Atrial Fibrillation in Patients With Hypertension
Trajectories of Risk Factors in Yet Another Manifestation of Hypertensive Target Organ Damage

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See related article, pp 597–605

Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia, with an increasing prevalence and incidence with age and associated cardiovascular comorbidities. The prevalence and incidence of hypertension also increases with increasing age, and hypertension is the commonest pathogenic risk factor for the development of AF. The development of AF is most evident in the presence of hypertensive left ventricular hypertrophy, especially where there is associated heart failure with preserved ejection fraction.

Not only does hypertension increase the risk of incident AF but also both conditions commonly coexist in the same patient. Both conditions individually lead to complications, such as stroke and heart failure, with the risks accentuated when both the disorders are present. Other epidemiological links are also evident, with the intimate relationship of AF and hypertension individually to coronary artery disease (especially myocardial infarction), obesity, and obstructive sleep apnea and to alcohol excess. Associated renal dysfunction or proteinuria (commonly seen in association with hypertension) can predispose to the development of AF. Uncontrolled hypertension leads to more strokes, whether in AF or non-AF patients. When anticoagulants are used, uncontrolled blood pressure increases the risk of serious bleeding.

Underlying these epidemiological relationships are the pathophysiological similarities. AF confers a prothrombotic or hypercoagulable state, leading to the higher risk of thromboembolism. A prothrombotic state is also seen with hypertension, given the observation that despite the blood vessels being exposed to high pressures the complications of hypertension, that is, stroke and myocardial infarction are paradoxically thrombotic, rather than hemorrhagic (the Birmingham paradox). AF is more common with diastolic dysfunction, often with associated left ventricular hypertrophy. Systemic vascular dysfunction (as quantified by abnormal flow-mediated dilatation or other biomarkers) is evident in hypertension, and it is also related to AF.

In this issue of Hypertension, Rahman et al report that among 4351 Framingham Study participants, longitudinal disease patterns, referred to as trajectories, of AF risk could be related to the development of AF. The highest risks of incident AF were seen with group 4 (hypertensive initially with decreasing BP) and group 5 (hypertensive and increasing BP) for systolic blood pressures, particularly where longer antihypertensive treatment was needed. Interestingly, distinct trajectories for diastolic blood pressure, smoking, and diabetes mellitus were not associated with increased 15-year risk of AF. The authors conclude that longitudinal trajectories (ie, longitudinal systolic blood pressure data) may distinguish how exposures related to AF contribute toward the prospective risk of incident AF, especially where prolonged hypertension is present and antihypertensive treatment is used.

What are the implications of this elegant work from the Framingham study? It seems obvious that longitudinal trajectories make much more sense when assessing pathogenic relationships. Numerous studies have measured baseline one off measurements of particular biological variables and related them to events occurring many years afterward, most typically seen in much of biomarker-based research to predict outcomes. For the latter, one off single (baseline) measures of biomarker(s) have often been used to refine clinical risk stratification, for predicting end points occurring many years later. Indeed, patients do not remain static, in relation to age and risk. Repeated measures of physiological measures have been proposed as being far more reflective of actual reality with regard to clinical status. Indeed, one could clearly argue that for (any) physiological measures open to possible clinical variability, it only seems sensible to measure the parameter repeatedly and multiple times over a period to improve their clinical relevance, especially for risk prediction. Cardiovascular risk is also a continuum of risk, and patients do not fall into neat (and artificially defined) low-, moderate-, or high-risk categories.

Nonetheless, analysis of longitudinal trajectories of blood pressure would not account for other parameters that would change over time that could influence cardiovascular risks (including the predisposition to AF), for example, renal function, cardiac function, and obesity. Changes in individual drug therapies or doses over time may be added confounders that would not be adequately addressed by Rahman et al.
What are the practical aspects of associated hypertension in the management of AF? As shown by Rahman et al., patients with (mainly systolic) hypertension are more likely to develop incident AF; and thus, all hypertensive patients should be opportunistically screened for AF, by pulse palpation and confirmatory ECG if an irregular pulse is present. Where suspected, Holter monitoring should be performed, especially for underlying paroxysmal AF, which may be asymptomatic yet prognostically serious. The presence of uncontrolled hypertension leads to more target organ damage, whether in the heart, brain, kidneys, or eyes. In the heart, this has been referred to as hypertensive heart disease, where left ventricular hypertrophy, diastolic dysfunction, atrial dilatation, and heart failure with preserved ejection fraction are evident manifestations. To such presentations of hypertensive target organ damage, we can certainly add AF.

The concomitant presence of AF and hypertension requires strict blood pressure control, especially because stroke and systemic embolism have been related to uncontrolled blood pressures. In terms of stroke risk assessment, hypertension (whether history of hypertension or uncontrolled blood pressure) scores 1 point on the CHA2DS2-VASc score (congestive heart failure, hypertension, age ≥75 years [doubled], diabetes mellitus, stroke/transient ischemic attack/thromboembolism [doubled], vascular disease [prior myocardial infarction, peripheral arterial disease, or aortic plaque], age 65 to 74 years, sex category [female]), and thus, stroke prevention (ie, oral anticoagulation) should be considered in hypertensive patients with AF. Even a single stroke risk factor confers risks of stroke and mortality, and oral anticoagulation confers a positive net clinical benefit compared with aspirin or no antithrombotic treatment. Effective stroke prevention in AF means oral anticoagulation, whether as a vitamin K antagonist (eg, warfarin) or a non–vitamin K antagonist oral anticoagulant; importantly, aspirin has no role to play.

Bleeding risk assessment also requires consideration of blood pressure levels. Uncontrolled hypertension represents the H criterion on the HAS-BLED score (hypertension, age, stroke, bleeding tendency/predisposition, labile INRs, elderly age/frailty, drugs [eg, concomitant aspirin/nonsteroidal anti-inflammatory drugs or alcohol excess]) score for assessing bleeding risks in patients with AF, and this score flags up patients for regular review and follow-up and directs attention to the correctable bleeding risk factors, so that, for example, uncontrolled blood pressure should be proactively managed.

In conclusion, longitudinal trajectories and repeated measures of blood pressure may distinguish how hypertension contributes toward the risk of developing AF and probably, its associated complications. Hypertension and AF are intimately related pathogenically, epidemiologically, pathophysiological, and from the aspect of clinical implications (or complications). Perhaps, both conditions are not so strange bedfellows after all, given that AF is a likely manifestation of hypertensive target organ damage and should be proactively managed accordingly.

Disclosures

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