REVIEW

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Hypertension – The Silent Killer

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Abstract

Hypertension is often called 'the silent killer' because it shows no early symptoms and, simultaneously, is the single most significant risk factor for atherosclerosis and all clinical manifestations of atherosclerosis. It is an independent predisposing factor for heart failure, coronary artery disease, stroke, renal disease, and peripheral arterial disease. It is the most important risk factor for cardiovascular morbidity and mortality in industrialized countries.

Key words

hypertension, complications of hypertension

INTRODUCTION

The leading cause of mortality, responsible for roughly one-third of all deaths globally, is cardiovascular disease. The majority of these events are caused not by one single cardiovascular risk factor, but rather a mixture of several factors. The most important of these in industrialized countries is not only hypertension, but also high levels of blood lipids, obesity, physical inactivity, smoking, glucose intolerance/diabetes and age. High blood pressure certainly represents a modifiable risk factor [1]. In the year 2000 it is estimated that nearly one billion people (~26% of the adult population worldwide) had hypertension. The number patients with hypertension increases every year, and by 2025 is expected to rise to 29% of the population [2].

Definition and etiology. Hypertension, also known as high blood pressure, is defined as systolic blood pressure of 140 mmHg or higher and/or diastolic blood pressure of 90 mmHg or higher. The classification of blood pressure used in the 2007 ESH/ESC Guidelines comprises categories of optimal (systolic blood pressure less than 120 mmHg and diastolic blood pressure less than 80 mmHg), normal (systolic blood pressure 120-129 mmHg and/or diastolic blood pressure 80-84 mmHg), and high-normal (systolic blood pressure 130-139 mmHg and/or diastolic blood pressure 85-89 mmHg) blood pressure, followed by 3 grades of hypertension, and a separate category for isolated systolic hypertension. The 3 grades of hypertension correspond to:

1) mild (systolic blood pressure 140-159 mmHg and/or diastolic blood pressure 90-99 mmHg);
2) moderate (systolic blood pressure 160-179 mmHg and/or diastolic blood pressure 100-109 mmHg);
3) severe hypertension (systolic blood pressure 180 or greater and/or diastolic blood pressure 110 mmHg or greater).

Isolated systolic hypertension (systolic blood pressure 140 mmHg or higher), is graded as 1, 2, or 3, according to the systolic blood pressure level, provided that the diastolic blood pressure is less than 90 mmHg. When systolic and diastolic blood pressure fall into different categories, the highest category is used in assessing total cardiovascular risk [1, 3].

There are 2 types of hypertension depending on etiology – 'primary' (also called 'essential') hypertension and 'secondary' hypertension. Essential hypertension is the most prevalent type, affecting 90-95% of hypertensive patients [4]. The pathogenesis of primary hypertension is multifactorial and complicated. Genetic factors play an important role. Environmental factors, such as sedentary lifestyle, stress, smoking, obesity [5], salt (sodium) sensitivity [6] and alcohol intake, also are significant. The aforementioned factors, for example increased salt intake and obesity, have long been known culprits. These factors alone are probably not sufficient to raise blood pressure to abnormal levels, but are synergistic with a genetic predisposition. Other factors that may be involved in the pathogenesis of primary hypertension are hyperactivity of the renin-angiotensin-aldosteron system and sympathetic nervous system, abnormal production of natriuretic peptides, and deficiency in endothelial vasodilatation substances [1, 3].

Approximately 5-10% of patients with hypertension have identifiable secondary hypertension. It is important to recognize this type hypertension since it is treated differently to essential hypertension, by treating the underlying cause of the elevated blood pressure. The history, examination, and routine laboratory tests may identify such patients, in particular, patients who suddenly develop severe hypertension at an early age and which is treatment resistant. The causes include renal disease (renal artery stenosis), obstructive sleep apnea, primary aldosteronism, Cushing's syndrome, pheochromocytoma, coarctation of the aorta (uncommon), hypertension associated with pregnancy, estrogen use, as well as other causes (eg. medications) [1, 3].

Complications of hypertension. Hypertension is often called 'the silent killer' because it is a disease that shows no early symptoms, and simultaneously, is the single most significant risk factor for heart disease: myocardial infarction, left ventricular hypertrophy, congestive heart failure, aneurysm, stroke, as well as chronic kidney disease (hypertensive nephropathy) and hypertensive retinopathy [1, 3]. The complications of hypertension are related either to sustained elevations of blood pressure, with consequent changes in the

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vasculature and heart, or to the accompanying atherosclerosis that is accelerated by long-standing hypertension.

Mild to moderate primary hypertension is largely asymptomatic for many years. The most frequent symptoms, headache, fatigue, dizziness and facial flushing, are also very non-specific. Suboccipital pulsating headaches, occurring early in the morning and subsiding during the day, are said to be characteristic, but any type of headache may occur [1, 7]. Accelerated hypertension is associated with somnolence, confusion, visual disturbances, nausea and vomiting (hypertensive encephalopathy) [1].

Hypertension is a well-known risk factor that predisposes to the development of left ventricular hypertrophy, coronary flow abnormalities, and systolic and diastolic dysfunction. This complex of abnormalities is known as hypertensive heart disease and eventually leads to heart failure [8]. Already in the Framingham Study in which 5,127 people were followed up for 14-18 years, 492 cases of coronary heart disease were identified, and 142 cases of congestive heart failure [9].

Left ventricular hypertrophy in hypertension is associated with an increase in the size of cardiac myocytes, an increase in size as well as number of non-myocyte cells (e.g., fibroblasts), accumulation of collagens, and infiltration by monocytes and lymphocytes. Therefore, whereas myocytes can hypertrophy only because they are terminally differentiated, the interstitial cells undergo both hypertrophy and hyperplasia. The excess collagen produced and deposited by the fibroblasts leads to interstitial and perivascular fibrosis. This entire process has been referred to as cardiac remodeling and significantly alters the physical properties of the myocardium [10]. The intramyocardial vascular bed is also affected by the hypertrophic response of the heart – the hypertensive heart is characterized not only by increases in myocyte and interstitial mass, but also by abnormalities of the intramyocardial arterioles [8].

Clinically, hypertensive heart disease manifests itself through the sequelae of cardiac hypertrophy and/or the symptoms and signs of coronary insufficiency. Both of these conditions may lead to ischemic events, arrhythmias, and congestive heart failure. Hypertensive patients have anginal complaints or other signs of myocardial ischemia in the face of angiographically normal coronary arteries. In these cases, the imbalance between oxygen supply and demand is believed to be related to increased coronary resistance at the microvascular level. An abnormally high resistance of the coronary microvascular bed can be found even in the absence of left ventricular hypertrophy, but is more apparent when left ventricular hypertrophy is present. Hypertension may alter coronary flow patterns even before the development of left ventricular hypertrophy. The coronary flow reserve is greatly reduced in the presence of left ventricular hypertrophy. In such cases, there is increased wall stress and, when this occurs, ventricular dilation may physically compress the coronary vascular bed. In addition, altered diffusion of oxygen because of the hypertrophy may seriously threaten oxygen delivery to myocytes [1, 11].

Patients with hypertensive heart disease run a greater risk of ventricular arrhythmias and sudden death. The ventricular arrhythmias are more common in hypertensives with left ventricular hypertrophy than in those without [12].

The systolic dysfunction at rest develops relatively late as a complication of the hypertensive process, hypertension may exacerbate systolic dysfunction due to another cause, such as atherosclerotic coronary artery disease or valvular heart disease. In addition, patients with isolated systolic hypertension may encounter this complication a little earlier. In contrast, diastolic function in hypertension is impaired even at an early stage. The factors that affect diastolic function in hypertensive patients are multiple. One of these factors is aging, which is associated with a decline in left ventricular relaxation and increased diastolic stiffness [13, 14]. Diastolic dysfunction is also significantly related to myocardial ischemia and enhanced loading conditions on the heart. In addition, neurohumoral factors and alterations at the cellular level may be involved [15, 16]. It is generally accepted that diastolic dysfunction can lead to congestive heart failure even when systolic function is normal. Under such circumstances the heart is not dilated, but filling conditions of the left ventricular are impaired because of its inability to relax appropriately. As a consequence, stroke volume decreases, left ventricular filling pressure increases, and pulmonary congestion ensues [13, 14]. First apparent during exercise, the signs of left ventricular failure become increasingly evident at rest. Although it is not entirely clear which structural abnormalities dictate the transition from adaptive hypertrophy to congestive heart failure, molecular changes in contractile proteins as well as disturbances in collagen cross-linking are among the mechanisms potentially involved. Ventricular dilatation is accompanied by wall thinning, augmented systolic wall stress, and a reduction in the ejection fraction, the latter being aggravated by the increased afterload. Therefore, as the heart increases in size, pump function and contractility progressively deteriorate. Clinically, this situation manifests itself by dilated cardiomyopathy, hypokinesis, and congestive heart failure [14, 17]. Congestive heart failure was and still is a gloomy complication of the hypertensive process. Although its contribution to cardiovascular mortality in hypertensive patients has greatly diminished since the advent of effective antihypertensive drugs, it has not disappeared altogether. Aggressive control of hypertension can regress or reverse left ventricular hypertrophy and reduce the risk of cardiovascular disease. Diuretics have produced equal or greater reductions of left ventricular mass when compared with other classes of drugs. β-Blockers are less effective in reducing left ventricular hypertrophy and play a specific role in patients with established coronary artery disease or impaired left ventricular function [18].

Hypertension not only affects the microcirculation but also accelerates atherosclerosis in the larger (epicardial) vessels. There is an important risk factor for atherosclerosis by directly producing injury via mechanical stress on endothelial cells. High blood pressure might allow more lipoproteins to be transported through intact endothelial lining cells by altering permeability. Hypertension also markedly increases lysosomal enzyme activity, presumably owing to stimulation of the cellular disposal system by the internalization of increased amounts of plasma substances. This might lead to increased cell degeneration and release of the highly destructive enzymes into the arterial wall [19].

Uncontrolled hypertension, as well as arteriosclerosis, may result in a bulge in the aorta (aortic aneurysm) or in any large artery. Aneurysms may also occur in the chest (thoracic aneurysm) – ascending, arch, descending aorta, and in the abdomen (abdominal aneurysm). The complications of aneurysm are dissection and rupture of the aorta [1].

The neurologic effects of long-standing hypertension may be divided into retinal and central nervous system changes. Because the retina is the only tissue in with the arteries and arterioles can be examined directly, it is possible to observe the progress of the vascular effects of hypertension. The retinal circulation undergoes a series of pathophysiological changes in response to elevated blood pressure. In the initial, vasoconstrictive stage, there is vasospasm and an increase in retinal arteriolar tone owing to local autoregulatory mechanisms. This stage is seen clinically as a generalized narrowing of the retinal arterioles. Persistently elevated blood pressure leads to intimal thickening, hyperplasia of the media wall, and hyaline degeneration in the subsequent, sclerotic stage. This stage corresponds to more severe generalized and focal areas of arteriolar narrowing, changes in the arteriolar and venular junctions, and alterations in the arteriolar light reflex. This is followed by an exudative stage, in which there is disruption of the blood–retina barrier, necrosis of the smooth muscles and endothelial cells, exudation of blood and lipids, and retinal ischemia. These changes are manifested in the retina as microaneurysms, haemorrhages, hard exudates, and cotton-wool spots. These retinal lesions often produce scotoma, blurred vision, and even blindness, especially in the presence of papilledema or haemorrhages of the macular area [20, 21, 22].

Central nervous system dysfunction also occurs frequently in people with hypertension. High blood pressure – as well as age, diabetes mellitus, coronary artery disease, left ventricular hypertrophy, atrial fibrillation, obesity, total cholesterol, physical inactivity, smoking, and alcohol consumption – is an important risk factor for 2 quite different disorders: haemorrhagic and ischemic stroke. Cerebral infarction is secondary to the increased atherosclerosis observed in hypertension, while cerebral haemorrhage is the result of both the elevated arterial pressure and the development of cerebral vascular microaneurysms [23]. Approximately 85% of strokes are due to infarction. The incidence of stroke rises progressively with increasing blood pressure levels, particularly systolic blood pressure in people >65 years. A linear relationship between stroke incidence and blood pressure has been demonstrated in several epidemiological and clinical studies [24, 25]. The treatment of hypertension convincingly decreases the incidence of both ischemic and haemorrhagic strokes.

Hypertension has often been observed to be a risk factor for vascular dementia because there may be an acceleration of cerebral white matter lesions. Hypertension-related cognitive impairment and dementia may be a consequence of a single infarct due to occlusion of a 'strategic' larger vessel. or multiple lacunar infarcts due to occlusive small vessel disease resulting in subcortical white matter ischemia [26, 27].

Hypertensive encephalopathy – an acute syndrome with severe hypertension - is associated with headache, nausea, vomiting, convulsions, confusion, stupor and coma. Focal or lateralizing neurologic signs, either transitory or lasting, may occur but are infrequent and always suggest some other form of vascular disease (haemorrhage, embolism or atherosclerotic thrombosis). By the time neurologic manifestations appear, the hypertension has usually reached the malignant state, with retinal haemorrhages, exudates, papilledaema, and evidence of renal and cardiac disease. Usually, neuropathologic examination may reveal a cerebral swelling and/or haemorrhages of various sizes from massive to petechial. A cerebellar pressure cone reflects an increased volume of brain tissue and increased pressure in the posterior fossa; in some instances, a lumbar puncture may precipitate a fatality. Microscopically, in addition to small haemorrhages, there are clusters of microglial cells, minute cerebral infarcts, and necrosis of arterioles [28, 29].

Chronic hypertension can lead to nephrosclerosis, a common cause of renal insufficiency [30]. In the early stages of hypertension, the kidneys appear normal, whereas in advanced cases, loss of renal parenchyma results in small, diffusely contracted kidneys with a finely granular surface. This gradual reduction in renal size is primarily caused by diffuse cortical atrophy and fibrosis, which reflect the progressive vascular damage that occurs in people with uncontrolled or poorly controlled hypertension. The major pathologic findings are hyalinization and sclerosis of the walls of the afferent arterioles. The initial event appears to be an irregular subendothelial deposition of hyaline material along the course of the vessel wall. As the disease progresses, the hyaline deposition increases, gradually extends into the media, and ultimately replaces the entire wall of the arteriole. The arteriolar wall thickens, its cellularity is reduced, and the size of the vascular lumen is variably decreased. Changes in the afferent arterioles are almost always associated with changes in the interlobular arteries within the kidney [30-32].

The ischemia caused by these vascular lesions results in secondary changes in the renal parenchyma, which include glomerulosclerosis, tubular atrophy, and interstitial fibrosis with round-cell infiltration. Because the vascular lesions are usually distributed in a focal, irregular fashion throughout the renal cortex, the secondary ischemic changes assume a similar pattern of distribution. When the vascular lesions are very severe and generalized, the entire kidney undergoes ischemic atrophy [31-33].

In most patients with non-malignant, untreated hypertension, clinical evidence of renal involvement never develops. Early markers of renal injury are microalbuminuria or macroalbuminuria, with or without azotemia [1, 2].

CONCLUSIONS

Elevated arterial pressure is the most important public health problem in developed countries – being common, asymptomatic, readily detectable, usually easily treatable, and often leading to lethal complications if left untreated. Effective hypertension treatment can reduce the risk of stroke, heart attack and congestive heart failure, hypertensive retinopathy and nephropathy. The goal of hypertension treatment is to reduce blood pressure levels. Treatment of hypertension and proper lifestyle changes reduce the risk of serious hypertension complications.

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