Hypertension, Left Ventricular Hypertrophy, and Myocardial Ischemia

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KEYWORDS

• Hypertension • Ischemia • Perfusion • Mechanisms • Management

KEY POINTS

- Myocardial ischemia contributes in a major way to the morbidity and mortality associated with hypertension and hypertensive heart disease (HHD).
- There are a variety of mechanisms that contribute to the production of myocardial ischemia in hypertension. Although coronary artery disease (CAD) may be an important associated factor in the production of ischemia, it is not a prerequisite and many patients with hypertension have ischemia with normal coronary arteries.
- Management of such patients should include a search for myocardial ischemia and, if present, a tailored approach to treatment that encompasses both risk factors management and selection of medications that can effectively control arterial pressure and prevent or lessen myocardial ischemia.

INTRODUCTION AND OVERVIEW

The devastating effects of hypertension on the heart prior to the introduction of antihypertensive therapy are inclined to be forgotten. Patients graphically describe a feeling of drowning as pulmonary edema takes hold. One of the authors (FD) remembers being a young physician treating such patients. One of the most dramatic benefits of antihypertensive therapy has been the reduction in morbidity and mortality from HHD. This considerable benefit is comparable with the reduction in stroke and in renal failure using similarly well-selected antihypertensive therapy.

Hypertension, dyslipidemia, glucose intolerance, cigarette smoking, and left ventricular hypertrophy (LVH) are the main, independent modifiable risk factors for cardiovascular disease.[1] In addition, hypertension is a pathophysiologic template for

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myocardial ischemia and there is secure epidemiologic evidence demonstrating its importance as a risk factor for angina, myocardial fibrosis, myocardial infarction, and sudden death.[1,2] Furthermore, this relationship strengthens progressively as the arterial pressure rises and when LVH coexists as identified by Electrocardiography (ECG) or echocardiography.[2] An excess of 40% of the attributable risk for these manifestations of ischemia is due to hypertension.

It is worth dwelling in particular on sudden death. Men with hypertension and LVH have a 6-fold to 8-fold, and women 3-fold, increased risk of sudden cardiac death presumably due to ventricular arrhythmias. Despite major ongoing research, this problem remains a most elusive condition to predict and, therefore, to prevent. Myocardial ischemia is a potent stimulus for ventricular tachydysrhythmias and hypertension provides a perfect medium for these catastrophic events, which are increased further in the presence of LVH.

The development of CAD in patients with hypertension is a complex interaction of direct hemodynamic effects, genetic predisposition, endothelial dysfunction, oxidative stress, and humoral factors. Although associated obstructive CAD is a key factor in this kaleidoscope, other factors are involved as a consequence of hypertension and LVH. Understanding the background pathophysiology to myocardial ischemia allows therapy to be targeted more effectively with subsequent reduction in these clinical sequelae (**Fig. 1**).

PATHOPHYSIOLOGY OF MYOCARDIAL ISCHEMIA IN HYPERTENSIVE HEART DISEASE

HHD is the heart's response to sustained arterial hypertension. It is initially a functionally adaptive process in response to increased left ventricular (LV) afterload. The hallmarks of this process are the development of LVH, myocardial ischemia, diastolic dysfunction, myocardial fibrosis, apoptosis, cardiomyocyte growth, endothelial dysfunction, and increased arterial stiffness.[3] These factors combine to produce a maladaptive feedback loop (**Fig. 2**). The most easily identifiable phenotypic expression of HHD is LV remodeling, which ultimately leads to LVH.

Types of Left Ventricular Remodeling

Cardiac remodeling is defined as "alterations in size, geometry, shape, composition and function of the heart resulting from cardiac load or injury."[4] There are 3 recognized types of remodeling[5]: concentric, eccentric, and post–myocardial infarction, which has particular relevance to this article. A mixed picture occurs as the infarcted myocardium becomes stretched, leading to an increase in LV cavity size, with subsequent increased pressure on the noninfarcted myocardium to maintain stroke volume.

In hypertension, the development of LVH occurs as the heart remodels in the presence of increased LV load. This sustained rise in blood pressure (BP) produces increased LV wall stress. This is compensated for physiologically with the changes in wall thickness and radius.

As BP increases there is increased LV wall stress, compensated for by thickening of the LV wall (concentric remodeling).[6] Thus, the increased LV wall stress is a major determinant of myocardial oxygen demand and myocardial ischemia is a hallmark of this process.

FACTORS PREDISPOSING TO LEFT VENTRICULAR HYPERTROPHY

Nonhemodynamic Factors

Hypertension provides a sustained hemodynamic load on the LV, which remodels in an attempt to normalize wall stress and regulate myocardial oxygen consumption.