A new predictor for the onset of atrial fibrillation?

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In this issue of the Netherlands Heart Journal, the results of a substudy of the PREVEND trial are published.¹ This prospective registry of presumably healthy citizens of Groningen aims to establish the association between microalbuminuria and the emergence of renal and cardiovascular diseases.² This general population based long-term study extends the series of previous large-scale epidemiological trials conducted in the Netherlands. We recall among them the 1970 Vlagtwedde study for epidemiological cardiology and ischaemic heart disease, the 1982 Zutphen study of diet and cardiovascular diseases, the 1997 Maastricht study of circulatory arrest and sudden death, the 1998 Amsterdam study of out-of-hospital cardiac arrest and the 1999 Rotterdam study of prolonged QT interval and mortality. In this substudy of the PREVEND trial the investigators demonstrated the association between an elevated pro B-type natriuretic peptide (NT-proBNP) at baseline and the presence of atrial fibrillation (AF) recorded four years later on the ECG while sinus rhythm was present at baseline. A new predictor for the emergence of AF was born.

AF is characterised by many clinical aspects and its genesis is clearly of multifactorial nature. Risk factors for AF vary from age to high systemic blood pressure, left ventricular hypertrophy, valvular heart disease and heart failure. These determinants initiate intrinsic atrial changes leading to elevated left atrial pressure and stretch, and eventually to structural and electrophysiological abnormalities that make the atria prone to sustained AF. Furthermore, both the autonomic nervous system and the RAAS system modulate the incidence and manifestations of AF. Various epidemiological studies predict a substantial increase

in AF, specifically in elderly people. Because AF impairs lifestyle and daily activities, provokes heart failure and most importantly leads to stroke, timely detection of AF followed by rhythm or rate control strategy and of course anticoagulation are the measures of daily practice. This is of importance because AF can arise with or without symptoms, an observation often seen in the same AF patient. This knowledge belongs to the 'professional kit' of the cardiologist, and an elevated NT-proBNP as predictor for later arising AF is suggested as a new tool.

To appreciate the message of this substudy several aspects need to be addressed. The term 'population based' is not a straightforward concept in this subpopulation of the PREVEND programme because 70% had a urinary albumin excretion $\geq 10\text{mg/l}$ whereas more than 24% were subsequently excluded from the cohort, mainly because the four-year follow-up ECGs were missing. In addition, the low incidence of AF (0.6%) during the ECG registration at four years after baseline undermines the sensitivity of the predictor. Furthermore the diagnostic power of a single ECG recording of 20 seconds is very limited. Many large-scale AF studies using daily trans-telephonic recordings have shown the lack of sensitivity and specificity of a single ECG to diagnose AF. Of importance, a statistical association satisfies the investigators but does not always disclose the underlying mechanism and makes the clinical relevance of the observation a matter of ongoing debate. The mathematical model applied handled elevated NT-proBNP, left ventricular hypertrophy and ischaemic heart disease as confounders. The multivariate model subsequently computed independent odds ratios. It is conceivable that elevated NT-proBNP is not confounded by e.g. left ventricular hypertrophy but that elevated NT-proBNP BNP is a measure of severity of left ventricular hypertrophy, likewise any other condition causing cardiomyocyte stretch as discussed by the authors. Taking these considerations one step further one can argue that AF leads to higher plasma NT-proBNP concentration and vice versa. A hypothesis that is compatible with the presented data.

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All limitations of this substudy have been sincerely admitted by the investigators who underlined that NT-proBNP screening for later AF is nowadays not advocated but can be considered in high-risk patients such as those with diabetes and systemic high blood pressure and/or left ventricular hypertrophy. In the mean time one can assume that the clinician would rather classify an elevated NT-proBNP at the initial visit or during follow-up as the reflection of haemodynamic or structural cardiac abnormalities than impending onset of AF, an arrhythmia that is so often of secondary origin.

We conclude that all efforts to identify predictors of new AF should be welcomed because this arrhythmia affects negatively quality of life as well as life expectancy. The investigators of the PREVEND study, encouraged by preliminary results of the Framingham Offspring³ study, confirmed that an elevated NT-proBNP might

predict AF and this observation is worthwhile. Because the power of this predictor requires prospective trials and thus its applicability as a screening tool for daily practice is debatable, we rely on the well-established risk factors for AF and have sufficient tools for timely AF detection as the medical history and Holter recording, external and implantable loop recorders and the memories of implantable brady and tachy devices. ■

References

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