of position change on diastolic (dAix) and systolic augmentations (sAix@75) were in mirror image of each other (Fig. 3). In addition, the timing of the diastolic wave was delayed in the supine, compared with the sitting position (Fig. 4). The reciprocal relationship between systolic and diastolic reflected waves is compatible with a concept that would consider them, not as separate entities but rather as parts of a single wave. This single wave would result from the summation of multiple components originating from a range of reflection sites and reaching the aorta sometimes predominantly before, sometimes predominantly after and sometimes in an interval straddling end-ejection, depending on arterial mechanics and hemodynamic conditions [24].

We shall now consider factors specific to the gravid state that might contribute to explain our observations. It has been known for decades that, in advanced pregnancy, the force exerted in the supine position by the uterus on the inferior vena cava leads to its almost complete obliteration [28]. The impact on venous return, cardiac output and arterial BP is variable, depending on the functionality of parallel venous channels, notably the paravertebral sinuses [29]. In a minority of cases, cardiovascular collapse may ensue (the supine hypotensive syndrome), relieved by moving the patient from dorsal to lateral decubitus [28,30]. In the present study, the hemodynamic effects of position changes may have been affected somewhat by pregnancy status, as ongoing from sitting to supine ejection duration increased less in pregnant than in nonpregnant women (Table 1). In comparison with an erect posture, recumbency is expected to favor venous return and ventricular filling, leading to larger ejection volume and duration. This effect of posture might be less in pregnant than in nonpregnant conditions, due to compression of the great veins by the gravid uterus in recumbency. However, it is relevant to note that none of our pregnant volunteers were intolerant to the supine position and that their BP remained essentially constant during the protocol (Table 1). Could compression of the abdominal aorta by the gravid uterus contribute to modifications of the central pressure waveform induced by the sitting to supine transition in the pregnant participants? This possibility seems remote, first because, although documented in isolated cases, aortic compression is not a constant phenomenon in these circumstances [31,32], and also considering the similarity of positional effects on reflected waves in pregnant and nonpregnant conditions (Figs 2–4).

What other mechanisms, then, could underlie this impact of body position? One clue is given by the changes noted in the timing of waves, which appeared delayed, suggesting a lower propagation velocity of pressure waves (pulse wave velocity, PWV) in the supine compared with the sitting position (Fig. 4; dT1r, dMTT). The direct measurement of PWV in any position other than supine is technically difficult and, for this reason, was not part of our protocol. Indeed, the effects of body position on PWV have rarely been documented [33]. However, one major difference to be expected between sitting and supine is, for simple hydrostatic reasons, a much higher intraluminal pressure, in the former condition, within arteries of the lower body half. The direct relationship between PWV and BP is well known [23] and explained by the progressive stiffening of the arterial wall as vessel distension increases, with a stiffer artery conducting faster according to the Moens–Korteweg equation [34]. Thus, in all arteries located caudally to the heart, one would expect a lower PWV in horizontal, as compared with erect body positions. To our knowledge, the only data relevant to that issue are those by Hasegawa and Rodbard [33], which in healthy volunteers support this hypothesis. Thus, a general transmission delay of reflected waves in supine compared with sitting conditions would explain the associated reciprocal modifications of systolic and diastolic augmentations displayed in Fig. 3. In short, we submit that the attenuation of systolic and enhancement of diastolic reflections in the supine as opposed to the sitting position are due, at least in part, to a slower propagation of pressure waves mediated by a decrease in the transmural pressure of major conduit arteries. A similar mechanism has been invoked to explain that, either in healthy individuals following a Valsalva maneuver [35], or in patients with cardiovascular shock [36], the central arterial pulse is modified according to the same pattern found in the present study.

Systolic augmentation did not differ between healthy pregnant and nonpregnant women, whether expressed as sAix or sAix@75, and whatever the position in which each it was evaluated. This is in accordance with our previous work that was carried out in sitting conditions only [16]. The discrepancy with other studies [15] reporting a decrease in these indices in third trimester normal pregnancies, in comparison with nonpregnant controls, is, thus, apparently due to factors other than variations in body position, with possible causes remaining to be determined. By contrast, the present results provide a clear explanation of the persistent diastolic wave observed by Ronnback *et al.* [7] in third trimester pregnancies, as opposed to its marked blunting previously reported by us [16], because their participants were examined in the supine, and ours in the sitting position.

In summary, body position has a major impact on the pattern of central aortic pressure augmentation by reflected waves in healthy young women examined either during third trimester pregnancy or in the nonpregnant state. The effect of position on wave reflections seems predominantly due to changes in the transmural pressure of conduit arteries mediated by gravity and operates similarly in the nonpregnant and pregnant state. This fact should be taken into account when using applanation tonometry of the radial artery to characterize arterial stiffness, at least in young pregnant or nonpregnant women. Whether the statement can be generalized to young men and older age classes remains to be determined.

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Conflicts of interest

There are no conflicts of interest for any of the authors.

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