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Happy New Year and welcome back to Atrial Fibrillation Research Review.

Issue 34 begins with the development and testing of a multimarker risk score for use in patients with AF to evaluate their stroke, systemic embolic event or death risk. COPD has been confirmed to increase the rates of several outcomes, including death from any cause, in patients with AF. Another paper in this issue found that patients with CKD (chronic kidney disease) undergoing ablation for AF had similar rates of postprocedural complications as those without CKD, except for a higher rate of hospitalisation for HF. There is also an interesting comprehensive review by our Australian colleagues on the association between alcohol consumption and AF risk. This issue concludes with research reporting that patients with AF and diabetes treated with insulin were at greater risk of thromboembolism than not only those without diabetes, but also those with diabetes not treated with insulin.

I hope you are finding these regular updates in AF research helpful in your everyday practice. Please don’t hesitate to email your comments and suggestions.

Kind Regards,

Dr Andrei Catanchin
andrei.catanchin@researchreview.com.au

Cardiovascular biomarker score and clinical outcomes in patients with atrial fibrillation

Authors: Ruff CT et al.

Summary: These authors developed and tested a CV biomarker score for predicting stroke, systemic embolic events or mortality risk using a subanalysis of data from 4680 evaluable participants with baseline cardiac troponin I, NT-proBNP (N-terminal pro-B-type natriuretic peptide) and D-dimer level data from the ENGAGE AF-TIMI 48 randomised trial, which compared two once-daily edoxaban regimens with warfarin in patients with AF at moderate to high risk of stroke. For comparisons of highest versus lowest baseline levels, cardiac troponin I, NT-proBNP and D-dimer were associated with 2.8- to 4.2-fold gradients of risk after adjusting for CHA₂DS₂VASc score (p<0.001 for trend for each), and the multimarker risk score identified a >15-fold gradient of risk after adjusting for CHA₂DS₂VASc score. When the multimarker risk score was added to the CHA₂DS₂VASc score, its C-statistic increased from 0.586 to 0.708 (p<0.001) and its net reclassification improved by 59.4% (p<0.001).

Comment: It’s highly likely we’ll see cardiac biomarkers such as troponin, BNP and D-dimer, as reported here, feature in future iterations of the CHA₂DS₂VASc score (or new scores altogether); recall the ABC (Age, Biomarkers, Clinical history) stroke risk score reported in issue 31 of Atrial Fibrillation Research Review last year.

Reference: JAMA Cardiol 2016;1(9):999–1006

Abstract

Abbreviations used in this issue:

AF = atrial fibrillation; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CV = cardiovascular; DAPT = dual antiplatelet therapy; ECG = electrocardiography; HF = heart failure; HR = hazard ratio; INR = international normalised ratio; VKA = vitamin K antagonist.
Efficacy of intravenous and oral sotalol in pharmacologic conversion of atrial fibrillation

Authors: Milan DJ et al.

Summary: This was a systematic review and meta-analysis of ten clinical trials comparing sotalol with other antiarrhythmics, placebo or no treatment for AF conversion. Compared with placebo or no treatment, sotalol was superior for AF conversion (p<0.001), but it was not significantly better than class IA or IC antiarrhythmic drugs or amiodarone. One trial reported that ibutilide 2mg was superior to sotalol, but with more proarrhythmia.

Comment: Sotalol or flecainide are generally the first-line agents for reverting acute AF and are more rapidly effective than amiodarone; sotalol has the added benefit of effective ventricular rate control (compared with flecainide). Ibutilide is not available in Australia.

Reference: Cardiology 2017;136(1):52–60

Impact of chronic obstructive pulmonary disease on prognosis in atrial fibrillation

Authors: Proietti M et al., on behalf of EORP-AF Investigators

Summary: The prevalence of and clinical factors associated with COPD were investigated in AF registry patients. COPD was diagnosed in 339 (11.0%) of the patients with AF. The patients with COPD had significantly more risk factors and comorbidities, including diabetes mellitus and chronic HF, and they were significantly less likely to have received a prescription for a β-blocker. After 1 year of follow-up, patients with AF and COPD were significantly more likely to have died from a CV cause or from any cause, and were significantly more likely to have experienced a thromboembolic event, bleeding or CV-related death. A Cox regression analysis identified COPD as an independent predictor of all-cause mortality (HR 1.55 [95% CI 1.05–2.28]).

Comment: In this European study (note higher smoking rates and therefore COPD more prevalent than in Australia) COPD was independently associated with all-cause mortality in AF patients. Note that β-blockers are often withheld in COPD patients, often unnecessarily, and likely contribute to the findings.

Reference: Am Heart J 2016;181:83–91

Screening for atrial fibrillation in 13 122 Hong Kong citizens with smartphone electrocardiogram

Authors: Chan N-Y & Choy C-C

Summary: These authors reported on the feasibility of a community screening programme for AF using a smartphone-based wireless single-lead ECG in 13,122 Hong Kong citizens. Only 0.4% of the single-lead ECG recordings could not be interpreted. New AF was diagnosed in 101 participants, with 66 being asymptomatic. Participants with newly diagnosed AF had a mean CHA2DS2-VASc score of 3.1. The respective prevalence rates for AF detected by single-lead ECG only and by single-lead ECG or self-report were 1.8% and 8.5%. A multivariable logistic regression analysis revealed that AF was independently predicted by age, sex, height, bodyweight, body mass index, HF history, valvular heart disease, stroke, hyperlipidaemia, coronary artery disease, peripheral artery disease and cardiothoracic surgery.

Comment: Many Australian cardiologists (and some patients!) now own the AliveCor device as used in this study. Only 0.4% of traces were ‘uninterpretable’ confirming this product’s high quality. There was a steep rise in AF detection with age >60 years and >40% of AF was previously undiagnosed, with a mean CHA2DS2-VASc score of 3.1 – the implication being that many new patients would be anticoagulated. What we do with this from a public health perspective remains to be seen.


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Safety and clinical outcomes of catheter ablation of atrial fibrillation in patients with chronic kidney disease

Authors: Ullal AJ et al.

Summary: Safety and clinical outcomes were reported according to renal disease for 21,091 patients who underwent AF ablation, 1593 (7.6%) of whom had CKD. Compared with patients without CKD, those with CKD were significantly older (64 vs. 59 years [p<0.001]), had higher CHA2DS2-VASc scores (3.2 vs. 1.8 [p<0.001]) and were more likely to be hospitalised for HF (2.1% vs. 0.4% [p<0.001]), but did not differ significantly for 30-day rates of stroke/transient ischaemic attack (0.13% vs. 0.13%), perforation/tamponade (2.3% vs. 3.1%) or vascular complications (2.4% vs. 2.2%). A multivariate analysis revealed that CKD did not significantly impact on the 1-year risk of hospitalisation for AF (adjusted HR 1.02 [95% CI 0.87–1.20]), cardioversion (0.99 [0.87–1.12]) or repeat AF ablation (0.89 [0.76–1.06]).

Comment: Although renal failure is generally linked to complications in a wide range of CV interventions as well as ischaemic stroke and major haemorrhage, it’s comforting to see here that these ‘high-risk patients’ appeared to have equal risk and efficacy from this invasive procedure (AF ablation).


Abstract

Impact of baseline stroke risk and bleeding risk on warfarin international normalized ratio control in atrial fibrillation

Authors: Hellyer JA et al.

Summary: Associations between baseline stroke, bleeding risk and time in INR therapeutic range were explored in 167,190 participants with newly diagnosed AF treated with warfarin in TREAT-AF, a retrospective cohort study of the US Veterans Health Administration. The proportion of patients with time in INR therapeutic range of >65% decreased across increasing CHA2DS2-VASc and HAS-BLED score strata, with significant associations between the odds of achieving time in INR therapeutic range of >65% and high CHA2DS2-VASc and HAS-BLED scores. The rate of INR monitoring did not differ significantly across risk strata.

Comment: This interesting finding is worth bearing in mind when selecting appropriate anticoagulation in high-risk patients – although we may feel we have more 'control' with warfarin, in fact carefully selected NOAC (nonvitamin K oral anticoagulant) therapy may well be the better option.


Abstract

Atrial Fibrillation among patients with atrial fibrillation undergoing intracoronary stenting treated with 2 treatment strategies of rivaroxaban or a dose-adjusted oral vitamin K antagonist treatment strategy

Authors: Gibson CM et al.

Summary: Stented patients with nonvalvular AF (n=2124) were randomised 1:1:1 to receive: i) rivaroxaban 15mg daily plus a P2Y12 inhibitor for 12 months; ii) rivaroxaban 2.5mg twice daily with stratification to a prespecified duration of DAPT of 1, 6 or 12 months; or iii) dose-adjusted VKA daily with a similar DAPT stratification. Compared with the VKA plus DAPT arm, the risk of all-cause mortality or recurrent hospitalisation was lower in the rivaroxaban plus P2Y12 inhibitor and rivaroxaban plus DAPT arms (34.9% and 31.9%, respectively, vs. 41.9%; respective HRs 0.79 [95% CI 0.66–0.94] and 0.75 [0.62–0.90]; respectively needed numbers to treat, 15 and 10), as were the risks of all-cause death plus hospitalisation potentially resulting from bleeding (8.6% and 8.0% vs. 12.4% [respective p values 0.032 and 0.012]) and all-cause death plus potentially CV-related rehospitalisation (21.4% and 21.7% vs. 29.3% [0.001 and 0.011]); other forms of rehospitalisation did not differ significantly.

Comment: This remains a highly topical and frequently encountered clinical scenario (AF patients receiving stents). This further analysis of PIONEER (which showed less bleeding with rivaroxaban versus warfarin) suggests an all-cause mortality and rehospitalisation benefit with both rivaroxaban regimens compared with warfarin.

Reference: Circulation 2017;135(4):323–33

Abstract

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Alcohol and atrial fibrillation: a sobering review

Authors: Voskoboinik A et al.

Summary: These Australian authors comprehensively reviewed the role of alcohol consumption in AF, including the place of abstinence for patients with AF. They discuss the effects of alcohol on electrophysiology, the autonomic system and the structure of the atria. The contributions of alcohol consumption on hypertension, obesity and sleep-disordered breathing are also mentioned. The authors also note the impact of excessive (binge) alcohol consumption on emergency department visits resulting in diagnoses of AF, particularly during holiday periods, but also an increased risk of AF even with habitual moderate drinking. They caution that the cardioprotective effects of the consumption of small amounts of alcohol do not extend to AF.

Comment: This excellent review made the local Melbourne mainstream media and is important reading. We have known for some time that even modest regular alcohol intake predisposes to the subsequent development of AF and this paper is a synthesis of the currently available data in this respect. It also reminds us of the beneficial effects of regular alcohol intake.

Reference: J Am Coll Cardiol 2016;68(23):2567–76

Insulin-requiring versus noninsulin-requiring diabetes and thromboembolic risk in patients with atrial fibrillation

Authors: Patti G et al.

Summary: This analysis of individual participant data from the PREFER in AF study assessed thromboembolic risk in 5717 patients with AF, including 1288 with diabetes, of whom 22.4% required insulin. Compared with nondiabetics and diabetics not receiving insulin, diabetics treated with insulin were significantly more likely to have experienced a stroke/systemic embolism at 1 year (5.2% vs. 1.9% and 1.8%, respectively; HRs 2.89 [95% CI 1.67–5.02] and 2.96 [1.49–5.87]), with no significant difference between nondiabetics and diabetics not receiving insulin; the increased risk among insulin recipients was independent of potential confounders (e.g., diabetes duration) and persisted in various subpopulations (including anticoagulant therapy recipients).

Comment: Diabetes and AF have a complex inter-relationship with one predisposing to the other. Diabetes is of course an independent stroke risk factor and confers 1 point in the CHA₂DS₂-VASc score. The findings of this registry suggest that diabetes not requiring insulin therapy may be a weaker stroke predictor than previously appreciated, but insulin-requiring diabetes is a strong risk factor.

Reference: J Am Coll Cardiol 2017;69(4):409–19

Abstract

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