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Cardiovascular Changes during Chronic Hypertensive States

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Abstract

Hypertension is currently the single most important contributor to death around the world in both developed and developing regions. Elevated blood pressure is a major risk factor for coronary heart disease, atrial fibrillation, heart failure, cerebrovascular disease and peripheral artery disease.

Hypertensive heart disease consists of both vascular and myocardial changes. Various mechanisms are responsible for hypertensive heart disease, including endothelial dysfunction and coronary arteriolar constriction causing ischemia of the myocardium, increased fibrosis, apoptosis and inflammatory changes. Studies also shown that major risk factors such as dyslipidemia and also diabetes stratifies the patient into high risk group. Hypertension induces a compensatory thickening of the ventricular wall in an attempt to normalize wall stress, which results in concentric LVH, which in turn decreases LV compliance and LV diastolic filling, causing heart failure. Enlargement of the left atrium results in stretching of the atrial fibers, causing arrythmias and increased blood flow causes damage and narrowing of arteries resulting in coronary artery disease.

Key Words: *Hypertension, heart failure, endothelial dysfunction, left ventricular hypertrophy.*

INTRODUCTION

Hypertension remains a major public health problem associated with considerable morbidity and mortality. Hypertensive heart disease is a constellation of abnormalities that includes left ventricular hypertrophy (LVH), systolic and diastolic dysfunction, and their clinical manifestations including arrhythmias and symptomatic heart failure. The classic paradigm of hypertensive heart disease is that the left ventricular (LV) wall thickening in response to elevated blood pressure as a compensatory mechanism to minimize wall stress. Subsequently, after a series of poorly characterized events ("transition to failure"), the left ventricle dilates, and the LV ejection fraction (EF) declines. (1) The prevalence of HTN increases in adult populations, because of aging, lifestyle changes and also due to the obesity epidemic. Elevated BP, cholesterol levels and obesity in children or teenagers persist

into adulthood and increase the risk for CV events later in life. [2] HTN in adults is defined as a Systolic blood pressure of >140 mmHg and/or Diastolic blood pressure of >90 mm Hg.[3] In adult populations the stratification of CV risk is based on BP level, risk factors, subclinical organ damage (SOD) and established CV disease (CVD) and kidney disease.

The main risk factors include systolic and diastolic blood pressure (DBP)levels, aging (man >55 years, women >65 years), smoking, dyslipidemia, fasting plasma glucose of 5.6–6.9 mmol/l, abnormal glucose tolerance test, abdominal obesity and family history of premature CVD (man at age <55 years, women at age <65 years). Young and middle aged adults do not have any risk for CV events even in the presence of risk factors (smoking, dyslipidemia) for HTN while old aged people are more prone to CV attacks in the presence of HTN grade 1 and 2.[4]

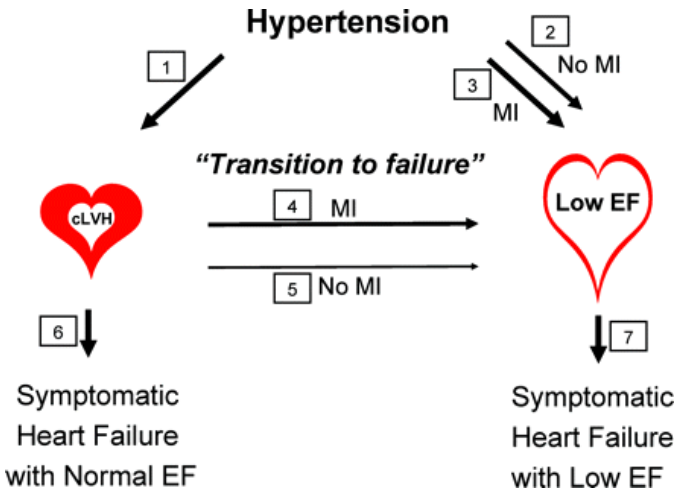

FIGURE 1

PATHOPHYSIOLOGY OF HYPERTENSIVE HEART DISEASE

Hypertensive heart disease consists of both vascular and myocardial changes. Various mechanisms are responsible for hypertensive heart disease, including endothelial dysfunction and coronary arteriolar constriction causing ischemia of the myocardium, increased fibrosis, apoptosis and inflammatory changes.[5][6]A major role in structural remodeling of the heart is played by cardiomyocyte and vascular smooth muscle cell hypertrophy, the conversion of fibroblasts to myofibroblasts, expansion of interstitial and perivascular collagen and decreased intramyocardial capillary density. Fibrosis of the myocardium is an important risk factor for arrhythmias. HTN induces a compensatory thickening of the ventricular wall in an attempt to normalize wall stress, which results in concentric LVH, which in turn decreases LV compliance and LV diastolic filling, causing heart failure. Diastolic dysfunction develops in hypertensive patients even in the absence of LVH. Impaired isovolumic relaxation leads to decreased velocity of early diastolic filling. [7]

LEFT VENTRICULAR HYPERTROPHY

Left Ventricular Hypertrophy is an important phenotype in the progression of hypertensive and the progression from hypertension to concentric LVH is an important step on the pathway toward heart failure.[9] Pathological changes present in patients with hypertensive LVH include an increase in the size of the cardiomyocyte, alterations in the extracellular matrix, with accumulation of fibrosis, and abnormalities of the intramyocardial coronary vasculature, including medial hypertrophy and perivascular fibrosis.[10] The mechanisms responsible for progression to hypertrophy include not only a response to the mechanical stress from elevated blood pressure but also the influences of neurohormones, growth factors, cytokines.[11] Recent trials demonstrated that tighter control of systolic blood pressure (target of <130 mm Hg versus <140 mm Hg) was associated with a reduction in the development of LVH on ECG, emphasizing the importance of the pressure load itself.[12]

LVH is important subclinical organ damage in hypertensive subjects and an independent CV risk factor both in children and adult populations. In several studies the relationship between left ventricular mass and subsequent CV risk was found to persist after adjustment for traditional risk factors. In the recent study, LVH doubled the

risk of CV events. The following events developed during follow-up in a group of uncomplicated subjects with essential HTN: sudden cardiac death, MI, stroke, transient ischemic attack, heart failure, new onset unstable angina, arterial occlusive disease and progressive renal failure. Left ventricle geometry can be classified into four categories: normal geometry, concentric remodelling [normal LVM, increased relative wall thickness (RWT)], concentric hypertrophy (elevated LVM and RWT) and eccentric hypertrophy. [13]

Adult patients with concentric remodelling and hypertrophy have the highest peripheral resistance, and those with eccentric hypertrophy have a supernormal cardiac index, thereby demonstrating the role of pressure and volume overload as mechanisms involved in developing LVH. Moreover, in the group with concentric remodelling, the highest peripheral resistance was accompanied by reduced LV end-diastolic dimension, which suggests that pressure overload is balanced by a decreased volume load. In adults, concentric hypertrophy was found to be associated with the highest risk of CVD. [19][20] In concentric hypertrophy, the degree of impaired LV filling (left atrial after load) increases in LV stiffness, which results in an increase in the size and function of the left atrium.

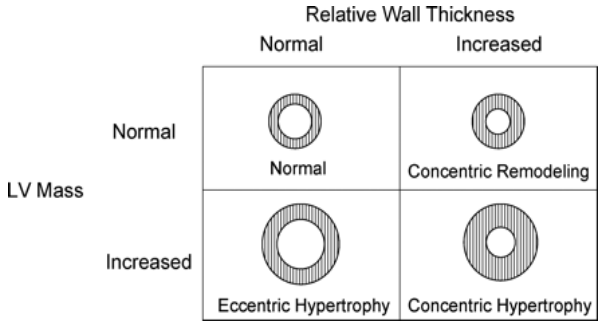

FIGURE 2

HEART FAILURE

In adults, HTN is a very important risk factor for coronary artery disease, arrhythmias (atrial and ventricular), MI and systolic heart failure. The impact of HTN on developing systolic heart failure is well established, and research focus is currently directed towards diastolic heart failure. The mechanisms underlying diastolic heart failure include abnormal matrix dynamics, altered myocyte cytoskeleton, impaired active relaxation and marked increase in fibrosis. The stiffness of the left ventricle influences the volume– pressure relationship during diastole, with small changes in LV volume resulting in greater rise in pressure. [14] Increased ventricular stiffness results from changes in extracellular matrix and cytoskeleton isoforms. An increase in activation of matrix metalloproteinase and tissue inhibitors of metalloproteinase can shift the type of collagen from type I to type III which has increased stiffness and cross-linking. Titin, a thick filament protein, is responsible for anchoring the thick filament to the Z disc in a sarcomere. Shifts to a stiffer isoform of titin (N2B) alter the properties of the myofilament cytoskeleton and contribute to ventricular stiffness.

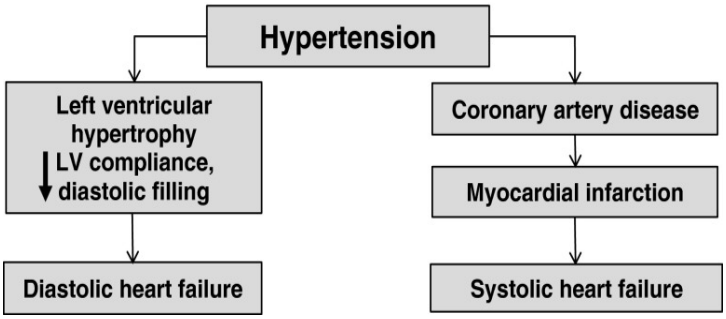

FIGURE 3

STROKE

In adults, the brain is an early target for organ damage by elevated BP. HTN causes vascular brain injury directly [small-vessel disease (SVD)] or by promoting atherosclerosis or cardiac damage. HTN results in increased brain vascular resistance and the loss of the physiological mechanism of autoregulation. Hypertensive SVD is thought to be the main cause of silent brain infarcts, which, by definition, lack clinically overt stroke-like symptoms; rather, they are associated with subtle deficits in physical and cognitive function. Moreover, the presence of silent infarcts doubles the risk of subsequent stroke and dementia. The etiology of stroke in children is

mostly multifactorial and varied: congenital and acquired heart disease, arteriovenous malformations and sickle cell disease, thrombophilias and infectious diseases such as varicella, sepsis, meningitis and even minor infection. [15] Arteriovenous malformations, cavernous malformations and aneurysms are the most common causes of pediatric hemorrhagic stroke. HTN is also counted among hemorrhagic stroke risk factors, since it rarely occurs in children it is considered to be a less important risk factor. The most sensitive method to diagnose acute ischemic stroke is brain magnetic resonance imaging, which requires sedation in younger children. [16] Nephrologic pediatric patients with vasculitis are at a high risk of stroke. HTN, connective tissues diseases, migraine, increases the risk of vertebral artery dissection and cervical artery dissection, both of which are a common cause of strokes in young adults after injuries.

ENDOTHELIAL DYSFUNCTION

Endothelial cells play an important role in vessel homeostasis and through their production of nitric oxide, prostacyclin and thrombomoudlin they regulate vasodilatation and fibrinolysis and inhibit coagulation processes. [17] Endothelial dysfunction is an early stage of atherosclerosis. Stimuli leading to vaso relaxation in the presence of intact vascular endothelium (such as acetylcholine) produce vasoconstriction when acting directly on the underlying smooth muscle cells in vascular areas with an injured endothelium. [18]

CONCLUSION

Hypertension is currently one of the major cause of death around the world. Elevated BP represents an important risk factor for CV diseases, such as coronary heart disease, heart failure, stroke, peripheral artery disease and renal failure, in adults. Based on observational and interventional studies, specific recommendations have been developed for the treatment of HTN and other risk factors (e.g. hypercholesterolemia) with the aim of reducing global CV risk. Long-term follow-up multicenter studies are necessary to assess CV risk stratification in children and adolescents with HTN and to work out standards for diagnostic and treatment procedures.

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