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Hypertension and Atrial Fibrillation: the "why" behind their coexistence

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Abstract

Hypertension and atrial fibrillation commonly coexist, uncontrolled blood pressure being considered a major risk factor for several cardiac complications including new-onset atrial fibrillation. Systolic blood pressure is an important determinant of recurrent AF and overall AF burden in patients with left ventricular dysfunction (LVEF≤40%). On the other side, atrial fibrillation is considered the most prevalent concomitant condition in hypertensive patients, a common cause of cardiovascular complications like stroke, enhanced disability and mortality. Antihypertensive treatment may contribute to a reduction of risk of AF development and complications, and it appears that some classes of drugs are superior to others in preventing new-onset AF and stroke.

Keywords: blood pressure, atrial fibrillation, risk factor, treatment

In the general population, systemic hypertension (HTA) is a major risk factor for a significant number of cardiovascular complications such as heart failure, coronary artery disease, atrial fibrillation (AF), stroke, and so forth. Concerning AF, HTA is one of the major risk factors, approximately 80% of AF patients associate increased blood pressure. AF is usually diagnosed with opportunistic screening, in patients 65 years and older, using pulse palpation together with auscultator measuring blood pressure (BP) [1].

In Framingham Heart Study, HTA was associated with a 1.9-fold increased risk of developing new-onset AF, whilst in the Manitoba Follow-Up Study the risk was 1.4 times higher [2]. Moreover, HTA is associated with a 1.5-fold increased risk of progression from paroxysmal to permanent AF [3]. On the other side, AF is the most prevalent concomitant condition in hypertensive patients, greatly enhancing the disability and mortality in these subjects [2]. Increased BP promotes morphological and functional alterations of the myocardium leading to left ventricular hypertrophy, concentric left ventricle remodeling and diastolic dysfunction. Subsequently, increased left atrial pressure

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may cause atrial stretch and dilation, which may favor the development of AF [4]. A 16-years prospective study on hypertensive subjects with no other major predisposing conditions, revealed that risk of atrial fibrillation increases most with age and left ventricular mass [5]. According to another study results, nighttime BP levels plays the most important role in left atrial remodeling and enlargement, possibly due to RAAS activation [4].

Neurohormonal activation in patients with atrial fibrillation

Biomarkers including atrial natriuretic peptides (ANP) and brain natriuretic peptides (BNP) have been correlated with myocardial structural alterations, although the mechanism by which these natriuretic peptides are elevated in hypertension remains unclear. It has been hypothesized that elevated natriuretic peptides, specifically ANP, are more closely associated with blood pressure per se, than with ventricular remodeling secondary to hypertension [4]. An accepted player influencing the development of AF is the renin-angiotensin- aldosterone system (RAAS), presumably through two main mechanisms: first, by promoting myocardial fibrosis, primarily at the atrial level, thereby acting as a potentially arrhythmogenic anatomical substrate, and secondly, by inducing structural changes such as left ventricular hypertrophy and atrial enlargement, which are also responsible for the neurohormonal activation involved in the development of AF [4]. Angiotensin II is involved in the regulation of cardiomyocyte proliferation and collagen deposition in the interstitial matrix. Therefore, RAAS activation may act as a promoter of growth and tissue fibrosis in the atrial myocardium [4].

AF-CHF and AFFIRM analysis

A newly published analysis from AFFIRM (The Atrial Fibrillation Follow-up Investigation of Rhythm Management) and AF-CHF (The Atrial Fibrillation and Congestive Heart Failure) trials, conducted on 2.715 patients with paroxysmal or persistent AF, assessed the influence of systolic blood pressure on atrial fibrillation recurrence and burden (proportion of time spent in AF). In patients with LVEF >40%, systolic blood pressure did not influence the AF recurrence. In contrast, in patients with LVEF ≤40%, the AF recurrence rate was higher in those with hypertension compared to normotensives ($p = 0.005$). Consistently, the proportion of time spent in AF was not influenced by systolic blood pressure in patients with LVEF >40%, but in subjects with LVEF ≤40%, the adjusted mean proportion of time spent in AF was much higher in patients with hypertension. The conclusion of the analyses was that systolic blood pressure is an important determinant of recurrent AF and overall AF burden in patients with left ventricular dysfunction (LVEF≤40%), but not in those with preserved ventricular function [6].

Optimal blood pressure in patients with atrial fibrillation

As reminded earlier, systemic hypertension is associated with a linear increase in cardiovascular complications such as heart failure, AF, and death. Yet, in the presence of specific cardiovascular conditions such as coronary heart disease and heart failure, low blood pressure is paradoxically associated with an increase in mortality. In a post-hoc analyses of the AFFIRM subjects, a J-shaped relationship was revealed between BP, all-cause mortality and secondary outcome (a composite of all-cause mortality, sustained ventricular tachycardia, ventricular fibrillation, pulseless electrical activity, clinically significant bradycardia, stroke, major bleeding, myocardial infarction and pulmonary embolism). The lowest expected event rates were associated with SBP of 130 - 140 mm Hg and DBP of 70 - 80 mm Hg. Low BP (< 110/60 mm Hg) seemed to be more dangerous than high BP in the AF population [7].

Another post-hoc combined analysis on pooled data from AFFIRM and AF-CHF trials assessed the relationship between baseline systolic blood pressure (SBP) and mortality and hospitalizations. In patients with LVEF ≤40%, SBP <120 mmHg and SBP >140 mmHg were both associated with a significant increase in total mortality compared with normotensives. Hospitalizations were unrelated to SBP regardless of LVEF. The authors concluded that blood pressure is independently related to mortality in a U-shaped pattern in patients with impaired systolic function, but not in those with a normal EF [8,9].

Blood pressure treatment in atrial fibrillation

Treatment of hypertension in AF needs to take into consideration characteristics of the underlying AF such as chronicity and ventricular rate. Antihypertensive treatment may contribute to a reduction of risk of AF development and complications, and it appears that some classes of drugs are superior to others in preventing new-onset AF and stroke. This is presumably related to the coexistent clinical conditions and to the distinguishing property of a specific drug in reversing structural cardiac damage caused by HTA [2]. The most important target of antihypertensive treatment is the regression and prevention of electrocardiographic left ventricular (LV) hypertrophy [2].

Considering the significant role that RAAS plays in AF occurrence, drugs that interfere with the system (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers or mineralocorticoid antagonists) seem to be more effective in preventing new-onset AF than treatment with beta-blockers and calcium antagonists in hypertensive patients. However, RAAS inhibitors are helpful in subjects with early or reversible cardiac structural changes and they are less effective in patients with more advanced or heterogeneous cardiac disease [2]. It is believed that RAAS blockade prevents atrial electrical remodeling and fibrosis by improving left ventricular function and decreasing filling pressures.

A recent meta-analysis specifies telmisartan as a more efficient drug in preventing AF recurrences among hypertensive patients with paroxysmal AF, the mechanisms involved including strong binding affinity to angiotensin II type 1 receptors, the specific property to block potassium channels in atrial myocytes and its effect in facilitating parasympathetic activity as well as reducing QT dispersion [10].

The 2016 European Society of Cardiology guidelines for the management of atrial fibrillation and The American Heart Association/American College of Cardiology/ Heart Rhythm Society guidelines, recommend the use of angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs) for new-onset AF prevention in patients with hypertension, heart failure with reduced ejection fraction, and left ventricular hypertrophy. ACEIs or ARBs are not recommended for the secondary prevention of paroxysmal AF in patient with no underlying heart disease. Still, it may be considered in patients with recurrent AF undergoing electrical cardioversion [11,12].

In a review of approximately 12 000 patients with systolic heart failure, the addition of a beta-blocker to RAAS inhibitor compared with RAAS blocker alone reduced the incidence of new-onset AF by 27% [3]. Beta-blockers are preferred in hypertensive patients with underlying coronary artery disease particularly after myocardial infarction [3]. In patients with AF and a high ventricular rate, beta-blockers and non-dihydropiridine calcium antagonists (verapamil, diltiazem) are recommended. Beta-blockers and mineralocorticoid antagonists (spironolactone) may prevent atrial fibrillation in hypertensive patients with heart failure.

Dihydropiridine calcium antagonists such as amlodipine are very effective agents for BP control; they reduce pulse pressure and therefore may have a potential role in AF reduction; however, amlodipine was shown to be inferior to valsartan in reducing new incidence of AF. Studies comparing RAAS blockers (ACEIs or ARBS) vs calcium channel blockers have shown that the prior agents are superior in reducing AF- related hospitalizations [3,13].

There are no recognized studies assessing the effects of diuretics on the incidence or recurrence of AF. Nonetheless, these effective agents in reducing blood pressure do often induce electrolyte abnormalities which may contribute to arrhythmias.

Hypertension and atrial fibrillation ablation

Within the context of AF catheter ablation through pulmonary vein antrum isolation (PVI), hypertension represents one of the main pre-procedural risk factors for AF recurrence [2]. A recently published study, which evaluated the impact of hypertension on the outcome of atrial fibrillation (AF) ablation, showed no statistical difference in AF recurrence rate following catheter ablation between patients with controlled hypertension and normotensives in the long-term follow-up. By contrast, pharmacologically uncontrolled hypertensives presented higher AF recurrence risk and required more extensive ablation [14].

Several studies have tried to investigate the relationship between renal artery denervation (RDN) and AF, after certain evidence of incremental AF suppression

in patients treated with pulmonary vein isolation combined with RDN for the treatment of resistant hypertension. One study published in 2016 demonstrated that when RDN is added to PVI, it significantly decreases the rate of AF recurrences and AF burden and is in part related to improvement in BP control. Still, the antiarrhythmic mechanism by which RND functions is unknown [15].

Hypertension and atrial fibrillation: a two-way road

Atrial fibrillation is considered the most prevalent concomitant condition in hypertensive patients [10]. In this population, AF is a common cause of cardiovascular complications like stroke, enhanced disability and mortality. Prevention of new episodes of AF is warranted, particularly in hypertensive patients whose CHADS2-VASc score is already high.

Restoring SR in hypertensive patients with AF can lead to a significant increase in systolic BP (especially at nighttime) and a decrease in diastolic BP. Adjustments of the antihypertensive treatment may be necessary in patients with AF undergoing cardioversion to sinus rhythm [16]. Additionally, close monitoring for AF recurrence should be recommended.

Conclusion

Hypertension is the most common cardiovascular disorder, and atrial fibrillation is the most prevalent concomitant condition in hypertensive patients. Antihypertensive treatment may contribute to a risk reduction of atrial fibrillation development and complications, and it appears beneficial to use an angiotensin-converting enzyme inhibitors or angiotensin receptor blockers as an antihypertensive in patients with atrial fibrillation, adding a beta-blocker or nondihydropiridine calcium channel blocker when rate control is desired. With normal renal function and normokalemia, we should consider an mineralocorticoid antagonists in patient with heart failure. When atrial fibrillation ablation is considered, strictly controlled blood pressure is required, since atrial fibrillation recurrence risk is higher with increased blood pressure.

Conflict of interest

The authors confirm that there are no conflicts of interest.

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