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Original Contribution

STRUCTURAL AND FUNCTIONAL VASCULAR CHANGES IN HIGH NORMAL ARTERIAL PRESSURE

P. Nikolov*

First Department of Internal Medicine, Section of Cardiology, Faculty of Medicine, Medical University - Plovdiv, Bulgaria

ABSTRACT
The PURPUSE of the present study is changes in function and structure of large arteries in individuals with High Normal Arterial Pressure (HNAP) to be established. MATERIAL and METHODS: Structural and functional changes in the large arteries were investigated in 80 individuals with HNAP and in 45 with optimal arterial pressure (OAP). In terms of arterial stiffness, pulse wave velocity (PWV), augmentation index (AI), central aortic pressure (CAP), pulse pressure (PP) were followed up in HNAP group. Intima media thickness (IMT), flow-induced vasodilatation (FMD), ankle-brachial index (ABI) were also studied. RESULTS: Significantly increased values of pulse wave velocity, augmentation index, central aortic pressure, pulse pressure are reported in the HNAP group. In terms of IMT and ABI, being in the reference interval, there is no significant difference between HNAP and OAP groups. The calculated cardiovascular risk (CVR) in both groups is low. CONCLUSION: Significantly higher values of pulse wave velocity, augmentation index, central aortic pressure and pulse pressure in the HNAP group are reported.

Key words: high normal blood pressure, optimal arterial pressure, arterial stiffness, carotid artery thickness, flow induced vasodilatation, ankle-brachial index.

INTRODUCTION

High normal blood pressure (HNBP) is that the reference interval for systole is between 130-139 mmHg and for diastole- between 85-90 mmHg (1). In the recommendations of the European Association for Hypertension (ESH) since 2013, no drug treatment was needed in this category (2). There is increasing evidence that HNBP has a twice as high cardiovascular risk (CVR) compared with normotensive individuals (3-6). CVR is calculated by the so-called EUROSCORE, which is insensitive to young patients (7). The risk profile of hypertensive objects is increasingly relying on subclinical organ changes. Changes in the structure and function of large arteries may be a surrogate for early and accurate assessment of changes in HNBP and an argument for medication treatment. Blood pressure changes reflect arterial rigidity, flow-induced vasodilation, intima-media thickness, and ankle-hand index.

The **PURPUSE** of the present study is to establish changes in function and structure of large arteries in HNBP individuals. The working hypothesis is that in objects with HNBP there are changes in function and structure of the large arteries, increasing the CVR and even in some may be an argument for earlier start of medication treatment.

MATERIAL AND METHODS

On the basis of office blood pressure registration (BP), two groups were defined -a group with HNBP, consisting of 81 individuals and control group with optimal blood pressure – OBP (systolic pressure below 120 mmHg and diastolic - below 80 mmHg) of 45 objects. The measurement of BP under basic conditions was carried up in two different examinations, in three times, on the forearm with an electronic apparatus "Microlife" –Switzerland.

***Correspondence to:** *Petar Nikolov, First Department of Internal Medicine, Section of cardiology, Faculty of Medicine, Medical University - Plovdiv, Bulgaria, Plovdiv 4002, Silistra St.8, e-mail address: peponik@yahoo.com*

The averaged values were taken into consideration. The groups do not differ in gender and age, with the average age being about 40 **(Table 1)** The HNBP group has a less favorable metabolic profile and a greater incidence of metabolic syndrome (MS) than that with optimal blood pressure (OBP).

Table 1*. Characteristics of the groups.*

Indices	**HNBP**(81)	Standard deviation	**OBP**(45)	Standard deviation	**P**
age	44,1	±3,4	41,2	±2,3	NS
Gender(m/f)	40/41	-	24/21	-	NS
Weight(sm)	105,56	± 6,35	75,57	±8,62	<0,01
Waist(sm)	107,06	±3,11	82,43	±4,84	<0,01
Total cholesterol(TC) mmol/l	5,57	±1,23	4,03	±0,96	<0,05
Triglycerides (TG) mmol/l	2,11	±0,21	1,13	±0,11	<0,05
High density lipoproteins-ch(HDL) mmol/l	1,14	±0,21	1,31	±0,25	NS
Low density lipoproteins-ch(LDL) mmol/l	3,58	±0,67	2,25	±0,53	<0,05
Plasma sugar level mmol/l	4,96	±0,56	4,74	±0,61	NS

The individuals were tested for arterial rigidity by Arteriograph, TensioMed, Hungary, a device based on an oscillometric method for pulse wave velocity (PWV) measurement, central aortic pressure (CAP) and augmentation index (AI). The pulse pressure, giving the difference between systolic and diastolic values, was also calculated. In case of an impaired aortic compliance, the upper mentioned indices increase, indicating thus increased arterial rigidity and unfavorable vascular remodeling. PWV (8) is of greatest clinical and prognostic significance. Flow mediated vasodilatation (FMD) was also measured in the followed up individuals. Brachial artery diameter measurement can be done manually or automatically. The automatic measurement of the brachial artery diameter is more accurate and has better reproducibility than manual one. This index reflects well endothelial function and deviations may be indicative of early endothelial dysfunction in HNABP individuals (9-11). Intima media thickness (IMT) was measured at the distal portion of the common carotid artery (CCA) at its anterolateral position, 1-2 cm (4 cm) from the bifurcation. The thickening is an indicator of the acceleration of the atherosclerotic process and may have a correlation with the severity of the coronary disease (12). The methodology for ankle brachial index (ABI) measurement is non-invasive and easy to implement. Measurement of ABI was performed by a Huntleheigh Dopplex Doppler Apparatus and a sphygmomanometer. Systolic blood pressure (SBP) of both hands was measured by checking Doppler blood flow at the antecubital portion. Similarly, the systolic pressure of lower limbs was measured by doppler blood flow assay of a.tibialis posterior and a.dorsalis pedis. The ABI is determined individually for each lower limb, with the lower of the two values being taken from the left and right ABI measurements. The pathological index is an expression of a more advanced atherosclerotic process and it is of less importance in the initial vascular changes expected in HNBP individuals.

RESULTS

Assessment of changes in large arteries.Arterial rigidity: In clinical terms, it is importantthe indices reflecting the rigidity of arterial vessels, in concern of HNABP based unfavorable vascular remodeling to be measured. Increased rigidity causes changes in PWV, thus being an independent predictor for cardiovascular morbidity and mortality. A velocity above 12 m/s confirms increased rigidity. In contrast, to PWV, which is a direct index of assessing arterial rigidity, CAP and AI are indirect parameters, measuring it. **Table 2** presents the parameters reflecting arterial vascular wall behavior in HNBP and OBP groups.

Table 2. *Indices for arterial rigidity.*

Indices	Group Number	Mean value	Standard deviation	P
PWV- m/s (pulse wave velocity)	HNBP-81	7,31	±1,431	P<0,05
	OBP-45	6,34	±0,579	
CAP- mmHg (central aortic pressure)	HNBP-81	109,87	±11,342	P<0,05
	OBP-45	100,81	±4,281	
AI % (augmentation index)	HNBP-81	7,95	±8,752	P<0,05
	OBP-45	3,89	±2,170	
PP- mmHg (pulse pressure)	HNBP-81	51,06	±5,963	P<0,05
	OBP-45	44,28	±3,683	

Significantly increased values of PWV, AI, CAP and PP in the HNBP group are registered. These objects experience initial changes in large vessels (aorta) leading to increased rigidity and higher PWV. Reflected wave returns faster and increases central aortic pressure, augmentation index, and pulse pressure. Apparently, the changes in the cardiac vessels go in parallel. The above-mentioned haemodynamic abnormalities resulting in increased arterial rigidity are an incentive for left ventricular hypertrophy with subsequent changes in systolic and diastolic left ventricular (LV) function.

Table 3. *Flow mediated dilation (FMD) in HNBP and OBP groups.*

Index	Група Брой	Mean value	Standard deviation	P
FMD%	HNBP-81	10,32	±9,125	P<0,05
	OBP-45	16,07	±8,751	

The transition from norm to pathology is not leap, but smooth. Trends are important. In hyperhypertensives, there is definite evidence of increased arterial rigidity leading to structural and functional changes in the left ventricle. Apparently, a gradual increase in AP although still within the so-called norm is a process leading to changes in the vessels and the heart. **Determination of flow induced vasodilatation (FMD):** While IMT and ABI report structural changes in large arterial vessels, FMD takes into account the functional one. FMD of brachial artery is of highest clinical value. Impaired FMD% reflects the degree of endothelial dysfunction. In recent years, many authors have found that FMD is in directly propotional relationship to endothelial dysfunction. It is a classic commentary that endothelial dysfunction is the beginning of the atherosclerotic process and it precedes the morphological vascular changes. The most sensible method of endothelial dysfunction checking is FMD. Impaired FMD marks the onset of vascular damage. In the comparative assessment of FMD in objects with HNBP and OBP, **Table 3** presents thatthe rate of dilation is considerably lowerer in HNBP. This speaks of suppressed physiological phenomena, such as the flow of induced vasodilation. Impaired dilation reflects changes in the other vascular functional indices too, discussed above: PWV, AI, CAP and PP. This in turn leads to a change in the heart's structure: greater muscular mass, impaired diastolic function and reduced velocity of constriction**. Intima media thickness (IMT) and ankle-brachial index (ABI)**: Intra-carotid artery thickness or intima-media thickness (IMT) is an accessible index for assessing vascular changes in peripheral circulation and also a precursor to major cardiovascular events. IMT could be used the stages of atherosclerotic process to be assessed as well as its response to treatment to be monitored. The intimal thickness of the inner carotid artery over 1.2 mm is a sure sign of atherosclerotic vascular alterations. It is clear that this is a stage of advanced vascular damage and could not be registered in HNBP, being , a pre-clinical condition in which no significant changes could be expected. Changes in ABI are in concern with even more advanced vascular changes. Then the systolic BP of the lower limbs becomes lower than in the upper limbs and ABI becomes lower. Values below 0.9 are certainly pathological and indicate significant atherosclerotic changes in the lower limbs. In the comparative assessment of these two parameters, it was found that there was no significant difference between HNBP and OBP groups. IMT and ABI are in the reference interval in both groups - **Table 4.**

Table 4. *Changes in IMT (intima-media thickness) and ABI (ankle-brachial index) in HNBP and OBP groups.*

Indices	Group Number	Mean value	Standard deviation	P
IMT(mm)	HNBP-81	0,54	±0,131	P<0,05
	OBP -45	0,55	±0,123	
ABI	HNBP -81	1,15	±0,135	P<0,05
	OBP -45	1,22	±0,123	

DISCUSSION

A key question posed by considering HNBP as a problem is whether it is a norm or pathology. The answer to this question is also related to the decision if it should be treated by drugs or not. The current recommendations of ESH since this year (2018) say that only individuals with HNBP with higher CVR according to the SCORE system should be treated medically. Applying this scale, it turns out that the two groups - tested and controlled are with low CVR, i.e. no drug therapy is needed. The results obtained show that functional changes occur in the HNBP category, resulting in increased arterial stiffness and endothelial dysfunction. Knowing that the endothelium has regulatory and protective functions for the vessels, it is considered that endothelial dysfunction is the initial and early stage of atherosclerosis. Thus, we have the opportunity to intervene early in the pathological process. Changes that are registered in large arterial vessels, such as increased pulse wave velocity, increased central aortic pressure, increased pulse pressure, are a sign of reduced vascular compliance. The increased pulse wave velocity is followed by an increased velocity of the reflected wave, burdening thus the heart and triggering LV hypertrophy. A stimulus for LV hypertrophies canbe the activated system of renin angiotensin aldosterone (SRAA) too. Indirect evidence of this is the results of our previous studies presenting the favorable reverse changes of the heart and vessels in HNBP individuals due to the use of ACE inhibitors. The autonomous role of PWV is great as a predictor of total and cardiovascular mortality, coronary events and stroke. On the other hand, this is an index of high sensitivity.What more, the role of PWV, as a predictor of cardiovascular events, is of most significance in patients less than 50 years of age.Considering the drawbacks of the SCORE scale for assessing CVR, in the assessment of individuals with baseline hypertension and those with borderline values such as HNBP, as well as the high potency of PWV, the latter should be taken into account when considering a drug therapy to this category(14).

CONCLUSION

Changes in the structure and function of large arteries are reported in individuals with HNBP.They are an expression of the fact that high normal blood pressure affects arterial stiffness and makes endothelial function appear. All of this changes the cardiovascular risk of individuals with HNBP.When making a decision for medication treatment in HNBP category, the existing SCORE scale is insufficient. More sensational markers for CVR, such as PWV, are needed.

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