UNIVERSITE DE LAUSANNE - FACULTE DE BIOLOGIE ET DE MEDECINE

Département de Médecine
Division de Physiopathologie clinique

Bilateral symmetry of radial pulse in high-level tennis players: implications for the validity of central aortic pulse wave analysis

THESE

préparée sous la direction du Professeur Bernard Waeber
avec la collaboration du Professeur François Feihl et du Docteur
Gérald Gremion, Privat-Docent et Maître d'Enseignement
et de Recherche

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

Boris GOJANOVIC

Médecin diplômé de la Confédération Suisse
Originaire de Lausanne (VD)

Lausanne

2010

Unil
UNIL | Université de Lausanne
Faculté de biologie
et de médecine

Ecole Doctorale
Doctorat en médecine

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Directeur de thèse	*Monsieur le Professeur* ***Bernard Waeber***
Co-Directeur de thèse	
Expert	*Madame le Professeur* ***Lucia Mazzolai***
Directrice de l'Ecole doctorale	*Madame le Professeur* ***Stephanie Clarke***

la Commission MD de l'Ecole doctorale autorise l'impression de la thèse de

Monsieur Boris Gojanovic

intitulée

Bilateral symmetry of radial pulse in high-level tennis players : implications for the validity of central aortic pulse wave analysis

Lausanne, le 20 avril 2010

pour Le Doyen
de la Faculté de Biologie et de Médecine

Madame le Professeur Stephanie Clarke
Directrice de l'Ecole doctorale

Rapport de synthèse

Ce travail de thèse s'articule autour de l'importance de l'évaluation de la fonction vasculaire et des répercussions au niveau central, cardiaque, des perturbations du réseau vasculaire. Les maladies cardiovasculaires sont prédominantes dans notre société et causes de morbidité et mortalité importante. La mesure de la pression artérielle classique reste le moyen le plus utilisé pour suivre la santé des vaisseaux, mais ne reflète pas directement ce qui se passe au niveau du cœur. La tonométrie d'aplanation permet depuis quelques années de mesurer l'onde de pouls radial, et par le biais d'une fonction mathématique de transfert validée, il est possible d'en déduire la forme et l' amplitude de l'onde de pouls central, donc de la pression aortique centrale. Cette dernière est un reflet bien plus direct de la post-charge cardiaque, et de nombreuses études cliniques actuelles s'intéressent à cette mesure pour stratifier le risque ou évaluer l'effet d'un traitement vasculaire. Toutefois, bien que cet outil soit de plus en plus utilisé, il est rarement précisé si la latéralité de la mesure joue un rôle, sachant que certaines propriétés des membres supérieurs peuvent être affectées par un usage préférentiel (masse musculaire, densité osseuse, diamètre des artères, capillarisation musculaire, et même fonction endothéliale). On a en effet observé que ces divers paramètre étaient tous augmentés sur un bras entraîné. Dès lors on peut se poser la question de l'influence de ces adaptations physiologiques sur la mesure indirecte effectuée par le biais du pouls radial.

Nous avons investigué les deux membres supérieurs de sujets jeunes et sédentaires (SED), ainsi que ceux de sujets sportifs avec un développement fortement asymétrique des bras, soit des joueurs de tennis de haut niveau (TEN). Des mesures anthropométriques incluant la composition corporelle et la circonférence des bras et avant-bras ont montré que TEN présente une asymétrie hautement significative aux deux mesures entre le bras dominant (entraîné) et l'autre, ce qui est aussi présent pour la force de serrage (mesurée au dynamomètre de Jamar).

L'analyse des courbes centrales de pouls ne montre aucune différence entre les deux membres dans chaque groupe, par contre on peut observer une différence entre SED et TEN, avec un index d'augmentation diastolique qui est 50 % plus élevé chez TEN. Les index d'augmentation systolique sont identiques dans les deux groupes.

On peut retenir de cette étude la validité de la méthode de tonométrie d'aplanation quel que soit le bras utilisé (dominant ou non-dominant) et ce même si une asymétrie conséquente est présente. Ces données sont clairement nouvelles et permettent de s'affranchir de cette variable dans la mesure d'un paramètre cardiovasculaire dont l'importance est actuellement grandissante. Les différences d'index diastolique sont expliquées par la fréquence cardiaque et la vitesse de conduction de l'onde de pouls plus basses chez TEN, causant un retard diastolique du retour de l'onde au niveau central, phénomène précédemment bien décrit dans la littérature.

Bilateral symmetry of radial pulse in high-level tennis players: implications for the validity of central aortic pulse wave analysis

Boris Gojanovic[a], Bernard Waeber[a], Gerald Gremion[b], Lucas Liaudet[c] and François Feihl[a]

Background Reconstruction of the central aortic pressure wave from the noninvasive recording of the radial pulse with applanation tonometry has become a standard tool in the field of hypertension. It is not presently known whether recording the radial pulse on the dominant or the nondominant side has any effect on such reconstruction.

Method We carried out radial applanation tonometry on both forearms in young, healthy, male volunteers, who were either sedentary ($n = 11$) or high-level tennis players ($n = 10$). The purpose of including tennis players was to investigate individuals with extreme asymmetry between the dominant and nondominant upper limb.

Results In the sedentary individuals, forearm circumference and handgrip strength were slightly larger on the dominant (mean ± SD respectively 27.9 ± 1.5 cm and 53.8 ± 10 kg) than on nondominant side (27.3 ± 1.6 cm, $P < 0.001$ vs. dominant, and 52.1 ± 11 kg, $P =$ NS). In the tennis players, differences between sides were more conspicuous (forearm circumference: dominant 28.0 ± 1.7 cm nondominant 26.4 ± 1.5 cm, $P < 0.001$; handgrip strength 61.4 ± 10.8 vs. 53.4 ± 9.7 kg, $P < 0.001$). We found that in both sedentary individuals and tennis players, the radial pulse had identical shape on both sides and, consequently, the reconstructed central aortic pressure waveforms, as well as derived indices of central pulsatility, were not dependent on the side where applanation tonometry was carried out.

Conclusion Evidence from individuals with maximal asymmetry of dominant vs. nondominant upper limb indicates that laterality of measurement is not a methodological issue for central pulse wave analysis carried out with radial applanation tonometry. *J Hypertens* 27:1617–1623 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Journal of Hypertension 2009, 27:1617–1623

Keywords: aorta, blood pressure, pulse, radial artery, tennis

Abbreviations: AIx, systolic augmentation index (central or radial); BMI, body mass index; BP, blood pressure; *VO2max*, maximal oxygen uptake

[a]Division de Physiopathologie Clinique, [b]Département de l'Appareil Locomoteur and [c]Service de Médecine Intensive Adulte, Centre Hospitalier Universitaire Vaudois et Université de Lausanne, Switzerland

Correspondence to François Feihl, MD, Associate Professor of Pathophysiology, PPA BH19-317, CHUV, CH-1011, Switzerland
Tel: +41 21 314 14 23; fax: +41 21 314 14 32;
e-mail: Francois.Feihl@chuv.ch

Received 10 October 2008 **Revised** 27 February 2009
Accepted 20 March 2009

Introduction

It is now widely recognized that the pulsatile component of arterial blood pressure plays a major pathogenetic role in the development of cardiovascular diseases, and that an abnormally high pulsatility, manifested by elevation of systolic and/or differential (pulse) pressure bears a strong relationship to ultimate outcome [1–4]. Regarding major target organs such as the heart and brain, the relevant pulsatility is that of central aortic pressure [5], which may substantially differ from its peripheral counterpart measured at the brachial level, due to the phenomenon of pulse wave amplification. [6]. Pulse wave amplification is mainly due to the existence of pressure waves generated by reflections in the periphery, which travel backwards along the arterial tree towards the aortic root, thus superimposing to the forward travelling pressure wave generated by left ventricular ejection [6].

The link between pulsatility of central blood pressure and the development of cardiovascular disease involving the heart and brain is now supported by a string of recent longitudinal studies. [4,7–14]. Therefore, there is now great interest for the noninvasive estimation of central systolic and pulse pressure, which seems to be possible with either carotid or radial tonometry. Due to proximity of the former vessel to the aortic arch, the shape of the carotid pulse is an acceptable surrogate to the central waveform, but carotid tonometry presents with some technical difficulties. In contrast, radial tonometry is easily carried out, but the radial substantially differs from the central pulse. The latter issue was circumvented by noting that the pattern of pulse wave amplification along the subclavian, brachial and radial arteries is relatively invariant between individuals, showing little dependence on age, sex, or mean level of blood pressure [15,16]. Furthermore, this pattern is unaffected by

0263-6352 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins DOI:10.1097/HJH.0b013e32832bffc0

arteriosclerosis, which usually spares arteries of the upper limb. Thus it was possible to define a unique mathematical operation (generalized transfer function), which allowed transforming the radial pulse – recorded tonometrically – into a reasonable approximation to its central counterpart [15,16].

It has been underscored that the reconstruction of the aortic from the radial pulse is only valid to an approximation [16]. Because transfer functions may indeed differ somewhat between individuals, the method does not necessarily provide an exact replica of an individual central waveform. In studies of large collectives however, such errors will tend to average out, unless some form of bias is also present. A numerical simulation of arterial pressure pulse propagation in the upper limb of humans has indicated that the transfer function may be rather sensitive to changes in the terminal load [17], determined in large part by resistance vessels where most of the reflections occur. The bulk of these vessels reside in skeletal muscle, which is systematically more developed in the dominant, in comparison with the nondominant arm. Thus, a systematic effect of laterality on the transfer function is conceivable. It is noteworthy that this possible source of bias has never been addressed experimentally, and that most studies using radial tonometry do not even mention the laterality of measurement.

Here, we have carried out a comparison of radial and derived central arterial pressure waveforms obtained from applying the tonometer to the dominant vs. the nondominant side in two groups of healthy men, one composed of sedentary individuals, and the other of high-level tennis players. Because the regular practice of tennis induces a large asymmetry of upper limb muscular development, we expected that any effect of laterality on the shape of the radial pulse would be magnified in the latter group.

Methods

Individuals

Two groups of young (20–35 years) healthy men were enrolled. Eleven individuals declaring no regular physical activity beyond that required by daily life were considered sedentary and constituted the sedentary group. The tennis group composed of 10 athletes who had been practicing tennis at regional or national competition level for the last 5 years. Recruitment was by advertisement. Exclusion criteria, based on medical history and summary clinical examination, included all of the following: current smoking, obesity, hypertension, diabetes, hyperlipemia, Raynaud disease, upper limb injury in the last 6 months, and intake of any drug. The study was approved by the Ethical Committee at our institution, and informed consent was obtained in writing from all individuals.

Measurements

Brachial blood pressure was obtained with oscillometry (Datascope Accutorr 1A; MS Cardio-Medical, Brunnen, Switzerland) by averaging the last two of three readings. Tonometry of the radial artery was carried out in triplicate, using the Sphygmocor device (AtCor Medical, Sydney, Australia) as previously described by our group [18]. 10 s recordings were accumulated until three were available that fulfilled all quality criteria defined by the manufacturer; that is, 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. Recordings not fulfilling these criteria were discarded. Arm and forearm circumference was determined with measuring tape. Handgrip strength was obtained with a Jamar dynamometer. Physical fitness was assessed from the maximal oxygen consumption (*VO2max*), using the CPX/MAX system (MedGraphhics, St. Paul, Minnesota, USA) and the Wasserman treadmill protocol.

Protocol

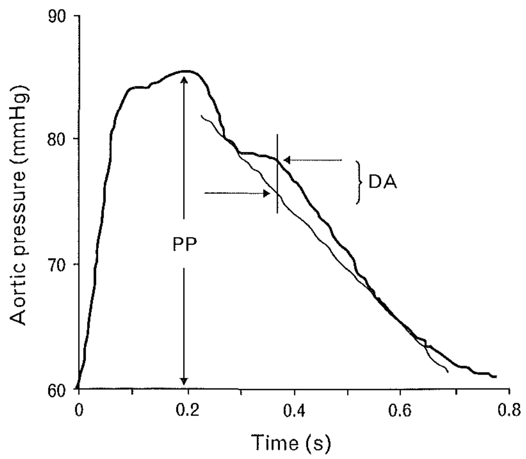
The study was carried out between 0800 and 1000 h in a quiet, temperature-controlled examination room, with individuals lying comfortably in the supine position on a hospital bed. Brachial blood pressure was obtained, and then radial tonometry carried out, first on one side and then on the other. The order in which the dominant and nondominant sides were investigated was randomized. After all tonometric data were recorded, arm diameter, forearm diameter, and handgrip strength were measured on both sides.

Data analysis

To obtain a graphical overview of the influence of experimental conditions on the radial and central arterial pulse waveforms, these were ensemble-averaged and expressed as a percentage of the corresponding pulse pressure as previously described [18].

From the reconstructed central aortic waveform, the Sphygmocor software calculates various indices, including duration of cardiac cycle, duration of ventricular ejection, and 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 due to reflection (sometimes termed central systolic augmentation index, central systolic AIx) 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. The Buckberg index is the ratio of diastolic to systolic time-aortic pressure integrals; it has been related to the efficiency of myocardial perfusion (which occurs mainly in diastole) [19]. In addition, the deviation of the central waveform from monoexponential decay in diastole was interpreted as due to backwards travelling waves reaching the aorta in that part

Fig. 1



Calculation of the central diastolic augmentation index. DA, diastolic augmentation; PP, pulse pressure. Index calculated as 100 x DA/PP.

Table 1 **Demographic and metabolic characteristics**

	Sedentary group	Tennis group
Number of individuals	11	10
Age (year)	26.6 ± 1.0	25.2 ± 4.3
Weight (kg)	81.6 ± 13.9	72.0 ± 8.1
Height (cm)	1.79 ± 0.08	1.79 ± 0.06
BMI (kg/m^2)	25.5 ± 2.9	22.4 ± 1.8††
Waist (cm)	90.3 ± 8.7	79.5 ± ± 5.9††
Hip (cm)	98.3 ± 6.0	93.1 ± 4.6†
Waist/hip	0.92 ± 0.05	0.85 ± 0.04††
VO2max (ml/min per kg)	46.4 ± 4.4	57.1 ± 4.7†††
Heart Rate (beat/min)	60.2 ± 5.2	52.3 ± 8.0†

Data are means ± SD. BMI body mass index. *VO2max* maximal oxygen consumption. $^{†}P<0.05$. $^{††}P<0.01$. $^{†††}P<0.001$ tennis players vs. sedentary men.$^{*}P<0.05$.$^{**}P<0.01$.$^{***}P<0.001$ dominant vs. nondominant upper limb.

of the cardiac cycle [6,20]. We computed the amplitude of the diastolic reflection wave, as previously described [18]. Briefly, this central diastolic augmentation index corresponds to the maximal distance between the upward convexity seen on the diastolic part of the aortic waveform and a straight line passing through the onset of the incisura and tangent to the last diastolic part of the central waveform (Fig. 1). Use of straight line was preferred to that of a (theoretically more appealing) single decreasing exponential, because it avoided the potential instabilities that would have been introduced by the need to estimate an unknow asymptote. As in the case of the central systolic AIx, the central diastolic augmentation index is expressed as a percentage of aortic pulse pressure. Finally, we also report the radial systolic augmentation index (radial AIx), as calculated by the Sphygmocor software. The radial AIx is derived directly from the radial waveform, as the ratio of the second to the first systolic peak amplitudes, as described [21].

Statistical analysis of variables obtained only once in each individual (e.g. demographic data) was carried out with bilateral *t*-tests. Variables obtained in more than one condition in each subject were analyzed with repeated measures analysis of variance, using a model including group (sedentary/tennis), laterality (dominant/nondominant), and the interaction of these factors. When the relevant F statistic was significant, further pairwise comparisons were done using Fisher's protected least significant difference [22]. The alpha level of all tests was set at 0.05. The data were summarized as mean ± SD.

Results

As shown in Table 1, the two groups of individuals were matched for age and sex, and sedentary individuals were clearly overweight with respect to tennis players. A higher *VO2max* and lower heart rate confirmed the superior physical fitness of the latter with respect to former.

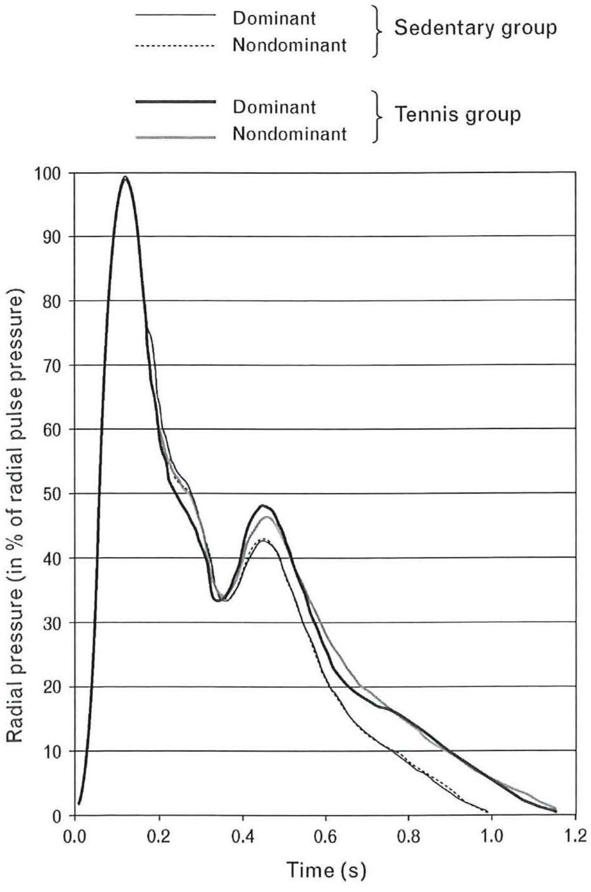
Bilateral upper limb characteristics in the two study groups are shown in Table 2. In the sedentary individuals, the average circumference of both the upper-arm and the forearm was 2% greater on the dominant, as compared with the nondominant side, a difference that reached statistical significance in the forearm only ($P<0.001$). As expected, upper limb asymmetry was much larger in tennis players, in whom the average circumference difference between dominant and nondominant sides reached 6%, and was statistically significant not only in the forearm ($P<0.001$), but also in the upper arm ($P<0.001$). In tennis players, the nondominant upper limb was thinner than in sedentary individuals ($P<0.001$), a difference probably related to a higher fat mass in the latter. As expected again, the handgrip strength of tennis players

Table 2 **Upper limb characteristics**

	Sedentary group		Tennis group	
	Dominant	Nondominant	Dominant	Nondominant
Upper arm circumference (cm)	31.0 ± 2.4	30.5 ± 2.8	30.0 ± 2.2†††,***	28.4 ± 2.6†††
Forearm circumference (cm)	27.9 ± 1.5***	27.3 ± 1.6	28.0 ± 1.7***	26.4 ± 1.5†††
Systolic BP (mmHg)	123 ± 7	122 ± 9	120 ± 12	118 ± 13
Hand grip strength (kg)	53.8 ± 10.0	52.1 ± 11.1	61.4 ± 10.8†††,***	53.4 ± 9.7
Diastolic BP (mmHg)	71 ± 6	68 ± 5	62 ± 8††	63 ± 8††

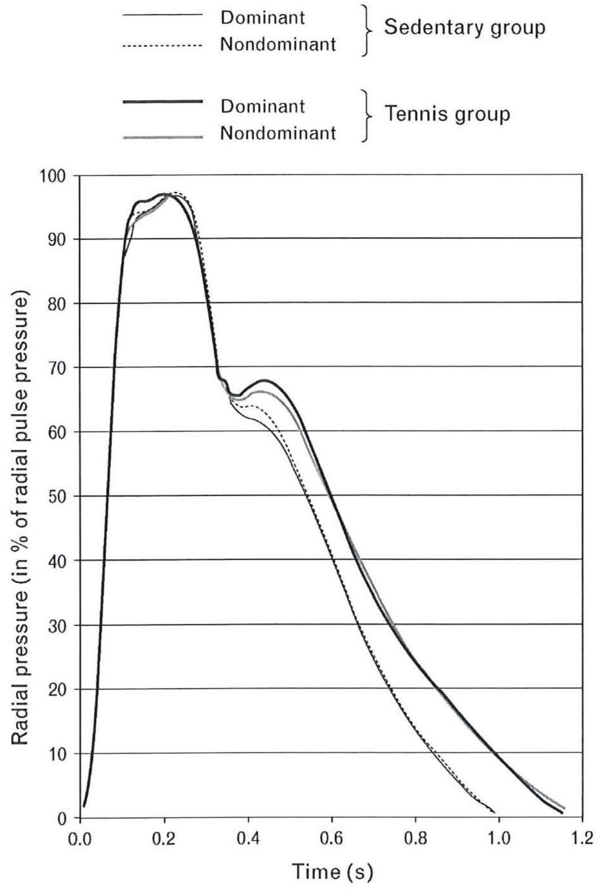
Data are means ± SD. BP oscillometric value of blood pressure. $^{†}P<0.05$. $^{††}P<0.01$. $^{†††}P<0.001$ tennis players vs. sedentary men.$^{*}P<0.05$.$^{**}P<0.01$. $^{***}P<0.001$ dominant vs. nondominant upper limb.

Fig. 2



Ensemble-averaged radial pulse waveforms recorded from the dominant and nondominant arm in the sedentary and tennis groups.

Fig. 3



Ensemble-averaged aortic pulse waveforms, as reconstructed from radial tonometry carried out on the dominant and on the nondominant arm in the sedentary and tennis groups.

was much larger on the dominant than on the nondominant side (on average by 15%, $P < 0.001$), an asymmetry that was far less marked in the sedentary group (3%, $P > 0.1$). Within groups, the values of oscillometric blood pressure taken on both sides were practically identical. Systolic brachial pressure was similar, and diastolic brachial pressure somewhat lower in tennis players, in comparison with the sedentary individuals.

There was no effect of laterality on the shape of either the radial or the reconstructed central pressure waveform (Figs 2 and 3). The systolic part of the aortic waveform was of similar shape and duration in both groups. In contrast, the upper convexity seen in the first half of diastole, interpreted as due to reflection waves reaching the aorta within that part of the cardiac cycle [6,18], appeared more prominent in the tennis players than in the sedentary individuals (Fig. 3). The longer pulse duration of tennis players' diastole in comparison with sedentary individuals, which is obvious in Figs 2 and 3 and is consistent with their lower heart rate (Table 1), appeared due to a selective prolongation of diastole.

Consistent with the pulse shapes shown in Fig. 3, there was no effect of laterality on any of the pulsatility indices derived either directly from the radial or from the reconstructed central aortic waveforms, whether in the tennis or in the sedentary group (Table 3). Both the radial and the central systolic AIx were the same in both groups. In contrast, the central diastolic augmentation index was more than 50% larger in tennis players ($P < 0.05$). These athletes also had a significantly higher Buckberg index ($P < 0.01$), reflecting both the larger central diastolic augmentation and the longer duration of diastole. As a final note, the larger value of central diastolic augmentation in comparison with central systolic AIx is not amenable to physiologic interpretation, considering the different modes of computation of these two parameters.

Discussion

The main new finding of this study is the identity of radial pulse waveforms recorded with aplanation tonometry on both forearms of the same individual. This identity holds even in the presence of gross asymmetry

Table 3 **Parameters derived from radial applanation tonometry**

	Sedentary group		Tennis group	
Arm used for applanation tonometry	Dominant	Nondominant	Dominant	Nondominant
Central systolic pressure (mmHg)	105 ± 6	103 ± 8	98 ± 7	99 ± 9
Central diastolic pressure (mmHg)	72 ± 6	69 ± 4	63 ± 8	64 ± 8
Peripheral minus central systolic pressure (mmHg)	17.5 ± 4.1	19.4 ± 4.2	21.7 ± 7.0	19.3 ± 4.2
Central AIx (%)	4.2 ± 11.3	4.3 ± 10.9	3.2 ± 6.6	4.6 ± 8.0
Central diastolic augmentation (%)	8.2 ± 3.7	9.0 ± 3.5	14.0 ± 7†	13.0 ± 6.4†
Buckberg index (%)	164 ± 15	163 ± 13	211 ± 45††	203 ± 45†
Radial AIx (%)	52.0 ± 13.2	50.8 ± 9.9	45.4 ± 13.8	50.3 ± 13.3

Parameters calculated from the radial pulse, as recorded with applanation tonometry carried out on the dominant and nondominant arm of study individuals. Central parameters obtained from the reconstructed central aortic pressure waveform. AIx: systolic augmentation of either the central or the radial pulse, expressed in % of the corresponding pulse pressure. Data are means ± SD. † $P < 0.05$. †† $P < 0.01$. ††† $P < 0.001$ tennis players vs. sedentary men. There were no statistically significant difference between dominant and nondominant arm.

between the dominant and the nondominant upper limb, as existed in the tennis players. Consequently, the central aortic pressure waveform reconstructed with the use of a generalized transfer function is robustly independent of the side on which applanation tonometry of the radial artery is performed.

The asymetry of upper limb circumferences noted in the tennis players and, to a lesser degree, also in control individuals (Table 2) was entirely consistent with values reported in the literature [23,24], and was in all likelihood related to bilateral differences in mass of skeletal muscle, due to asymmetrical training, as indicated by the larger handgrip strength of the dominant side.

The possibility that asymmetrical training could cause differences in pulse wave amplification between the dominant and nondominant upper limb arises first because of the known effects of training on the structural and mechanical properties of conduit arteries. There is ample evidence that the lumen diameter and wall cross-sectional area of these vessels both increase with the activity level of the dependent muscle groups [25–28], with associated changes in vascular mechanics [24,28]. These effects are believed to be mediated locally rather than systemically, by the higher shear stress exerted on the arterial endothelium by an augmented blood flow [29]. Accordingly, unilateral endurance training of either the upper or lower limb has been associated with unilateral changes in the morphology and function of the corresponding conduit arteries [24,27,28,30]. In short, bilateral asymmetry in the geometry and mechanics of upper limb conduit arteries may be expected in the tennis players of the present study, and are also possible, although to a lesser degree, in the control individuals whose dominant arm exercises more than does the opposite arm.

Two simulation studies provide insight into how such differences could affect pulse wave amplification. Karamanoglu *et al.* [17] constructed a numerical model of the human upper limb arterial tree and concluded that changes of up to 50% in the Young modulus of conduit artery wall (one determinant of arterial compliance) had only a minor impact on the aortic to radial transfer function, translating into no impact at all on pulse wave amplification. However, this study did not explore effects related to changing vessel geometry. The latter were addressed by Westerhof *et al.* [31]. With an analogous approach, these authors found that a spatially uniform 25% increase or decrease in the internal diameter of subclavian, brachial and radial arteries would not substantially modify the aortic to radial transfer function below 3 Hz, that is, within the frequency band where most of the pressure wave energy is concentrated at resting normal heart rate. Consequently, such changes in diameter, which exceeded the asymmetry actually observed with unilateral upper limb training [24,27, 28,30], had a negligible impact on the shape of the radial pulse. These simulation results are therefore consistent with the identity of radial pressure waveforms found in the present study (Fig. 2).

The second reason why asymmetrical training could cause differences in pulse wave amplification between the dominant and nondominant upper limb resides in the effects of exercise on muscle microcirculation. It is well known that regular activity of muscles promotes their capillarization [29]. However, the part of microcirculation relevant to pressure transfer along the arterial tree lies upstream from the capillaries, that is in the resistance small arteries and arterioles, believed to be the major site of pressure wave reflection. There is surprisingly little data available on how training affects skeletal muscle vascularization at that level. One might reasonably assume a multiplication of parallel resistance channels commensurate at least to the increase in muscle mass, as found in the myocardium with exercise-induced cardiac hypertrophy [32,33]. Consistent with this possibility, investigators found the racket arm of tennis players to be 6% larger than the other arm in terms of circumference (as in the present study, Table 2), and thus roughly 12% larger in terms of volume, whereas the resting forearm blood flow measured with plethysmography and thus expressed per unit volume of tissue did not differ between sides [23]. This data implies that the global peripheral resistance which loaded the conduit arteries was 12% lower in the racket arm. The aforementioned simulation by Westerhof *et al.* [31] indicated that a fourfold increase or decrease in peripheral resistance of the upper limb would not substantially affect pulse wave aortic to radial pulse wave amplification. We must, however, consider that peripheral resistance, which measures the extent to which the vascular bed opposes the nonpulsatile component of blood flow, is not the sole determinant of peripheral pressure wave reflection. The latter depends in fact on the impedance mismatch between the distal conduit arteries and the resistance vessels, as measured by the peripheral reflection coefficient, a frequency-dependent quantity. The simulation by Karamanoglu *et al.* [17] indicates a potential high sensitivity of the aortic to radial transfer function to changes in the peripheral reflection coefficient in the whole frequency range (that is below 3 Hz too), such that the shape of the radial pulse could be affected. The present data (Fig. 2) indicate that any asymmetry in peripheral wave reflection associated with unilateral muscle training of the upper limb is likely to be very small and insufficient to cause asymmetry of the radial pulses.

The study was not primarily designed to test for differences in central aortic pressure waveform between athletes and sedentary individuals. However, our results necessitate some comments in that respect. On the basis of previous observations by Edwards *et al.* [34], endurance training is expected to reduce the augmentation of central systolic pressure due to reflected waves. However, the central systolic AIx did not differ between the two study groups (Table 3). An explanation to this discrepancy can reside in the lower heart rate of tennis players (Table 1), which might have biased the index towards higher values [35], but this interpretation was not supported when we corrected the analysis for such an effect (not shown). Another possibility resides in the small study size, coupled with the large interindividual variation of the central systolic AIx relative to mean values (Table 3 and [34]), making up for low power to detect differences between groups. However, the radial AIx, which usually tracks its central counterpart [21], also did not differ between groups despite a much smaller coefficient of variation (Table 3). A last factor possibly accounting for discordant results between studies might be a higher level of endurance in the trained athletes examined by Edwards *et al.* (average *VO2max* 65 ml/kg per min, [34]) relative to the present group of tennis-players (57 ml/kg per min, Table 1).

In comparison with the central systolic AIx, the central diastolic augmentation index was less variable (coefficient of variation $\leq 50\%$, Table 3) and significantly higher in the tennis players, in comparison with the sedentary individuals. This difference would be consistent with reflected waves reaching the central aorta later, thus predominantly in diastole, due to higher arterial distensibility and lower pulse wave velocity in the former group.

What are the implications of our study? First, we show formally that the noninvasive estimation of central aortic pressure with radial artery tonometry is independent of the side on which pulse recordings are taken. The demonstration has an element of robustness to it, due to the inclusion of individuals with exaggerated asymmetry between the dominant and the nondominant upper limb. To establish this methodological point was quite important, because pulse wave analysis is widely applied in clinical cardiovascular research. In addition, the potential usefulness of central diastolic augmentation as a further index of arterial distensibility warrants further studies.

Acknowledgements
The study received financial support from departmental funding.

There are no conflicts of interest.

References
1 Haider AW, Larson MG, Franklin SS, Levy D. Systolic blood pressure, diastolic blood pressure, and pulse pressure as predictors of risk for congestive heart failure in the Framingham Heart Study. *Ann Intern Med* 2003; **138**:10–16.
2 Wang JG, Staessen JA, Franklin SS, Fagard R, Gueyffier F. Systolic and diastolic blood pressure lowering as determinants of cardiovascular outcome. *Hypertension* 2005; **45**:907–913.
3 Safar ME, Lacolley P. Disturbance of macro- and microcirculation: relations with pulse pressure and cardiac organ damage. *Am J Physiol* 2007; **293**:H1–7.
4 Jankowski P, Kawecka-Jaszcz K, Czarnecka D, Brzozowska-Kiszka M, Styczkiewicz K, Loster M, *et al.* Pulsatile but not steady component of blood pressure predicts cardiovascular events in coronary patients. *Hypertension* 2008; **51**:848–855.
5 Mitchell GF. Effects of central arterial aging on the structure and function of the peripheral vasculature: implications for end-organ damage. *J Appl Physiol* 2008; **105**:1652–1660.
6 Nichols WW, O'Rourke MF. *McDonald's blood flow in arteries*, 5th ed. London: A Hodder Arnold Publication; 2005.
7 London GM, Blacher J, Pannier B, Guerin AP, Marchais SJ, Safar ME. Arterial wave reflections and survival in end-stage renal failure. *Hypertension* 2001; **38**:434–438.
8 Safar ME, Blacher J, Pannier B, Guerin AP, Marchais SJ, Guyonvarc'h PM, London GM. Central pulse pressure and mortality in end-stage renal disease. *Hypertension* 2002; **39**:735–738.
9 de Luca N, Asmar RG, London GM, O'Rourke MF, Safar ME. Selective reduction of cardiac mass and central blood pressure on low-dose combination perindopril/indapamide in hypertensive subjects. *J Hypertens* 2004; **22**:1623–1630.
10 Weber T, Auer J, O'Rourke MF, Kvas E, Lassnig E, Lamm G, *et al.* Increased arterial wave reflections predict severe cardiovascular events in patients undergoing percutaneous coronary interventions. *Eur Heart J* 2005; **26**:2657–2663.
11 Chirinos JA, Zambrano JP, Chakko S, Veerani A, Schob A, Willens HJ, *et al.* Aortic pressure augmentation predicts adverse cardiovascular events in patients with established coronary artery disease. *Hypertension* 2005; **45**:980–985.
12 The CAFE Investigators. Differential impact of blood pressure: lowering drugs on central aortic pressure and clinical outcomes. *Circulation* 2006; **113**:1213–1225.

13 Roman MJ, Devereux RB, Kizer JR, Lee ET, Galloway JM, Ali T, *et al.* Central pressure more strongly relates to vascular disease and outcome than does brachial pressure: the Strong Heart Study. *Hypertension* 2007; **50**:197–203.
14 Pini R, Cavallini MC, Palmieri V, Marchionni N, Di Bari M, Devereux RB, *et al.* Central but not brachial blood pressure predicts cardiovascular events in an unselected geriatric population: the ICARe Dicomano Study. *J Am Coll Cardiol* 2008; **51**:2432–2439.
15 O'Rourke MF, Pauca A, Jiang XJ. Pulse wave analysis. *Br J Clin Pharmacol* 2001; **51**:507–522.
16 Gallagher D, Adji A, O'Rourke MF. Validation of the transfer function technique for generating central from peripheral upper limb pressure waveform. *Am J Hypertension* 2004; **17**:1059–1067.
17 Karamanoglu M, Gallagher DE, Avolio AP, O'Rourke MF. Pressure wave propagation in a multibranched model of the human upper limb. *Am J Physiol* 1995; **269**:H1363–1369.
18 Delachaux A, Waeber B, Liaudet L, Hohlfeld P, Feihl F. Profound impact of uncomplicated pregnancy on diastolic, but not systolic pulse contour of aortic pressure. *J Hypertens* 2006; **24**:1641–1648.
19 Buckberg GD, Fixler DE, Archie JP, Hoffman JI. Experimental subendocardial ischemia in dogs with normal coronary arteries. *Circ Res* 1972; **30**:67–81.
20 Kelly R, Hayward C, Avolio A, O'Rourke M. Noninvasive determination of age-related changes in the human arterial pulse. *Circulation* 1989; **80**:1652–1659.
21 Melenovsky V, Borlaug BA, Fetics B, Kessler K, Shively L, Kass DA. Estimation of central pressure augmentation using automated radial artery tonometry. *J Hypertens* 2007; **25**:1403–1409.
22 Winer BJ. *Statistical principles in experimental design,* 3rd ed. New York: McGraw-Hill; 1971.
23 Sinoway LI, Musch TI, Minotti JR, Zelis R. Enhanced maximal metabolic vasodilatation in the dominant forearms of tennis players. *J Appl Physiol* 1986; **61**:673–678.
24 Giannattasio C, Failla M, Grappiolo A, Calchera I, Grieco N, Carugo S, *et al.* Effects of physical training of the dominant arm on ipsilateral radial artery distensibility and structure. *J Hypertens* 2001; **19**:71–77.
25 Wijnen JA, Kuipers H, Kool MJ, Hoeks AP, van Baak MA, Struyker Boudier HA, *et al.* Vessel wall properties of large arteries in trained and sedentary subjects. *Basic Res Cardiol* 1991; **86 (Suppl 1)**:25–29.
26 Kool MJ, Struijker-Boudier HA, Wijnen JA, Hoeks AP, van Bortel LM. Effects of diurnal variability and exercise training on properties of large arteries. *J Hypertens Suppl* 1992; **10**:S49–52.
27 Huonker M, Schmid A, Schmidt-Trucksass A, Grathwohl D, Keul J. Size and blood flow of central and peripheral arteries in highly trained able-bodied and disabled athletes. *J Appl Physiol* 2003; **95**:685–691.
28 Schmidt-Trucksass A, Schmid A, Brunner C, Scherer N, Zach G, Keul J, Huonker M. Arterial properties of the carotid and femoral artery in endurance-trained and paraplegic subjects. *J Appl Physiol* 2000; **89**:1956–1963.
29 Prior BM, Yang HT, Terjung RL. What makes vessels grow with exercise training? *J Appl Physiol* 2004; **97**:1119–1128.
30 Miyachi M, Tanaka H, Yamamoto K, Yoshioka A, Takahashi K, Onodera S. Effects of one-legged endurance training on femoral arterial and venous size in healthy humans. *J Appl Physiol* 2001; **90**:2439–2444.
31 Westerhof BE, Guelen I, Stok WJ, Wesseling KH, Spaan JA, Westerhof N, *et al.* Arterial pressure transfer characteristics: effects of travel time. *Am J Physiol* 2007; **292**:H800–807.
32 Breisch EA, White FC, Nimmo LE, McKirnan MD, Bloor CM. Exercise-induced cardiac hypertrophy: a correlation of blood flow and microvasculature. *J Appl Physiol* 1986; **60**:1259–1267.
33 White FC, Bloor CM, McKirnan MD, Carroll SM. Exercise training in swine promotes growth of arteriolar bed and capillary angiogenesis in heart. *J Appl Physiol* 1998; **85**:1160–1168.
34 Edwards DG, Lang JT. Augmentation index and systolic load are lower in competitive endurance athletes. *Am J Hypertens* 2005; **18**:679–683.
35 Wilkinson IB, MacCallum H, Flint L, Cockcroft JR, Newby DE, Webb DJ. The influence of heart rate on augmentation index and central arterial pressure in humans. *J Physiol (Lond)* 2000; **525 (Pt 1)**:263–270.