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Effects of Isolated Systolic Hypertension and Essential Hypertension on Large and Middle-sized Artery Compliance

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Background: Systolic hypertension of the elderly is characterized by a reduction in arterial compliance. Whether and to what extent this involves arteries of various structure and size is not well known. *Objective:* To study carotid and radial artery compliance in systolic hypertension of the elderly, compared to essential hypertension and normotension. *Methods:* We investigated 28 elderly patients with systolic hypertension (age 68.6 ± 1.4 years, mean ± SE; systolic blood pressure $>$ 160 mmHg and diastolic blood pressure $<$ 90 mmHg) plus 17 age-matched patients with essential hypertension and 15 age-matched healthy normotensive subjects. Radial and carotid artery compliance were evaluated using echotracking techniques. In both arteries compliance was assessed statistically and dynamically, i.e. as compliance values throughout the diasto-systolic pressure range. Measurements included intima-media wall thickness of the radial artery. *Results:* Compared to normotensive subjects, carotid artery compliance was reduced in essential hypertension and more so in systolic hypertension. However, although in both groups radial artery wall thickness was markedly greater than in the normotensive group, radial artery compliance was markedly reduced in systolic hypertension, but unchanged in essential hypertension. *Conclusions:* In systolic hypertension of the elderly the reduction of arterial compliance is marked in both muscular and large elastic arteries, while in elderly essential hypertensives changes in arterial compliance are more heterogeneous, i.e. only carotid artery compliance is reduced. The different effects of these two types of hypertension on arterial mechanics are visible throughout the physiological range of blood pressure and probably accounted for by different alterations in vessel wall structure *Key words: arterial compliance, blood pressure, carotid artery, essential hypertension, peripheral circulation, systolic hypertension, vessels.*

INTRODUCTION

Several studies have shown that arterial compliance is reduced in systolic hypertension and that this reduction is majorly responsible for the blood pressure pattern typical of this condition, i.e. an increased systolic and a reduced diastolic blood pressure [1–4]. In these studies, however, methods have been used that allow global and often only indirect indices of compliance to be obtained throughout the arterial tree without addressing two important aspects of arterial mechanics that have recently emerged; one, the steep nonlinear relationship that links arterial compliance to blood pressure [5], and two, the heterogeneous effects of various diseases on arteries of different structure and size [6, 7]

In the present study we have addressed these issues using techniques that allow arterial compliance and distensibility to be continuously assessed from diastolic to systolic blood pressure in both a middle-sized muscular and a large elastic-type artery. The study was performed in subjects with systolic hypertension. For comparison, however, we also studied age-matched essential hypertensive and normotensive individuals

METHODS

Subjects

We investigated 60 subjects (24 males, 36 females) with an age ranging from 54 to 81 years; 15 subjects (age 63 ± 2.0 years) were healthy controls with a normal blood pressure at three sphygmomanometric measurements obtained in the outpatient clinics; 17 subjects (age 66.3 ± 1.5 years) had an essential hypertension of a moderate degree, i.e. a diastolic blood pressure equal or above 95 and equal or less than 110 mmHg. The remaining 28 patients (age 68.6 ± 1.4 years) had a systolic hypertension, i.e. a systolic blood pressure above 160 mmHg and a diastolic blood pressure below 90 mmHg. All hypertensive subjects were under antihypertensive treatment (which was withdrawn before the

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study; see below) based on a diuretic ($n = 6$), an ACE-inhibitor ($n = 11$), a calcium antagonist ($n = 13$) or a variable combination of the above drugs ($n = 15$). No hypertensive subjects had (i) clinical evidence of a major cardiovascular or non-cardiovascular disease, (ii) an abnormal plasma glucose ($\geq$110 mg%) or lipid (total cholesterol $\geq$ 220 mg%) profile, and (iii) hemodynamically significant atherosclerotic plaques at echo-Color-Doppler examinations of the aorta, carotid and femoral arteries. All subjects gave their informed consent to the study, which was approved by the Ethics Committee of our Institutions

Radial artery evaluation

Radial artery diameter and wall thickness were measured using an A-mode ultrasonic device (NIUS 02, Omega, Bienne, Switzerland and Capital Medical Services, Paris, France). Briefly, a highly focalized transducer operating at a frequency of 10 MHz was stereotaxically positioned over the radial artery 2–4 cm above the wrist, direct contact with the skin being prevented by use of a gel as a medium. With the subject supine and the arm immobile at the heart level, the transducer was oriented perpendicularly to the longitudinal axis of the vessel based on the acoustic Doppler signal. After switching to A-mode the echo beam corresponding to the posterior media-adventitia interface was visualized on a computer screen [5]. The wall thickness of the posterior wall of the artery could thus be electronically measured as the distance between the inner and outer wall echoes [5, 8]. The backscattered echoes from the inner posterior and anterior walls of the artery were also visualized on the computer screen and electronically digitized (via an analogical fast transducer) to allow internal diameter variations to be derived at 50 Hz. The resolution was 150 μm [8]

The device also made use of a photoplethysmographic system (Finapres 2003, Ohmeda, Englewood, CO) which allowed blood pressure to be recorded at 50 Hz from a finger ipsilateral to the radial artery examined, with an accuracy similar to intra-arterial blood pressure recording [9] and a resolution of 2 mmHg [9]. The concomitant acquisition of continuous arterial diameter and blood pressure signals allowed the diameter/pressure curve of the vessel to be calculated. The curve was then analysed for its fitting with the arctangent model of Langewouters, which is based on the formula:

$$S = \alpha\left[\frac{\pi}{2} + \tan^{-1}\left(\frac{P-\beta}{\gamma}\right)\right]$$

where S is the cross-sectional area, P is the intravascular pressure, and α, β and γ are three optimal parameters describing the spatial position of the diameter/pressure curve [10]. Cross-sectional compliance (C = ΔS/ΔP) was calculated from this formula as follows:

$$C = \frac{\alpha}{\gamma}\,\frac{1}{1+\left(\dfrac{P-\beta}{\gamma}\right)^2}$$

and expressed as consecutive values for blood pressure ranging from diastole to systole, i.e. as the cross-sectional compliance/pressure curve. The same formula was used to calculate the cross-sectional distensibility (cross-sectional compliance divided by the vessel area)/pressure curve. The measurements were made by two operators unaware of the clinical condition of the patient. The within-operator variation coefficients of radial artery diameter at diastole (see below) and wall thickness measurements were 4% and 3%. The corresponding between-operator variation coefficients were 8% and 7%

Carotid artery evaluation

With the subject supine and the neck in partial extension, the diameter and wall motion of the right common carotid artery were measured 2 cm below the carotid bifurcation using a B-M mode echo-tracking device based on Doppler shift (Wall Track System, PIE Medical, Maastricht, The Netherlands) and on a transducer operating at a frequency of 7.5 MHz [11, 12]. The transducer was oriented perpendicularly to the longitudinal axis of the vessel under B-mode guidance. After switching to A-mode the backscattered echoes from the anterior and posterior carotid artery walls were visualized on a screen and the corresponding radiofrequency signal was tracked by electronic tracers to allow the digitalized signal of the internal diameter variations to be derived at a 50 Hz. The resolution was 300 μm [12]

Blood pressure was measured from the ipsilateral arm by a mercury sphygmomanometer, taking the 1st and 5th Korotkoff sounds to identify systolic and diastolic values, respectively. Carotid artery compliance was derived in accordance with the Reneman formula [11]:

$$C = [\pi(Ddx\Delta d)]/2\Delta P$$

where C is the cross-sectional compliance, Dd the diastolic diameter of the vessel, Δd the systo-diastolic diameter change and ΔP the corresponding pulse pressure. The same formula was used to calculate carotid artery distensibility coefficient. All measurements were made by the same two operators who performed the radial artery measurements. The within-operator variation coefficient of carotid artery diameter measurements was 3.5%, while the between-operator variation coefficient was 5%

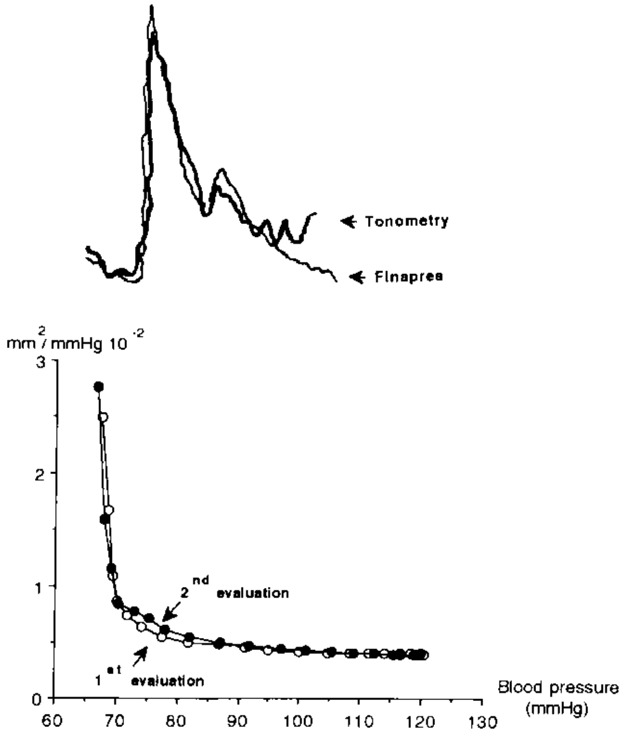

Fig. 1. The upper panel shows the original tracing from one subject of the carotid artery pressure waveform obtained by tonometry and the symultaneous waveform obtained by Finapres. The lower panel shows the carotid compliance (Reneman formula)-pressure curve obtained by using the ascending portion of the Finapres pressure waveforms taken in the same subject at two different times.

In 15 subjects (5 subjects per group) an attempt was made to obtain compliance-pressure curves also for the carotid artery. Tonometry was not used because the carotid artery compression required by this procedure was regarded as potentially risky in elderly patients. Blood pressure was thus continuously measured using the Finapres device (see above). The blood pressure and carotid artery diameter tracings were recorded as ASCII values and synchronized to obtain carotid artery diameter/pressure curves. The Reneman formula served again to derive carotid artery compliance/pressure curves, using consecutive pairs of diameter and blood pressure values for calculating Δ diameter vs Δ pressure. Only data derived from the ascending portion of the finger blood pressure wave were considered, because this portion showed (i) a close similarity with the ascending portion of the blood pressure wave obtained by tonometry from the carotid artery (Fig. 1, upper panel), (ii) a superimposable morphology over consecutive cardiac cycle, and (iii) a high reproducibility of the compliance/pressure curves derived at different times (Fig. 1, bottom panel). The descending portion of the finger pressure wave was not considered in order to avoid the wave form alterations caused by reflected wave phenomena

Protocol and data analysis

In all subjects, 2 weeks was allowed from the screening visit during which any antihypertensive drug taken by the

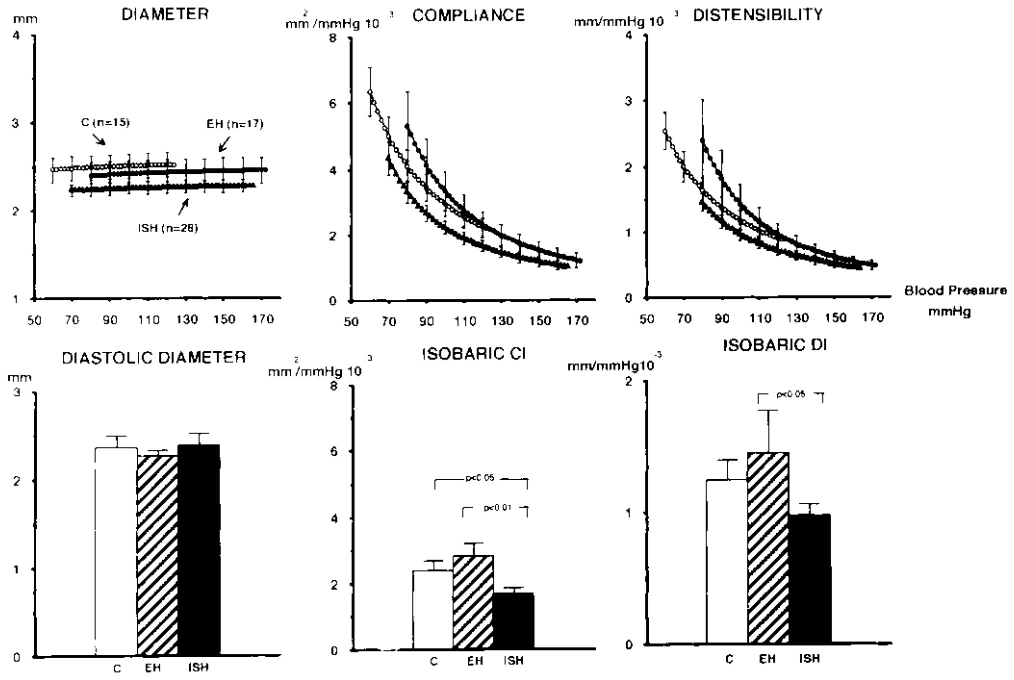

Fig. 2. Radial artery mechanics in 15 control healthy subjects (C), 17 subjects with essential hypertension (EH) and 28 subjects with systolic hypertension (ISH). Data are shown as means ± SE. CI: compliance index; DI: distensibility index.

hypertensive subjects was withdrawn. The patients were then visited a second time in the outpatient clinic to collect further sphygmomanometric blood pressure measurements. The study proper was conducted in the afternoon (following a 24-h abstinence from alcohol and coffee consumption) in accordance with the following protocol: (i) each subject was placed in the supine position and fitted with the finger blood pressure and the radial artery echo-tracking devices, (ii) following a 20-min time interval, blood pressure, heart rate and radial artery diameter were continuously measured for 15 min, (iii) the radial artery echo-tracking device was disconnected and the 7.5 MHz probe for carotid artery evaluation was manually positioned over the neck, (iv) five 6-sec acquisitions of carotid diameter were made during a 15-min period while blood pressure was measured at 5-min intervals with a mercury sphygmomanometry and continuously by the Finapres pressure device

Radial artery wall thickness was measured over 30 sec via the oscilloscopic image of the arterial walls. The radial artery diameter-pressure curve was obtained by averaging the values of 5 periods of 30 sec each, taken at 3-min intervals. These data were used to obtain (i) the compliance-pressure curve and (ii) the distensibility–pressure curve, (iii) the diameter corresponding to diastolic blood pressure, (iv) the integral of the area under the curve relating compliance to the blood pressure range common to each group (isobaric compliance index), and (v) the integral of the area under the curve relating distensibility to the blood pressure range common to each group (isobaric distensibility index). Carotid artery diastolic diameter, compliance and distensibility coefficient were calculated by averaging the values obtained in the five acquisition periods. In the subjects in whom finger blood pressure was measured continuously, the carotid isobaric compliance was calculated as mentioned before for the radial isobaric compliance index

Data obtained in individual subjects were averaged and shown as means ± SE. The statistical significance of the differences in mean values was assessed by two-way analysis of variance. The two-tailed *t*-test for unpaired or paired observations was used to locate the between-group differences. The Bonferroni correction was employed to account for multiple comparisons. A p value < 0.05 was taken as the level of statistical significance

RESULTS

As expected, the sphygmomanometric blood pressure values taken at the second medical visit were different in the three groups of subjects, i.e., systolic, mean and diastolic blood pressure were 133.0 ± 4.3 mmHg, 98.3 ± 2.7 mmHg and 81.0 ± 2.1 mmHg, respectively, in the normotensive group. All values were significantly and markedly elevated (197.9 ± 5.9 mmHg, 135.6 ± 3.0 mmHg and 105.0 ± 2.0 mmHg, $p < 0.01$) in the group with essential hypertension. In contrast, in the group with systolic hypertension, systolic and mean blood pressure were significantly and markedly elevated (191.6 ± 4.9 mmHg and 117.1 ± 4.4 mmHg, $p < 0.01$), whereas diastolic blood pressure was significantly but only slightly greater (85.5 ± 1.3 mmHg, $p < 0.01$) than that of the control group. Heart rate values (obtained via the finger pressure signal as the reciprocal of the interval between consecutive systolic beats) were similar in the three groups (65.8 ± 2.7 b/min, 69.0 ± 2.8 b/min and 69.1 ± 2.0 b/min)

Radial artery mechanics and wall thickness

Fig. 2 shows that in all three groups radial artery diameter increased slightly and progressively as blood pressure increased from diastole to systole, whereas radial artery compliance and distensibility showed a concomitant, marked and non-linear reduction. Radial artery diastolic diameter and diameter-pressure curves showed no significant between-group differences. Compared to controls, radial artery compliance and distensibility-pressure curves were displaced slightly upward in subjects with essential hypertension with a modest and non-significant increase in the isobaric compliance and distensibility index. In contrast, radial artery compliance and distensibility pressure curves were displaced markedly downward in subjects with systolic hypertension, with a marked and significant reduction in both the isobaric compliance and the distensibility index. Compared to controls, radial artery wall thickness was significantly, markedly and similarly greater in both hypertensive groups (Fig. 3) compared to controls

Carotid artery mechanics

Fig. 4 shows that carotid artery diameter at diastole was greater in subjects with essential and systolic hypertension than in normotensive subjects, although only in systolic hypertension was the difference statistically significant. Carotid artery compliance and distensibility (derived from the Reneman formula and the sphygmomanometric blood pressure) were reduced to a similar marked extent in both hypertensive groups. As shown in Fig. 5, the carotid compliance-pressure curve decreased steeply as blood pressure increased above diastole, with a further much flatter decrease when blood pressure values further increased towards systole. The shape of the curve was similar in controls, essential hypertensive patients and patients with systolic hypertension. In patients with systolic hypertension, but not in essential hypertensive patients, the compliance values were lower than those of controls over most of the curve. The isobaric compliance

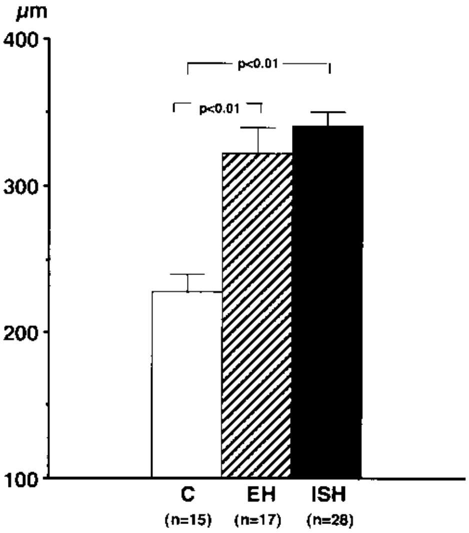

Fig. 3. Radial artery wall thickness in the subjects of Figure 2. Abbreviations as in Figure 2.

was reduced in both hypertensive groups, however, although the reduction was more marked in systolic hypertension (systolic hypertension 2.6 ± 0.4 mm^2/mmHg 10^{-2} $p < 0.05$ vs controls; essential hypertension 4.2 ± 1 mm^2/mmHg10^{-2}; controls 5.3 ± 0.8 mm^2/mmHg 10^{-2})

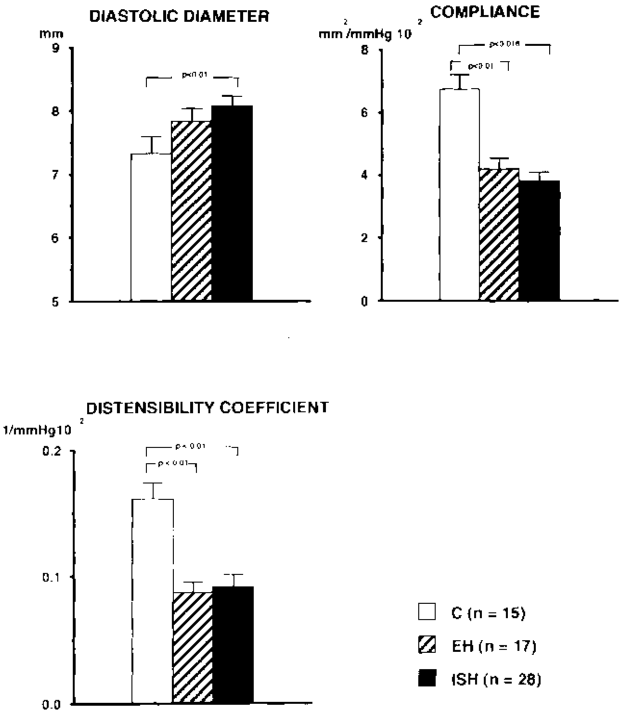

Fig. 4. Carotid artery mechanics in the subjects of Figure 2. Abbreviations and symbols as in Figure 2.

DISCUSSION

Our study confirms that arterial compliance is reduced in systolic hypertension [1–4, 13–16]. However, it also provides several new data which allow this phenomenon to be known in greater detail. First, the reduction of arterial compliance shown in systolic hypertension is a marked and diffuse one because, compared to control subjects, in subjects with systolic hypertension the compliance values were reduced by 39% in middle-sized muscular arteries and by 44% in large elastic arteries. Second, the generalized reduction of arterial compliance that characterizes systolic hypertension is different from that accompanying essential hypertension, in which large elastic artery compliance but not middle-sized muscular artery compliance is reduced [17–21]. And third, in both middle-sized muscular and large elastic arteries, the reduction of arterial compliance associated with systolic hypertension is paralleled by a reduction of arterial distensibility, both changes being evident throughout the diasto-systolic pressure range and marked also when assessed at similar blood pressures (isobaric compliance and distensibility). This demonstrates that these phenomena by no means result just from the fact that a greater vessel diameter or a higher blood pressure stretches the arterial wall near the point of inextensibility, but that they definitively reflect an increase in vessel wall stiffness

Several other results of our study deserve to be mentioned. One, previous studies have shown that in middle-aged essential hypertensive subjects, compared to age-matched normotensive individuals, radial artery compliance is either unchanged or moderately increased [17–19]. Our present observations show this to be the case also in elderly essential hypertensive subjects, leading to the conclusion that even when its duration is a long one, essential hypertension never results in an impaired mechanics of muscular middle-sized arteries. Because this contrasts with the reduction in large elastic artery compliance, we can speculate that factors acting selectively on muscular middle-sized arteries are responsible. We can also speculate that these factors consist in a stimulation of smooth muscle growth, i.e. a distensible tissue which at all ages balances or outweighs the effect of a stiffer tissue component such as collagen

Two, radial artery wall thickness was increased to a similarly marked degree in essential and systolic hypertension. However, while in the former radial artery compliance was slightly increased, in the latter it was markedly reduced. Thus, arterial wall thickening *per se* is not necessarily associated with a stiffening of the vessel wall, which presumably depends more critically on

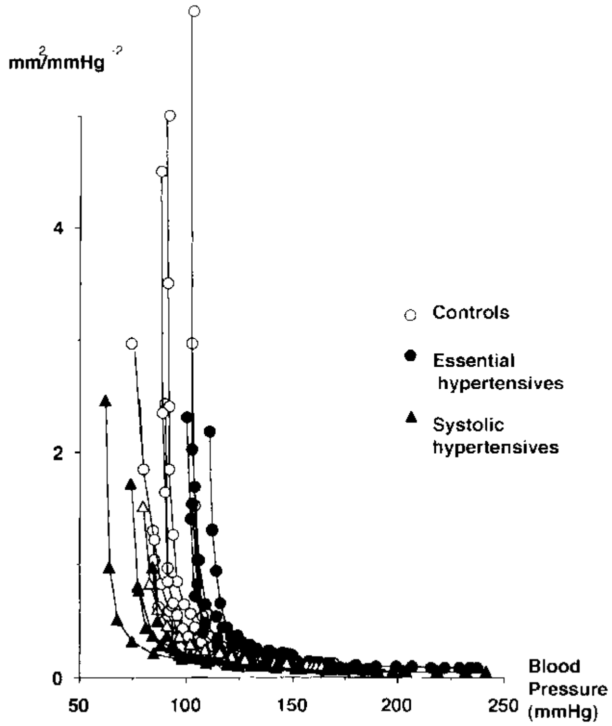

Fig. 5. Carotid artery compliance - pressure curves obtained by using the Reneman formula and the ascending portion of the Finapres pressure waveform in 5 controls, 5 subjects with EH and 5 subjects with ISH. Abbreviations as in preceeding Figures.

alterations in vessel wall structure. We can speculate that while in essential hypertension this alteration leads to an increased amount of smooth muscle (see above), in systolic hypertension it leads to a predominance of collagen on smooth muscle and elastine

Three, in the present study we made an attempt to obtain compliance-pressure curves for the carotid artery, as Laurent *et al*. [23] did in middle-aged essential hypertensive subjects. At variance with Laurent *et al*. [23], however, we did not use tonometry to obtain blood pressure waveforms because the compression of the carotid artery required by this procedure was regarded as potentially risky in elderly patients. Blood pressure waveforms were instead obtained through the finger blood pressure measuring device (Finapres), which was found to be suitable because (i) the ascending portion of its pressure waveform was superimposable to the one obtained by tonometry, (ii) the finger blood pressure waveforms were reproducible across consecutive cardiac cycles, and (iii) the delay between carotid and finger pressure waveforms was small presumably because in the elderly the pulse wave velocity is accelerated and thus the time-lag of pulse waveforms between different arterial sites is minimized. The results confirm that carotid artery is stiffer in essential and the more so in systolic hypertension. They further show, however, that in both normotensive and hypertensive elderlies carotid artery compliance is characterized by a non-linear reduction as blood pressure increased from diastole to systole that is much steeper than the one seen in the radial artery. This emphasizes the importance of obtaining compliance-pressure curves for characterizing carotid artery mechanics properly. Although pressure waveforms obtained from the carotid artery are obviously preferable, it would seem from our data that using the ascending portion of the finger blood pressure waveform may be an acceptable alternative in those instances (e.g. the elderly) in which application of tonometry to the carotid artery may raise safety concerns

In conclusion, our study shows that both middle-sized muscular and large elastic artery compliance and distensibility are markedly reduced in systolic hypertension of the elderly. On the contrary, in essential hypertension of the elderly compliance and distensibility are reduced in the carotid but slightly increased in the radial artery, the alterations thus being more heterogeneous. This heterogenity may not have a major or practical implication because total arterial compliance depends to a greater extent on large elastic arteries such as the carotid one than on the middle-sized muscle arteries, suggesting that in elderly patients its value is reduced in both conditions. This has an interesting pathophysiological implication, however, because it probably means that the different effects of these two types of hypertension on arterial mechanics are accounted for by different alterations in the vessel wall structure. Detailed information on arterial wall mechanics in these conditions is derived from compliance-pressure curves which can be obtained also at the carotid artery level by coupling continuous ultrasonographic measurement of diameter with continuous finger blood pressure measurement

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