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AORTIC RIGIDITY AND PLASMA CATECHOLAMINES IN ESSENTIAL HYPERTENSIVE PATIENTS

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ABSTRACT

Aortic rigidity, plasma noradrenaline and adrenaline, and hemodynamic parameters were measured in 48 essential hypertensive patients, 25 younger than 45 (Group I) and 23 of 45 years and over (Group II). Aortic rigidity was determined by the ratio of pulse pressure over stroke volume. Aortic rigidity and hemodynamic parameters were also determined after combined alpha-beta receptor blockade induced by Labetalol (mg 100 IV) or by Propranolol (mg 10 IV) plus Phentolamine (mg 10 IV). The aortic rigidity index was significantly higher in Group II, systolic arterial pressure being significantly higher. All other data, including plasma noradrenaline and adrenaline, were not significantly different in the two groups. In Group II a significant correlation ($r = 0.62$) was noted between aortic rigidity indexes and plasma noradrenaline values. The alpha-beta receptor blockade induced a decrease of aortic rigidity particularly in Group II, owing to a more marked decrease of systolic arterial pressure. A highly significant correlation was noted in Group II between the changes in aortic rigidity index and the basal plasma noradrenaline levels ($r = 0.81$). Therefore, the aortic rigidity in essential hypertensive patients older than 45 is influenced by the sympathetic nervous system activity, as judged by plasma noradrenaline levels. This influence seems related to an increase with age of aortic responsiveness to sympathetic stimulation.

INTRODUCTION

Systolic hypertension is an independent risk factor in cardiovascular disease (7, 8). Particularly in men older than 45, high systolic arterial pressure is considered a stronger risk factor for coronary heart disease than diastolic arterial pressure, which seems to be more important in younger men. This difference may indicate that the mechanisms involved in causing a high systolic arterial pressure are different in the young and old patients (1). Several factors may influence the level of systolic arterial pressure (4, 12), but aortic compliance is one of the most important mechanisms which can induce and sustain systolic hypertension (9). The sympathetic nervous system activity may also influence the level of systolic and diastolic arterial pressure, along with the stroke volume, the total peripheral resistance (2) and even the aortic compliance or its reverse, that is aortic rigidity (3).

In a previous study we suggested that an increased sympathetic nervous system activity decreases aortic compliance (3). As an extension of this work, the relationship between the sympathetic nervous system activity, as judged by plasma catecholamine levels, and aortic rigidity was examined in essential hypertensive patients of different age in relation to the effects of combined alpha-beta receptor blockade.

MATERIAL and METHODS

An informed consent to the study was given by 48 essential hypertensive patients. They were divided according to age: Group I, 25 patients (age 19-44, mean 36) and Group II, 23 patients (age 45-69, mean 53). WHO I n.6 in Group I and n.5 in Group II; WHO II n.17 in Group I and n.16 in Group II; WHO III n.2 in Group I and

n.2 in Group II. The hypertension was defined as essential on the basis of a complete clinical examination and of the results of the appropriate laboratory and radiological investigations. Urography and/or arteriography were all normal. None of the patients had renal failure nor a history or clinical signs of heart failure or of neurological disease. Four patients were classified WHO III on eye-ground changes only (hemorrages and exudates). The patients were untreated or discontinued any medication 4 weeks before investigation.

All studies were performed in the morning with the patient comfortably supine. Two catheters were introduced percutaneously, under local anaesthesia, one into an antecubital vein and the other into the brachial artery by a modified Seldinger technique (17). According to the method of cardiac output measurement, the venous balloon-tipped catheter was positioned in the right atrium (dye-dilution method) or in the main pulmonary artery (thermodilution method). The arterial catheter was advanced to the ascending aorta. Cardiac output was determined at least in triplicate by the dye-dilution (Cardiogreen) or the thermodilution (Dextrose 5%, ml 10 at 0°C) method (20), the two methods being quite comparable (personal data). The aortic pressure and an electrocardiographic lead (D II) were continuously recorded. At least 30 minutes after catheter positioning, samples of arterial blood were drawn for measurement in duplicate of noradrenaline and adrenaline plasma levels by fluorimetry (14). The arterial pressure was derived from the intra-aortic recorded tracing. The mean arterial pressure was obtained adding 1/3 of pulse pressure to the diastolic pressure.

Aortic compliance may be defined by the change in aortic volume (ΔV) over the change in aortic pressure (ΔP). The ΔV can be derived by the stroke volume (SV) and the ΔP by the pulse pressure

(PP), that is by the difference between systolic and diastolic arterial pressure. Therefore, the SV/PP ratio can be taken as an index of aortic compliance and its reciprocal as an index of aortic rigidity: PP/SV mmHg/ml of blood ejected. The higher the value of this index (PP/SV), the higher the aortic rigidity. The validity of this method in evaluating aortic compliance or its reciprocal, that is aortic rigidity, was assessed comparing it with the method proposed by Simon et al. (18). These authors estimated the arterial compliance from the analysis of the monoexponential blood-pressure time curve during diastole, according to a simple viscoelastic model. When these two methods were compared in 16 hypertensive patients a very good correlation ($r = 0.92$) was noted between the PP/SV ratio and the reciprocal of the aortic compliance index proposed by Simon et al. (18), with a regression line almost coincident with the identity line (personal observation).

Hemodynamic parameters and plasma catecholamines were measured in all patients in basal conditions. Then a combined alpha-beta receptor blockade was induced giving Labetalol mg 100 IV or Propranolol mg 10 IV followed by Phentolamine mg 10 IV. Both Labetalol and Propranolol plus Phentolamine, at the doses used, induce a comparable blockade of adrenergic receptors. In all patients hemodynamic data were controlled 15 minutes after the end of drug injections.

Statistical evaluations were made by standard techniques for Student's t-test and the calculation of correlation coefficients, using an Olivetti P6040 computer. Values were reported as Mean$\pm$SEM.

RESULTS

The systolic arterial pressure was significantly higher in Group II: 190$\pm$4.9 versus 171$\pm$4.9 mmHg of Group I ($p<.05$). The dif-

ferences were not significant in diastolic arterial pressure (108±3.0 in Group I and 107±3.3 mmHg in Group II), in cardiac index (3.5±0.2 in Group I and 3.1±0.1 l/m2 in Group II), in stroke index (45±1.5 in Group I and 46±1.4 ml/m2 in Group II) and in total peripheral resistance (40±1.9 in Group I and 44±1.4 U/m2 in Group II). The index of aortic rigidity, that is the pulse pressure (PP) over the stroke volume (SV) ratio (PP/SV), was significantly higher in Group II: 1.03±0.06 versus 0.76±0.05 mmHg/ml of Group I ($p<.005$). Plasma noradrenaline was slightly higher in Group II: 331±42 versus 276±29 ng/l of Group I (NS). Plasma adrenaline was similar in both groups: 103±13 in Group I and 79±7 ng/l in Group II (NS). The single values of the aortic rigidity index and of plasma noradrenaline with their Mean±SEM are shown in Figure 1.

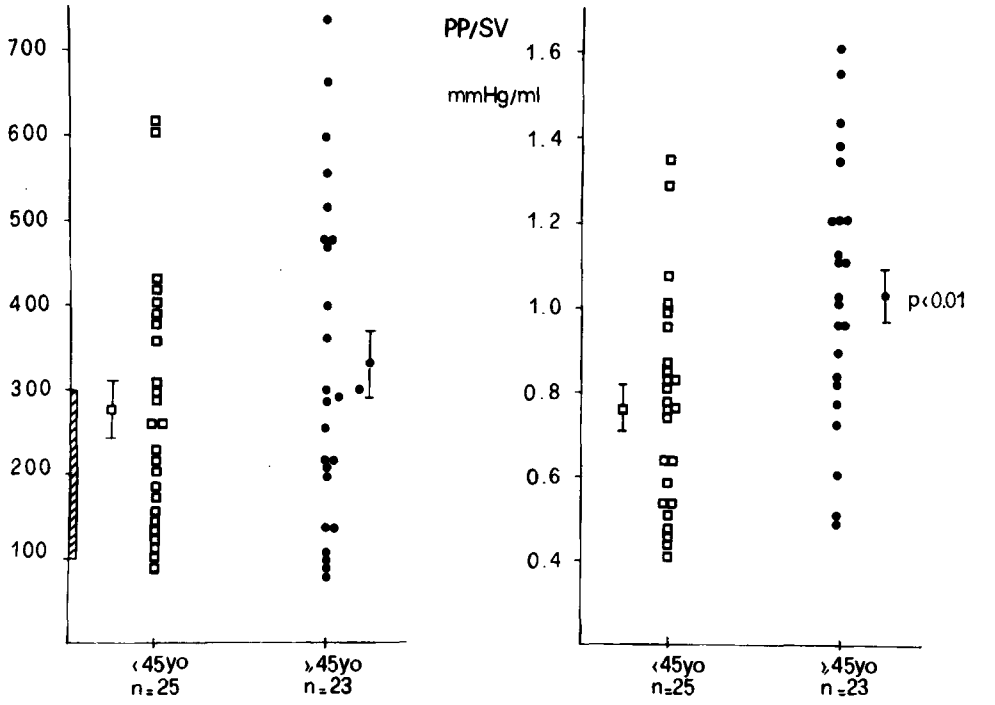

Fig. 1. Single values and their mean±SEM of plasma noradrenaline (NA) and aortic rigidity index (PP/SV).

Correlations

Group I: No significant correlations were found between the hemodynamic parameters, the index of aortic rigidity (PP/SV ratio) and plasma catecholamines.

Group II: A significant positive correlation was found between the index of aortic rigidity (PP/SV ratio) and plasma noradrenaline: $r = 0.62$, $p < .01$ (Fig. 2). A more detailed analysis demonstrates that PP was positively related to plasma noradrenaline ($r = 0.47$, $p < .05$) while a negative correlation was found between SV and plasma noradrenaline ($r = -0.44$, $p < .05$). The systolic arterial pressure was also significantly related to plasma noradrenaline ($r = 0.49$, $p < .05$). Among the others hemodynamic parameters, the total peripheral resistance was related to plasma noradrenaline ($r = 0.46$, $p < .05$). No significant correlations were noted with plasma adrenaline.

Effect of combined alpha-beta blockade: The hemodynamic changes induced by the alpha-beta blockade are shown in Figure 3. The

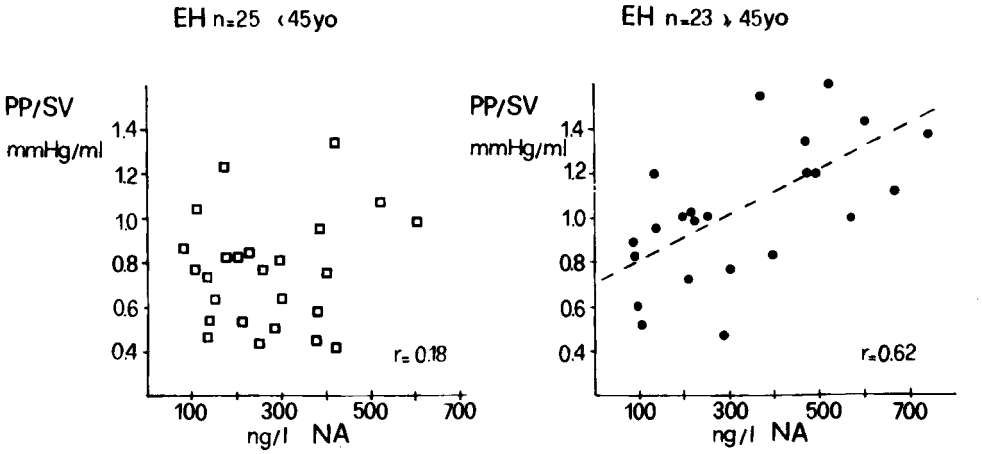

Fig. 2. Correlations between plasma noradrenaline (NA) and aortic rigidity index (PP/SV) in essential hypertensive patients (EH).

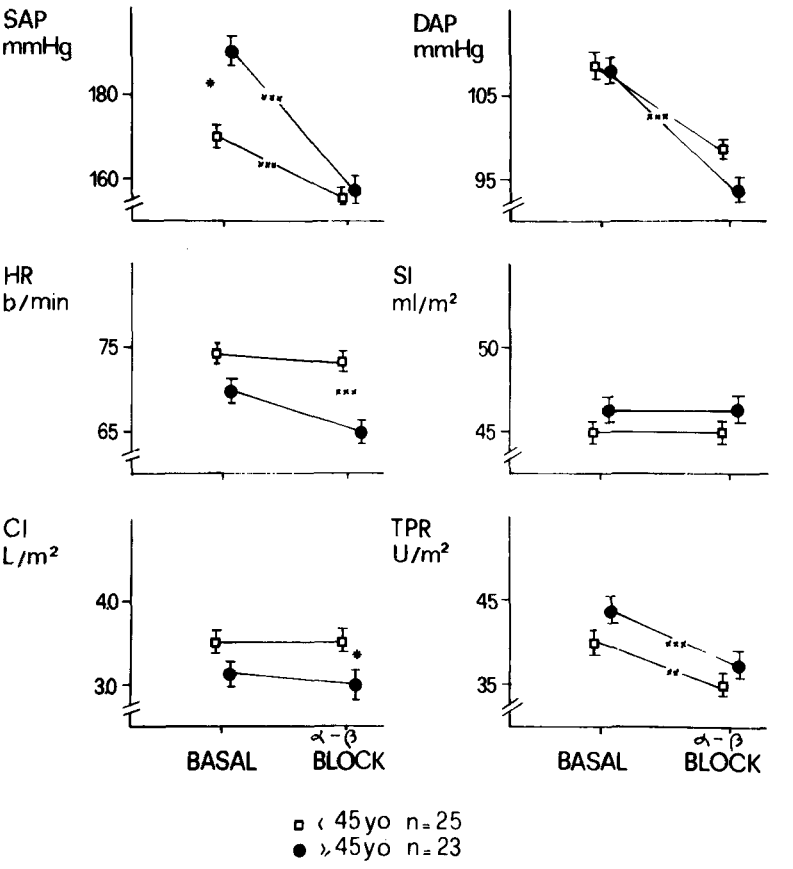

Fig. 3. The changes in systolic (SAP) and diastolic arterial pressure (DAP), heart rate (HR), stroke index (SI), cardiac index (CI) and total peripheral resistance (TPR) induced by combined alpha-beta blockade.

changes induced were similar in both groups. However, the decrease in systolic arterial pressure was more evident in the older age group in which the difference in systolic arterial pressure present in basal conditions was abolished by alpha-beta blockade. The aortic rigidity was significantly reduced in both groups: from 0.76±0.05 to 0.59±0.04 mmHg/ml ($p<.02$) for Group I and from 1.03± 0.06 to 0.79±0.04 mmHg/ml ($p<.005$) for Group II. The decrease of the PP/SV ratio was determined by the decrease of PP from 63±3.6

to 50±2.9 mmHg ($p<.01$) in Group I and from 84±4.1 to 63±3.2 mmHg ($p<.001$) for Group II, while SV was unchanged after the blockade. A highly significant correlation was found in Group II between the changes of aortic rigidity index induced by the alpha-beta receptor blockade and the basal plasma noradrenaline levels ($r = 0.81$, $p<.001$); this correlation was not significant in Group I (Fig. 4). When the % changes in the aortic rigidity index induced by the blockade in Group II were considered, the correlation with basal plasma noradrenaline was still highly significant ($r = 0.79$, $p<.001$).

DISCUSSION

Our study indicates that aortic rigidity is influenced by the sympathetic nervous system activity in hypertensive patients older than 45. As expected, aortic rigidity was higher in the group of older patients compared to the younger ones. This difference was accounted for by pulse pressure only, as stroke volume

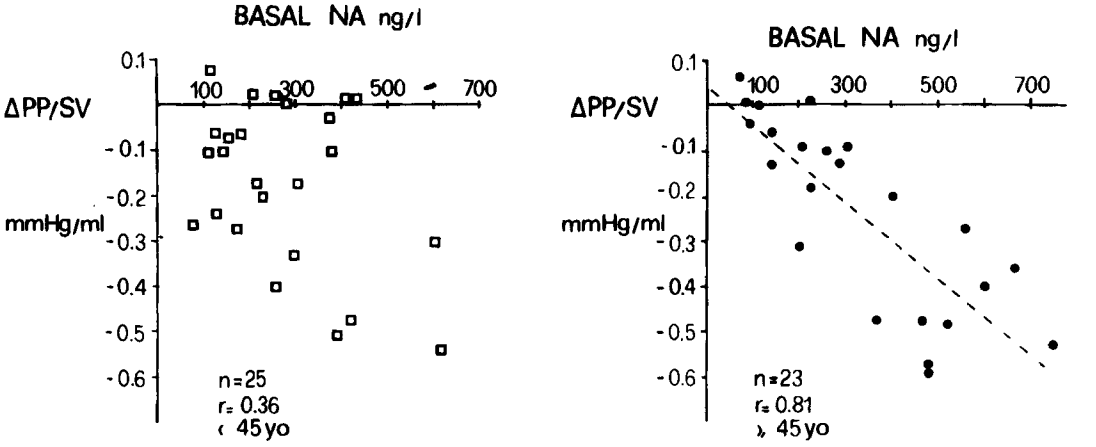

Fig. 4. Correlations between basal plasma noradrenaline (NA) and changes in aortic rigidity index (PP/SV) induced by combined alpha-beta blockade.

did not differ between the two groups. The higher pulse pressure in the older group was due to a higher systolic arterial pressure as diastolic pressure was almost identical in the two groups. Therefore, the higher aortic rigidity of Group II cannot be attributed to alterations in the pressure-volume relationship induced by a different initial stretch of the aorta (15). Plasma noradrenaline was only slightly higher in the older age group. However, in Group II plasma noradrenaline levels were significantly related to aortic rigidity values and the alpha-beta receptor blockade induced a decrease of aortic rigidity that was directly proportional to the basal plasma noradrenaline level. These acute changes in aortic rigidity suggest that the aortic rigidity is not only correlated to the anatomic structural characteristics of the aorta, but also to functional factors. The correlation of plasma noradrenaline with aortic rigidity, or even more with its changes induced by alpha-beta blockade, suggests that the sympathetic nervous system activity could directly influence the functional component of aortic rigidity. In a previous study (3) this influence was attributed to a higher sympathetic activity in hypertensive patients older than 45, on the basis of plasma noradrenaline levels higher than in younger patients. In the larger group of patients of the present study, however, the plasma noradrenaline levels were not significantly higher in the older age group. Therefore, an increased responsiveness of aortic smooth muscle to adrenergic stimulation with age may be postulated (12). A progressive reduction of beta adrenoceptor sensitivity and/or reactivity with increasing age was suggested by several studies (10,11,16). In our younger patients the more marked decrease of heart rate,and consequently of cardiac output as stroke volume was unchanged

(Fig. 3),points to a higher beta-receptor sensitivity in this group compared to older patients. Simon et al. (18) on the basis of the hemodynamic effect of beta-blockade have suggested that the sympathetic tone may be operative in sustaining systolic hypertension through beta-receptors in young hypertensive patients. It was also recently suggested that a defective beta-adrenoceptor mediated response with advancing age may result in a relative preponderance of alpha-mediated vasoconstriction in hypertensive patients (5,6). Therefore, the higher influence of the sympathetic nervous system activity on aortic rigidity of our older patients might be attributed to an enhanced vascular response mediated by an increased alpha and decreased beta-receptor sensitivity.

In conclusion, aortic rigidity may directly be influenced by the sympathetic nervous system activity in essential hypertensive patients of 45 years and over. This influence seems related to an increased responsiveness of the aorta,possibly mediated by an increased alpha-adrenoceptor sensitivity with age.

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