

Atrial Fibrillation Research Review™

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Issue 39 - 2017

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Abbreviations used in this issue:

AF = atrial fibrillation; CA = cancer antigen;
ECG = electrocardiography; HR = hazard ratio;
LAA = left atrial appendage; NOAC = nonvitamin K oral anticoagulant;
(NT-pro)BNP = (N-terminal pro-) B-type natriuretic peptide;
OR = odds ratio.

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Welcome to issue 39 of Atrial Fibrillation Research Review.

A Danish study comparing the effectiveness and safety of standard-dose NOACs and warfarin in patients with AF and a single risk factor for stroke begins this issue. I have also included the latest guidelines update from the EHRA (European Heart Rhythm Association) regarding the use of NOACs in patients with nonvalvular AF. Researchers from the US report that a significant proportion of patients ineligible for warfarin who received NOACs experienced repeat major bleeding, whereas there was a high success rate with LAA occlusion devices in high-risk patients. To conclude this issue, a German study has shown that the incidence of LAA thrombus in patients scheduled for catheter ablation of AF is low, supporting the current recommendations for NOACs and dispensing of transoesophageal echocardiography in patients with a CHA₂DS₂VASc score ≤1.

Thank you for all your valuable feedback and suggestions – please keep them coming.

Kind Regards,

Dr Andrei Catanchin

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Effectiveness and safety of standard-dose nonvitamin K antagonist oral anticoagulants and warfarin among patients with atrial fibrillation with a single stroke risk factor

Authors: Lip GYH et al.

Summary: The effectiveness and safety of dabigatran 150mg twice daily, rivaroxaban 20mg once daily and apixaban 5mg twice daily were compared with warfarin in an observational cohort of 14,020 Danish registry patients with AF and one low-risk, nongender-related risk factor for stroke. There was no significant difference between NOAC and warfarin recipients for ischaemic stroke/systemic embolism across strata. Compared with warfarin recipients, the incidences of 'any bleeding' were lower for apixaban and dabigatran recipients (respective HRs 0.35 [95% CI 0.17–0.72] and 0.48 [0.30–0.77]) but not for rivaroxaban recipients (0.84 [0.49–1.44]). Sensitivity analyses revealed broad consistency across most subgroups and between 1- and 2.5-year follow-up analyses; however, falsification endpoints generally did not falsify, suggesting that residual confounding may have been present across these comparisons.

Comment: It's comforting to confirm these NOACs have lower bleeding risks than warfarin even in low-risk patients. Remember that current guidelines state that anticoagulation 'should be considered' in patients with a CHA₂DS₂VASc score of 1, as compared with 'should be recommended' for CHA₂DS₂VASc scores of 2 or higher.

Reference: *JAMA Cardiol* 2017;2(8):872–81

[Abstract](#)

Alcohol consumption, sinus tachycardia, and cardiac arrhythmias at the Munich Oktoberfest

Authors: Brunner S et al.

Summary: The MunichBREW study enrolled 3028 volunteers attending the Munich Oktoberfest and obtained ECG and breath alcohol concentration measurements using a smartphone-based system; the study also evaluated cardiac arrhythmias with chronic alcohol consumption in 4131 participants from the community-based KORA S4 study. In the Munich Oktoberfest cohort, mean breath alcohol concentration was 0.85 g/kg, and 25.9% of the volunteers experienced sinus tachycardia and 5.4% experienced other arrhythmias. Each unit increase in breath alcohol concentration was associated with an increased likelihood of any cardiac arrhythmia (OR 1.75 [95% CI 1.50–2.05]), especially sinus tachycardia (1.96 [1.66–2.31]). Alcohol consumption was associated with a significant reduction in respiratory sinus arrhythmia measuring autonomic tone. In the KORA S4 cohort, chronic alcohol consumption increased the likelihood of sinus tachycardia (OR 1.03 [95% CI 1.01–1.06]).

Comment: There are no surprises here; alcohol causes sinus tachycardia in a dose-dependent fashion. No significant relationship with AF was seen in this study methodology; ECGs were only taken during alcohol consumption and we know AF often occurs hours afterward, so this would have to be confirmed with a different study method (e.g. more prolonged ECG monitoring).

Reference: *Eur Heart J* 2017;38(27):2100–6

[Abstract](#)

Updated European Heart Rhythm Association practical guide on the use of non-vitamin-K antagonist anticoagulants in patients with non-valvular atrial fibrillation

Authors: Heidbuchel H et al.

Summary: This paper reported the Executive Summary of the EHRA regarding updated guidance on NOAC use in patients with nonvalvular AF. The 15 clinical scenarios outlined in the previous 2013 version were preserved, but all the chapters have been rewritten. The main changes are: i) the definition of 'nonvalvular AF' and eligibility for NOACs; ii) inclusion of information on edoxaban; iii) tailored dosing information dependent on concomitant medications and/or clinical characteristics; iv) an expanded chapter on neurological scenarios; v) an updated anticoagulation card; and vi) more specific information on start-up and follow-up issues. Many flowcharts have been added, including the appropriateness of switching between vitamin K antagonists and NOACs, default scenarios for the acute management of coronary interventions, step-down protocols for long-term combined antiplatelet-anticoagulant management in patients with coronary heart disease, bleeding management and cardioversion for NOAC recipients.

Comment: This excellent publication contains an updated synthesis of the available evidence for NOACs and their use, and is a strongly recommended resource and reference for all anticoagulation prescribers.

Reference: *Eur Heart J* 2017;38(27):2137–49

[Abstract](#)

Cancer antigen-125 plasma level as a biomarker of new-onset atrial fibrillation in postmenopausal women

Authors: Sekiguchi H et al.

Summary: The relationship between plasma CA (cancer antigen)-125 level and new-onset AF was explored in 746 postmenopausal women. AF was recorded in 31 women during a 10-year observation period. Compared with women who did not experience AF, those who did were older (mean age 75 vs. 68 years) and had higher plasma levels of CA-125 (11.4 vs. 7.7 U/mL [$p<0.01$]) and high-sensitivity C-reactive protein (0.10 vs. 0.07 mg/dL [$p<0.05$]); independent predictors of AF were age (HR 1.3 [95% CI 1.08–1.57]) and plasma CA-125 level (1.29 [1.10–1.51]).

Comment: In line with a number of other well-described biomarkers associated with AF (e.g. troponin, BNP, C-reactive protein), we now see this tumour marker added to the list. Advancing age is of course well accepted as a predictor. These results support the increasingly clear notion of AF as a 'systemic' disease.

Reference: *Heart* 2017;103(17):1368–73

[Abstract](#)

N-terminal pro B-type natriuretic peptide in systematic screening for atrial fibrillation

Authors: Svennberg E et al.

Summary: The value of NT-proBNP level measurements for detecting AF during systematic screening was explored in the Strokestop study of 7173 Swedish residents aged 75–76 years who were screened for AF using twice-daily intermittent ECG recordings over 2 weeks. NT-proBNP levels were determined in a substudy of 815 consecutive participants and 71 individuals with newly detected AF. Compared with participants without AF ($n=742$), those with newly detected AF ($n=96$) had a higher median NT-proBNP level (330 vs. 171 ng/L [$p<0.001$]). There were no significant differences in CHA₂DS₂-VASc parameters between participants with newly detected AF versus those without AF, nor between those with newly detected AF in the NT-proBNP cohort versus the cohort in which NT-proBNP levels were not measured. An NT-proBNP cutoff of ≥ 125 ng/L in a nonacute setting resulted in a negative predictive value of 92%, translating into 35% fewer patients requiring systematic AF screening; the number requiring screening fell further, with no impact on sensitivity, when bodyweight was added to NT-proBNP level.

Comment: We know BNP is a biomarker associated with AF and it seems low BNP levels might predict against AF, but we are a long way from incorporating this into wider screening programmes.

Reference: *Heart* 2017;103(16):1271–7

[Abstract](#)



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Chocolate intake and risk of clinically apparent atrial fibrillation: the Danish Diet, Cancer, and Health Study

Authors: Mostofsky E et al.

Summary: The impact of chocolate consumption on incident clinically apparent AF or atrial flutter was explored using data from 55,502 participants from the Danish Diet, Cancer, and Health prospective cohort study. There were 3346 cases of AF/flutter recorded over a median follow-up period of 13.5 years. Compared with chocolate intake rate of less than once per month, chocolate consumption rates of 1–3 servings per month, 1 serving per week, 2–6 servings per week and ≥ 1 serving per day were associated with lower AF/flutter rates (respective HRs 0.90 [95% CI 0.82–0.98], 0.83 [0.74–0.92], 0.80 [0.71–0.91] and 0.84 [0.65–1.09]); the results were similar for men and women when analysed separately.

Comment: Chocolate (and other caffeine) intake is known to be relatively 'protective' when it comes to AF in population studies, possibly by subtly increasing baseline heart rate. As in all observational studies, it's not possible to exclude confounding, and it's unlikely this will be able to be proven prospectively.

Reference: *Heart* 2017;103(15):1163–7

[Abstract](#)

Role of the burden of premature atrial contractions during the blanking period following second-generation cryoballoon ablation in predicting late recurrences of atrial arrhythmias

Authors: Coutiño H-E et al.

Summary: The impact of the burden of premature atrial complexes for predicting atrial arrhythmia recurrence was assessed in 107 consecutive, retrospectively included patients with drug-resistant paroxysmal AF who underwent index pulmonary vein isolation using second-generation cryoballoon ablation. Compared with patients who experienced ≤ 76 premature atrial complexes per day, those who experienced more had a higher atrial arrhythmia recurrence rate (47.5% vs. 11.9% [$p < 0.001$]). A multivariate analysis revealed that > 76 documented premature atrial complexes per day registered at 1 month and at the end of a blanking period were predictors of late atrial arrhythmia recurrence.

Comment: Although 76 atrial extrasystoles per day would not be considered clinically frequent or relevant by most, in fact this predicted recurrent AF postablation and suggests these extrasystoles may be AF triggers, presumably from pulmonary veins.

Reference: *J Interv Card Electrophysiol* 2017;49(3):329–35

[Abstract](#)



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Replacing warfarin with a novel oral anticoagulant: risk of recurrent bleeding and stroke in patients with warfarin ineligible or failure in patients with atrial fibrillation (The ROAR study)

Authors: Turagam MK et al.

Summary: Outcomes were reported for 263 warfarin-ineligible patients with AF who received NOACs. The repeat major bleeding event rate on NOAC therapy was 63%, and this was greater in patients with versus without prior gastrointestinal bleeding (74.5% vs. 30% [$p < 0.0001$]). The repeat systemic thromboembolism rate was 5%, and these patients had a higher mean CHA₂DS₂VASc score than those who did not experience repeat systemic thromboembolism (6.5 vs. 3.3 [$p = 0.001$]). Interventions to manage repeat major bleeding events were administered to ~34% of affected patients. Successful LAA occlusion device use was recorded for 67% of high-risk patients who underwent interventions to manage major bleeding events.

Comment: We don't yet have comparison data for the NOACs and LAA occlusion devices, but this study shows that major bleeding on warfarin is likely to recur on alternative anticoagulation; for these patients LAA occlusion/exclusion remains the only alternative option for stroke prevention. Recall that aspirin is not adequate and also causes major bleeding.

Reference: *J Cardiovasc Electrophysiol* 2017;28(8):853–61

[Abstract](#)

Catheter ablation for the treatment of atrial fibrillation is associated with a reduction in health care resource utilization

Authors: Samuel M et al.

Summary: These researchers analysed data from a cohort of 1556 patients who had undergone catheter ablation for AF in Canada to evaluate the impact of the procedure on long-term healthcare resource utilisation. There were progressive increases in hospitalisations, emergency department visits, outpatient visits, cardioversions and echocardiograms during the 24 months prior to index catheter ablation ($p < 0.05$ for all trends). Decreases were seen for all-cause hospitalisations, AF hospitalisations, emergency department visits, cardioversions and echocardiograms during the 12 months after index catheter ablation compared with the 12 months prior ($p < 0.05$ for all trends), with continued declines out to 24 months for all-cause hospitalisations, cardioversions and echocardiograms ($p < 0.05$ for all trends).

Comment: The cost effectiveness of AF ablation has long been well established. This report goes further and nicely demonstrates the incremental costs as AF progresses, then a clear reversal with ablation and continued decline in cost out beyond 2 years.

Reference: *J Cardiovasc Electrophysiol* 2017;28(7):733–41

[Abstract](#)

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RESEARCH REVIEW

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Risk stratification of patients with left atrial appendage thrombus prior to catheter ablation of atrial fibrillation: an approach towards an individualized use of transesophageal echocardiography

Authors: Gunawardene MA et al.

Summary: Risk factors for LAA thrombus prior to AF catheter ablation in daily clinical practice, according to guideline-recommended oral anticoagulation strategies (withheld 24-hours preablation or continuous vitamin K antagonists [international normalised ratio 2.0–3.0]), were identified in a group of 1658 patients; all patients underwent preprocedural transoesophageal echocardiography on the day of ablation. The patients were grouped into those with (n=13) and without LAA thrombus. None of the 640 patients with a CHA₂DS₂VASc score of ≤1 experienced LAA thrombus, regardless of underlying AF type. Independent predictors for LAA thrombus were higher CHA₂DS₂VASc scores (OR 1.54 [95% CI 1.07–2.23]), history of nonparoxysmal AF (7.96 [1.52–146.64]), hypertrophic cardiomyopathy (9.63 [1.36–43.05]) and left ventricular ejection fraction <30% (8.32 [1.18–36.29]); oral anticoagulation type was not a significant predictor.

Comment: Transoesophageal echocardiography is usually performed for a number of reasons: to exclude LAA thrombus and to guide trans-septal puncture and other aspects of the ablation procedure. In centres where this is only performed preprocedure for the exclusion of thrombus, it appears it could be omitted in low-risk patients who have received adequate anticoagulation (similar to the approach for elective cardioversion).

Reference: *J Cardiovasc Electrophysiol*; Published online July 26, 2017
[Abstract](#)

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Atrial Fibrillation Research Review™

Independent commentary by Dr Andrei Catanchin, a cardiologist/electrophysiologist specialising in the management of AF and other arrhythmias at Epworth HealthCare in Melbourne. He performs catheter ablation, implants pacemakers and ICDs (defibrillators) and his research interests include alternatives to warfarin (e.g. NOACs) in AF management. Dr Catanchin is a Senior Lecturer with the University of Melbourne, teaches at all levels and regularly presents at local and national meetings.



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