Welcome to issue 24 of Atrial Fibrillation Research Review.

We begin this issue with Australian research reporting that a diagnosis of OSA (obstructive sleep apnoea) and its severity are independent predictors of incident AF. Other research included found that postoperative AF independently predicted late AF, while an independent association was seen between late, but not postoperative, AF and long-term mortality. Two studies have reported on systemic embolism in AF, and another two have explored relationships between physical activity and AF. This issue concludes with a randomised trial showing no benefit of a strategy of early initiation and interruption of anticoagulation based on remotely detected atrial tachyarrhythmia in patients with implanted defibrillators.

I hope you find the research selected relevant to your everyday practice. I appreciate your feedback, questions and suggestions, so please keep them coming.

Kind Regards,
Dr Andrei Catanchin
andrei.catanchin@researchreview.com.au

Severity of OSA is an independent predictor of incident atrial fibrillation hospitalization in a large sleep-clinic cohort

Authors: Cadby G et al.

Summary: These researchers explored the impact of OSA on AF risk in 6841 sleep clinic attendees referred for possible OSA whose data were linked to hospital data to determine hospitalisation for incident AF. AF was recorded for 455 of the sleep clinic attendees during follow-up of median 11.9 years. Multivariable independent predictors of incident AF were an AHI (apnoea-hypopnea index) >5 per hour (adjusted HR 1.55 [95% CI 1.21–2.00]), log AHI+1 (1.15 [1.06–1.26]) and log time with O2 saturation <90%+1 (1.12 [1.06–1.19]). No interaction was seen between AHI and age, sex or body mass index for AF development.

Comment: This West Australian study reminds us of the importance of sleep apnoea, an accepted risk factor for AF. OSA is frequently associated with obesity, hypertension and other factors that are also important in creating the AF substrate over time. Here we see that OSA itself is independently related to AF (seemingly related to degree and duration of hypoxia), and there appears to be a dose response with the most severe OSA carrying the highest risk of long-term AF.


Abstract

Independent commentary by Dr Andrei Catanchin, a cardiologist/electrophysiologist specialising in the management of AF and other arrhythmias in private practice in Melbourne. Dr Catanchin has a particular expertise in the management of AF and other rhythm disorders. He performs catheter ablation for AF and other arrhythmias, implant pacemakers and ICDs (defibrillators) and his research interests include alternatives to warfarin in AF management.

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**Trends and predictors of readmission after catheter ablation for atrial fibrillation, 2009–2013**

**Authors:** Noseworthy PA et al.

**Summary:** Rates of readmission after catheter ablation for AF were estimated and predictors were identified using administrative claims data for 10,705 procedures over a 5-year period. The 90-day all-cause readmission rate was 15.6% and the 90-day readmission rate with AF as the primary diagnosis was 5.4%. Furthermore, both the 90-day all-cause and AF-related readmission rates declined from 15.6% to 12.8% (p=0.04) and from 6.4% to 5.0% (p=0.03), respectively, over the study period. A multivariate analysis revealed that the risk of readmission was associated with earlier year of ablation and with nine chronic conditions (alone or in combination).

**Comment:** A number of potential factors have resulted in reduced hospital readmission following AF ablation, including technological improvements and other procedural advancements as well as better patient selection and perhaps more appropriate procedure/patient matching.

**Reference:** Am Heart J 2015;170(3):483–9

**Implications of new-onset atrial fibrillation after cardiac surgery on long-term prognosis**

**Authors:** Melduni RW et al.

**Summary:** This community-based research followed 603 residents from a US county with no prior documented AF history at baseline, who underwent coronary artery bypass graft and/or valve surgery, for mean 8.3 years, during which they were monitored for first late AF or death at >30 days postoperatively. Compared with individuals who had no postoperative AF, those who did had a lower rate of freedom from late AF (57.4% vs. 86.9% [p<0.001]). The late AF risk was greatest (18%) within the first year. Postoperative AF was an independent predictor of late AF (adjusted HR 3.52 [95% CI 2.42–5.13]) but not long-term mortality (1.16 [0.87–1.55]), whereas late AF was an independent predictor of long-term mortality (3.25 [2.42–4.35]). Diastolic dysfunction was also found to independently influence long-term mortality and late AF risk.

**Comment:** This very common ‘complication’ of cardiac surgery is often asymptomatic but prolongs the hospital admission and is associated with subsequent adverse outcomes, so a rhythm control approach is usually implemented, accompanied by anticoagulation if duration is prolonged, rhythm control is unsuccessful or AF develops late in the postoperative period. How long to then continue anticoagulation remains controversial – this study would suggest a longer period to be reasonable.

**Reference:** Am Heart J 2015;170(4):659–68

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**Systemic, noncerebral, arterial embolism in 21,105 patients with atrial fibrillation randomized to edoxaban or warfarin**

**Authors:** Geller BJ et al.

**Summary:** This was a prespecified analysis of 21,105 ENGAGE AF-TIMI-48 trial participants who had received high- or low-dose edoxaban or warfarin once daily for the prevention of stroke and systemic embolic events. Among 1016 participants who met the primary endpoint, the systemic embolic event rate was 6.6%, 13% of which were fatal. Extremities were affected in 85% of the 73 systemic embolic events, and 41% required surgical or percutaneous intervention. Systemic embolic events did not differ significantly between high- and low-dose edoxaban versus warfarin recipients (respective HRs 0.65 [95% CI 0.34–1.24] and 1.24 [0.72–2.15]). A meta-analysis of four warfarin-controlled phase 3 AF trials revealed a significant reduction in the systemic embolic event risk with NOAC use (RR 0.63 [95% CI 0.43–0.91]).

**Comment:** We are reminded that not all thromboembolic complications of AF involve the brain, and it’s interesting to note that 85% of systemic embolic events in the ENGAGE study involved limbs. Organs with end-arteries and poor vascular watershed such as the heart and gut (with poorer clinical outcomes), although receiving more of the cardiac output, were less represented. NOACs prevent systemic embolic events more effectively than warfarin.

**Reference:** Am Heart J 2015;170(4):669–74

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For more information click here
Extracranial systemic embolic events in patients with nonvalvular atrial fibrillation

Authors: Bekwelem W et al.

Summary: This research explored the incidence, risk factors for and outcomes following suspected systemic embolic events that were reported in 37,973 anticoagulated randomised trial participants with AF who were independently re-adjudicated for clinical and objective evidence of sudden loss of perfusion of a limb or organ. There were 221 systemic embolic events involving 219 participants over 91,746 participant-years; the respective incidences of systemic embolic events and stroke were 0.24 and 1.92 per 100 participant-years. Participants experiencing systemic embolic events were more likely than those experiencing stroke to be female (56% vs. 47% [p=0.01]), whereas age and mean CHADS2 scores were comparable. Most systemic embolic events (56%) involved the lower extremities, 31% were visceral and 10% were upper extremity. Most participants with systemic embolic events (60%) required endovascular or surgical intervention, 30% were hospitalised but did not require a procedure, 5% required amputation and 5% were managed with clinic assessments alone. The 30-day full recovery rate was 54%, 20% survived with deficits and the 30-day mortality rate was 25%; the latter was greater after visceral-mesenteric than lower- and upper-extremity systemic embolic events (55% vs. 17% and 9%, respectively [p<0.0001]). Compared with participants with neither event, those who experienced systemic embolic events and stroke during follow-up were at significantly increased risk of death (respective RRs 4.33 [95% CI 3.29–5.70] and 6.79 [6.22–7.41]).

Comment: This is the largest ever description of extracerebral embolic events, covering four large AF trials (ACTIVE-A, ACTIVE-W, AVERROES and RELY-NB), only the last had effective anticoagulation in both study arms and systemic embolic event rates were far lower). The legs were the commonest site affected (60%), followed by vescera (30%). Factors more prevalent in systemic embolic events in comparison with stroke included female sex, smoking, previous systemic embolic events, myocardial infarction and peripheral vascular disease; there were 8 times more strokes than systemic embolic events.

Reference: Circulation 2015;132(9):796–803

Abstract

Physical activity is associated with a reduced risk of atrial fibrillation in middle-aged and elderly women

Authors: Drc Na et al.

Summary: These researchers obtained physical activity information from 36,513 women free of AF at enrolment in a Swedish mammography programme to investigate the impact of different types of physical activity on the development of AF, which was determined from inpatient registry records. There were 2915 cases of AF diagnosed over median 12 years of follow-up. Compared with <1 hour of leisure-time exercise per week at study entry, ≥4 hours decreased the risk of developing AF (adjusted RR 0.85 [95% CI 0.75–0.95]), as did ≥40 minutes per day versus ‘almost never’ of walking/cycling (0.81 [0.72–0.92]).

Comment: In contrast to a recent similar study in men, this analysis shows a protective effect of exercise in women, including higher intensity training in youth. This area needs further exploration in (both sexes). Currently both extremes of physical activity (i.e. absent/low and high/extreme) can be considered risk factors for AF.


Abstract

Relation of physical activity and incident atrial fibrillation

Authors: Bapat A et al.

Summary: The relationship between physical activity and AF was explored using data from a diverse population of 8793 individuals without clinically recognised cardiovascular disease from the MESA (Multi-Ethnic Study of Atherosclerosis) database; 199 cases of AF were recorded over mean 7.7 years of follow-up. No association was seen between vigorous physical activity or total intentional exercise and incident AF after adjusting for covariates in the overall MESA population. However, among individuals reporting any vigorous physical activity, the risk of AF was significantly lower for those in the top tertile of total intentional exercise versus those with no total intentional exercise (adjusted HR 0.46 [95% CI 0.22–0.98]).

Comment: This study showed no relationship between higher levels of exercise and AF (and if anything AF was reduced in these patients). Note that these patients were not athletes and the highest level of activity here was lower than in previous studies linking endurance training to AF in later life.


Abstract

A comparison of atrial fibrillation monitoring strategies after cryptogenic stroke

Authors: Choe WC et al., for the CRYSTAL AF Investigators

Summary: These researchers compared a range of simulated intermittent monitoring strategies with continuous rhythm monitoring in a cohort of 168 patients with cryptogenic stroke from the CRYSTAL-AF (Cryptogenic Stroke and Underlying Atrial Fibrillation) trial; short-term (single 24-hour, 48-hour and 7-day Holter, and 21-day and 30-day event recorders) and periodic (quarterly 24-hour, 48-hour and 7-day Holter, and monthly 24-hour Holter) strategies were evaluated. The 24-hour Holter had the lowest (1.3%) and the 30-day event recorder the highest (22.8%) sensitivity for a single monitoring period for diagnosing AF, and the sensitivity of quarterly 24-hour Holter monitoring was 3.1%, but this increased to 20.8% with quarterly 7-day monitors. The single external monitoring strategies had NPVs (negative predictive values) of 82.3–85.6%, and repetitive periodic monitoring strategies had NPVs of 82.6–85.3%. Long-term continuous monitoring was significantly better than any of the intermittent monitoring strategies for detecting AF.

Comment: We have long known that some form of monitoring for AF is needed in cryptogenic stroke and implantable monitors represent a highly accurate and very well-tolerated approach, with increasingly high yield with longer term monitoring. It’s likely we’ll see this incorporated into guidelines as an accepted indication soon.


Abstract
Excessive atrial ectopy and short atrial runs increase the risk of stroke beyond incident atrial fibrillation

Authors: Larsen BS et al.

Summary: Whether increased atrial ectopy and short atrial runs increase stroke risk beyond incident AF was investigated in this analysis of 15-year data from a cohort of 678 individuals enrolled in the Copenhagen Holter Study with no earlier history of cardiovascular disease, stroke or AF. Excessive supraventricular ectopic activity was recorded for 15% of the cohort. An association was seen between excessive supraventricular ectopic activity and ischaemic stroke when participants were censored by time of AF (adjusted HR 1.96 [95% CI 1.10–3.49]) and when AF was modelled as time-varying exposure (2.00 [1.16–3.45]). Among participants with excessive supraventricular ectopic activity who experienced stroke, AF was recorded in 14.3% before their stroke. Participants with excessive supraventricular ectopic activity and a CHA2DS2-VASc score of ≥2 had a stroke incidence (2.4% per year) that was comparable with the risk observed in AF. A day-to-day analysis revealed that excessive supraventricular ectopic activity was consistent.

Comment: Frequent and multiple atrial premature beats (30 premature atrial contractions per hour or any >20-beat atrial runs in this study) predict AF and therefore stroke. Excessive supraventricular ectopic activity has high day-to-day reproducibility, as distinct from AF, which can easily be missed on random-day Holter monitoring. So should it be used as a surrogate marker of stroke risk? We need a trial randomising subjects with excessive supraventricular ectopic activity to ‘rhythm control’ and anticoagulation.


Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices

Authors: Martin DT et al., on behalf of the IMPACT Investigators

Summary: Patients with dual-chamber or biventricular defibrillators (n=2718) were randomised to start and stop anticoagulation based on remote rhythm monitoring or usual office-based follow-up; anticoagulation was established using standard clinical criteria. Atrial tachyarrhythmia occurred in 945 participants (34.8%), 264 of whom met criteria for anticoagulation. The confirmed AF or atrial flutter rate was 91%, and median time to start of anticoagulation was significantly shorter in the intervention arm than the control arm (3 vs. 54 days [p<0.001]); however, there was no difference for primary endpoint events (stroke, systemic embolism or major bleeding; 2.4 vs. 2.3 per 100 patient-years [p=0.732]) and the trial was terminated after median 2 years follow-up for futility. There was also no significant between-group difference for major bleeding, or for thromboembolism among patients with atrial tachyarrhythmia. No temporal relationship between atrial tachyarrhythmia and stroke despite an association between atrial tachyarrhythmia burden and thromboembolism.

Comment: The concept is attractive – only use anticoagulation during and after episodes of AF. However, accurate continuous rhythm monitoring in this complex study using anticoagulation (81% warfarin, remainder NOACs) according to perceived stroke risk did not improve outcomes compared with conventional management. More AF carried a higher stroke risk, but stroke events were not temporally associated with AF.

Reference: Eur Heart J 2015;36(26):1660–8

Abstract

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