Welcome to issue 38 of Atrial Fibrillation Research Review.

This issue begins with a paper reporting more non-PV (pulmonary vein) triggers and worse long-term outcomes following catheter ablation in patients with long-standing persistent AF compared with those with paroxysmal or persistent AF. An analysis of RE-LY data found that the benefits of dabigatran over warfarin for stroke prevention and intracranial bleeding were consistent across age groups. The use of apixaban has been reported to be as safe and effective as warfarin when used as uninterrupted oral anticoagulant therapy for patients undergoing catheter-based ablation of AF. This issue concludes with an evaluation of the CAAP-AF score for predicting AF recurrence in patients with AF treated by balloon cryoablation.

I hope you are enjoying keeping up to date with the latest AF research. As always, your comments and feedback are welcome.

Kind Regards,
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Characteristics and long-term catheter ablation outcome in long-standing persistent atrial fibrillation patients with non-pulmonary vein triggers
Authors: Hung Y et al.
Summary: Characteristics and long-term outcomes were reported for patients who had undergone catheter ablation for drug-refractory AF, split into patients with paroxysmal AF (n=579), persistent AF (n=103) and long-standing persistent AF (n=94). Patients with long-standing persistent AF were more likely to be male (93.6% \(p<0.001\)) and have non-PV triggers (44.7% \(p<0.001\)), longer AF duration (6.65 years \(p=0.029\)), larger LA diameter (44.44mm \(p<0.001\)) and longer procedure times (181.94 min \(p<0.001\)). Over average follow-up of 28.53 months after first catheter ablation, the AF recurrence rate was significantly greatest in patients with long-standing persistent AF (\(p<0.001\)). Independent predictors of AF recurrence in patients with long-standing persistent AF were larger LA diameter (HR 1.063 [CI 1.018–1.111]) and non-PV triggers (1.707 [1.037–2.809]).

Comment: These findings support our current approach to AF ablation; we are less likely to embark on a rhythm control approach because outcomes are poor in persistent (versus paroxysmal) AF and in particular long-standing persistent AF (>12 months duration). More frequent non-PV triggers and larger atria are markers of more advanced and complex electrical disease.

Reference: Int J Cardiol 2017;241:205–11
Abstract

Does perceived stress increase the risk of atrial fibrillation?
Authors: Graff S et al.
Summary: The relationship between incident AF risk and high levels of perceived stress was explored in a population-based cohort of 114,337 participants from the Danish National Health Survey, among whom 2172 had a first episode of AF over 424,839 person-years of follow-up. Individuals scoring in the highest Cohen’s 10-item Perceived Stress Scale quintile had a 28% greater risk of AF than those in the lowest quintile, but the association was not significant after adjustments for comorbidities, socioeconomic status and lifestyle factors (HR 1.01 [95% CI 0.88–1.16]).

Comment: The relationship between general stress and AF is often raised by patients, but has not been conclusively demonstrated or confirmed in formal studies. An acute event or illness, however, does of course carry a higher risk of AF.

Reference: Am Heart J 2017;188:26–34
Abstract
Effects of dabigatran according to age in atrial fibrillation

Authors: Lauw MN et al.

Summary: These researchers sought to estimate the effects of dabigatran versus warfarin on stroke, bleeding and mortality according to age in participants with AF from the RE-LY trial; there were 10,855 participants aged <75 years, 4231 aged 75–79 years, 2305 aged 80–84 years and 722 aged ≥85 years at baseline. Compared with warfarin, the benefit of dabigatran 150mg twice daily and 110mg twice daily for stroke and intracranial bleeding were maintained across all age groups (p values not significant for interactions). Both the 150mg twice daily and 110mg twice daily dosages of dabigatran were associated with lower rates of extracranial major bleeding compared with warfarin in the younger participants (relative HRs 0.78 [95% CI 0.62–0.97] and 0.72 [0.57–0.90], but the risks were higher in those aged ≥80 years (1.68 [1.18–2.41] and 1.50 [1.03–2.18]; p<0.001 for interaction).

Comment: This analysis supports local Australian recommendations of using the 110mg twice daily dose for patients >75 years old (and in some groups of younger patients, e.g. high bleeding risk or renal impairment).

Reference: Heart 2017;103(13):1015–23

Abstract

Gender differences in clinical presentation and 1-year outcomes in atrial fibrillation

Authors: Schnabel RB et al.

Summary: Gender differences in AF clinical presentation, management and prognosis were explored in a cohort of 6412 European registry patients. Compared with men, women were older (mean age 74.1 vs. 70.1 years [p<0.0001]), more frequently had ≥1 AF-related symptom at least occasionally (95.4% vs. 89.8% [p<0.0001]), were less frequently treated with electrical cardioversion (14.9% vs. 20.6%) or ablation (3.3% vs. 6.3%), and were less likely to undergo coronary revascularisation (adjusted odds ratio 0.35 [95% CI 0.22–0.56]) or develop an acute coronary syndrome (0.60 [0.38–0.93]) or heart failure at 1 year (0.80 [0.68–0.96]). There were no significant differences between genders for oral anticoagulation prescriptions or 1-year stroke/transient ischaemic attack/artrial thromboembolism and major bleeding events.

Comment: It is well known that women with AF have the same (if not more) symptoms than men and suffer the same (if not more) complications of AF, but overall receive less aggressive management, and this applies to other conditions in cardiology and other fields. The current ESC AF guidelines include strong recommendations to manage women and men equally in terms of diagnosis and therapy including catheter ablation.

Reference: Heart 2017;103(13):1024–30

Abstract

Safety and efficacy of uninterrupted apixaban therapy versus warfarin during atrial fibrillation ablation

Authors: Shah RR et al.

Summary: The safety and efficacy of uninterrupted oral anticoagulant therapy with warfarin (n=310) or apixaban (n=317) were reported for patients who had undergone catheter-based AF ablation and transoesophageal echocardiography on the same day for the detection of intracardiac thrombi. Eight complications occurred among the warfarin recipients and five occurred among the apixaban recipients, with no significant difference between these two groups (p=0.38). No thromboembolic complications were reported in either group.

Comment: Although major complications are rare and therefore difficult to research, this study adds to the growing evidence for uninterrupted NOAC therapy during AF ablation, and this practice is supported by recent guidelines. Operators need to be comfortable with ablation without a reversal agent available or, as some of us are doing, change the NOAC to dabigatran for the procedure.

Reference: Am J Cardiol 2017;120(3):404–7

Abstract

Rivaroxaban for stroke prevention in patients with nonvalvular atrial fibrillation and active cancer

Authors: Laube ES et al.

Summary: The safety and efficacy of rivaroxaban was evaluated in 163 evaluable patients with active cancer and AF who had received the agent at the Memorial Sloan Kettering Cancer Center in the US. The adjusted 1-year cumulative incidences of ischaemic stroke and major bleeding were estimated to be 1.4% and 1.2%, respectively, the 1-year risk of clinically relevant nonmajor bleeding leading to anticoagulation discontinuation was 14.0%, and the 1-year cumulative mortality incidence was 22.6%, similar to that of a population of patients with active cancer. There was one death due to an acute ischaemic cerebrovascular insult.

Comment: Active cancer confers additional thromboembolic (and bleeding) risk, and in this specific population, physicians might traditionally be more comfortable using warfarin. Although with relatively small numbers, the common cancer types were well represented here and the mean CHA2DS2VASc score was 3.2. The high cancer-related mortality would in some cases outweigh the benefits of anticoagulation (which also increases bleeding), and case-by-case consideration is required.

Reference: Am J Cardiol 2017;120(2):213–7

Abstract

Comparison of the incidences of complications after second-generation cryoballoon ablation of atrial fibrillation using vitamin K antagonists versus novel oral anticoagulants

Authors: Mugnai G et al.

Summary: These authors sought to analyse procedural characteristics and complications in consecutive patients with drug-resistant AF who underwent PVI by cryoballoon ablation, and also to investigate the impact of NOACs (n=164) versus VKAs (n=290) on adverse events. NOAC recipients were significantly older than VKA recipients (62.8 vs. 56.6 years [p<0.001]). Complications included peripheral vascular complications in six patients (1.3% per procedure), persistent phrenic nerve palsy in two (0.4%) and transient ischaemic attack in one (0.2%). Major complication incidences did not differ significantly between the VKA and NOAC recipients (2.4% vs. 1.2% [p=0.5]).

Comment: This analysis of contemporary cryoballoon ablation practice is reassuring; the complication rates are lower than previous reports with either cryo- or radiofrequency ablation studies, and in particular we see a very low rate of phrenic nerve injury (traditionally cited as a major disadvantage to using this technique compared with the more prevalent radiofrequency ablation with electroanatomic mapping).

Reference: Am J Cardiol 2017;120(2):223–9

Abstract

Single freeze strategy with the second-generation cryoballoon for atrial fibrillation

Authors: De Regibus V et al.

Summary: This multicentre, international, retrospective analysis, undertaken in a cohort of 818 consecutive patients with drug-resistant AF (74.1% paroxysmal; 25.9% persistent), investigated acute success, procedural complications and clinical outcomes for a single-freeze strategy using the second-generation cryoballoon, CB-A. A mean 1.4 veins per patient required additional freezes. Phrenic nerve palsy that persisted at last follow-up was reported for 0.2% of the patients. After median follow-up of 14 months, taking into consideration a 3-month blanking period, the freedom from arrhythmia recurrence rate was 84.6%. After a single procedure, clinical recurrence after the blanking period was predicted by AF recurrence during the blanking period and persistent AF.

Comment: With the growing popularity of the cryoballoon balloon approach to AF ablation, this ‘dosing’ technique promises even shorter procedure times while maintaining excellent efficacy.


Abstract
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TM

Warfarin remains an effective anticoagulant for patients with AF*1-3

Warfarin has a similar rate of ischaemic stroke (and undefined) and SE prevention compared to DOACs (RR = 0.93, 95% CI: 0.83 to 1.04; p = 0.19)**

*Based on a meta-analysis comparing warfarin to DOACs

Warfarin may be used in patients with severe renal impairment (creatinine clearance <30 mL/min)**

Established guidelines for warfarin reversal and bridging anticoagulation therapy**

A long history of clinical use in the prevention and treatment of venous thrombosis and pulmonary embolism**

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Minimum Product Information: COUMADIN and MAREVAN (warfarin sodium). Coumadin and Marevan have NOT been shown to be bioequivalent and should not be interchanged. Indications: Prophylaxis and/or treatment of venous thrombosis and its extension and pulmonary embolism; prophylaxis and/or treatment of thromboembolic complications associated with atrial fibrillation; use as an adjunct to the treatment of coronary occlusion. Administration: Tablets for oral use. Dosage: Must be individualised for each patient according to the particular patient’s sensitivity to the drug. Adjust dose based upon results of the one-stage prothrombin time (PT). Most patients are satisfactorily maintained on 2 to 10 mg daily. (See full PI). Contraindications: Any condition or personal circumstances in which the hazard of haemorrhage might be greater than the potential clinical benefits of anticoagulation. Pregnancy: Haemorrhagic tendencies or blood dyscrasias. (See full PI for other contraindications). Precautions: Do not interchange MAREVAN® and COUMADIN®. Haemorrhage in any tissue or organ; necrosis and/or gangrene of skin and other tissues. Adverse reactions: Fatal or non-fatal haemorrhage from any tissue or organ; bleeding which occurs when the PT/INR is within the therapeutic range; necrosis of skin and other tissues. Infrequent: Hypersensitivity/allergic reactions, systemic cholesterol microembolisation, “purple toes syndrome”; hepatitis, cholestatic hepatic injury, jaundice, elevated liver enzymes, (see full PI). Drug Interactions: Warfarin is known to interact with at least 250 different drugs – refer to full PI. Presentation: COUMADIN® tablet, 1 mg (brown, scored, embossed M/3) 50s; 3 mg (blue, scored, embossed M/3) 50s; 5 mg (pink, scored, embossed M/3) 50s; MAREVAN® tablet, 1 mg (light tan, scored, embossed COUMADIN/T) 50s; 2 mg (lavender, scored, embossed COUMADIN/2) 50s; 5 mg (green, scored, embossed COUMADIN/5) 50s, Minimum PI based on Coumadin® and Marevan® PI (last amended 19 January 2010 and 17 November 2009 respectively). | References: 1. European Heart Journal Aug 2016, 67(21): D01: 10.1002/ehj.12801 2. Australian Approved Product Information for Coumadin. 3. Australian Approved Product Information for Marevan. 4. Gomez A, et al. Thrombosis 2013, Article ID 640723, 16 pages. 5. Ansell, et al. Chest 2008;133:1625-1985. 6. Tran, et. al. MJA 2013;198(4):17-7. 7. eTG complete, [Internet]. Melbourne: Therapeutic Guidelines Limited. Accessed: Aug 2017; (www.http://online.tg.org.au/complete/). | All sales and marketing requests to: Aspen Pharma Pty Ltd, 34-36 Chancos Street, St Leonards NSW 2065 | Tel: +61 2 8436 8300 | aspen@aspenpharma.com.au | www.aspenpharma.com.au | © Coumadin and Marevan are registered trade marks of Aspen Pharma Pty Limited.

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a RESEARCH REVIEW publication
Left atrial appendage volume as a new predictor of atrial fibrillation recurrence after catheter ablation

Authors: Teixeira PP et al.

Summary: Using data from 52 patients with paroxysmal and persistent AF who had undergone a first AF catheter ablation preceded by contrast-enhanced cardiac CT, these researchers investigated the role of LAA volume as an independent predictor of postablation AF recurrence. The respective mean LA and LAA volumes were 98.9mL and 9.3mL. PVI was successful in all patients. During 24 months of follow-up, the AF recurrence rate was 33%. Compared with patients in whom AF did not recur, those in whom it did had a significantly greater LAA volume (11.3 vs. 8.2mL [p=0.0022]). A multivariable analysis using Cox regression revealed that AF recurrence was independently predicted by LAA volume (HR 1.32 [95% CI 1.12–1.55]) and persistent AF (4.22 [1.48–12.07]). An LAA volume >8.825mL predicted AF recurrence with sensitivity and specificity of 94% and 66%, respectively.

Comment: The LAA has long been known to have arrhythmogenic potential and some studies show its resection or electrical isolation improves freedom from AF. Here we see that patients with larger LAAs were more likely to have recurrent AF postablation, and the possible mechanisms for this remain to be established.


Predicators of arrhythmia recurrence after balloon cryoablation of atrial fibrillation

Authors: Sanhoury M et al.

Summary: These authors tested the value of the CAAP-AF score for predicting AF recurrence in 283 symptomatic patients with drug-refractory AF (92% paroxysmal AF) who had undergone PVI with a second-generation cryoballoon. Hypertension was present in 31% of the patients, and 4% had coronary artery disease. Mean LA diameter was 40.6mm, mean left ventricular ejection fraction was 60.0%, mean CHA2DS2-VASc score was 1.2, and the mean number of prior failed antarrhythmic drugs was 1.4. The overall AF recurrence rate over 16 ±6 months of follow-up was 8.87%, and the respective rates for CAAP-AF scores of 0–3, 4, 5, 6, 7 and ≥8 were 3.17%, 8.47%, 16.28%, 6.67%, 23.08% and 36.36%. At a CAAP-AF score cutoff of 5, the AF recurrence rate for scores <5 was 4.86%, whereas it was 16.49% for higher scores; this cutoff predicted AF recurrence with sensitivity and specificity values of 64% and 68%, respectively.

Comment: This neat scoring system synthesizes what we know about efficacy of rhythm control in AF (be it with drugs or ablation); larger atria, older age and persistent AF present more challenges. Coronary disease, female sex and failed drug therapy are further predictors.


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