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REVIEW

Diastolic dysfunction in hypertension

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Abstract Hypertension and coronary heart disease, often coexisting, are the most common risk factors for heart failure. The progression of hypertensive heart disease involves myocardial fibrosis and alterations in the left ventricular geometry that precede the functional change, initially asymptomatic. The left ventricular diastolic dysfunction is part of this continuum being defined by the presence of left ventricular diastolic dysfunction without signs or symptoms of heart failure or poor left ventricular systolic function. It is highly prevalent in hypertensive patients and is associated with increased cardiovascular morbidity and mortality. Despite its growing importance in clinical practice it remains poorly understood. This review aims to present the epidemiological fundamentals and the latest developments in the pathophysiology, diagnosis and treatment of left ventricular diastolic dysfunction.

PALABRAS CLAVE
Disfunción diastólica;
Hipertensión;
Enfermedad cardíaca hipertensiva;
Geometría ventricular izquierda;
Insuficiencia cardíaca con fracción de eyección preservada

Disfunción diastólica en la hipertensión

Resumen La hipertensión y la enfermedad coronaria, a menudo coexistentes, son los factores de riesgo más comunes para la insuficiencia cardíaca. La progresión de la enfermedad cardíaca hipertensiva implica fibrosis miocárdica y alteraciones en la geometría ventricular izquierda que preceden al cambio funcional, inicialmente asintomático. La disfunción diastólica ventricular izquierda es parte de este proceso y se define como la presencia de disfunción diastólica del ventrículo izquierdo sin signos ni síntomas de insuficiencia cardíaca o mala función sistólica ventricular izquierda. Es altamente prevalente en pacientes hipertensos y se asocia con un aumento de la morbimortalidad cardiovascular. A pesar de su creciente importancia en la práctica clínica, el conocimiento de la disfunción diastólica del ventrículo izquierdo sigue siendo

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escaso. Esta revisión tiene como objetivo presentar los fundamentos epidemiológicos y los últimos avances en la fisiopatología, el diagnóstico y el tratamiento de la disfunción diastólica del ventrículo izquierdo.

Introduction

In hypertension (HTN), the evolution of hypertensive heart disease for heart failure (HF) involves structural changes (myocardial fibrosis), and changes in left ventricular (LV) geometry (remodeling and left ventricular hypertrophy [LVH]) which cause deviations in diastolic function: changes in relaxation and LV filling.[1] The diagnosis of diastolic dysfunction (DD) in its early stage, asymptomatic, may allow early intervention, delaying or sustaining the emergence of symptomatic HF. HF proceeds from structural or functional changes, initially asymptomatic, that deteriorate the filling and/or the LV ejection fraction (LVEF). HF with preserved ejection fraction (HFpEF), typically $\geq$50%, affects mainly the elderly and hypertensive patients, is present in 40–50% of patients with HF and have ''evidence'' of what is commonly referred as DD; its prognosis is as bleak as the most widely spoken HF with reduced ejection fraction (HFrEF with LVEF < 40%).[2–4] Patients with a LVEF between 40% and 49% is now defined as HF with mid-range EF, a ''gray area'' of patients with features of primary mild systolic dysfunction, but also with DD (in fact, many of the patients with HFrEF also have DD).[5]

The importance of DD is often undervalued, due to the difficulty of diagnosing it and lack of effective therapeutic alternatives. It is, however, an increasingly significant problem in patients with HTN and we propose to review the epidemiological fundamentals and latest developments in pathophysiology, diagnosis and treatment of LV DD.

Epidemiology

A broad definition, published by American Society of Hypertension in 2005, stated that HTN is ''a progressive cardiovascular (CV) syndrome arising from complex and interrelated aetiologies. Early markers of the syndrome are often present before blood pressure (BP) elevation is observed; therefore, HTN cannot be classified solely by discrete BP thresholds. Progression is strongly associated with functional and structural cardiac and vascular abnormalities that damage the heart, kidneys, brain, vasculature, and other organs, and lead to premature morbidity and death''. It is estimated to affect about 1 billion people and it causes more than 7 million annual deaths worldwide (13% of total mortality). In Portugal, the overall prevalence of HTN in adult population of 18–90 years is 42.2% (44.4% in men, 40.2% in women). The prevalence increases with age, along with the increased risk of CV disease, being the most common risk factor for HF in general population.[2,6,7]

HF affects about 1–2% of adult population in developed countries and at least 10% of the population $\geq$70 years.[8] The risk of having HF is 20% for both gender and lifetime risk is even larger for those who have HTN.[9] HF is the leading cause of hospitalization in the elderly.[2,10] Portugal, in 2004, HF prevalence was 4.4% (roughly 80% had history of HTN, 39% coronary artery disease, and 15% atrial fibrillation [AF]).[11] Although traditionally defined as ''pump failure'', it is known that about half of the patients with HF maintain a preserved LVEF,[12] with an annual mortality of 10–30%. About 60% of patients with HFpEF die from CV causes, mostly sudden death or HF.[13] In asymptomatic individuals, the prevalence of DD varies between 11.1 and 34.7%, depending on diagnostic methods, criteria used and population characteristics.[14–17] Furthermore, the presence of LV DD is an independent risk factor for increased CV morbidity and mortality.[17,18]

DD is present in half of hypertensive patients.[12,19] A recent study suggests that hypertensive elderly women (>60 years) are more likely to develop DD.[20] The ASCOT-BPLA study highlighted increased susceptibility of hypertensive African-Caribbean compared to Caucasians Europeans.[21]

Arterial hypertension, left ventricular hypertrophy and diastolic dysfunction

HTN is the most common comorbidity present in HFpEF patients (~60–80% of the patients).[22] LVH is an important phenotype in the progression of hypertensive heart disease and its consequences. The myocardial remodeling process begins before the onset of symptoms. In early, mild HTN, LVH is not present but there is already evidence of impaired relaxation of LV, that may be present in half of individuals.[12,19,23]

LVH has been considered a natural response to stabilize LV function in the presence of high BP. The increase in BP causes a raise in the afterload and in mechanical stress on the ventricular wall. In order to normalize the parietal stress, there is a compensatory thickening of the ventricular wall with an increase in LV mass, but no increase in ventricular cavity size (concentric LVH). LVH causes reduction of AV pressure gradient and impairs LV filling[24,25] and structure, with alterations in the extracellular space, cardiomyocytes and an increase of chamber stiffness. There is a proliferation of fibroblasts with increased deposition, distribution and geometry changes of collagen, which accumulates in the interstitial and perivascular region. The extracellular matrix undergoes an intense turnover caused by the presence of various factors (e.g. B-type natriuretic peptide [BNP] and tissue inhibitors), which act on the metalloproteinases and other proteolytic enzymes modulating collagen degradation.[26,27] This process is enhanced by hyperactivation of renin–angiotensin–aldosterone system (RAAS) which matches with existing overload pressure, support and the progression of HTN, as well as of LVH.[6,28]

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