

Arrhythmogenesis mechanisms in hypertension

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Received: January 8, 2019, Accepted: February 26, 2019

Abstract

Hypertension is frequently associated with cardiac arrhythmias. Epidemiological and experimental studies have shown the link between hypertension and both atrial and ventricular arrhythmias but the importance of hypertension in the occurrence and management of these diseases is not well acknowledged in the medical practice. In particular left ventricular hypertrophy increases the incidence of atrial fibrillation, ventricular arrhythmias and sudden cardiac death. Prospective clinical trials have shown that antihypertensive therapy delays or prevents the occurrence of these arrhythmias, the highest benefit being obtained with angiotensin converting enzyme inhibitors and angiotensin receptor blockers.

Keywords: Hypertension, Arrhythmias, Atrial fibrillation, Sudden cardiac death, Ventricular arrhythmias

Introduction

Cardiac arrhythmias are commonly seen in hypertensive patients but the contribution of hypertension to the development of these arrhythmias is frequently unrecognized and as a consequence undertreated. The aim of this paper is to describe the pathophysiology, epidemiology and the clinical and therapeutical implications of hypertension in patients with atrial and ventricular arrhythmias. To do this we searched the PubMed using combinations of the terms “hypertension”, “atrial fibrillation”, “ventricular arrhythmias” and “sudden cardiac death”

Pathophysiology

Left ventricular hypertrophy

Left ventricular hypertrophy, a common finding in hypertensive patients, was positively correlated with a higher rate of both atrial and ventricular arrhythmias as well as with sudden cardiac death[1-7]. The proarrhythmic effect is caused by prolongation of the action potential duration, increased dispersion of refractoriness, interstitial fibrosis and collagen deposition, creating the conditions for myocardial reentry[8]. In mild LVH changes in K currents lead to action potential prolongation, predisposing to early afterdepolarisations. The changes occur differently at the endocardial and epicardial level, with a longer action potential duration subepicardially. This increased dispersion of refractoriness creates conditions for reentry. Another change in mild LVH is the decreased Ca

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ATPase at the sarcoplasmic level. The diminished capacity to handle intracellular Ca levels favors the occurrence of late afterdepolarisations. In severe LVH appear also conduction disturbances due to a decreased number of connexins at the gap junctions and to the interstitial fibrosis and collagen deposition[8].

Myocardial ischaemia

Myocardial ischaemia is the most pro-arrhythmic factor associated with LVH. Ischaemia may be caused by atherosclerosis of the epicardial arteries or by the decreased coronary flow reserve and perivascular fibrosis found in hypertrophic myocardium. The pro-arrhythmic mechanisms include increased dispersion of refractoriness between the ischaemic or non ischaemic areas and also inside the ischaemic area in the presence of LVH[8]. Triggered activity is also more frequent in the presence of myocardial ischaemia and LVH[8].

Neurohormonal activation

Sympathetic activity is increased in hypertensive patients, and hypertrophic myocardium is more sensitive to the electrophysiological effects of sympathomimetic.

Ventricular wall stress

Increased wall stress found in LVH promotes ventricular ectopy[8,9]. Acute increases of blood pressure produce ventricular premature beats [10,11]

Ion disturbances

In newly presenting hypertensive patients serum potassium level has been shown to be the most important independent factor contributing to the prevalence of arrhythmias[12]. Hypertensive patients using thiazide and loop diuretics are more exposed to this condition. Patients with LVH are more susceptible to arrhythmias in the presence of hypokalemia[12].

Hypertension and atrial fibrillation

Epidemiology

Atrial fibrillation is the most common sustained arrhythmia in adults. The incidence of AF increases

with age:- a prevalence of 0.1% in adults younger than 55 years increases to 9% in adults older than 80 years[13,14]. The Framingham Study cohort also demonstrated that hypertension and diabetes were the only cardiovascular risk factors that were responsible for the development of new-onset AF. In the Framingham study, hypertension brought an excess risk for AF by 50% in men and 40% in women, ranking 4th after heart failure, aging, and valvular heart disease. However, because of its higher prevalence in the population, hypertension accounts for more cases of AF(14%) than the other risk factors.

Clinical implications

The predominantly hemodynamic mechanisms (Figure 1) include the increase in left ventricular (LV) wall thickness, the rise in LV stiffness, and the impairment in LV diastolic function associated with hypertension. These processes lead to a rise in LA stretch and pressure, with subsequent remodeling and dysfunction of the LA, ultimately predisposing to AF. The activation of the renin-angiotensin-aldosterone system also contributes to the LA remodeling (figure 1). The risk of new-onset AF increases with LV mass in hypertensive patients in sinus rhythm at entry and no other major predisposing conditions, whereas increased LA

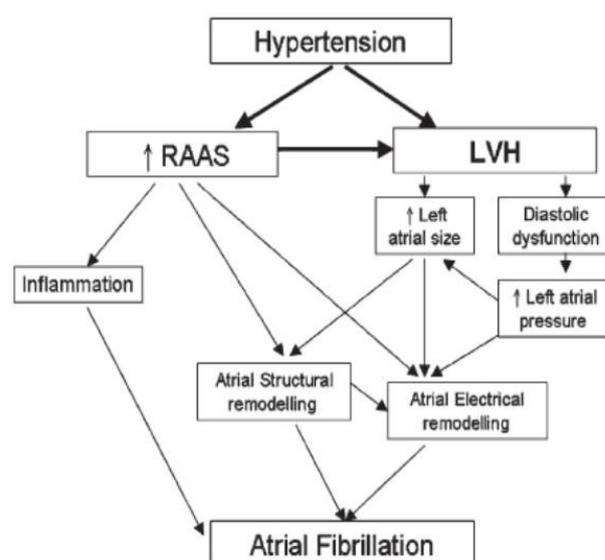


Figure 1. Potential mechanisms of atrial fibrillation related to hypertension
254x190mm (96 x 96 DPI)

size is more closely associated to the development of permanent AF. At any level of LV mass, the risk of permanent AF increases with LA diameter[16] (figure2).

The blood pressure levels influence the risk for AF. While the impact of diastolic BP is not significant, systolic BP increases the incidence of AF and pulse pressure – a marker of arterial stiffness – is superior to both systolic and diastolic BP in predicting the risk for AF[17]. The 24 h distribution of BP levels is also important. Hypertensive patients with a nondipping pattern have a 2-fold higher risk of developing AF when compared with those with a normal diurnal BP rhythm[18].

Therapeutical considerations

There is a well-established association between hypertension and atrial fibrillation since high systolic blood pressures (SBP) are long-term predictors of incident AF. The BP strict control is an effective method to reduce the incidence of AF. LIFE study compared patients with left ventricular hypertrophy and in-treatment SBP ≤ 130 mm Hg and SBP between 131 and 141 mm Hg with patients with in-treatment SBP ≥ 142 mm Hg showing a lower of new AF of 40% and respectively 24% over a follow up of 4.6 years[19].

The type of blood pressure lowering therapy may also be of importance. ACE inhibitors and

sartans, acting on the RAAS activation, prove in several studies a benefit over other antihypertensive drugs in reducing the incidence of new AF, although evidence is not yet conclusive[17].

The presence of hypertension changes the prognosis of atrial fibrillation, increasing both the CHA₂DS₂-VASC score and, when uncontrolled, the HAS-BLED score, being associated with a higher risk of both ischaemic and hemorrhagic stroke. The presence of LVH is also important, making the use of class I antiarrhythmics and Sotalol contraindicated[20].

Hypertension and ventricular arrhythmias

Epidemiology

In untreated hypertensive patients, non-sustained ventricular arrhythmia was observed in up to 5% of patients during 24-h Holter monitoring. The most important determinant for the occurrence of ventricular arrhythmia in patients with hypertension is the presence of LVH. In Framingham study the risk factor-adjusted HR for sudden cardiac death in patients with LV hypertrophy was 2.16 (figure 3). Both ECG and echocardiographically determined LVH are associated with an increased risk, with the presence of both having the highest risk. It is interesting that electrical LVH seems to have a higher impact than the presence of echo LVH only[24](figure 4).

Clinical implications

Since the presence of LVH increases the risk in hypertensive patients cardiac echography should be performed in all hypertensive patients with ventricular arrhythmias. Exercise stress test is useful to evaluate the presence of myocardial ischaemia. A thorough evaluation for dyselectrolytemia, thyroid status, personal habits of drug abuse or increased alcohol, caffeine or other stimulants intake should be effectuated[23].

Therapeutical considerations

The regression of LVH is shown to reduce the incidence of VAs[21]. In addition to the degree of BP lowering several classes of antihypertensive drugs have shown an increased benefit – ACE

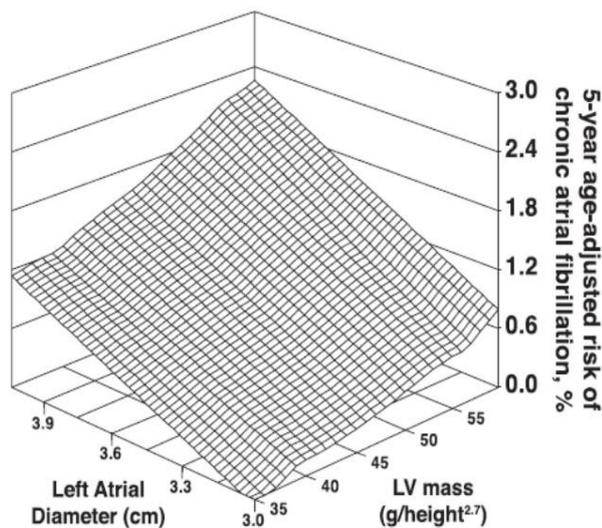


Figure 2. 5-year risk of permanent atrial fibrillation in relation to LV mass and left atrial diameter
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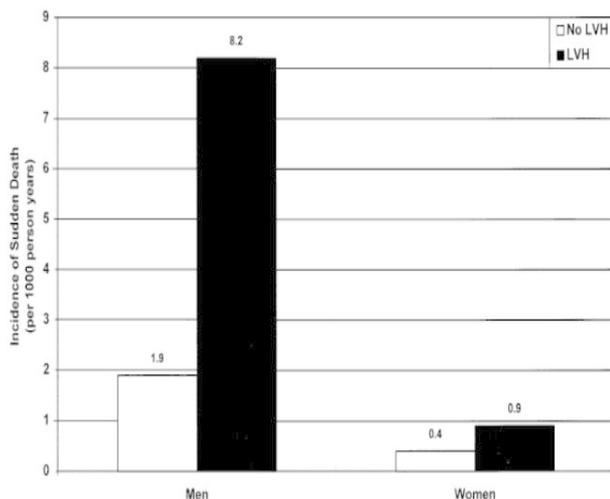


Figure 3. Incidence (unadjusted) of sudden death in men and women according to LV hypertrophy status
254x190mm (96 x 96 DPI)

inhibitors and ARBs. On the other way, the use of thiazide diuretics is associated with an increased risk of SCD.

In hypertensive patients with asymptomatic and non-sustained ventricular arrhythmias, there is no role for prophylactic use of antiarrhythmic agents. In those with LV dysfunction and those who suffered from sustained and symptomatic ventricular tachycardia not related to a reversible cause, implantable cardioverter defibrillator should be considered for prevention of SCD[21].

Conclusions

Hypertension is a frequently unrecognized risk factor for cardiac arrhythmias and its incidence is growing[25]. Better BP control strategies can therefore reduce the incidence of this pathology. On the other side in patients with arrhythmias hypertension increases the risks, therefore adequate therapy may improve their individual prognosis. High BP and especially the presence of LVH also change the therapeutical options in these patients. Educational programs to improve population awareness and to update the current medical knowledge in this field of all the medical specialists who see patients with hypertension and have to take decisions in the clinical evaluation and treatment of these patients are required.

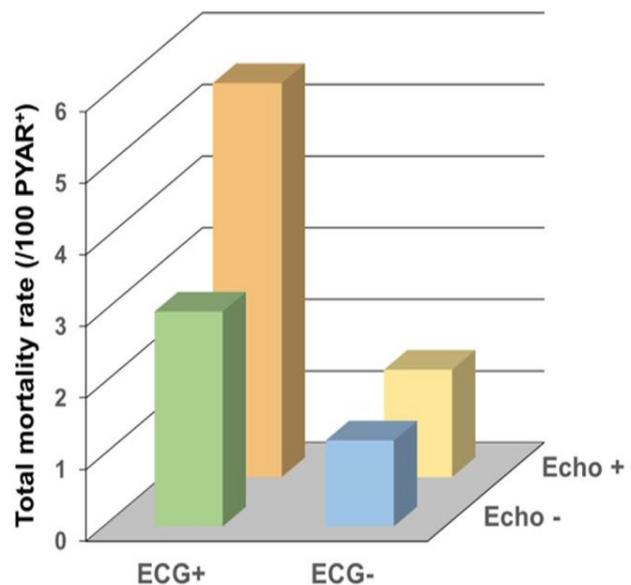


Figure 4. Risk of overall mortality associated with LVH (*Person Years at Risk)
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Conflict of interest

The authors confirm that there are no conflicts of interest.

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