Arterial hypertension in the elderly

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Introduction

More than half of the individuals older than 65 are affected by hypertension. Isolated systolic hypertension, characterized by an increase in systolic arterial pressure without an increase in diastolic one, is the most frequent type of hypertension in persons over 50 years of age. It occurs de novo or after a long period of inadequately treated systolic-diastolic arterial hypertension. The main reason for its occurrence is many years mediated increase in stiffness of the large elastic arteries. This structural change is responsible for the occurrence of high systolic pressure in the following two ways: by blood ejection from the left ventricle into the stiff arterial system of decreased distensibility, and by the increase in the pulse wave velocity with the reflection wave occurring during late systole. The increased peripheral vascular resistance, sympathetic stimulation and activities of the Renin Angiotensin Aldosteron (RAA) system play a less significant role in the incidence of arterial hypertension in the elderly than is the case with individuals affected by structural and functional changes of the aorta.

Previously, vascular stiffness and an increase in systolic pulse pressure were considered as a part of the aging process and there was no insistence on treating this type of hypertension. Nowadays, when it is known that arterial hypertension in the elderly increases the risk of cardiovascular diseases three to four times more than in younger persons, it is insisted that this significant risk factor be corrected.

In addition to necessary life style modifications, the advantage in medical treatment is given to thiazide diuretics and dihydropiridines from the group of calcium channel blockers. The therapy should be always adjusted to comorbidities.

Elderly persons are defined as individuals at the age of 65 and older. They represent a growing segment of the population. In 1990, elderly persons comprised 13% of the total population of the USA and it is estimated that until 2040 they will constitute 20% of the population 1. As regards the number of elderly persons, Serbia is ranked as the fourth country in the world, after Greece, Italy and Japan. According to the data of the Statistical Office of the Republic of Serbia, approximately 17.24% of the population was elderly at the end of the last century, and it is estimated that this number will increase to 30% as far as 2025 2.

Similarly, the percentage of very old persons (older than 85) is constantly growing and it is assumed that there will be 16 million very old persons in the world by the middle of the 21st century 1.

More than half of the individuals over 65 years of age have hypertension 1. The principal reason for the increased incidence of arterial hypertension in the elderly is the growing number of persons suffering from isolated systolic hypertension (ISH), which is also the most frequent type of hypertension found in this age group 3, 4. Isolated systolic hypertension is defined as an elevated systolic blood pressure ≥ 140 mmHg with the diastolic pressure value < 90 mmHg.

Much more significant fact than the increased incidence of the elderly is the fact that the elderly with arterial hypertension, whether it is isolated systolic or both systolic and diastolic, are at three to four times higher risk to develop cardiovascular diseases than young individuals. It is an important risk factor for stroke, heart failure, coronary artery disease, terminal renal failure and death 1.

Epidemiology of arterial hypertension in the elderly

The results of the thirty-year follow-up of patients included in the Framingham Heart Study have shown that systolic blood pressure (SBP) continually increases from the age of 30 to 84. Unlike systolic blood pressure, diastolic blood pressure (DBP) increases until the fifth decade and...
then gradually decreases through the age of 60. This results in the increase of pulse pressure (PP) \(^5\), which is illustrated in Figures 1 and 2.

As it is already mentioned ISH is the predominant type of arterial hypertension among individuals older than fifty. ISH is present in 8% to 15% of all individuals over 60 years of age \(^6\). The third National Health and Nutrition Examination Survey (NHANES III) has shown that more than 80% of persons over 50 who suffer from arterial hypertension have systolic hypertension (Figure 3) \(^7\). Its incidence progressively increases with age by 5%, 15%, and 25%, in the sixth, seventh and eighth decade, respectively \(^6\).

Despite the general pattern of arterial blood pressure changes are similar for both genders, the arterial pressure, which is lower in women younger than 50, gradually increases from that age and results in values significantly higher than in men over sixty \(^8\). This phenomenon is a consequence of menopause, which enhances the age-induced increase of arterial blood pressure.

**Structural changes of large arteries in elderly persons and the reasons of their occurrence**

The age-associated increase in stiffness of large arteries is the main characteristic of arterial hypertension in the elderly \(^2\). Structural changes affect the aorta and elastic arteries, whereas the structure of muscular arteries does not change significantly. Elastic arteries undergo thickening of the tunica intima and their tunica media loses the ordered structure of elastic fibre and lamina that become thinner due to ruptures and fragmentation. Levels of collagen and matrix protein rise. Calcium binds to elastin and the undifferentiated muscle cells of the tunica media that proliferate and migrate into the intima. Proliferation of connective tissue results in the thickening of the intima and media fibrosis, along with the loss of distensibility and partial loss of its contractility.

A logical explanation for these alterations lies in the fact that the stress cycle accumulated in six decades as a result of more than two billion expansions of the aorta in the course of ventricular contraction leads to fatigue of the material and consequential structural changes \(^9, 10\).

Genetic polymorphism also plays a role in the process of cardiovascular aging \(^11\). A combination of two or three polymorphisms may influence the characteristics of the vascular wall much more consistently than a single polymorphism. In elderly persons suffering from ISH, the DD genotype of angiotensin-converting enzyme gene polymorphism, combined with the specific genotype of aldosterone synthetase and α-adducin gene polymorphism influence the reduction of arterial compliance and distensibility, which in turn are responsible for the incidence of ISH and augmentation of PP.

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The age-induced structural changes in large arteries occur independently of other risk factors, but the role of hypercholesterolemia, smoking, insulin resistance, etc. cannot be ignored in the development of endothelial dysfunction, and thereby the development of arterial hypertension. On the other hand, high systolic blood pressure increases wall stress that causes the damage of endothelium, which, in a vicious circle, maintains high levels of arterial blood pressure.

**Pathophysiology of arterial hypertension in elderly persons**

The value of systolic blood pressure (SBP) is a result of the interaction among the following three factors: characteristics of left ventricular ejection, and compliance of large arteries, and propagative and reflective properties of the pulse wave in the arterial tree.

As noted above, the dominant reason for the increased SBP in the elderly with ISH is an increased stiffness of the arteries, which produces negative effects in two ways — through direct and indirect mechanisms. The direct mechanism involves the creation of high systolic pressure by the ejection of blood from the left ventricle into the stiff arterial system of decreased distensibility. The indirect mechanism implies the influence that the arterial stiffness has on the velocity of pulse wave and on the pressure wave reflection time. With the increase of arterial stiffness and the velocity of the pulse wave, the reflection wave returns into the central artery earlier, usually during late systole and less often during early diastole. This causes increase in the aortic and left ventricular pressure during systole and a reduction aortic pressure during diastole. This is shown in Figure 4.

![Fig. 4 – With aging large arteries stiffen, and the reflected wave, which travels faster, is superimposed over the forward wave in early systole, increasing both systolic and pulse pressure](https://example.com/fig4)

In our research, published ten years ago, we found that aortic distensibility estimated by echocardiography inversely correlated with pulse wave velocity in patients with isolated systolic hypertension older than 65.

One of the characteristics of arterial hypertension in the elderly is an increase in the activity of the sympathetic nervous system which leads to down-regulation of adrenergic receptors. On the other hand, beta-adrenergic receptor sensitivity is diminished, which reflects in a decreased chronotropic response to beta antagonists and indicates a lesser significance of sympathetic stimulation in the development of arterial hypertension and less efficiency in treatment with beta blockers in elderly individuals.

Another mechanism contributing to the development of arterial hypertension in the elderly is endothelial dysfunction. It is manifested in decreased nitric oxide-mediated dilatation. Taking the increase in aortic pulse wave velocity as the measure of stiffness of large arteries, Wallace et al. have shown that it correlates with endothelial dysfunction.

Additionally, the number of nephrons decreases with age and a total of 800,000 nephrons at birth reduces by half at the age of 70. The nephrosclerosis developed as a result of aging and arterial hypertension leads to the decreased secretion of renin from the kidneys. Thus, in elderly with arterial hypertension we usually find decreased levels of renin in circulation and lower plasma renin activity. Low levels of renin can also occur as a result of the salt retention tendency with consequential volume load, which leads to increase of arterial pressure and suppression of renin release from the juxtaglomerular cells. This characteristic of the arterial hypertension in elderly persons explains better responsiveness of arterial hypertension to the application of diuretics and calcium channel blockers, and its lower responsiveness to the treatment with ACE inhibitors, AT1-receptor blockers and beta blockers.

Elderly hypertensive persons, as well as the normotensive ones, show salt sensitivity, which is indirectly proven by significant decrease of blood pressure values with the loss of salt or reduction of salt intake.

Elderly persons who suffered from arterial hypertension at younger age and sustained it at old age show a more significant increase in peripheral vascular resistance than those whose aging was the reason for the occurrence of arterial hypertension.

Hemodynamically, ISH is characterised by a decrease in cardiac output, stroke volume and intravascular volume. Baroreceptor sensitivity to changes in blood pressure levels is decreased, which results in significant variations of the arterial blood pressure values.

**Specific characteristics of arterial hypertension in the elderly**

Diagnosing arterial hypertension in the elderly, especially very old ones, may be accompanied with problems. In approximately 2% to 5% of elderly persons with rigid, calcified arteries, it is impossible to ensure the collapse of the brachial artery, which gives false high values of the arterial blood pressure. This phenomenon is called pseudohypertension. Pseudohypertension is suspected in persons with minimal vascular damage of the retina in spite of the high measured values of arterial blood pressure, and in those who show postural symptoms after discontinuation of therapy.

Arterial hypertension in the elderly is characterised by significant oscillations in the values of arterial pressure.
which can be proved by 24-hour ambulatory blood pressure monitoring. In one of our researches we found that variations of systolic pressure values in hypertensive subjects older than 60 years correlated with their age and they were the most frequent in patients older than 80 years of age. We also determined that reduction of systolic blood pressure during night inversely correlated with age. However, significant individual variations of systolic arterial pressure in elderly persons during the night indicate the risk of brain stroke. The risk of cardiovascular events is also increased during the early morning increase in the values of arterial pressure. The white coat hypertension was detected in 24% of elderly persons. In one of our investigations we found that the prevalence of the white coat hypertension was higher in the elderly with isolated systolic hypertension than in patients with combined systolic and diastolic hypertension which were the same age. Another phenomenon that may be seen in the elderly is the phenomenon of reverse white coat hypertension, which implies that the values obtained during 24-hour monitoring of arterial pressure are higher than those obtained through conventional measuring in the doctor’s office.

Moreover, another phenomenon characteristic of the elderly population is orthostatic hypotension, which is defined as a fall in SAP by at least 20 mmHg and a fall in diastolic pressure by 10 mmHg within three minutes after getting up. The main reasons for its occurrence are the decrease in baroreceptor sensitivity and the deficit of heart-rate response to the change in body position. The incidence of occurrence of orthostatic hypotension increases from 17% in persons 65 to 74 years of age to 26% in persons older than 85. Orthostatic hypotension poses the risk of traumatism, and, on the other hand, it is a risk factor for cardiovascular diseases. Likewise, orthostatic hypotension increases the risk of brain stroke and dementia. Reduction of arterial blood pressure may also occur after eating, which is referred to as postprandial hypotension. The basic reason for its occurrence is an inadequate response to vasodilatory effects of gastrointestinal peptides and insulin. It has been established that approximately 70% of individuals older than 70 show fall in arterial pressure values after meals, and that in 24% of the cases reduction is over 16 mmHg for systolic and over 12 mmHg for diastolic arterial pressure. Not a small number of the elderly have a weakness, even syncope after breakfast which, besides all the possible metabolic reasons, can be also explained with the postprandial hypotension that is easily detected by the 24-hour blood pressure monitoring. However, if the evidence of postprandial hypotension is missing then the 24-hour blood pressure monitoring should be repeated at least twice if there are no conditions for hospitalization.

The implications of high pulse pressure

This characteristics of arterial hypertension in the elderly complicate the treatment of these patients. Yet, they cannot be a barrier to the medical treatment, which is extremely important due to the subclinical and clinical consequences of arterial hypertension in elderly persons. The left ventricle becomes stiff, in addition to the stiffness of the large arteries. Moreover, left ventricle hypertrophy is often found in the elderly suffering from ISH. In our examination of the influence of the aortic distensibility on systolic and pulse pressure in patients with isolated systolic hypertension, we found that the patients with this form of arterial hypertension in addition to impaired left ventricular relaxation also have concentric remodeling pattern of left ventricle as dominant pattern. Stiffness of the left ventricle combined with decreased distensibility of the arterial system increases the risk of cardiovascular diseases in several ways. Among other problems, the wall stress increases, which in turn enlarges the energy necessary for cardiac cycle. The increase in left ventricular stress during late systole leads to incomplete diastolic relaxation, and eventually to heart failure with preserved ejection fraction.

Isolated systolic hypertension is often combined with coronary artery disease, thrombotic and hemorrhagic strokes, dementia, peripheral arterial disease and slow progressing heart and renal failure. Comparing the results of normotensive elderly persons with the elderly suffering from ISH it has been shown that the increase of systolic blood pressure by 1 mmHg raises the incidence of coronary artery disease, stroke and overall mortality by 1%. This finding is real evidence for the significance and severity of this type of arterial hypertension.

Treatment of arterial hypertension in the elderly

The purpose of treating arterial hypertension in elderly persons is identical to the purpose of treating it in young and middle-aged populations – its reduction to values below 140/90 mmHg, ie reduction to values below 130/80 mmHg in the high-risk patients with clinical damage (after acute myocardial infarction, due to renal failure, after cerebrovascular insult) and those suffering from diabetes mellitus. Like in the case with hypertensive patients in younger age, reduction of body weight, restriction of salt intake according to DASH (Dietary Approaches to Stop Hypertension), increased physical activity and moderate alcohol intake (one serving per day for women and two servings for men) is advised for the elderly regardless of the type of arterial hypertension.

According to our experience an essential precondition to achieve the target values of arterial blood pressure in patients older than 65, and especially older than 70 years of age, is the reduction in salt intake of 100 mmol/day (ie 4.7 to 5.8 g NaCl). This can be explained by the above-mentioned salt sensitivity which increases through the lifetime. One of the problems in the modification of a lifestyle is the changes in the bones and joints, which restrict mobility and require a combined medical approach including physiotherapist who will show these patients some exercises that are crucial for maintaining and prevention of the reduction of large arteries distensibility as well as for the sustenance of a desired weight and the decline of body overweight.

In drug treatment, there are five available large groups of antihypertensives: thiazide diuretics, calcium channel blockers, angiotensin–converting enzyme (ACE) inhibitors,
angiotensin (AT1)-receptor blockers, and beta blockers. Each of these groups reduces the values of arterial blood pressure in a similar way, thus reducing the incidence of cardiovascular events. Different clinical trials have shown that medicament treatment of these patients reduced the risk of cerebrovascular insult, coronary artery disease, acute myocardial infarction, mortality of coronary artery disease and total mortality (Tables 1 and 2). The specificity of treating elderly persons is in introducing smaller dosage of the drugs due to the significant occurrence of adverse effects in this population.

The initial randomized controlled studies showed the benefit from the use of diuretics or beta blockers compared with placebo in the treatment of various forms of arterial hypertension in the elderly 27-30. However, Masserli et al. 31 using meta-analysis showed that beta blockers used in the treatment of arterial hypertension in the elderly were less effective than diuretics in the prevention of cardiovascular events. Based on the results of large randomized studies (SHEP and Syst-Eur) thiazide diuretics and calcium channel blockers (especially dihydropiridines) were suggested as the first-line therapy in the treatment of ISH 32, 33. The studies that followed examined the advantage of the "new" (new generation dihydropiridines, ACE inhibitors and AT1 recep- tor blockers) in relation to the "old" (beta blockers and thiazide diuretics) antihypertensives. The ALLHAT study showed that thiazide diuretic, ACE inhibitor and calcium channel blocker reduced the frequency of cardiovascular events in the subgroup of patients older than 65 years of age equally well 34. The LIFE study showed that the AT1 receptor blocker was more effective than beta blocker in the prevention of cardiovascular events, especially cerebrovascular insult in hypertensive patients aged 55 to 80 with left ventricle hypertrophy 35. The advantage of AT1 receptor blockers

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<td>HYVET 37</td>
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<td>LIFE 35</td>
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Stop-Hyper – Swedish Trial in Old Patients with Hypertension; SHEP – Systolic Hypertension in the Elderly Program; Syst-Eur – Systolic Hypertension-Europe; MRC – Medical Research Council trial of treatment of hypertension in older adults; HYVET – Hypertension in the Very Elderly Trial; LIFE – Losartan Intervention for Endpoint reduction in hypertension; SBP – systolic blood pressure; DBP – diastolic blood pressure; LVH – left ventricle hypertrophy

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<td><strong>Trial</strong></td>
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The prevention of the nonfatal cerebral stroke in patients older than 70 years of age with ISH was confirmed by the results of SCOPE study 36.

Last year the results of the HYVET study which demonstrated the benefit of treatment of very old hypertensive patients (older than 80) were published. It was shown that the use of indapamide with or without perindopril in this population of patients led to a reduction of death counts from cerebral stroke, heart failure and total mortality. This eliminated the suspicion about necessity of treatment of very old hypertensive patients 37.

As it can be concluded from the above-mentioned, the large randomized studies have shown the benefit from the

applying of all groups of antihypertensives in treatment of old hypertensive patients. However, in everyday practice we face the dilemma about which medication to use first. The basic thing in these circumstances is the information about the associated risk factors and the information about subclinical and clinical manifestations of target organs damage. Undoubtedly, in patients with ISH without associated risk factors and organs damage we will apply thiazide diuretics with or without calcium channel blockers (Table 3). In other

taking three antihypertensives (thiazide diuretic is one of them) do not have optimal regulation of arterial pressure. If arterial hypertension exists in spite of compliance of proposed lifestyle changes and advised polytherapy, after excluding secondary forms of arterial hypertension (stenosis of renal artery usually of atherosclerotic nature), we can conclude that it is a resistant arterial hypertension in question. The reason for resistant arterial hypertension in the elderly are the structural changes of large arterial blood vessels. In

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<td>Recommendations for arterial hypertension treatment in the elderly</td>
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<td>• The aim of the treatment of arterial hypertension in the elderly is the reduction of systolic pressure values to less than 140 mmHg, diastolic pressure below 90 mmHg and in patients with ISH the value of systolic pressure &lt; 140 mmHg;</td>
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<td>• In order to achieve the blood pressure regulation it is necessary to modify the lifestyle, firstly to reduce salt intake and body weight in obese patients, then to stop smoking and reduce alcohol intake;</td>
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<td>• In medicament treatment we should start with a half of the usual dose because of a significant manifestation of adverse effects in this group of patients;</td>
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<td>• In patients with ISH without associated risk factors and target organs damage the advantage is given to thiazide diuretics and calcium channel blockers;</td>
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<td>• In all other circumstances (which are to appear far more often in everyday practice) the choice of medications should be adjusted in accordance with associated risk factors and clinical and subclinical target organs damage.</td>
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these circumstances, we use different modifications of a medical treatment to achieve a regular blood pressure, which is sometimes impossible.

Additionally, there is one more problem in treatment of the elderly. Namely, it is difficult to maintain optimal values of diastolic arterial pressure in these subjects with ISH. Protergerou et al. 38 have shown that the values of diastolic pressure ≤ 60 mmHg reduce survival despite of the stiffness of large arteries and the function of the left ventricle 38. They have suggested that it requires optimization of therapy not only regarding the values of systolic, but also diastolic arterial pressure.

In these circumstances where we have a significant reduction of diastolic pressure value (≤ 60 mmHg) in patients with ISH we are satisfied with accomplished but not optimal regulation of systolic blood pressure, like in the resistant arterial hypertension.

**Conclusion**

From all the abovementioned we can conclude that there is no dilemma whether the treatment of arterial hypertension of the elderly is necessary. Furthermore, it should be adapted to each patient and the success of the treatment is not always guaranteed.

**References**


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