Atrial Fibrillation

Tackling a growing healthcare challenge: atrial fibrillation epidemiology, prevention, and underlying causes

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Europe has had a high prevalence of atrial fibrillation (AF) for decades, while the global incidence has been projected to rise sharply during the coming years.[1] This poses a growing challenge for healthcare systems as AF is associated with hospitalisation and other outcomes such as stroke, heart failure, and dementia. Three papers published in *The Lancet Regional Health—Europe* for the Series on "Atrial Fibrillation" provide an overview of AF with regards to preventive measures,[2] genetics,[3] and the contribution of socioeconomic and lifestyle factors.[4]

Linz et al. review the current knowledge on clinical epidemiology and the potential of screening and digital solutions to mitigate the burden of AF on public health.[2] First, they describe the epidemic of AF, highlighting the impact of population ageing on the increasing prevalence. All projections may underestimate the impact of AF diagnoses made by means of screening, both in- and outside the traditional clinical setting. As noted by the authors, AF screening remains a hot topic in cardiology, and now with evidence to support the discussion. AF may be a reasonable candidate according to the Wilson and Jungner criteria; it is an often asymptomatic condition associated with preventable outcomes and screening may be both net-beneficial and feasible. A recent trial found that a pragmatic screening programme was cost-effective and slightly decreased a combined outcome of stroke, bleeding and mortality,[5,6] which was also supported by a summary-level meta-analysis of four trials using vastly different methodologies.[6,7] But, the perceived benefits of screening for AF is still deducted mostly from studies of AF yield—i.e. screening leads to more diagnoses than no screening,[8] and the knowledge on outcomes from studies of clinically diagnosed AF, opposed to screening-detected AF, which be an inherently different entity.

We still need to better understand appropriate screening target populations and methods, and how this can be integrated in clinical care. To this regard, the authors move on to discuss care pathways including digital screening and management. The knowledge about digital care is still preliminary, but in their systematic review, the authors identified several studies with promising results for a future of more efficient identification and management of patients with AF using digital tools such as apps, artificial intelligence, and so-called wearables to improve both clinical and patient-reported outcomes.

Another opportunity for risk stratification and prevention may arise from a better understanding of the genetics associated with AF. Vinciguerra et al. reviewed the genetic, transcriptomic, and epigenetic mechanisms of AF.[3] They note that genetic predisposition seems to have the highest impact on AF in populations of European ancestry, where the vast majority of associations are with common variants across several hundred locations in the human genome (genetic loci). These genetic variations form the basis of polygenic risk scores (PRS), which are slowly seeing more use in risk prediction.[9] However, non-European population groups remain understudied in genetic investigations, which may hinder the generalizability. Also, the absolute risk differences according to PRS groups are often modest, though implementation among patients with cardiovascular disease seems encouraging.[10] Nevertheless, new knowledge of the genetic underpinnings of AF may help elucidate the diverse pathophysiological pathways involved in AF, including inflammation, electrical disturbances, and cardiac structural remodelling.

Although numerous associations are near or within genes involved in established arrhythmogenic pathways, most identified variants are in non-protein coding regions of the genome, where they may have mediating effects through changed expression of transcription factors like Pitx2. Consequently, researchers have studied both gene regulation and expression, through epigenetic and transcriptomic studies, and have found genes and proteins to be up- or downregulated in AF. Some studies have indicated that AF itself could modify the expression of the Pitx2 transcription factor and lead to altered intracellular calcium handling, although results have been conflicting. In the near future, advances in artificial intelligence may offer useful tools for a better understanding of genetics, epigenetics and transcriptomics.

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Adequate health care requires that patient-, lifestyle, and socioeconomic factors are addressed, which is discussed in the review by Shantsila et al.[4] The authors note that obesity increases AF risk and subsequent weight loss may reduce both symptoms and rate of recurrence, and that modifiable risk factors such as smoking and alcohol consumption also play an important role. A wide range of comorbidities are associated with AF: Hypertension, ischaemic heart disease, diabetes and chronic obstructive lung disease, leading to polypharmacy in many patients. Pill burden and potential drug–drug interactions in multimorbid patients still represent an obstacle to clinicians when considering appropriate treatment for AF, such as anticoagulation. The authors note that direct oral anticoagulants (DOACs) in polypharmacy were associated with reduced risk of stroke or embolism, without affecting bleeding risk.

Mental health disorders may also contribute to AF risk: most studies point to an increased risk of AF and reduced adherence to anticoagulation in individuals with schizophrenia. Depression has also been linked with a ~35% increased AF risk and an increased symptom burden. Associations with other mental health disorders seem less robust. Finally, patient factors such as sex, ethnicity, and socioeconomic status should be considered. Notably, low socioeconomic status was associated with an up to 1.5-fold higher mortality rate and increased risk of complications like stroke and heart failure. This may in part be driven by access to care (either by geographical difference or through price in areas where healthcare is not free at point of need), differences in health literacy, and adherence to treatment and risk reducing regiments.

The three papers present a comprehensive overview of the tools necessary to understand AF and mitigate its burden on public health. Emerging technologies in digital health and artificial intelligence show promise in diagnostic and preventive efforts, and new pathophysiological insights may help inform risk stratification, although more studies with appropriate control groups and hard clinical outcomes are needed. To tackle the challenge posed by the growing prevalence of AF, prevention and risk stratification could improve by integrating information from heritable components, clinical risk factors, socioeconomics, biomarkers, and digital technologies.

Contributors

All authors contributed equally.

Declaration of interests

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