Welcome to issue 28 of Atrial Fibrillation Research Review.

This issue begins with Australian research reporting that PVI by single ring isolation is associated with minimal adverse effects on LA function during medium-term follow-up, despite isolating a larger region of the LA myocardium. Other research included showed that procedural safety during LAA occlusion with the Amplatzer™ cardiac plug for the prevention of AF-related thromboembolism was similar between patients with and without chronic kidney disease. There is also research from our colleagues across the Tasman reporting that warfarin anticoagulation in dialysis patients with AF didn’t significantly reduce embolic events or mortality, and did increase the risk of intracranial bleeds. Australian research also concludes this issue, reporting on the prevalence and incidence of AF in patients before and after presentation with acute PE.

I hope you find the research selected for this issue of interest to you, and that you also find the comments helpful.

Kind Regards,
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Atrial fibrillation ablation by single ring isolation versus wide antral isolation: effects on left atrial size and function
Authors: Lee A et al.

Summary: The differential effects of PVI by single ring isolation versus wide antral isolation, for prevention of AF recurrence, on LA size (LA maximum and minimum volumes) and function (LA emptying fraction and LA expansion index) over 6 months were investigated in 187 participants from an RCT comparing the two techniques. Participants who underwent wide antral isolation had a small but statistically significant decrease from baseline in LA maximum volume at 6 months (67.3 vs. 62.7mL [p=0.02]) but no significant change in LA function. Participants who underwent single ring isolation had a small but significant reduction from baseline in LA expansion index at 6 months (80.6 vs. 66.6% [p=0.02]), but no significant change in LA maximum volume. However, there was no significant between-group difference for any of the LA size or function measures at 6 months.

Comment: Wide antral isolation involves an ablation ring around the upper and lower pulmonary vein pairs on each side (i.e. two rings). The single ring approach consists of a large ring encircling all four (or more) pulmonary veins, thereby electrically isolating all veins and the posterior wall from the remainder of the left atrium. The more extensive atrial area isolated with the single ring isolation technique did not affect measures of atrial size and function.

Reference: Int J Cardiol 2016;206:1–6
Abstract

Abbreviations used in this issue:
AF – atrial fibrillation; BMI – body mass index; CV – cardiovascular; HF – heart failure; LA(A) – left atrial (appendage); PE – pulmonary embolism; PVI – pulmonary vein isolation.

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Relation of female sex to left atrial diameter and cardiovascular death in atrial fibrillation

Authors: Prioretti M et al.

Summary: This was a post hoc analysis of available LA dimension data from 2615 AFFIRM trial participants. Two-thirds of the participants had LA enlargement. Patients with LA enlargement were more likely to be women (p = 0.032), have a higher BMI, and were more likely to have hypertension, diabetes, structural heart disease, prior coronary artery disease or HF; significant associations were seen with BMI, left ventricular mass, female sex and mitral valve insufficiency (p < 0.001). Females with AF and LA enlargement were at increased risk of CV-related death (p = 0.011), with LA diameter also showing a significant association with this outcome (p < 0.001). A Cox regression analysis confirmed that CV-related death among women with AF was independently predicted by LA diameter (p = 0.009).

Comment: More women than men with AF have atrial enlargement (diameter >38mm and >40mm for women and men, respectively) and this was associated with a higher CV mortality risk, independent of left ventricular mass, mitral valve pathology or antithrombotic therapy. Mortality in women was also related to raised BMI, diabetes and HF (in men only HF and myocardial infarction were significant).

Reference: Int J Cardiol 2016;207:258–63
Abstract

Impact of chronic kidney disease on left atrial appendage occlusion for stroke prevention in patients with atrial fibrillation

Authors: Kefer J et al.

Summary: These researchers evaluated the safety and efficacy of LA occlusion in patients enrolled in the Amplatzer™ cardiac plug multicentre registry, including 375 with and 639 without chronic kidney disease. Compared with the patients without chronic kidney disease, those with chronic kidney disease had higher CV risk scores (CHA₂DS₂VASc score, 4.9 vs. 4.2; HASBLED score, 3.4 vs. 2.9 [p < 0.001 for both]). Procedural and occlusion success rates were similarly high in all stages of chronic kidney disease at 97% and 99%, respectively, and periprocedural major adverse event and mortality rates were also similar at 5.1% and 0.8%, respectively. The respective annual stroke/transient ischaemic attack and observed bleeding rates among patients with complete follow-up (1319 patient-years) were 2.3% and 2.1%—these rates were 62% and 60% lower than expected and similar between patients with versus without chronic kidney disease. A Kaplan-Meier analysis revealed that patients with estimated GFR <30 mL/min/1.73m² had lower 1-year and 2-year overall survival rates (84% vs. 96% and 84% vs. 93%, respectively [p < 0.001]).

Comment: Patients with renal impairment (estimated GFR <60 mL/min/1.73m² here) and AF have both high stroke and bleeding risks (particularly diaylsis patients—only a small number here), as well as more procedural complications. LA occlusion may be a viable option, reducing stroke risk while avoiding the high bleeding risks of anticoagulation. Renal failure patients did not have more procedural complications than those with normal renal function in this study.

Reference: Int J Cardiol 2016;207:335–40
Abstract

Computer-guided normal-low versus normal-high potassium control after cardiac surgery: no impact on atrial fibrillation or atrial flutter

Authors: Hoekstra M et al.

Summary: Patients who had undergone coronary artery bypass graft and/or valvular surgery were assigned to a normal-low (4.0 mmol/L) or normal-high (4.5 mmol/L) potassium target in alternating blocks of 50 patients; potassium levels were regulated with GRIP-II, a validated computer-assisted potassium replacement protocol. The mean daily potassium dose in the normal-low target group was significantly lower than in the normal-high target group (30 vs. 52 mmol [p < 0.001]), resulting in a lower mean potassium concentration in the intensive-care unit (4.22 vs. 4.33 mmol/L [p < 0.001]). There was no significant difference between the normal-low and normal-high potassium target groups for the primary endpoint of AF/atrial flutter incidence on 12-lead ECG during postoperative week 1 (38% vs. 41%), and this lack of difference extended to several subgroups.

Comment: Potassium replacement in cardiac patients is a widely accepted practice. Although targeting 4.5 mmol/L (vs. 4.0 mmol/L) resulted in much more replacement, only a minor difference was seen in mean levels and there was no effect on AF. Magnesium was managed the same in both groups.

Reference: Am Heart J 2016;172:45–52
Abstract

Relationships between anticoagulation, risk scores and adverse outcomes in dialysis patients with atrial fibrillation

Authors: Wang TKM et al.

Summary: These authors reported on the management and outcomes over 4.4 ±2.5 years of follow-up for 141 patients with AF and end-stage renal failure on dialysis at a New Zealand hospital; 41.8% of the patients were receiving warfarin. The respective incidences of embolic events, ischaemic stroke, all bleeding events and intracranial bleeding events were 4.1, 3.1, 9.6 and 0.82 per 100 person-years. Patients receiving warfarin anticoagulation had a higher intracranial bleed risk (hazard ratio 11.1 [p = 0.038]), but their risks of total embolic events, bleeding events and mortality were not significantly increased. Embolic events were detected by CHADS₂, CHA₂DS₂VASc and HAS-BLED scores (c statistics 0.808–0.838), but bleeding events were not (0.459–0.498).

Comment: In keeping with previous reports in this difficult area, this New Zealand study shows warfarin in dialysis patients with AF confers greater bleeding risk, but not a reduction in thromboembolic events or mortality. Decisions remain to be made on a case-by-case basis.

Abstract

Left atrial appendage closure for atrial fibrillation is safe and effective after intracranial or intracranial hemorrhage

Authors: Fahmy P et al.

Summary: These authors reported on consecutive patients with nonvalvular AF and prior intracranial haemorrhage (n=24) or intracranial haemorrhage (n=2) who underwent LAA closure with the Amplatzer™ cardiac plug (n=9), Amplatzer™ Amulet™ (n=3) or Watchman™ (n=7) device. The patients’ mean CHADS₂, and CHA₂DS₂VASc scores were 3.2 and 4.9, respectively. There were no procedure-related complications. Over mean follow-up of 11.9 months, there was one (procedure-unrelated) death at 13 months and one patient experienced a transient ischaemic attack at 20.6 months postprocedure; no ischaemic strokes, haemorrhagic strokes or bleeding problems were recorded.

Comment: History of major haemorrhage (in particular intracerebral) is a not uncommon contraindication to anticoagulation for AF. This (albeit relatively small) study reports excellent results in this specific group of patients using contemporary LAA occlusion devices.

Reference: Can J Cardiol 2016;32(3):349–54
Abstract

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Established standards in anticoagulation therapy1,2,4

A long history of clinical use in the prevention and treatment of venous thrombosis and pulmonary embolism2,4

Reduces the relative risk of stroke by 64% in patients who have atrial fibrillation compared to placebo or no treatment5,6

1 meta-analysis: number needed to treat for 1 year to prevent 1 stroke is 37 (for primary prevention) and 12 (for secondary prevention)

Weekly treatment cost of warfarin
10mg/day – $12.547,8

1 based on April 2016 non-concession card PBS (maximum price to consumer) and medicare benefits schedule for x prothrombin pathology tests/month

Established guidelines for warfarin reversal and bridging anticoagulation therapy1,6

* Coumadin and Marevan have NOT been shown to be bioequivalent and should not be interchanged.

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Minimum Product Information: MAREVAN® and COUMADIN® (warfarin sodium). Indications: Prophylaxis and/or treatment of venous thrombosis and its extension and pulmonary embolism; prophylaxis and/or treatment of the thromboembolic complications associated with atrial fibrillation; use as an adjunct in 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 inter exchange 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; anaphylaxis which occurs when the PT-INR is within the therapeutic range; necrosis of skin and other tissues. Infrequent: hypersensitivity/allergic reactions, systemic cholesterol microembolizations, “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: MAREVAN® tablet, 1 mg (brown, scored, embossed M/1) 50s; 3 mg (blue, scored, embossed M/3) 50s; 5 mg (pink, scored, embossed M/5) 50s. Presentation: COUMADIN® tablet, 1 mg (light tan, scored, embossed COUMADIN/1) 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 2008 respectively).


PBS Information: This product is listed on the PBS as an antithrombotic agent.

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a RESEARCH REVIEW publication
Novel usage of the cryoballoon catheter to achieve large area atrial substrate modification in persistent and long-standing persistent atrial fibrillation

Authors: Su WW et al.

Summary: Cryoballoon ablation was performed in 225 patients with varying degrees of AF disease; the balloon was used for more than PVI in several cases. This paper on 11 anatomical cardiac locations where extra-PV lesion sets were utilised showed that such ablations can be performed safely with the balloon catheter. The complication rate was 3.6%, and the respective 12-month rates of freedom from all atrial arrhythmias in patients with paroxysmal AF (n=88), persistent AF (n=75) and long-standing persistent AF (n=62) were 88%, 71% and 55%. The mean procedure time associated with this protocol was 2.2 hours and the average fluoroscopy time was 4.2 minutes.

Comment: Although there are reports of the cryoablation balloon being used for delivering lesions other than around the pulmonary veins, this is by no means standard practice, and no real conclusions can be drawn from this study.

Reference: J Interv Card Electrophysiol; Published online Mar 3, 2016
Abstract