PRAXISMEDICA

REVIEW ARTICLE

SECONDARY HYPERTENSION AND CONTINUUM OF RISING CASES

Miloš Mijalković[1] Saddam Shawamri[2] Dalila Šačić[3] Slavica Pajović[4]

1 Univerzitet u Prištini sa privremenim sedištem u Kosovskoj Mitrovici, Medicinski fakultet, Republika Srbija, 2 Faculty of Medicine, University of Belgrade, Serbia, 3 Clinic for Cardiology, University Clinical Center of Serbia, Belgrade, Serbia, 4 University of Priština, Faculty of Medicine - Internal Medicine Clinic - Kosovska Mitrovica, Serbia

Arterial hypertension is well-known strong risk factor that can lead to the development of coronary artery disease, heart attacks, heart failure, stroke, and other heart-related issues. Arterial hypertension has increased exponentially in the last few decades in adult men and women. Traditionally arterial hypertension is classified as primary, when no specific cause has been identified and is usually associated with multiple genetic polymorphisms and various environmental factor interactions, and secondary when there are conditions with biological plausibility to cause hypertension. Traditional data in medical textbooks indicate that in 90-95% of cases, arterial hypertension is primary, while only a small percentage of cases have secondary hypertension. European guidelines for elevated blood pressure and hypertension from 2024 indicate a higher prevalence of secondary hypertension, ranging from 10-35% of cases. Secondary hypertension is still not fully understood and often remains undiagnosed. Identifying the underlying cause of secondary hypertension is crucial, as treating the root condition can significantly reduce the risk of heart disease, stroke, and improve overall quality of life. Obesity is a major global health problem and the prevalence of obesity is constantly increasing and simultaneously leads to an increase in the prevalence of both primary and secondary arterial hypertension. Some forms of secondary hypertension cause more severe cardiac damage than primary hypertension and are associated with a higher cardiovascular risk. Secondary hypertension is more often resistant hypertension, which means that it is difficult to achieve target blood pressure values. It is important to timely conduct appropriate examinations and begin treatment promptly.
Keywords: secondary hypertension, blood pressure, cardiac damage, myocardial hypertrophy, obesity

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Miloš Mijalković[1] Saddam Shawamri[2] Dalila Šačić[3] Slavica Pajović[4]

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Arterijska hipertenzija je dobro poznat i glavni faktor rizika koji može dovesti do razvoja koronarne arterijske bolesti, infarkta miokarda, srčane insuficijencije, moždanog udara i drugih kardiovaskularnih komplikacija. U poslednjih nekoliko decenija prevalenca arterijske hipertenzije eksponencijalno raste kod odraslih muškaraca i žena. Tradicionalno se arterijska hipertenzija klasifikuje na primarnu, kada se ne može identifikovati specifičan uzrok i kada je obično povezana sa brojnim genetskim polimorfizmima i interakcijama različitih faktora sredine, i sekundarnu, kada postoje stanja sa jasnom biološkom osnovom koja mogu izazvati hipertenziju. Tradicionalni podaci iz medicinskih udžbenika pokazuju da je primarna arterijska hipertenzija zastupljena u 90–95% slučajeva, dok samo manji procenat obolelih ima sekundarnu hipertenziju. Evropske preporuke za povišen krvni pritisak i hipertenziju iz 2024. godine ukazuju na višu prevalencu sekundarne hipertenzije, koja se kreće od 10 do 35% slučajeva. Sekundarna hipertenzija i dalje nije u potpunosti razjašnjena i često ostaje nedijagnostikovana. Identifikovanje osnovnog uzroka sekundarne hipertenzije od suštinskog je značaja, jer lečenje osnovnog stanja može značajno smanjiti rizik od kardiovaskularnih oboljenja, moždanog udara, čime se poboljšava ukupni kvalitet života. Gojaznost predstavlja veliki globalni zdravstveni problem, a njena prevalenca je u stalnom porastu, što istovremeno dovodi i do porasta prevalence kako primarne, tako i sekundarne arterijske hipertenzije. Određeni oblici sekundarne hipertenzije dovode do izraženijeg oštećenja srca u odnosu na primarnu hipertenziju i povezani su sa većim kardiovaskularnim rizikom. Sekundarna hipertenzija je češće rezistentna hipertenzija, što znači da je teško postići ciljne vrednosti krvnog pritiska. Važno je blagovremeno sprovesti odgovarajuće dijagnostičke pretrage i započeti lečenje na vreme.
Ključne reči: sekundarna hipertenzija, krvni pritisak, oštećenje miokarda, hipertrofija miokarda, gojaznost

Korespondent:
Miloš Mijalković
Polyclinic Kardio Medika, Nis, Serbia
Mail: m.mijalkovic84@gmail.com

INTRODUCTION

Arterial hypertension is the leading cause of cardiovascular disease, stroke and premature death worldwide. According to the World Health Organisation (WHO) globaly report, only 54% of adults with hypertension are diagnosed, 42% receive treatment, and 21% have their hypertension controlled. These data underscore the necessity for improved awareness and management of hypertension. The region of South-East Asia and the Western Pacific region experienced a significant increase of hypertension since 1990 (1).

Arterial hypertension is traditionally classified as primary or essential when no specific cause has been identified and is usually associated with multiple genetic polymorphisms and various environmental factor interactions, and as secondary when there are conditions with biological plausibility to cause hypertension regardless of other factors. Traditional data in medical textbooks indicate that in 90-95% of cases, arterial hypertension is primary, while only a small percentage of cases have secondary hypertension (1).

The prevalence of primary hypertension is rising globally owing to ageing of the population and increases in exposure to risk factors, such as high sodium intake, low potassium intake, obesity, alcohol consumption, smoking cigarettes, physical inactivity and unhealthy diet (2).

According to the 2003 European guidelines for the managment of arterial hypertension, the prevalence of secondary hypertension is 5-10% of cases, while the 2024 European guidelines for elevated blood pressure and hypertension indicate a higher prevalence of secondary hypertension, ranging from 10-35% of cases (2,3).

Secondary hypertension is still not fully understood and often remains undiagnosed. It has long been known that secondary hypertension is more likely to affect younger individuals and those whose high blood pressure is difficult to control with standard treatments. Identifying the underlying cause of secondary hypertension is crucial, as treating the root condition can significantly reduce the risk of heart disease, stroke, and other serious health issues, improving overall quality of life (4).

The importance of identifying secondary hypertension cannot be exaggerated. Chronic hypertension, regardless of the cause, can lead to serious damage to vital organs, including the heart, blood vessels, kidneys, brain, and eyes. While most patients with hypertension have primary hypertension (with no known cause), identifying secondary causes is essential because, with proper treatment, secondary hypertension can often be cured. Therefore, recognizing and addressing secondary hypertension is a key step in the effective management and prevention of long-term health complications (4).

The common suggestive clinical signs that require investigation into the cause of secondary hypertension are listed in (Table 1) (5,6).

Table 1. Patient characteristics that should raise the suspicion of secondary hypertension

- An acute and significant increase in blood pressure in patients who previously had stable blood pressure
- Age of onset of hypertension before puberty
- Age of onset of hypertension in individuals younger than 30 years who are not obese and have no family history of hypertension
- Severe hypertension with blood pressure higher than 180/110 mmHg, accompanied by target organ damage
- Resistant hypertension, which represents persistent elevation of blood pressure above 140/90 mmHg despite the use of optimal doses of at least three or four antihypertensive medications from different classes, including a diuretic
- Refractory hypertension, which refers to persistent elevation of blood pressure despite the use of five or more antihypertensive medications

Causes of secondary hypertension

Secondary hypertension is categorized based on its underlying causes into various subgroups. As is well known, more common causes of secondary hypertension include: renal parenchymal disease, chronic kidney disease, renovascular hypertension (atherosclerotic renovascular disease, fibromuscular dysplasia), primary hyperaldosteronism, obstructive sleep apnea, the effects of alcohol and certain medications (non-steroidal antiinflammatory drugs, corticosteroids, mineralocorticoids, sympathomimetics, oral contraceptives, antineoplastic drugs, immunosuppressants, erhytropoetin) etc. Less common causes of secondary hypertension include: pheochromocytoma, paraganglioma, acromegaly, Cushing's syndrome, hyperthyroidism, hypothyroidism, hyperparathyroidism, pregnancy-induced hypertension, coarctation of the aorta, etc. (7-9).

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Common causes of secondary hypertension

Kidney and renal artery disease

The kidneys play a central role in blood pressure regulation. Arterial hypertension can lead to kidney damage, while renal and renal artery diseases can contribute to an increase in blood pressure. Possible secondary forms of renal hypertension include glomerular kidney disease (e.g. glomerulonephritis) and tubulointerstitial processes (e.g. polycystic kidney disease) or microvascular kidney damage and renovascular hypertension (10).

Renal artery stenosis may be suspected as a cause of hypertension in younger individuals, mainly females with fibromuscular dysplasia, without a family history of arterial hypertension or in elderly patients presenting with hypertensive crises, flash pulmonary edoema (commonly in the context of bilateral renal artery stenoses, or of unclear progressive deterioration of renal function. The prevalence of the different aetiology of renal artery stenosis varies according to age and cardiovascular risk factor but it is reported that atherosclerotic renal artery stenosis account for 60–90% and fibromuscular dysplasia for 10-30% of the cases. Aetiologically, fibromuscular dysplasia, which typically affects young women needs to be distinguished from atherosclerotic artery stenosis, which is more common in older patients. Renal artery disease can lead to the narrowing of the renal vessel lumen, which reduces the pressure in the afferent arteriole and impairs renal perfusion. This triggers the kidneys to release renin, resulting in elevated levels of angiotensin II and aldosterone. These hormones raise blood volume by increasing the reabsorption of sodium and water in the kidneys, which in turn boosts cardiac output via the Frank-Starling mechanism. Elevated angiotensin II also causes systemic vasoconstriction, increasing systemic vascular resistance, and stimulates sympathetic activity. Chronic angiotensin II elevation further promotes cardiac and vascular hypertrophy. As a result, hypertension associated with renal artery stenosis is driven by both an increase in systemic vascular resistance and a rise in cardiac output (10).

Chronic kidney disease is a global health problem, with its prevalence on the rise. It is well known that primary arterial hypertension and chronic kidney disease are intrinsically related, with hypertension being a strong determinant of worsening kidney function. On the other hand, chronic kidney disease has a high prevalence of secondary hypertension (11-13).

Primary hyperaldosteronism

Primary hyperaldosteronism is the leading cause of secondary hypertension in middle-aged adults (ages 40–64 years). Elevated aldosterone levels cause heart damage and increase cardiovascular morbidity and mortality. It is actually a collection of conditions, including aldosterone-producing adenomas and bilateral idiopathic hyperaldosteronism. An adrenal adenoma or adrenal hyperplasia can lead to excessive aldosterone secretion. The elevated levels of aldosterone cause the kidneys to retain sodium and water, which results in increased blood volume and higher arterial blood pressure. As the body tries to suppress the renin-angiotensin system, plasma renin levels are typically low. Additionally, high aldosterone levels are often associated with hypokalemia. It is believed that the prevalence of primary hyperaldosteronism is also on the rise, and in a certain number of cases, it remains unrecognized as a cause of secondary hypertension (14-16).

Sleep apnea

Obstructive sleep apnea (OSA) is characterized by recurrent episodes of complete or partial collapse of the upper airway during sleep, resulting in apnea or hypopnea, and it is an independent risk factor for cardiovascular disease such as arterial hypertension, heart failure, arrhythmias, and coronary heart disease. The mechanism underlying the development of arterial hypertension in sleep apnea involves multiple factors, including increased sympathetic tone and decrease in parasympathetic tone, inflammation through mechanisms such as obesity, decreased intrathoracic pressure, pulmonary stretch receptor stimulation, chemoreceptor stimulation, hypoxemia, and hypercapnia. Consequently, renin-angiotensin-aldosterone system is activated, the endothelin-1 level is increased, and the nitric oxide level is decreased, all of which contribute to the increase in vascular resistance and the development of hypertension. The presence of OSA has been related to an increase in the prevalence and incidence of hypertension, regardless of other factors. In fact, approximately 50% of patients with OSA present hypertension. Recent studies show that the rise in obesity continues, and the prevalence of sleep apnea is also increasing, but in Asia there are many non-obese sleep apnea patients. Furthermore, many mild

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cases of sleep apnea with minimal symptoms are difficult to detect (17-19).

Drug-induced hypertension

Due to their widespread use, nonsteroidal anti-inflammatory drugs (NSAIDs), including acetylsalicylic acid and acetaminophen, represent the most common medications associated with worsening blood pressure control. Both cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) inhibitors can elevate blood pressure. NSAIDs increase blood pressure primarily by altering prostaglandin synthesis, which leads to adverse renal effects. In addition, NSAIDs raise systemic vascular resistance through enhanced endothelin-1 production and disturbances in arachidonic acid metabolism. Systemic corticosteroids such as dexamethasone, fludrocortisone, methylprednisolone, prednisone, and prednisolone may cause an elevated blood pressure. Corticosteroids can cause sodium and fluid retention, and can lead to an increase in blood pressure. The increase in blood pressure is dose dependent. Sympathomimetics such as the decongestants containing phenylephrine or pseudoephedrine may cause an elevated blood pressure. Estrogens, androgens, and oral contraceptives may cause an increase in blood pressure.
Antidepressants such as monoamine oxidase inhibitors, serotonin-norepinephrine reuptake inhibitors, and tricyclic antidepressants may cause an elevated blood pressure. Some immunosuppressants like cyclosporine and tacrolimus can affect kidney function, which can lead to the retention of sodium and water, ultimately causing blood pressure to rise. Several classes of antineoplastic drugs, including mainly vascular endothelial growth factor (VEGF) inhibitors, proteasome inhibitors, and cisplatin derivatives, can cause an increase in blood pressure due to their anti-tumor effects (20,21).

Less common causes of secondary hypertension

Phaeochromocytoma

Phaeochromocytomas or paragangliomas are tumors that secrete excessive amounts of catecholamines. These lesions may occur in the adrenal glands (phaeochromocytomas) or in sympathetic ganglia found along the sympathetic chain (paragangliomas or extra-adrenal phaeochromocytomas). Phaeochromocytomas are rare tumors, accounting for about 0.2-0,6% of all cases of sustained hypertension and hypertensive crisis. Catecholamine-secreting tumors can result in extremely high levels of circulating catecholamines (epinephrine, norepinephrine and dopamine). The elevated catecholamine levels induce systemic vasoconstriction, with cardiac stimulation leading to a substantial increase in arterial blood pressure and tachycardia (22).

Thyroid and parathyroid diseases

Dysregulation of thyroid function is reversible cause of secondary hypertension. Thyroid disorders lead to various hemodynamic changes that contribute to elevated blood pressure through their effects on endothelial function, vascular reactivity, renal hemodynamics, and the RAAS system. In hyperthyroidism, the increased endothelial responsiveness is a result of shear stress from the hyperdynamic circulation, which helps lower vascular resistance. On the other hand, hypothyroidism leads to a marked reduction in sensitivity to sympathetic agonists, resulting in higher peripheral vascular resistance and arterial stiffness. Thyroid disorders, specifically hypothyroidism and hyperthyroidism, have also been on the rise in recent decades and can certainly be important causes of secondary hypertension. Sporadic primary hyperparathyroidism is an endocrine disorder often characterized by persistent fasting hypercalcemia, caused by the autonomous overproduction of parathyroid hormone due to parathyroid adenoma or hyperplasia (hypercalcemic primary hyperparathyroidism). Primary hyperparathyroidism is associated with a higher risk of arterial hypertension (23-26).

Cushing's syndrome

In Cushing's syndrome arterial hypertension develops due to multiple pathophysiological mechanisms that contribute to increased plasma volume, peripheral vascular resistance, and cardiac output. Glucocorticoids may also affect blood pressure control by acting on the central nervous system, where they activate both glucocorticoid and mineralocorticoid receptors. As a result, glucocorticoids lead to changes that elevate cardiac output, total peripheral resistance, and renovascular resistance, which contributes to persistent hypertension. It is also known that the incidence of Cushing's syndrome have been increasing in the last period. Present in about 80% of Cushing's syndrome patients, secondary

hypertension is one of the pathology's most prevalent features (27-29).

Pregnancy-induced secondary hypertension

Pregnancy-induced secondary hypertension refers to a spectrum of hypertensive disorders unique to pregnancy, with preeclampsia and Hemolysis, Elevated Liver Enzymes, and Low Platelet (HELLP) syndrome being the most severe forms. Women with HELLP syndrome are at the highest risk for cardiovascular morbidity, including pulmonary edema and cardiac dysfunction. Preeclampsia, diagnosed after 20 weeks of gestation, is marked by new-onset hypertension, often accompanied by proteinuria or evidence of organ damage. Large studies published in recent years have also shown that there is an increase in the prevalence of pregnancy-induced hypertension. Obese women over 35 years of age have an increased risk of developing pregnancy-induced hypertension and preeclampsia, which can be a major cause of maternal and perinatal morbidity and mortality (30-35).

Aortic coarctation

Coarctation of the aorta, a congenital narrowing of the aorta, is a rare but significant cause of secondary hypertension, accounting for less than 1% of cases. It causes a narrowing of the descending aorta, usually located at the insertion of the ductus arteriosus distal to the left subclavian artery, which typically results in a left ventricular pressure overload. The obstruction reduces blood pressure in the lower body while raising pressure in the head and upper limbs. Coarctation is diagnosed by comparing blood pressure readings in the upper and lower limbs. Typically, these pressures are comparable, but in coarctation, blood pressure in the upper limbs is often significantly higher than in the lower limbs (36,37).

Mechanisms of obesity-induced hypertension and Discussion

Obesity is a common health disorder that develops from the interaction between genotype and environment and involves social, behavioral, cultural, physiological, metabolic and genetic factors. There is much evidence that obesity has a significant negative impact on population health. Therefore an important role is assigned to the treatment of this condition and its associated comorbidities such as arterial hypertension, hyperlipidemia, hyperinsulinemia, and insulin resistance. Obesity is a major global health problem and the prevalence of obesity is constantly increasing in most countries in the world, dominantly in younger-aged individuals both women and men. Sedantery behavior, constantly lower physical activity, urbanization, unhealthy nutrition contribute to obesity (38,39).

Link between obesity and arterial hypertension involves multiple mechanisams of origin such as sympathetic nervous system (SNS) overactivation, stimulation of the renin-angiotensin-aldosterone system (RAAS), alterations in adipose-derived cytokines such as leptin, insulin resistance and hyperinsulinaemia, elevated cortisol levels, as well as structural and functional renal changes (40).

Activation of the sympathetic nervous system (SNS) has been considered to have a crucial function in the pathogenesis of hypertension among obese individuals. Sympathetic nervous system overactivity include elevations in heart rate, cardiac output, and renal tubular sodium reabsorption, as a direct result of a α-adrenergic and β-adrenergic receptor stimulation and indirectly through activation of other systems such as the renin-angiotensin-aldosterone system RAAS. Causative mechanisms of SNS activation in obesity include abnormal adipokine secretion from adipose tissue, stimulation via the RAAS, insulin resistance, and baroreceptor dysfunction (40).

The arterial pressure control mechanism of diuresis and natriuresis according to the principle of infinite feedback gain seems to be shifted toward higher BP values in obese patients. Abnormalities in these mechanisms that would tend to raise blood pressure increase sodium and water excretion through pressure natriuresis and diuresis. As long as excretion exceeds intake, extracellular-fluid volume decreases reducing venous return and cardiac output until blood pressure returns to normal. Conversely, when blood pressure decreases, the kidney retains salt and water until arterial pressure returns to normal. Thus, pressure natriuresis acts as the key component of the feedback system that normally stabilizes blood pressure and body-fluid volumes. During the early phases of obesity, before loss of nephron function because of glomerular injury, primary sodium retention occurs as a result of increase in renal tubular reabsorption. This may be compensated by renal vasodilation, increased glomerular filtration rate and increased filtered amount of water and electrolytes. As a consequence of an incomplete compensation, however, extracellular-fluid volume is expanded, resulting in a hypertensive

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adjustment of the pressure natriuresis. This resetting of the kidney-fluid apparatus to a hypertensive level is consistent with the model of hypertension because of volume overload. Another significant cause of shift of pressure natriuresis toward higher blood pressure levels in obesity is the possibility of alterations in intrarenal forces caused by histological changes in the renal medulla that may compress the loops of Henle and vasa recta. Increased renal sodium reabsorption and volume expansion play an important role in initiating hypertension associated with obesity. Ultimately, however, the elevated glomerular hydrostatic pressure leads to progressive glomerular sclerosis and impaired renal function, and a deleterious cycle ensues in which nephrons are injured, sodium retention is exacerbated, and arterial pressures rise to maintain sodium delivery to the macula densa (41).

Obesity is associated with a state of insulin resistance and hyperinsulinaemia, which may contribute to hypertension. Insulin is known to act as a vasodilator, but in obese individuals with chronic hyperinsulinemia this response is blunted secondary to endothelial dysfunction, resulting in a state of increased vasoconstrictor tone. Chronic hyperinsulinemia has been associated with impairment of the vasodilator action of insulin. Hyperinsulinemia promotes an altered profile of vascular function. Vascular dysfunction seems to be the important factor in understanding the long-term implication of insulin in the causation of hypertension. Finally, insulin resistance has also been exhibited as an effect of heightened sympathetic drive, through b-adrenergic stimulation and/or vasoconstriction with subsequent reduction of muscular blood flow (42).

Also the leptin has been shown to stimulate sympathetic nervous system activity in the central nervous system and exerts a presssor effect on the cardiovascular system. Endothelial dysfunction has also been reported as another important aspect of leptin's effects. This has led to the notion that hyperleptinemia, largely through activation of the SNS, may contribute to obesity-related hypertension (42).

Adipose tissue is a heterogeneous endocrine organ. The deposition of fat tissue and the type (white versus brown) in obese individuals plays equally a large role in the development and progression of hypertension. Therefore, we can say that white adipose tissue represents the largest proportion of fat in the entire body and can be found around the major organs and vasculature in the abdominal cavity and subcutaneously. White adipose tissue serves to maintain energy homeostasis, storing excess in the form of triglycerides. Individuals with increased accumulation of white adipose tissue particularly in visceral depots have a higher prevalence of hypertension, dyslipidemia, and insulin resistance compared with those with less visceral fat. Ectopic fat surrounding the vasculature is also important in blood pressure regulation through excess proinflammatory response and the release of inflammatory adipokines, such as tumor necrosis factor-alpha, interleukins, resistin, visfatin, and leptin (Figure 1) (43).

Overweight and obesity are well-established risk factors that can lead to cardiovascular morbidity and mortality. There is also a multifaceted and dynamic relationship between obesity and cancer. Obesity can serve as a risk factor for cancer development (43).

In this framework, a key factor in the development of hypertension in obesity is genetic susceptibility. Genome-wide association studies have identified over 50 single-nucleotide polymorphisms associated with hypertension and over 250 genes/loci involved in obesity. Recent clinical and preclinical studies investigate gene-environment interactions in the genesis of obesity-related hypertension, including data to support maternal and offspring obesity-related cardiovascular disease. Epigenetic modifications, including DNA methylation, noncoding RNAs,
and histone modifications, are defined as mitotically and meiotically heritable modulation of gene function in these early life origins of hypertension (Figure 1) (43).

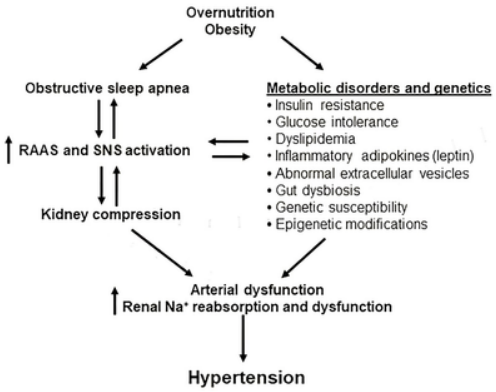


Figure 1. Mechanisms of obesity-induced hypertension

Obesity frequently coexists with obstructive sleep apnea, which results in chronic intermittent hypoxia and leads to the activation of carotid body chemoreceptors that reflexively upregulate SNS activity. Obese individuals have

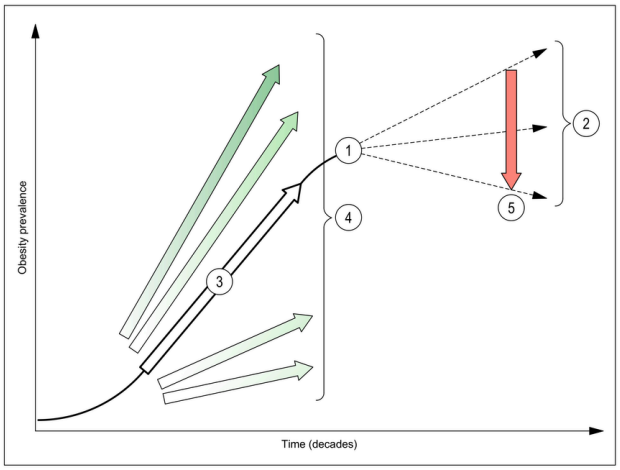
higher levels of plasma renin activity, angiotensinogen, angiotensin-converting enzyme (ACE), and aldosterone. Activation of the RAAS leads to increased formation of angiotensin II, which induces systemic vasoconstriction and simulates the production of aldosterone. Both angiotensin II and aldosterone increase renal tubular sodium reabsorption and water retention, resulting in intravascular volume expansion and hypertension. The prevalence of arterial hypertension in mild, moderate, and severe OSA is different, with the highest prevalence expected in severe forms of sleep apnea. The OSA severity index and the apnea–hypopnea index (AHI) are significant independent predictors of both systolic blood pressure and diastolic blood pressure. It has been shown that systolic blood pressure and diastolic blood pressure increase in line with increasing OSA severity, but there is a more significant increase in diastolic blood pressure. Obstructive sleep apnea is also an important risk factor in the development of resistant hypertension (44).

Obesity simultaneously leads to an increase in the prevalence of both primary and secondary arterial hypertension. The increase in the prevalence of obesity is certainly one of the dominant reasons for the increase in the prevalence of secondary hypertension. As shown above, obesity significantly contributes to the increase of the most common causes of secondary hypertension, such as chronic kidney disease, primary hyperaldosteronism, sleep apnea, etc.

In the mid-20th century, several large long-term prospective cohort studies (Framingham Heart Study, Nurses Health Study, CARDIA Study) were initiated and are still ongoing. These studies show that obesity is an independent significant risk factor contributing to the potential development of coronary heart disease, heart failure, stroke, arterial hypertension etc. (45-47).

In Figure 2. we can see the aims of obesity modeling at the population level. Descriptive studies quantify the present burden and potential future trends of obesity. Explanatory studies analyse the causes of the rise in obesity prevalence with time and the variability across populations. Evaluative models assess the likely effect of interventions to reduce future prevalence (48).

Figure 2. Diagram of the major uses of modelling of population prevalence of obesity



The black line is the trajectory of increases in obesity prevalence with time, with the present burden (1) and projected future burdens (2) being descriptive uses of modelling. Explanatory uses of modelling include explaining the rise in obesity with time (3) and the differences in prevalence rates (4). Evaluative uses include assessment of the potential for solutions to reduce the future burden of obesity (5) (48).

Some forms of secondary hypertension, if left untreated, cause more severe cardiac damage than primary hypertension and are associated with a higher cardiovascular risk. Cardiac damage includes not only myocardial hypertrophy, but also inflammation, fibrosis, apoptosis, and necrosis. Complications of secondary hypertension include hypertensive crisis, stroke, aortic dissection, myocardial infarction, arrhythmias, and congestive heart failure. Excessive secretion of catecholamines, aldosterone, angiotensin II, and cortisol leads to myocardial damage in secondary hypertension, and in addition to myocardial hypertrophy, it can cause both systolic and diastolic dysfunction, stress-induced cardiomyopathy, myocarditis, and dilated cardiomyopathy (49).

CONCLUSION

Secondary hypertension is more often resistant hypertension, which means that it is difficult to achieve target blood pressure values and takes more time. The possibility of existence of secondary hypertension should be considered in the diagnosis and treatment of all hypertensive patients. Blood pressure can be effectively reduced by identifying its etiology and treating the

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condition. Therefore, it is important to timely conduct appropriate examinations and begin treatment promptly. The use of personalized medical approaches allows for greater precision in patient treatment. In conclusion, if healthy lifestyle, increasing physical activity and dietary habits are not implemented, we can certainly expect a further rise in the prevalence of secondary hypertension in the future, in younger and middle-aged individuals, as well as partly in older patients.

On the one hand, it seems that since the appearance of the first drug for the treatment of primary arterial hypertension in the last year of the 19th century, it is much easier to achieve good blood pressure regulation, considering that several groups of antihypertensive medications have been developed in the meantime until today. This has resulted in the use of proven effective therapies to progressively improve control rates of hypertension, leading to reductions in cardiovascular, stroke, and kidney outcomes. On the other hand, today at the beginning of the 21st century, the increase in secondary hypertension and the discovery of its causes, which sometimes require a much more complex approach, are more worrying. And we can freely say that we have "A stable tree that grows like primary hypertension and a wind that shakes the canopy like secondary hypertension."

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