Commentary

Risk prediction of new AF – is there a role for artificial intelligence?

Jaspal S Taggar[1], Nadeem Qureshi[2], Stephen Weng[3]

Corresponding Author
[1]Jaspal S Taggar
Division of Primary Care,
University of Nottingham,
Room C34, Medical School,
Queen's Medical Centre,
Nottingham,
NG7 2UH
Email: Jaspal.taggar@nottingham.ac.uk
Tel: +44 115 8230462
Fax: +44 115 82 30214

[2]Division of Primary Care, University of Nottingham

[3]Division of Primary Care, University of Nottingham

The problem

Atrial fibrillation (AF) is the most common cardiac arrhythmia encountered in clinical practice.[1] AF conveys significant health risks, most notably from a 5-fold increased risk of stroke.[2] Strokes attributable to AF are of a greater severity, cause greater disability and mortality, and result in greater healthcare costs than non-AF related strokes.[3]

Around 40% of people with AF are asymptomatic and are described as having 'silent' AF.[4] It is therefore unsurprising that over 12% of people are found to have AF at the first presentation of a stroke. Early identification and treatment of AF before the occurrence of stroke is, therefore, of paramount importance to improve population health.

AF screening has been recommended but is yet to be implemented. Recommendations currently suggest screening in patients ≥65 years of age[5] but the yield of interventions for detecting new AF varies considerably according to the age of populations screened and interventions tested.[6] Identifying those at high risk of developing new AF, including those with "silent AF", would enable better targeting of screening interventions and consequently has the potential to improve the effectiveness and cost-effectiveness of future AF screening programmes.

Predicting the risk of developing AF

A variety of clinical, electrocardiographic (ECG) and biochemical markers have been identified as risk factors for the development of new AF. From these risk factors a number of risk prediction models have been developed (Table 1). Whilst all studies have utilised large patient datasets to derive and validate risk prediction models, only some have been developed using unselected primary care populations and all have been developed in non-UK populations.

Limitations of risk prediction models for new AF

Existing models only have moderate abilities to predict new AF and do not evaluate the incremental effects of different risk predictors for AF. Furthermore, risk models predominately use clinical characteristics to predict the occurrence of new AF and, of those that use ECG parameters, only a few ECG markers have been utilised. No models have incorporated biochemical markers for AF risk prediction. There remains an opportunity to improve the predictive abilities and risk stratification against AF outcomes by combining clinical, ECG and biochemical parameters.

Research suggests that existing risk prediction models may not be transferrable across populations. The US derived CHARGE-AF prediction tool was applied to the UK EPIC Norfolk cohort (n=24,020). Although CHARGE-AF was found to have reasonable discrimination (C-statistic (95% CI) 0.81 (0.75-0.85) there was weak calibration of this model with a nearly 2-fold overestimation of AF incidence.[7] Therefore an important consideration for future research would be to develop and validate prediction models using data from the target population.

Existing risk prediction models have been developed using epidemiological methods which can be improved upon using newer techniques, such as "artificial intelligence" or "machine learning". Previous approaches to developing risk prediction models rely on statistical modelling of 'survival rates' associated with patient baseline characteristics. These methods

assume linearity in relationships between individual characteristics on outcomes (e.g. the relationship between increasing age and developing new AF is linear) and linearity in the effect of multiple characteristics on outcomes (e.g. the increased risk of developing AF from the combined effects of hypertension and increased age is linear). These assumptions may be inaccurate and novel approaches to determining risk prediction, such as artificial intelligence technology, may overcome such limitations.

The role of Artificial Intelligence (AI) technology

Machine learning is computer-based learning using artificial intelligence technology to derive and enable pattern recognition within routinely collected clinical data.[9, 10] Machine learning could be used to better analyse integrated healthcare datasets for the derivation of better clinical evidence as it can overcome the assumptions of linearity when modelling multiple interacting risk factors. Machine learning was recently found to improve the accuracy of predicting all-cause mortality than conventional risk factor modelling in a prospective cohort of patients (n=502,628) from UK-Biobank.[8] Moreover, machine learning enables pattern recognition within data with a potential to identify new risk factors for disease that may previously have been unrecognised.

Potential for research

With the rapid emergence of artificial intelligence technology, researchers are increasingly questioning if there is an opportunity to improve the methodological interrogation of routinely collected patient data to improve healthcare outcomes. With regards to AF, should researchers be considering who may develop AF in the future to enable better targeting of AF detection interventions? There is now an opportunity to use technological advances to identify new risk factors for AF within large patient datasets and to develop tools for predicting those at greatest risk of developing AF. Indeed, primary care systems currently have risk prediction tools embedded within clinical systems (e.g. Q-Risk) so translation of such research into clinical practice is no longer a barrier.

Table 1: Studies of risk prediction models for the development of new AF

Study	Country	Design and sample size	Risk predictors used in model	Prediction time	Predictive ability using C-Statistic* or Hazard Ratio** (95% CI)
Alonso 2013	United States	CHARGE-AF Cohort (3 amalgamated cohorts for derivation; external validation in AGES and Rotterdam study cohorts) N = 18,556 (derivation) N = 7,672 (validation)	Clinical: Age, Race, Height, Weight, BP, treatment for hypertension, smoking, diabetes, previous MI, heart failure ECG: PR interval, LVH	5 years	AGES: *0.66 (0.63-0.70) Rotterdam: *0.71 (0.66-0.75)
Saliba 2016	Israel	Retrospective analysis of national healthcare database N = 1,062,073	Clinical: $CHADS_2$ (Congestive heart failure, hypertension, Age>75, diabetes, stroke) $CHA_2DS_2VAS_c$ (Congestive heart failure, hypertension, Age>75, diabetes, stroke, vascular disease, Age>65, sex category)	2 years	$CHADS_2$: *0.73 (0.73-0.74) $CHA_2DS_2VAS_c$: *0.74 (0.74-0.75)
Schnabel 2009	United States	Cohort (Framingham Heart Study) N = 4,764	Clinical: Age, Sex, BMI, SBP, treatment for hypertension, cardiac murmur, heart failure ECG: PR interval	5 years	*0.78 (0.76-.080)
Chamberlain 2011	United States	ARIC Cohort study Cohort study of Black population N = 14.546	Clinical: Age, Race, Height, SBP, treatment for hypertension, smoking, cardiac murmur, diabetes, IHD, heart failure	1 year	*0.78 (95% CI not reported)

			ECG: LVH		
Cabrera 2016	Spain	Cross-sectional analysis of Holter monitor results N = 299	Clinical: Age, heart failure/cardiomyopathy ECG: PAC>=0.2%; PR interval	2 years	*0.79 (0.71-0.88)
Brunner 2014	United states	Retrospective analysis of outpatient medical records database N = 100,000	Clinical: Age, IHD, diabetes, sex, heart failure, hypertension, valvular disease	5 years	*0.81 (0.81-0.82)
Suenari 2017	Taiwan	Retrospective analysis of national health insurance database (HATCH score) N = 670,804	Clinical: hypertension, age >75 years, stroke or TIA, COPD, heart failure	2 years	**2.06 (2.03-2.09) for each 1 point increment in score

ECG: Electrocardiogram; BMI = Body Mass Index; BP = blood pressure, SBP = systolic blood pressure; MI = Myocardial infarction; LVH = Left Ventricular Hypertrophy; IHD = ischaemic heart disease; PAC = premature atrial complexes; TIA = Transient Ischaemic Attack; COPD = Chronic Obstructive Pulmonary Disease.

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