Atrial fibrillation and its complications: a focus on identifying risk factors and risk stratification

Farhan Shahid¹, Eduard Shantsila¹, and Gregory Y. H. Lip¹,²*

¹University of Birmingham Institute of Cardiovascular Sciences, City Hospital, Birmingham, UK; and ²Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

This editorial refers to ‘Risk factor changes and incident atrial fibrillation among middle-aged men in the Malmö Preventive Project cohort’, by L.S.B. Johnson et al., on page 81.

Although traditionally described as a diagnosis of the elderly, a growing population with high prevalence of cardiovascular risk factors and overt cardiovascular disorders makes the problem of atrial fibrillation (AF) highly relevant. Therefore, early risk assessment and management of cardiovascular risk factors are of primary importance in improving cardiovascular health and reducing the incidence of AF. Despite a clear association between AF and various risk factors such as hypertension, diabetes mellitus, and heart failure, very few AF patients simply fall into a single, simple homogeneous category with respect to predisposing factors for developing AF or its complications.

In this issue of European Heart Journal: Cardiovascular Pharmacology, Johnson et al. report an observational study on the relationship between conventional risk factors and the incidence of AF in middle-aged patients in Malmö, Sweden. Risk factors analysed during the 6-year period were those of systolic and diastolic blood pressure, a 2-h oral glucose tolerance test, weight, and screening spirometry. Using Cox regression analysis, an independent relationship was found between the incidence of AF after 6 years follow-up, and the recorded changes in systolic and diastolic blood pressure, weight gain and fasting blood glucose. Interestingly, a link between AF and lung function was not significant, in contrast to previous cohort studies in patients with obstructive sleep apnoea. Limitations include residual confounding from variables that were not necessarily available in this dataset and the limited participation of female subjects.

Despite this, Johnson et al. provide interesting epidemiological insights into the development of risk factors in relation to AF, and provide some food for thought as to whether early recognition and intervention of risk factors may indeed reduce the risk of AF occurrence.

However, one must appreciate that the incidence of AF goes beyond conventional cardiovascular risk factors that have long been established. For example, data from the Framingham Heart Study show that parental AF increases AF in the offspring, independent of risk factors such as hypertension and diabetes. However, up to 30% of AF patients have no underlying cause and are labelled as ‘lone AF’. The latter term should be used with some caution as further close analysis of such patients with more detailed investigation techniques, not only aids in showing the aetiology of such patients but also provides important prognostic information.

On the other hand, multiple risk factors clearly increase the likelihood of developing AF (or AF-related complications), and the list is probably endless. Perhaps some balance is needed between simple clinical practicality and complex multivariate scores that may well be statistically significant with only marginally improved predictive ability. Indeed, even the CHA₂DS₂-VASc score is a good predictor of incident AF. As a further example, the metabolic syndrome is a group of risk factors associated with high risk of atherosclerotic disease, which have been strongly likened to the incidence of AF. Such common risk factors including hypertension, central obesity, insulin resistance, and low HDL with raised triglycerides are suggested to reduce incidence of AF if rigorously treated.

To add further to complexity (and expense), we can add in biomarker risk factors (whether blood, urine, imaging, genetic factors, etc.) that have been related to the development of AF or its complications. Also, some biomarkers seem in predictive in one cohort but not another, not to mention assay and laboratory variability and calibration.

Nonetheless, there exists a population of patients that develop AF but do not fit into our traditional risk factor profiles. In such patients, the use of novel biomarkers may perhaps be of benefit in the future in identifying incident AF. In patients with multiple stroke risk factors, perhaps AF is simply a bystander or ‘not yet documented’ as (for example) stroke and thromboembolism rates seem broadly similar whether or not AF is present, where multiple CHA₂DS₂-VASc score risk factors are evident.

Ultimately, does it matter? Clinical risk scores have modest predictive value for incident AF or its complications. The harder we look, the more AF we are likely to find. Some simple risk scores are better at defining ‘low-risk’ patients who do not need treatment.
(e.g., patients with CHA2DS2-VASc score 0 in males and 1 in females do not need antithrombotic therapy); following this step, stroke prevention can be considered for those with ≥1 stroke risk factor.13,14 Indeed, there is a positive net clinical benefit for treating such patients with vitamin K antagonists (VKAs, e.g. warfarin),15 a benefit which is even greater with the non-VKA oral anticoagu-
lants.16 Ultimately, we perhaps need to balance simplicity and prac-
ticality with the same approach to identifying incident AF, to be relevant to our everyday clinical practice.

Conflict of interest: G.Y.H.L.: consultant for Bayer/Janssen, Astel-
las, Merck, Sanofi, BMS/Pfizer, Biotronik, Medtronic, Portola, Boeh-
ringer Ingelheim, Microlife, and Daiichi-Sankyo. Speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Microlife, Roche, and Daiichi-Sankyo.

References
15. Lip GY, Skjøth F, Nielsen PB, Larsen TB. Non-valvular atrial fibrillation patients with none or one additional risk factor of the CHA2DS2-VASc score: A comprehensive net clinical benefit analysis for warfarin, aspirin, or no therapy. Thromb Haemost 2015;114:826–834.