Kidney International, Vol. 47 (1995), pp. 169–176

Vascular compliance in sodium-sensitive and sodium-resistant borderline hypertensive patients

PETRA DRAAIJER, MIRIAN J.F. KOOL, LUC M.A.B. VAN BORTEL, FRED NIEMAN, PETER W. DE LEEUW, JOHANNES P. VAN HOOFF, and KAREL M.L. LEUNISSEN

Vascular compliance in sodium-sensitive and sodium-resistant borderline hypertensive patients. Recently, we demonstrated a reduction in the compliance of the carotid, femoral and brachial arteries in sodium-sensitive subjects who had consumed a regular sodium intake of approximately 120 mmol per day, as compared to both sodium-resistant borderline hypertensive subjects and normotensive controls. Venous compliance was not different between the two borderline hypertensive groups and was only slightly lesser than in controls. Large artery compliance was studied using a non-invasive ultrasound vessel wall movement detector system, while venous compliance was determined by means of strain gauge plethysmography. The borderline hypertensive subjects were subsequently treated with enalapril 10 mg/day, felodipine 5 mg/day or placebo during six months. Despite similar reductions in blood pressure, enalapril induced a significant increase of the muscular femoral and brachial artery compliance, but not of the elastic carotid artery, while felodipine did not influence large artery compliance at all in the sodium-sensitive group. The effect of enalapril on muscular artery compliance was established through a dose-dependent increase in distension and not through a change in arterial diameter. Arterial compliance was not influenced by either of the drugs in the resistant group. Venous compliance was also not altered by the medication. In conclusion, femoral and brachial artery compliance in sodium-sensitive borderline hypertensive subjects, which was found to be lower than that of sodium-resistant subjects, improved with antihypertensive treatment with enalapril but not with felodipine, despite the similar reductions in blood pressure induced by both drugs. This finding implies that firstly, reduced arterial compliance is caused by more than just blood pressure elevation, and secondly, the renin-angiotensin system may play a role in the reduced arterial compliance of sodium-sensitive subjects.

Recently, we demonstrated that under conditions of a regular sodium intake of approximately 120 mmol sodium per day [1], sodium-sensitive borderline hypertensive subjects display a reduced compliance of the carotid, femoral and brachial arteries as compared to sodium-resistant patients and normotensive controls. Furthermore, despite the slight increase in blood pressure, arterial compliance in resistant subjects did not differ appreciably from normal. The diminished compliance in the sensitive group was the consequence of reduced arterial wall distension upon the pulse wave since arterial diameter, blood pressure and pulse pressure were similar in the sensitive and resistant groups.

The mechanisms underlying the difference in large artery compliance remain elusive. It could be argued that differences in the activity of the renin-angiotensin system between sodium-sensitive and sodium-resistant subjects play a role, as sodium sensitivity has been linked to inadequate suppression of the renin system after a sodium load [2]. In this respect, sodium-sensitive hypertensive subjects are thought to exhibit an inappropriately high intrarenal production of angiotensin II, while sodium-resistant subjects do not [3]. Thus, it may be hypothesized that by virtue of its vasocontrictor and/or growth promoting effects [4], angiotensin II could be responsible for decreased arterial compliance in sodium-sensitive subjects.

On the other hand, a disturbance in intracellular calcium metabolism may induce stiffer arteries in sodium-sensitive subjects. Indeed, in vascular smooth muscle cells a raised level of free calcium may increase muscular tone, thereby contributing not only to the pressor action of sodium, but also to increased vascular stiffness. In this respect, it is relevant to note that in essential hypertensive patients the pressure response to high sodium intake correlates positively with the increase in lymphocytic intracellular free calcium concentration [5].

The above-mentioned pathophysiologic considerations may not only apply to arterial compliance, but also to venous compliance. Takeshita and coworkers described a reduced venous compliance in sodium-sensitive hypertensive subjects as compared to sodium-resistant ones on a high sodium diet of 345 mmols per day [6]. In our study population, venous compliance tended to be decreased in the sodium-sensitive and resistant borderline hypertensive subjects as compared to normotensive controls [1].

Based upon these considerations, treatment with either an ACE-inhibitor or a calcium entry blocker may improve vascular compliance. Therefore the aim of this study was to investigate the effect of six months of treatment with either enalapril or felodipine on the compliance of carotid, femoral and brachial arteries in sodium-sensitive and -resistant borderline hypertensive subjects. In addition, we measured venous compliance during enalapril and felodipine treatment to investigate whether these agents confered any benefit on this variable.

Large artery compliance may be a major determinant of left ventricular hypertrophy in hypertension [7]. The reduced large artery compliance that was found in sodium-sensitive borderline hypertensives may well be related to increased left ventricular mass. Finally we determined echo-Doppler cardiographic measurements, not only to study whether there are differences in left ventricular mass between the groups and how pharmacological intervention interferes, but also to study stroke volume, since arterial distension and thus compliance depend on stroke volume.

Received for publication November 15, 1993
and in revised form July 18, 1994
Accepted for publication July 28, 1994

Methods

Patient characteristics

Forty-seven previously untreated borderline hypertensive patients were included in the study. Borderline hypertension was defined as a diastolic blood pressure of 90 to 95 mm Hg and a systolic blood pressure of 140 to 160 mm Hg [8]. All subjects were 20- to 45-year-old males and non-smokers. The patients were recruited with the aid of general practitioners, blood banks and local advertising. Besides the slight increase in blood pressure, all subjects were in good health. Secondary hypertension was excluded on the basis of medical history, physical examination and laboratory test results. The protocol of this study was approved by the hospital's ethics committee, and informed consent was obtained from all the participants before they entered the study.

Sodium-sensitivity assessment

The sodium-sensitivity status of the borderline hypertensives was determined five weeks before the onset of this study. A diet method was used in which the subjects consumed, at random order, a low sodium diet, containing 20 mmol sodium per day or a high sodium diet containing 220 mmol sodium per day during one week, with the alternative diet during the following week. The potassium content of both diets was 70 mmol per day. An arbitrarily chosen cut-off point of 8 mm Hg difference in mean arterial pressure between the end of the high sodium and the end of the low sodium diet was taken as an index of sodium sensitivity. The reproducibility of this approach was tested by restudying 10 subjects, approximately one year after the initial investigation. An excellent agreement between the first and the second test was found [9].

Protocol

After the initial study, that revealed the difference in arterial compliance between the groups, the subjects were randomly and in a double blind manner assigned to three treatment stategies: enalapril 10 mg/day, felodipine 5 mg/day or placebo. Before and again after three months of therapy, at the end of the treatment period at six months, and three months after stopping treatment, the subjects were investigated. During the week preceding the day at which the investigations took place, they consumed a diet containing 120 mmol sodium and 70 mmol potassium per day, while 24 hour urines were collected in order to estimate adherence to the diet.

The subjects used a light breakfast and entered the hospital at 8:00 a.m., at the days of the investigations. At first, body weight was measured. All subsequent investigations were performed in supine position, in a temperature controlled room of approximately 24°C. Blood pressure was measured after at least 15 minutes of rest. Systolic and diastolic pressure were measured every five minutes for half an hour, and the average of these blood pressure values was determined. Mean arterial pressure was calculated as the sum of diastolic pressure and one third of the pulse pressure. Simultaneously the heart rate was determined. Subsequently, arterial and venous compliance were measured. Finally, echo-Doppler cardiographic measurements were performed.

Arterial distensibility and compliance

The carotid, femoral and brachial arteries were studied using a non-invasive ultrasound wall movement detector system. This system, developed by Hoeks et al., has been described in detail [10]. In brief, it consists of a conventional ultrasound imager (Ultramark-V, ATL, Bothell, USA), with a 7.5 megahertz transducer, a data acquisition system and a personal computer. The transducer was positioned on the skin surface perpendicularly to the artery under study. An ultrasonic gel was used to optimize signal transduction. Subsequently, the arterial diastolic diameter (Dd), with a precision of approximately 10 μm, and the arterial wall distension (ΔD), with a precision of less than 10 μm, were recorded during 5 seconds.

Simultaneously with the vessel movement registration, blood pressure was measured every two minutes with an automated device (Dinamap, Tampa, FL, USA). The averages of these blood pressures and pulse pressures (ΔP) were calculated.

From the arterial diameter, the change in diameter during the heart cycle (distension), and the pulse pressure, arterial distensibility and compliance were calculated according to the following equations:

$$\text{DC (distensibility coefficient)} = (2\Delta D/Dd)/\Delta P,\ 10^{-3}/\text{kPa} \quad (1)$$

$$\text{CC (compliance coefficient)} = (\pi Dd x \Delta D)/2\Delta P,\ \text{mm}^2/\text{kPa} \quad (2)$$

which means that CC can be calculated by multiplying DC and the cross sectional area of the vessel lumen [11].

The intraobserver variability of the diameter measurements was determined and appeared to be less than 10% in the carotid artery and between 10% and 15% in the femoral and brachial arteries [12]. All measurements were performed by the same experienced investigator.

Venous compliance

Venous compliance was measured by strain gauge plethysmography (Periflow, Janssen Scientific Instruments, Beerse, Belgium) with direct intravenous pressure measurements. An antecubital vein was canulated (Venflon, internal diameter 1 mm) and the canula was connected to a pressure dome (Hewlett Packard), that was positioned at right atrial level, approximately 5 cm under the sternal angle. Venous pressure was displayed on a Hewlett Packard monitor as well as graphically. An inflatable cuff was applied to the upper part of the cannulated arm, and a mercury-filled strain-gauge was positioned around the forearm at one third of the forearm length from the lateral epicondyl. The plethysmograph and the pressure monitor were subsequently calibrated and a stabilization period of 15 minutes was taken into account. Subsequently, the arm cuff was inflated at a cuff pressure of 25 mm Hg and kept inflated during three minutes. This time interval was chosen to obtain stable values for arm volume and intravenous pressure. Thereafter, the cuff was deflated for two minutes to prevent accumulation of interstitial fluid due to capillary filtration. The change in arm volume and intravenous pressure were both measured after cuff deflation, in order to exclude any effect of capillary filtration on the obtained volume-pressure ratio. Subsequently, the procedure was repeated at stepwise increasing cuff pressures of 30, 35, 40 and 45 mm Hg, which yielded 5 volume-pressure ratios. These ratios were used in a linear regression analysis to obtain the volume-pressure relationship and thereby

an estimate of venous compliance, since venous compliance is defined as the slope of this relationship [13].

The between-day coefficient of variation of this technique was 15.5% [14].

Echo-Doppler cardiography

The measurements were performed using a Hewlett Packard sonos 100 echo-Doppler cardiograph, with the subjects in the partial left lateral decubitus position. Parasternal B-mode short and long axis images were obtained to provide reference points for subsequent M-mode investigation (3.5 MHz transducer). Left ventricular internal diameter (LVID), interventricular septum (IVS) and left ventricular posterior wall thickness (LVPW) were measured distally to the tips of the mitral valve at the onset of the QRS complex on the ECG, during three consecutive cardiac cycles. Average values were determined. Left ventricular mass (LVM) was calculated according to the formula of Devereux:

$$LVM = 1.04 * [(IVS + LVID + LVPW)^3 - LVID^3) - 13.6.$$

The reliability of this method has been amply demonstrated [15, 16]. Left ventricular hypertrophy was considered to be present when the left ventricular mass index exceeded 125 g/m^2 [17].

In order to obtain cardiac stroke volume, ascending aortic blood flow velocity was measured using a continuous wave Doppler system with a 10 megahertz transducer, positioned at the apex, while the aortic diameter was determined by means of B-mode echocardiography, positioned at the third or fourth intercostal space at the left sternal edge. Cardiac output was calculated by multiplying stroke volume with heart rate. It has been shown, that when performed by a skilled investigator, the results of this method correlate well with other (invasive and non-invasive) techniques [18]. In our clinic, the intra- and inter-observer variability of this method to assess stroke volume has been established to be 9% and 11%, respectively [19]. Cardiac output, stroke volume and left ventricular mass were normalized for body surface area.

Data analysis

Data were first checked for normality. Because no great discrepancies were found in the data, differences in characteristics of the investigated groups were tested by means of independent Student *t*-tests. Repeated measurement multivariate analysis of variance was used to analyze treatment effects.

Doubly multivariate analysis of variance was done to ascertain the elimination of blood pressure as confounding factor in the relation between type of treatment and arterial measurements [20]. Doubly multivariate analysis of variance is an analysis of variance which handles variates in two ways: first, each variate is repeated in time, and second, to that there is more than one measure that is repeated [21]. The design used in the study concerning doubly multivariate analysis can be characterized as a double within-factors design. The first within-factor is "time" having four catagories; the second one is "clinical outcome" such as arterial compliance and blood pressure. Eventually the design becomes a mixed one, because the treatment factor (enalapril, felodipine or placebo) and the patient groups (sodium-sensitive and sodium-resistant) are clearly between factors.

Blood pressure cannot be analyzed as a co-variant, for it tends to change in time. Therefore we had to include it as a repeated measurement within the design mentioned above. The co-variance between blood pressure and vascular compliance could be analyzed in this way given the treatment categories.

All data analyses were done using SPSS-pc programs; $P \leq 0.05$ was regarded as statistically significant.

Table 1. Patient characteristics at the beginning of the study

X	Sodium sensitive	*P*	Sodium resistant
N	17		28
Age	41 ± 6	0.41	40 ± 6
Body surface area	2 ± 0.2	0.74	2 ± 0.2
Systolic blood pressure *mm Hg*	155 ± 13	0.43	153 ± 16
Diastolic blood pressure *mm Hg*	87 ± 6	0.42	85 ± 8
MAP *mm Hg*	110 ± 7	0.48	108 ± 10
HR *bpm*	67 ± 13	0.20	63 ± 10

Abbreviations are: MAP, mean arterial pressure; HR, heart rate. Data are mean ± SD.

Results

Sodium-sensitivity status

Two subjects were excluded because of non-compliance to the diet; the difference in sodium excretion between low and high salt regimens was smaller than 150 mmol/day in these subjects. According to the definition used in this study, 17 borderline hypertensive patients were classified as being salt-sensitive and 28 as being salt-resistant. Sodium and potassium excretion at the end of the high and low salt diets was comparable for the two groups.

The difference in mean arterial pressure at the end of the low and high salt diets was 12 ± 5 (range 8 to 22) mm Hg for the sensitive and −2 ± 7 (range −16 to 5) mm Hg for the sodium-resistant group. The weight gain after the high sodium diet as compared to the low sodium diet was 1.7 ± 1 kg for the sodium-sensitive group and 0.9 ± 1 kg ($P = 0.08$) for the sodium-resistant group.

Subject characteristics

Table 1 shows characteristics of the sodium-sensitive borderline hypertensive (SS) and the sodium-resistant borderline hypertensive groups (SR) at the start of the study. There were no significant differences in age or body surface area between the groups. The estimated duration of hypertension was seven years in both groups. Systolic and diastolic pressures, as well as mean arterial pressures were comparable in the groups. Likewise, the heart rates did not differ between the groups.

Five sodium-sensitive borderline hypertensives were treated with enalapril (SS-E), five with felodipine (SS-F) and seven with placebo (SS-P), while 11 sodium-resistant subjects had enalapril (SR-E), 10 felodipine (SR-F) and seven placebo (SR-P) during the treatment period. The two excluded subjects were initially grouped as SR-P. The average decrease in mean arterial pressure after six months of treatment was SS-E:14 (range 2 to 28) mm Hg, SS-F:11 (1 to 25) mm Hg, SS-P:3 (−6 to 16) mm Hg in the sodium-sensitive group and SR-E:12 (−5 to 33) mm Hg, SR-F:6 (−7 to 21) mm Hg, SR-P:5 (−25 to 24) mm Hg in the resistant group (NS).

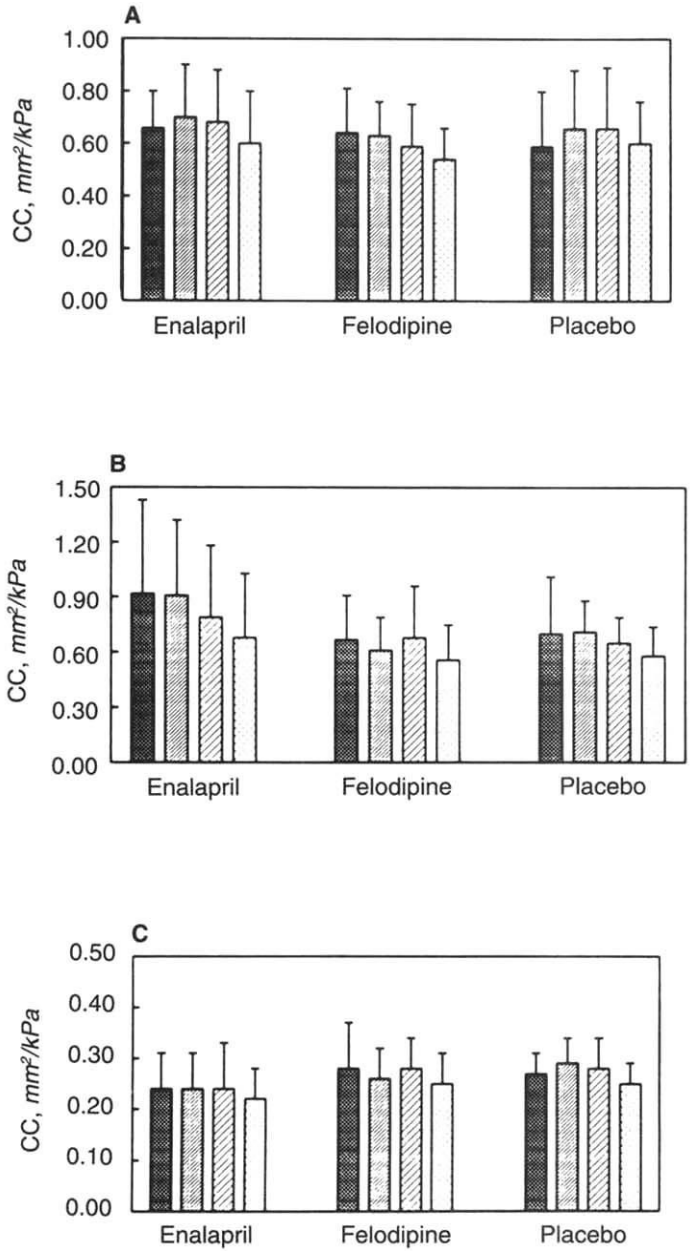


Fig. 1. *Effects of treatment on arterial compliance in the sodium resistant group.* **A.** Carotid artery. **B.** Femoral artery. **C.** Brachial artery. Symbols are: (▦) 0 months; (▨) 3 months; (▨) 6 months; ( ) 9 months.

Arterial distensibility and compliance

Treatment with enalapril, felodipine or placebo did not significantly influence arterial diameter and distension of the three investigated arteries of the sodium-resistant group. Pulse pressure was not significantly altered during the treatment period. As a consequence arterial compliance was not improved by the pharmacological agents in the resistant group (Fig. 1).

Carotid artery compliance did not change significantly in the enalapril or felodipine treated sodium-sensitive subjects (Fig. 2). In contrast, femoral and brachial artery compliance improved significantly in the enalapril treated sodium-sensitive subjects. Table 2 gives details about the sodium-sensitive group. The improvement in femoral and brachial artery compliance was due to increased distension rather than increased diameter. The improvement of the elastic properties of the femoral and brachial artery reached a maximum after six months of treatment and fell towards baseline values in the wash-out period. Baseline compliance of the femoral artery in the enalapril-treated sodium-sensitive subjects tended to be somewhat lower than that of the felodipine treated group, although the difference was not statistically significant. In the other muscular artery under study (brachial artery) baseline values are very comparable. Felodipine did not induce an improvement of the elastic properties of the femoral and brachial arteries (Fig. 3 and 4). Since pulse pressure was not significantly influenced by either enalapril or felodipine [mean decrease in pulse pressure after 6 months: SS-E:2 (range −7 to 10) mm Hg, SS-F:3 (range −4 to 15) mm Hg, SS-P:3 (range −6 to 9) mm Hg] and was not significantly different between the groups, a higher pulse pressure cannot be held responsible for the increased distension of the femoral and brachial arteries upon enalapril.

Since the enalapril induced reduction in blood pressure *per se* may induce improvement of distensibility of the arteries, a doubly multivariate analysis of variance was performed in order to evaluate whether the improvement of femoral distension was entirely achieved through a decrease in blood pressure, or whether enalapril exerts additional effects independently of blood pressure. This analysis indicated that the treatment effect of enalapril on both femoral and brachial distension remained significant when mean blood pressure values were taken into account, suggesting an effect of enalapril on arterial distension independent from its blood pressure lowering action (femoral artery $P = 0.01$, brachial artery $P = 0.02$).

Venous compliance

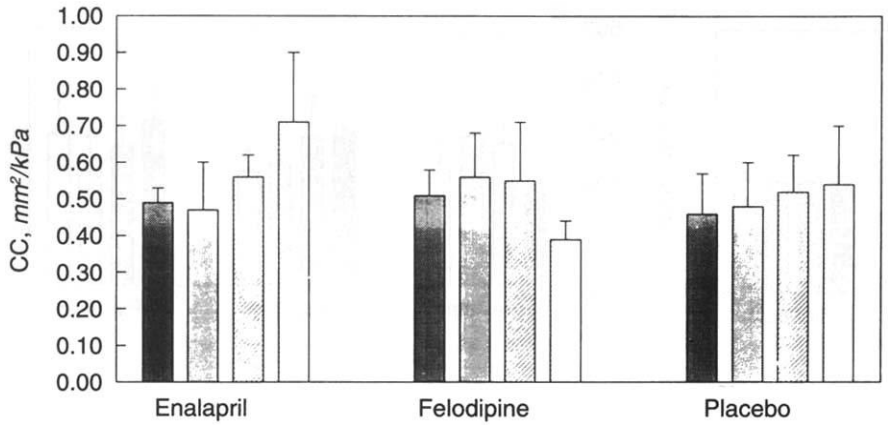
Venous compliance was comparable and only slightly below normal in the sodium-sensitive and sodium-resistant groups at the start of the study. Pharmacological intervention with either enalapril or felodipine, did not induce changes that were significantly different from placebo.

Echo-Doppler cardiography

Although left ventricular mass index tended to be somewhat larger in the sodium-sensitive group than in the resistant one after the initial investigation (SS: 109 ± 25 g/m^2, SR: 95 ± 37 g/m^2, $P = 0.2$), the slightly elevated blood pressure in the investigated groups has not yet led to left ventricular hypertrophy. In the entire group of borderline hypertensive subjects, after adjustment for blood pressure, significant inverse correlations were found between large artery distension and left ventricular mass index (carotid: $r = -0.64$, $P < 0.0001$, femoral: $r = -0.43$, $P = 0.013$, brachial $r = -0.31$, $P = 0.022$). Pharmacological intervention did not significantly influence left ventricular mass, stroke index or cardiac index.

Discussion

Six months of enalapril treatment induced a significant improvement of the femoral and brachial artery distensibility and compliance in the sodium-sensitive, but not in the sodium-resistant borderline hypertensive group. This improvement was achieved by an effect of enalapril on the vascular distension rather



Fig, 2. *Effects of treatment on the compliance of the carotid artery in the sodium sensitive group.* Symbols are as in Figure 1.

Table 2. Sodium sensitive group characteristics

	Enalapril		Felodipine		Placebo	
	−E	+E	−F	+F	−P	+P
Systolic BP *mm Hg*	151 ± 5	134 ± 14	156 ± 12	148 ± 15	156 ± 13	144 ± 17
Diastolic BP *mm Hg*	84 ± 7	72 ± 13	91 ± 7	78 ± 10	87 ± 4	87 ± 8
PRA *ng/ml · hr*	1.0 ± 0.6	7.9 ± 5	1.0 ± 0.6	1.4 ± 0.8	1.1 ± 0.7	0.7 ± 0.4
U_{Na} *mmol/24 hr*	122 ± 38	130 ± 40	128 ± 24	132 ± 38	136 ± 21	119 ± 36

Data are mean ±SD. Abbreviations are: PRA, plasma renin activity; U_{Na}, urinary sodium excretion; (−) before and (+) after six months of treatment in sodium sensitive subjects.

than by enlargement of the vascular diameter. The effect of enalapril on the distension of the two arteries reached a maximum after six months of treatment and returned to baseline levels at the end of the wash-out period. Furthermore, doubly multivariate analysis suggested that the improvement of femoral and brachial artery distention could not be explained by the decrease in blood pressure only. Thus, although the investigated groups are small, these data suggest that enalapril chronically modulates the viscoelastic properties of the femoral and brachial artery wall in sodium-sensitive subjects. Furthermore, the fact that enalapril did not appreciably influence large artery compliance in the sodium-resistant group may favour the hypothesis that the renin-angiotensin system is involved in determining the difference between sodium-sensitive and sodium-resistant borderline hypertensive subjects as far as large artery compliance is concerned.

The compliance of the carotid artery was not significantly altered in the sodium-sensitive group. It may be expected that enalapril, through its relaxant effect on vascular smooth muscle, has a more pronounced effect on muscular arteries such as the femoral and brachial arteries, than on elastic arteries, such as the carotid.

ACE inhibitors are known to exert a beneficial effect on arterial compliance in established and experimental hypertension [22–24]. Information on effects of ACE inhibition on large arteries in borderline hypertensive subjects is not widely available. Unlike the arterial dilatory effect of both enalapril [21] and felodipine [25] in essential hypertensives, no such effect was present in our borderline hypertensive population. The positive effect on compliance in this long-term experiment was entirely achieved through an increase in arterial distension.

Apart from a vasodilatory effect, ACE inhibitors are known to interfere with growth factors [26] and may induce regression of hyperthrophy of arterial walls.

Although blood pressure, pulse pressure, stroke and cardiac index were equally influenced by enalapril and felodipine treatment in all investigated groups, felodipine did not alter large artery compliance in the sodium-sensitive group. This suggests that the positive effect of enalapril and the lack of effect of felodipine on femoral and brachial distension are not related to changes in hemodynamics.

However, one has to keep in mind that something must have changed in the arterial wall of sodium-sensitive subjects under felodipine treatment, otherwise one would have expected a passive decline in arterial diameter upon the blood pressure reduction. Counterregulatory mechanisms may prevent this diameter reduction, thereby contributing to the lack of improvement in the compliance in the felodipine-treated sodium-sensitive subjects.

A critique on the vessel wall movement detector method, as used in the present study, is that pulse pressure was measured in the brachial rather than in the carotid and femoral arteries. The calculations of distensibility and compliance as performed in this study are only valid if the brachial pulse pressure is representative for that of the carotid and femoral arteries. Although we assume that such is the case, there can be a mismatch, especially when early pulse wave reflections ('shoulders') are present in the distension curves. Though not discussed in the present paper, at the onset of the study 41% of the sodium-sensitive subjects and 36% of the resistant subjects had 'shouldered' carotid distension curves, while no overt early pulse wave reflections were detected in the brachial and femoral arteries. Since there were no great discrepancies in the distribution of shouldered curves over the groups, we assumed a systematic error when we used brachial

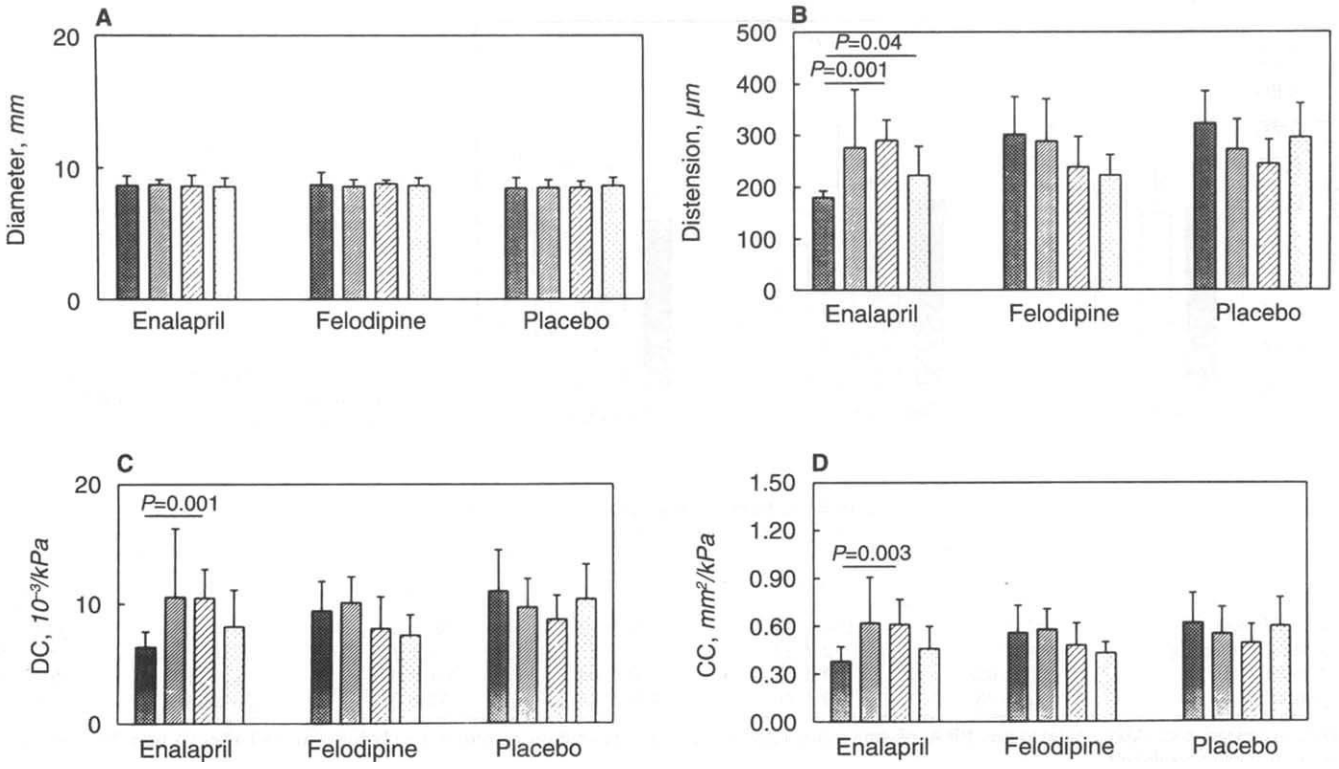


Fig. 3. *Effects of treatment in the sodium sensitive groups on femoral artery diameter* (**A**)*, distension* (**B**)*, distensibility* (**C**)*, and compliance* (**D**)*. Symbols are as in Figure 1.*

artery pulse pressure in the calculations of carotid and femoral compliance. Moreover, the 5% higher occurrence of 'shoulders' in the sensitive group may indicate that the calculations based on brachial pulse presure overestimate the actual compliance of the carotid artery in the sensitive group. Thus, the actual difference in carotid compliance between the sensitive and resistant group may be even more pronounced.

The reason that we used brachial artery pulse pressure in the calculations of carotid and femoral distensibility and compliance is that non-invasive methods to assess pulse pressure in the femoral and carotid arteries are scarce. Applanation tonometry may be a candidate [27], but technical difficulties and problems of reproducibility must be resolved. Taken together, we think that using brachial pulse pressure as a model for carotid and femoral pulse pressures induces a similar and systematic error in both groups, at least in the untreated situation.

Treatment with two antihypertensive agents, however, complicates the situation since they may induce differential effects on various macro- and microvascular beds, thereby specifically influencing pulse wave reflections. The error that is induced by using the brachial artery pulse pressure in the calculation of carotid and femoral artery compliance may no longer be a systematic one that is comparable in the sodium-sensitive and sodium-resistant groups.

Aware of this problem, we again studied distension curves in the sodium-sensitive subjects that were treated during six months with either enalapril or felodipine. Since there were no shouldered distension curves in the femoral and brachial arteries, we concluded that the difference in arterial wall properties that was found after six months of treatment with enalapril or felodipine in two sodium-sensitive groups may therefore be valid.

Previously, we found that despite a slight, but similar reduction in venous compliance in sodium-sensitive and -resistant borderline hypertensive subjects, the differences were not statistically significant from normal. Consequently, no major effects of treatment on venous compliance were expected in the present study. Indeed, venous compliance was not appreciably modified by antihypertensive treatment in our subjects. Similarly, no effect of enalapril or felodipine treatment on left ventricular mass was found.

In conclusion, six months of enalapril treatment induced a significant dose-dependent improvement of femoral and brachial artery distention and compliance in sodium-sensitive borderline hypertensive subjects that could not be explained by changes in blood pressure, pulse pressure or cardiac index.

No effects of enalapril were seen in the carotid artery of the sodium-sensitive subjects, suggesting inhomogeneity in the response of large arteries to enalapril treatment. Felodipine did not induce significant changes in the arterial compliance of sodium-sensitive subjects. As was expected, neither drug modified arterial compliance in sodium-resistant subjects or venous compliance in the sensitive and the resistant groups.

Acknowledgments

The work was performed in and financially supported by the Cardiovascular Research Institute of the University of Limburg (CARIM). Moreover, it was financially supported by the Dutch divisions of Astra

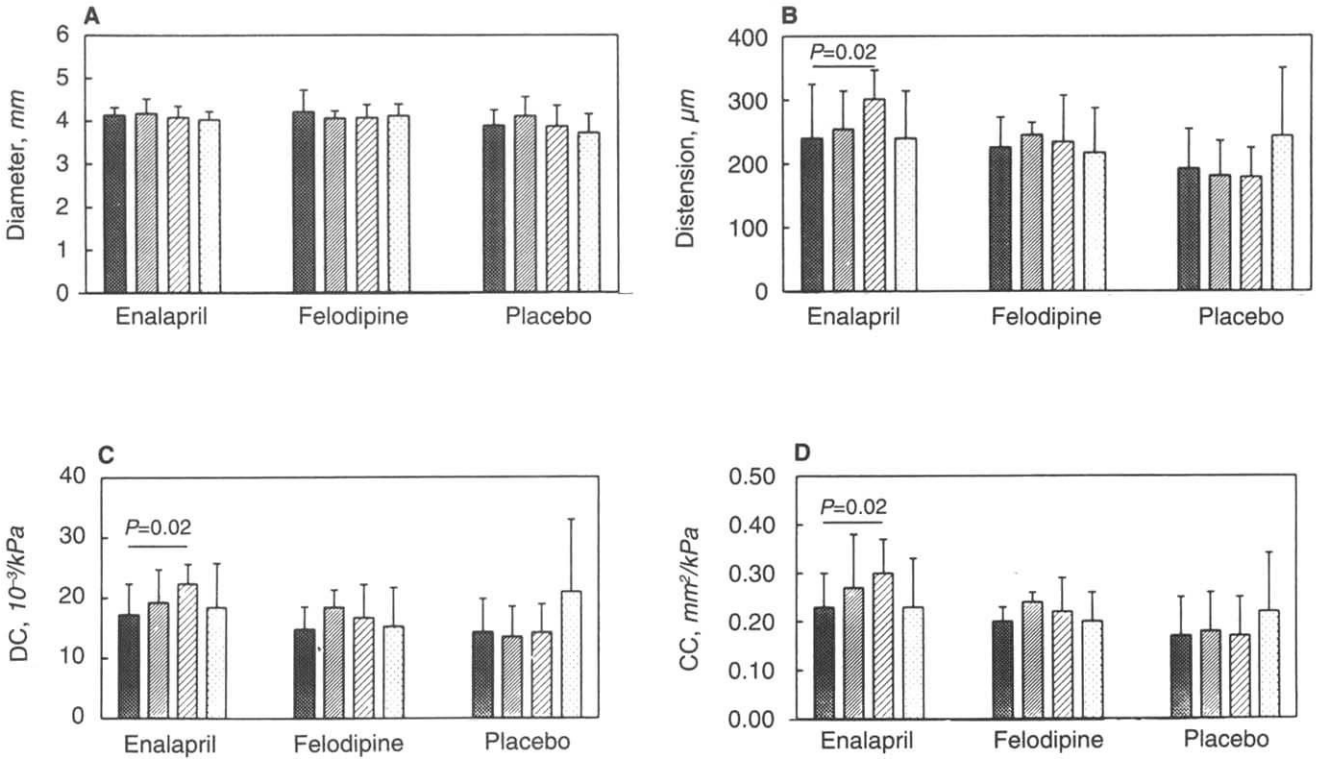


Fig. 4. *Effects of treatment in the sodium sensitive group on brachial artery diameter* (**A**)*, distension* (**B**)*, distensibility* (**C**)*, and compliance.* (**D**)*. Symbols are as in Figure 1.*

Pharmaceutica and Merck, Sharp and Dohme. The authors greatfully acknowledge the advice of Mr. L. Meems from Astra Pharmaceutica.

Reprint requests to P. Draaijer, University Hospital of Maastricht, Department of Medicine, PO Box 5800, 6202 AZ Maastricht, The Netherlands.

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