

# Features of endothelial dysfunction in chronic renocardiac syndrome

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## OBJECTIVES

The main pathogenetic mechanisms of high blood pressure in renal diseases are numerous and include an increase in the volume of circulating fluid, sodium retention, the emergence of autonomic dysregulation, activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system, and the emergence of endothelial dysfunction with increased levels of circulating vasoactive substances, resulting in increased cardiac output and peripheral vascular resistance, respectively. An integral part of the pathogenesis of arterial hypertension (AH) is a remodeling of the vascular system and the state of the vascular endothelium, which functions as a trigger mechanism for the implementation vasoregulating devices. Furthermore vascular endothelium involved in providing hemostasis local processes, proliferation, migration of blood cells in the vascular wall is also connected with regulation of vascular tone and atherosclerosis. Formed an idea of endothelial dysfunction, which is defined as an imbalance between the factors that provide all of these processes. It is still not possible to determine whether the causes of hypertension violation of endothelial dysfunction or endothelial dysfunction is one of the main mechanisms for the development of hypertension. Therefore, a study of the functional state of the vascular endothelium contributes to the further study of the mechanisms of disease and to find new ways for their pharmacological correction.

Objective: To study the endothelial vascular motor function in hypertensive patients with chronic kidney disease (CKD) - chronic renocardiac syndrome./

## METHODS

Vascular mechanisms of the pathogenesis of hypertension in patients with chronic kidney disease were studied in 172 patients age (54.2±6.2) years, 84 men and 88 women meeting the criteria for CKD, defined by the results of clinical and laboratory examination. The diagnosis of uncomplicated hypertension involved the presence of II-III degree, increase in blood pressure, the absence of severe comorbidities. The control group consisted of 25 healthy subjects matched for age and sex.

For ultrasonic echography imaging system used Acuson 128/HR/10 (USA) with the sensor 2.5 and 5 MHz. The endothelium-dependent and endothelium-independent vasodilatation was investigated according to the results of the use of vasodilation: reactive hyperemia in the compression of the brachial artery and nitroglycerin samples (500 mg of nitroglycerin on the tongue) by the method proposed D.Celermajier et al., and from 8.00 to 9.00 in a state of fasting patients in the supine position. Brachial artery was found 3-10 cm above the elbow. The study was conducted in triplex mode with synchronous ECG recording: B-mode diameter of the brachial artery was measured in Doppler mode evaluated changes of blood flow velocity indices before and during the trial with hyperemia and decompression in patients receiving 500 mg of nitroglycerin. Changes in vascular diameter (an increase in brachial artery diameter) and blood indices were evaluated every 15 seconds - 1 minute during the test with reactive hyperemia and 1 min at independent study endothelium-dependent vasodilation and expressed in percentage of the initial value.

Measured the diameter of the brachial artery (D, mm), flow velocity (V, m / s), the ratio  $D / V$ ,  $\Delta d$  (%) - an increase in the diameter of the artery decompression,  $\Delta dN$  (%) - increase in the diameter of the artery on trial with nitroglycerin and ratio  $\Delta d / \Delta dN$ .

Studied the frequency of vasoconstrictive response to decompression and nitroglycerin. Defining normal vasodilatory response >10%, 7-10% and reduced vasoconstrictive <7%.

The obtained data were processed using the software Statistica 5.0 for Windows 95 and Microsoft Excel 7.0 MS Office 97. The significance of differences was determined using paired and unpaired Student's t test for parametric variables, for nonparametric sequence variant used the Mann-Whitney and Wilcoxon tests.

## CONCLUSIONS

In the study of vascular-motor response to decompression and the sample with nitroglycerin in patients with chronic renocardiac syndrome in 60% of cases occur reduced vasodilator and constrictor response in 12.6%. Normal character vasodilation was 27.4%. Endothelium-independent vasodilatation brachial artery decompression was reduced by 51.1% compared with the control.

The growth of endothelium-independent vasoconstriction in the III degree of hypertension was reduced to a lesser degree than the endothelium-dependent - by 6.5% and 19.4% ( $p < 0.01$ ), respectively, which is reflected in the increase of the reliable  $\Delta d / \Delta dN$ : from 0.55 (0.18, 0.81) to 0.65 (0.24, 1.02) or 15.4% ( $p < 0.01$ ).

The attention that is being given to the role of endothelial dysfunction in the development of cardiovascular lesions in renal patients in the future will help to expand the understanding of the damaging factors associated with the appearance of endothelial dysfunction. This in turn determines the character of the preferred choice of antihypertensive drugs such as normal blood pressure and at the same time having a positive effect on the endothelium, which is also associated with the reduction of cardiac hypertrophy and the vascular wall.

## RESULTS

Compared with healthy individuals, average diameter of the brachial artery in the total group of patients with hypertension in CKD were lower by 54.3%: in patients with Stage II level 55, 1% and AH stage III 48.7% ( $p < 0.01$  compared with the control,  $p = 0.031$  for the comparison between the degree of hypertension). On the background of decrease in brachial artery diameter was also reduced blood flow in the total group of 36.4%, which is equally dependent on the degree of hypertension ( $p < 0.01$ ).

Conduct tests on decompression and nitroglycerin showed that reduced growth in brachial artery diameter in the total group on the decompression was compared with the norm of 51.1%: in AH II - by 48.8% and in AH III - by 52.2% ( $p < 0.01$  compared to control).

A similar pattern was obtained by carrying out the test with nitroglycerine: a total group of patients with hypertension decrease vasodilation was 21.1%, AH II - 13.8%, and AH III - 30.7% ( $p < 0.01$  compared with control in all cases).

Conduct tests to decompression showed that the normal type of vasodilator response occurred only in 27.4% of patients: in AH II - 8%, and in AH III - 22%.

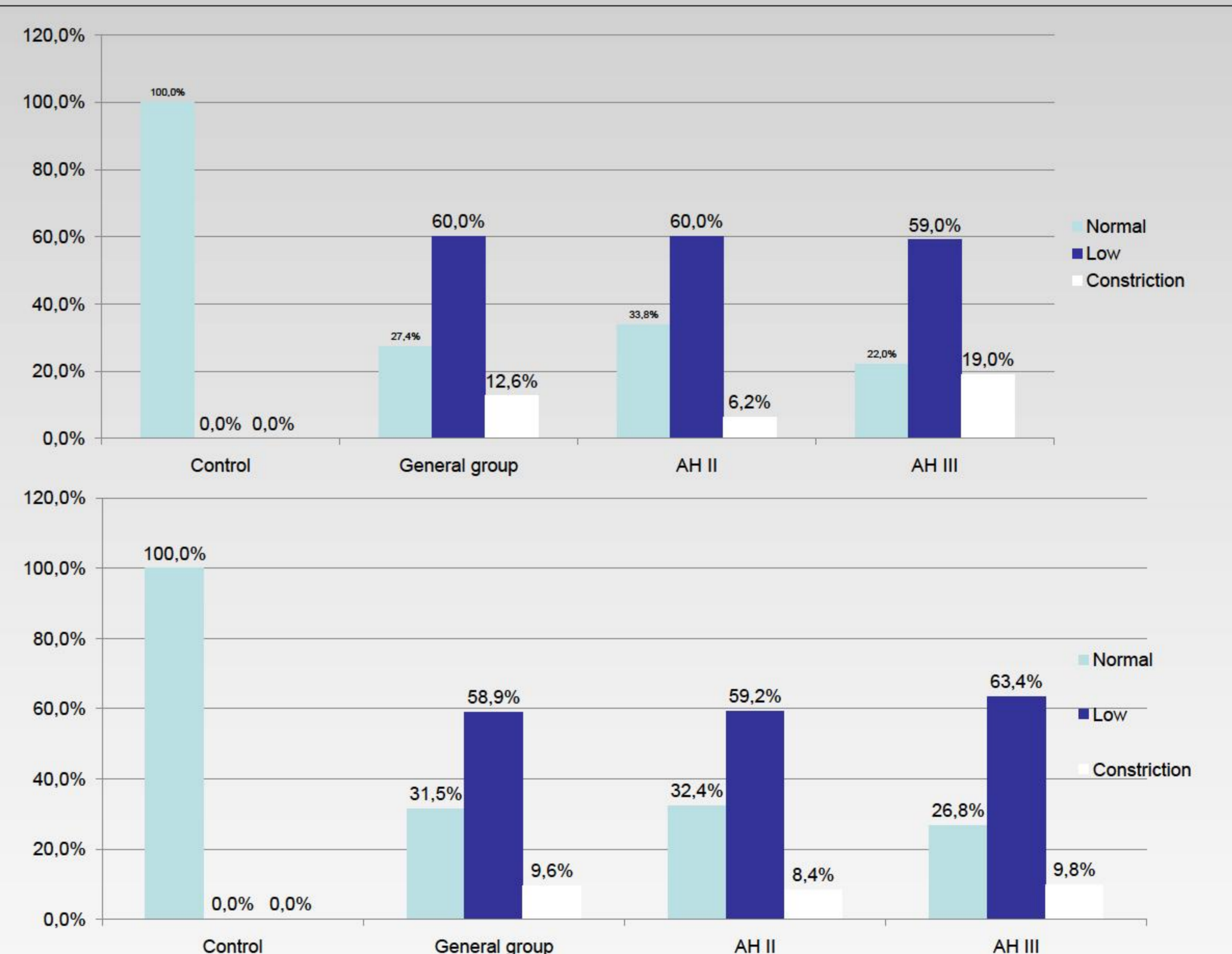
The reduced response to decompression was 60% of patients with hypertension II - in 43.2%, and AH III - in 56.8%, and constrictor - in 12.6%, of which in AH II - 6.2% and 17% in AH III, respectively.

When carrying out the test with nitroglycerin normal vascular response occurred in 33.5% of patients with hypertension, decreased from 59.9% to 9.6% of constrictor in patients and reduced vasoconstrictor response to nitroglycerin more frequent in patients with AH II (Table).

Describing the vasomotor response to decompression and test with nitroglycerin, it must be emphasized that in hypertensive patients with chronic kidney disease most often, in 60% of cases, found a reduced vasodilator and constrictor response in 12.6% (Fig.). Normal character vasodilation was only 27.4%, which means a significant reduction in vasodilatory properties related to endothelial function. Thus an endothelium-independent vasodilatation brachial artery decompression was reduced to a greater degree compared to the control - 51.1%.

Any type of frequency dependence of the reaction vessel on the nature of the sample (due to compression or nitroglycerin) was not significant: normal type of reaction is met more frequently in 31.5% of cases and to nitroglycerin in 27.4% of cases in the sample for decompression ( $p < 0.05$ ). Pathological constrictor reaction occurred in the overwhelming number of patients: in 72.6% of patients on decompression and 68.5% for nitroglycerin ( $p < 0.05$ ). This indicates a decrease in the independent and dependent vasodilatory response of the vascular endothelium as the main manifestations of vascular dysfunction in the endogenous (hypoxia) and exogenous (nitroglycerin) vasodilator stimuli.

Analysis of test with vasodilatory effects decompression and nitroglycerin showed that growth of endothelium-independent degree of vasoconstriction in hypertension III was reduced to a lesser extent than endothelium dependent - 6.5% and 19.4% ( $p < 0.01$ ) respectively, reflected in the increase of the reliable  $\Delta d / \Delta dN$ : from 0.55 (0.18, 0.81) and 0.65 (0.24, 1.02) or 15.4% ( $p < 0.01$ ). Therefore, increasing the frequency of vasoconstrictor responses to vasodilator tests are as much at AH II and AH III is an important element of the pathogenesis of hypertension in CKD.



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