THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

NUMBER 127 AUGUST/SEPTEMBER 2013 13th YEAR

The antiarrhythmic drug dronedarone (Multaq) was developed as a replacement for amiodarone (Cordarone) which has the potential for causing serious adverse effects such as thyrotoxicosis, pulmonary failure and liver failure. Early trials showed dronedarone to be significantly less effective than amiodarone, but possibly somewhat safer. A recent German trial concludes that dronedarone is not only almost totally ineffective (keeping only 20% of patients taking it in normal sinus rhythm), but also has the potential to cause serious side effects including bradycardia, atrioventricular block, QT interval prolongation and gastrointestinal problems (32% of patients discontinued the drug because of adverse effects).

The main difference between amiodarone and dronedarone is that the amiodarone contains 39% by weight of iodine. Thus a patient taking 200 mg/day of amiodarone would ingest 78 mg/day of iodine or about 500 times the recommended daily allowance of 150 micrograms. Is it possible that amiodarone owes much of its efficacy to its iodine component and that supplementing with safe amounts of iodine would be beneficial for afibbers?

Also in this issue we report that a right atrial flutter ablation on its own is a waste of time when trying to deal with coexisting atrial fibrillation and atrial flutter, that the LARIAT procedure for closing off the left atrial appendage has been found safe and effective, that Chinese EPs have been successful in the first trial of a simpler variant of the standard pulmonary vein isolation procedure, and that Danish researchers have found that a long QT interval is a potent risk factor for the development of lone atrial fibrillation.

Last but not least, if you need to restock your supplements, please remember that by ordering through my on-line vitamin store you will be helping to defray the cost of maintaining the web site and bulletin board. You can find the store at [*http://www.afibbers.org/vitamins.htm*](http://www.afibbers.org/vitamins.htm) *- your continuing support is greatly appreciated.*

Wishing you good health and lots of NSR,

Hans

Highlights

LETTERS TO THE EDITOR

Once again Hans, thank you for all of your excellent and very valuable work. You will be interested to know that I have been afib-free for over 18 months – since I eliminated gluten from my diet. Prior to my last episode (January 2012), I was afib-free for 4 months on a gluten-free diet. I consumed gluten over the Christmas holidays and lo and behold – AF!! So no more gluten for me, and I hope no more AF.

JF

Is it OK to take magnesium supplements with Tikosyn?

JSD

I am not aware of any contraindications to supplementing with magnesium when on Tikosyn (dofetilide). As a matter of fact, low blood levels of magnesium and potassium may increase the risk of torsades de pointes associated with Tikosyn therapy.

Hans

I found the recipe for magnesium bicarbonate water on the afibbers.org website and have been experimenting. Since most commercial milk of magnesia contains additives (i.e. sodium hypochlorite), I've been trying to make the concentrate directly with magnesium hydroxide powder rather than the powder + water = milk of magnesia. Unfortunately, I haven't been able to figure out how much powder to use: I calculate (two different ways) that it should be about 0.87 teaspoons per liter of carbonated water, yet when I try that, I get much more fizzing and much more undissolved powder that I did with the commercial milk of magnesia, so 0.87 teaspoons seems to be too much.

Where am I going wrong? How much magnesium powder should I be adding to the carbonated water to get a result equivalent to adding milk of magnesia as in the recipe?

JL

If you are using magnesium hydroxide $Mg(OH)_2$ (molecular weight 58) then you would need to add 3.6 grams to 1 liter of carbonated water in order to end up with a concentrate containing 1500 mg of elemental magnesium. The bulk density of powdered $Mg(OH)_2$ varies between about 0.4 g/mL and 1.0 g/mL, so 3.6 grams could be anywhere between 9 mL (2 teaspoons) and 3.6 mL (about ¾ teaspoon) depending on the fineness of the magnesium hydroxide powder.

Hans

Dronedarone (Multaq) found ineffective

LEIPZIG, GERMANY. A new study supports the contention that the antiarrhythmic drug dronedarone (Multaq) is largely ineffective and associated with a high incidence of adverse events. Dronedarone is a benzofuran derivative similar to amiodarone but without the iodine component. Initial trials showed it to be substantially less effective than amiodarone, but having fewer serious side effects. Later studies indicated that the drug is associated with an increased risk of liver and kidney damage.

The German study was carried out at Leipzig Heart Centre and involved 91 patients with atrial fibrillation (AF) and 29 patients with atypical (non-isthmus-dependent) atrial flutter (AFL). Of the 91 patients with AF, 30 had paroxysmal AF, while 61 had persistent AF. The average age of the study participants was 67 years, 53% were women, 67% had mild to moderate heart failure (New York Heart Association Class II or III), 93% had hypertension, 24% were diabetic, and 28% had undergone a previous catheter ablation.

The patients with persistent AF underwent cardioversion after a 3 to 5 day pre-treatment with 400 mg of dronedarone twice daily. All patients were then followed up at 4 weeks and 6 to 9 months after initiation of dronedarone therapy (400 mg twice daily). Follow-up visits included 12-lead electrocardiography, 7-day Holter monitoring, and assessment of liver and kidney function. Recurrence of AF and AFL was defined as atrial arrhythmia lasting 30 seconds or longer.

After the initial 3 to 5 day drug treatment phase, 6% of patients discontinued the drug after a failed cardioversion and 10% discontinued it after experiencing an adverse event. Discontinuation rates at 4 weeks were 23% because of inefficacy and 14% because of adverse events. Corresponding discontinuation rates at the 6 to 9 months check-up were 13% and 9%. Overall, only 27% of the original study group were still taking dronedarone at the last check-up. Discontinuation was due to inefficacy in 42% of patients and due to adverse events in 32%. The most common adverse event was bradycardia or atrioventricular block followed by gastrointestinal problems and QT-interval prolongation. One patient experienced acute renal failure after 6 weeks of dronedarone therapy.

At the 4 week check-up only 33% of patients were in sinus rhythm and this percentage declined to 20% at the 6 to 9 months check-up. Sinus rhythm maintenance was not significantly greater in patients who had undergone one ablation or therapy with Class I (flecainide and propafenone) or Class III (amiodarone, sotalol or dofetilide) antiarrhythmics. Reversal from persistent to paroxysmal AF was observed in 23 patients, while progression from paroxysmal to persistent AF occurred in 6 patients. Ten patients converted from AF to AFL as compared to only 2 patients who converted from AFL to AF.

The researchers conclude that dronedarone is associated with frequent adverse events and moderate antiarrhythmic efficacy requiring discontinuation in most patients (73% of the study group) within the first 9 months of use.
Lobe, S, et al. Usefulness of dronedarone in patients with atrial arrhythmias. **American Journal of Cardiology**, *Vol. 111, 2013, pp. 1311-14*

Editor's comment: Several electrophysiologists have previously expressed their misgivings about the drug. Dr. Steven Nissen of the Cleveland Clinic believes dronedarone is outright dangerous and Dr. Sanjay Kaul of Cedar-Sinai Medical Center in Los Angeles says that the drug does not even appear to be safe in intermediate-risk patients.[1] I think dronedarone deserves a place, alongside digoxin and sotalol, as the most useless pharmaceutical drug for AF patients.
[1] http://www.theheart.org/article/1283205/print.do

Ablation of coexisting atrial flutter and fibrillation

AUSTIN, TEXAS. Atrial fibrillation (AF) and atrial flutter (AFL) often coexist. Symptoms can be debilitating and may include palpitations, shortness of breath, chest discomfort, fatigue, dizziness and fainting; thus seriously affecting one's quality of life (QoL). A catheter ablation for "stand alone" right atrial flutter (cavotricuspid isthmus [CTI] ablation) is relatively simple and has a high chance of being successful. However, the probability that an AFL ablation will also eliminate AF is very low and, as a matter of fact, a CTI ablation may actually "unmask" previously undetected AF.

An American/Italian research team led by Dr. Andrea Natale now reports that an AF ablation by itself or a combined AF + AFL ablation is effective in eliminating both AF and AFL, whereas an AFL ablation by itself is not. Their single-blind, randomized study involved 360 patients with documented, coexisting paroxysmal AF and AFL. The patients were randomized into Group 1 comprising 182 patients who underwent AF or AF + AFL ablation, while Group 2 comprised 178 patients who underwent only AFL ablation.

A total of 124 patients in Group 1 had only a pulmonary vein antrum isolation (PVAI) procedure with additional lesions as required. The remaining 58 patients in Group 1 underwent both a PVAI and a CTI ablation. The decision to perform the added CTI procedure was made if the patient presented with typical right atrial flutter at the start of or during the PVAI, or if flutter was provoked by the isoproterenol challenge following the PVAI.

All procedures were performed under general anesthesia. NOTE: A left atrium diameter in excess of 5 cm (50 mm) was grounds for exclusion from the study. After overnight observation, patients were prescribed their previously ineffective antiarrhythmics and discharged. A recurrence was defined as any episode or AF, AFL or tachycardia lasting 30 seconds or longer, with episodes occurring during a 12-week blanking period being ignored.

Follow-up at 3, 6, 9 and 12 months included 7-day Holter monitoring as well as extended event recording. Quality of life was assessed prior to the ablation procedure and at the 12-month follow-up using 4 different questionnaires – the Medical Outcome Study Short Form, the Hospital Anxiety and Depression Score, the Beck Depression Inventory, and the State-Trait Anxiety Inventory.

At an average of 21 months follow-up, 64% of the group having undergone PVAI only were in normal sinus rhythm (NSR) without the use of antiarrhythmics as was 66% of the group having undergone PVAI + CTI. In contrast, only 19% of Group 2 (AFL ablation only) was in NSR without the use of antiarrhythmics. Assessment of the 1-year follow-up clearly showed that study participants who had undergone a successful ablation had improved their QoL scores very significantly with particular gains in scores related to anxiety, depression, vitality, and general physical and emotional well-being. Somewhat surprisingly, the post-ablation improvement in QoL was significantly less in Group 2 even if their CTI ablation had been successful.

The researchers conclude that in coexisting AF and AFL having a stand-alone PVAI or a combined PVAI + CTI is associated with a much lower recurrence rate than having just a CTI procedure. As a matter of fact, just undergoing a PVAI may be sufficient as there is some evidence that AFL may be triggered by ectopic activity in the pulmonary veins. Furthermore, it is clear that quality of life directly correlates with freedom from arrhythmia.

Mohanty, S, et al. Results from a single-blind, randomized study comparing the impact of different ablation approaches on long-term procedure outcome in coexistent atrial fibrillation and flutter (APPROVAL). **Circulation**, *Vol. 127, May 7, 2013, pp. 1853-60*

Editor's comment: This and previous studies clearly show that having just a right atrial flutter ablation, when both AF and AFL are present, is a waste of time. The observation that a successful ablation is associated with a greatly improved quality of life confirms the experience of afibbers who have regained permanent NSR through a successful ablation.

LARIAT procedure found effective

PHOENIX, ARIZONA. There is considerable evidence that the left atrial appendage (LAA) is an important source of blood clots (thrombi) in atrial fibrillation (AF) patients with underlying heart disease. Clot formation may occur when the rate of blood flow in and out of the LAA is significantly reduced. The most common cause of reduced blood flow is an inadequate left ventricular ejection fraction. Thus, LAA clot formation is rare among lone afibbers unless they have undergone a catheter ablation targeting the area around the opening of the LAA.

The LAA is a remnant of the original embryonic left atrium formed during the third week of gestation. The LAA lies within the pericardium in close contact with the free wall of the left ventricle. Thus, blood flow in and out of the LAA depends, to a significant degree, on a properly functioning left ventricle. The LAA empties into the left atrium through an orifice located between the left upper pulmonary vein and the left ventricle. The diameter of the opening varies between 10 and 40 mm, the overall volume of the LAA varies between 0.77 and 19.27 cubic centimeters (mL), and its length can vary between 16 and 51 mm.

Prevention of clot formation and the associated risk of ischemic stroke and TIA (transient ischemic attack) are usually attempted through the use of oral anticoagulants such as warfarin. However, a significant proportion of AF patients cannot tolerate anticoagulants because of high risk for hemorrhagic stroke and major bleeding. For these patients, there are two options – remove the LAA or close it off. Removal is a fairly simple matter if the patient is undergoing a maze or mini-maze procedure, but is not an option in the case of catheter ablation. Thus several techniques and devices have been developed to effectively isolate the LAA from the left atrium.

One such device is the WATCHMAN which is a nitinol (nickel-titanium alloy) cage covered with a polyethylene membrane and having barbs for anchoring it to the inside of the LAA. The device is inserted with a special catheter entering the left atrium through the femoral vein – a procedure similar to that used in pulmonary vein ablation procedures. The first trial of the device involved 66 patients with AF and one or more risk factors for ischemic stroke; it was performed at the Mayo Clinic. After 45 days, 93% of participants had achieved satisfactory sealing of the LAA. Unfortunately, there have been reports of the device working itself loose and there are also concerns about leaving a foreign, metallic object in the heart for an extended period of time.

The newly developed LARIAT device overcomes these concerns as it is made from Teflon-coated polyester, which is non-metallic and non-absorbable. The LARIAT device is essentially a noose which is permanently tightened around the LAA where it empties into the left atrium, thus preventing any blood flow in and out of the LAA. Early trials showed that 95 to 98% of patients undergoing the LARIAT procedure retained complete closure 3 to 12 months after. The procedure is a two-stage process involving access to both the inside of the heart with a catheter (endocardial access) and access to the outside of the heart (epicardial access) via a small incision at the bottom of the rib cage. It is usually carried out by a team of two physicians (by an EP for the endocardial phase and by an EP or cardiologist for the epicardial phase). For an excellent video of the procedure see http://link.brightcove.com/services/player/bcpid1966016647001?bckey=AQ~~,AAAByWTdcAE~,okzfB_eXtXleN8AYKFkzy7QTnuGzsxt0&bctid=2196073081001

Cardiologists at the Good Samaritan Medical Center now report their experience with a group of 27 AF patients who were at high risk for stroke. Anticoagulation was not an option since all the patients were also at high risk for major bleeding. Most of the patients (52%) had permanent AF, while 41% had paroxysmal, and 7% had persistent AF. Average age was 75 years, 74% were male, 96% had hypertension, 67% had congestive heart failure, and 37% had suffered a pervious stroke or TIA.

The trial participants had the LARIAT device installed while under general anesthesia and constant monitoring with TEE (transesophageal echocardiography). At the 45-day follow-up, complete closure was confirmed in 22 of 22 patients in whom the procedure was completed and who had TEE data. Three cases of procedure-related pericarditis (inflammation of heart lining) and one procedure-related stroke were noted. The authors conclude that percutaneous LAA exclusion with the LARIAT device can be achieved successfully with an acceptable rate of procedural complications.

Stone, D, et al. Early results with the LARIAT device for left atrial appendage exclusion in patients with atrial fibrillation at high risk for stroke and anticoagulation. **Catheterization and Cardiovascular Interventions**, *June 13, 2013 [Epub ahead of print]*

Comparison of apixaban (Eliquis) and warfarin

UPPSALA, SWEDEN. Although there is no evidence that otherwise healthy lone afibbers have an increased risk of ischemic stroke, it is clear that atrial fibrillation (AF) patients with heart failure, diabetes or hypertension have a significantly increased risk and this risk is further magnified if the patient has already suffered a heart attack or stroke. Oral anticoagulation with vitamin K antagonists such as warfarin (Coumadin) is still considered to be the best preventive therapy for patients at risk for stroke. Unfortunately, warfarin interacts with many foods and drugs and treatment requires constant, costly monitoring. Its use also substantially increases the risk of hemorrhagic stroke and major internal bleeding, particularly in older people, a group that, ironically, is also most at risk for an ischemic stroke. Effective warfarin therapy is based on maintaining an INR (international normalized ratio) between 2.0 and 3.0. Too low a ratio increases the risk of ischemic stroke, while too high a ratio increases the risk of hemorrhagic stroke and major bleeding. Warfarin acts by inhibiting the activation of the vitamin K-dependent coagulation factors V, VII, and X in the extrinsic and common pathways of the coagulation cascade. Research aimed at replacing warfarin has focused on developing new pharmaceutical drugs which will inhibit specific coagulation factors. A recent entry to the field is apixaban (Eliquis) a direct inhibitor of factor Xa, the first member of the common pathway in the coagulation cascade.

A very large study (ARISTOTLE) compared apixaban to warfarin. It involved 18,200 patients with AF and at least one additional risk factor for ischemic stroke. The average (median) age of the patients was 70 years and 35% were female. Most of the participants (85%) had persistent or permanent AF and had a $CHADS_2$ score of at least 1 (mean score of 2.1). All in all, the trial involved a group of very sick people, in no way comparable to a group of otherwise healthy afibbers. Almost 90% were being treated for hypertension, 35% had heart failure or abnormally low left ventricular ejection fraction, over 30% had experienced a prior heart attack, stroke, TIA (transient ischemic attack) or systemic embolism, and 25% had diabetes. None of the study participants had a $CHADS_2$ score of 0.

The participants were randomized to receive standard therapy with oral warfarin (INR range of 2.0 to 3.0) or 5 mg twice daily of apixaban (2.5 mg twice daily for elderly or frail persons and those with impaired kidney function). The warfarin-treated patients were within INR target range 66% of the time (median value). During an average (median) follow-up of 1.8 years, 212 patients (1.3%/year) in the apixaban group experienced a stroke, TIA or systemic embolism as compared to 265 patients (1.6%/year) in the warfarin group. The rate of major bleeding was 2.13%/year in the apixaban group compared to 3.09%/year in the warfarin group. The incidence of hemorrhagic stroke (intracranial bleeding) was 0.24%/year in the apixaban group compared to 0.47%/year in the warfarin group. The incidence of major gastrointestinal bleeding was 0.76%/year in the apixaban group and 0.86%/year in the warfarin group. Overall, 1009 patients (6.13%/year) in the apixaban group and 1168 patients

(7.20%/year) in the warfarin group died (from any cause) or suffered a stroke, systemic embolism or major bleeding during follow-up.

The ARISTOTLE AF investigators concluded that apixaban is superior to warfarin in regard to preventing stroke and systemic embolism and non-inferior in all other aspects where a comparison was made.

Now the same investigators have re-analyzed the ARISTOTLE data to determine if the superiority of apixaban is related to the quality of INR control in warfarin-treated patients. In other words, "would apixaban still be superior if INR control was optimal?" INR control is measured by the percentage of INR measurements for a given patient or treatment center that are within the therapeutic range of 2.0 to 3.0. This percentage is known as time in therapeutic range or TTR.

The ARISTOTLE trial included centers in 40 countries. Average TTR was highest in Sweden (83.2%) followed by Norway, Australia, Denmark, and Finland. Canada was #8 and the USA #9 (TTR 74%) and India was last at 49%. Not surprisingly, the rate of stroke (including systemic embolism) was lower in centers with a high TTR. However, the incidence of major bleeding was higher in centers with high TTR, although the difference noted was not statistically significant.

TTR vs Outcome (events in %/year)

	Stroke		Major Bleeding		All-Cause Death	
TTR	Apixaban	Warfarin	Apixaban	Warfarin	Apixaban	Warfarin
24.3 - 60.5	1.72	2.36	1.44	2.89	4.00	4.39
71.2 - 83.2	0.91	1.04	2.48	3.31	2.81	3.10

It is clear that apixaban is superior to warfarin in all centers, but the advantage would appear to be most pronounced in centers with poor TTR.

In an accompanying editorial British and Spanish researchers point out that INR control (TTR) with warfarin depends on numerous factors and that it actually is possible to predict with reasonable accuracy how a patient will respond. The recently developed Apostolakis score assigns 1 point each for being female, over the age of 60 years, having a medical history of two or more of the following conditions – hypertension, diabetes, coronary artery disease, heart attack, peripheral arterial disease, congestive heart failure, previous stroke, pulmonary disease, or liver or kidney dysfunction. Therapy with interacting drugs such as amiodarone also warrants 1 point, while smoking and non-white race warrants 2 points. Thus the score gives a total value between 0 and 8. The Apostolakis score correlates well with actually measured TTR and a score of 2 or more requires more regular INR monitoring and other interventions to achieve appropriate anticoagulation control. NOTE: The conflict of interest disclosures for the authors of the study takes up over 100 lines of fine print.

Wallentin, L, et al. Efficacy and safety of apixaban compared with warfarin at different levels of predicted international normalized ratio control for stroke prevention in atrial fibrillation. **Circulation**, *Vol. 127, June 4, 2013, pp. 2166-76*

Gallego, P, et al. Apixaban compared with warfarin for stroke prevention in atrial fibrillation. **Circulation**, *Vol. 127, June 4, 2013, pp. 2163-65*

Editor's comment: The above study confirms the superiority of apixaban over warfarin in the prevention of ischemic stroke, especially in centers and countries with less than optimum INR control. Apixaban (Eliquis) would appear to be the best overall choice for anticoagulation and will likely be the leading medication for this purpose once a reliable antidote to apixaban-induced bleeding becomes routinely available.

Importance of contact force in catheter ablation

PRAGUE, CZECH REPUBLIC. Despite significant, recent improvements in catheter ablation strategies to treat atrial fibrillation (AF), recurrence remains a continuing concern. Recurrence (after the blanking period) follows 20-55% of initial procedures and is almost always attributable to gaps in the isolation lines separating the pulmonary veins (PVs) and the left atrium. Isolation gaps may result either from areas omitted during initial treatment or from lesions that are not sufficiently transmural (extending through the entire thickness of the heart wall) to prevent conduction. The force (contact force or CF measured in grams) applied to the catheter, the position of the catheter in relation to the point ablated, and the length of time radiofrequency (RF) energy is applied (Force-Time Integral or FTI measured in gram-seconds) are the most important variables in determining the durability of any particular lesion.

A group of American, Czech, German and Swiss researchers now reports their experience with a new 3.5 mm irrigated catheter (*TactiCath*) that automatically measures CF and FTI every 100 milliseconds. Forty-six consecutive patients with predominantly paroxysmal (98%) AF participated in the study. The patients underwent an anatomically-guided pulmonary vein isolation procedure using the *EnSite* mapping system. The electrophysiologists doing the procedures followed their usual practice, but did not have access to the CF and FTI data being recorded. After a blanking period of 3 months, 40 of the patients underwent a second electrophysiologic study (similar to catheter ablation, but without necessarily creating new lesions). At this follow-up, 26 of the 40 patients (65%) showed one or more gaps. The number of gaps was found to correlate strongly with the minimum CF and the minimum FTI at the site of the gaps. The median CF for all initial ablations was 15 g and the median FTI was 479 gs.

The researchers observed that the average number of ablations per segment (the area around the PVs was divided into 8 segments for analysis purposes) was inversely correlated to isolation. This suggests that once an inadequate lesion has been produced trying to redo it only makes things worse. They make the following recommendations for increasing the probability of a successful ablation:

1. Position the catheter carefully before ablation, preferably with a CF of 20 g, but not less than 10 g.
2. Ensure positional stability by monitoring CF before applying RF energy.
3. Sustain RF delivery until a minimum FTI of 400 gs is achieved before moving the catheter to a new location.

Neuzil, P, et al. Electrical reconnection after pulmonary vein isolation is contingent on contact force during initial treatment. **Circulation Arrhythmia and Electrophysiology**, *Vol. 6, April 2013, pp. 327-33*

Editor's comment: The real-time measurement of CF and FTI during catheter ablation will no doubt prove to be of great value to EPs performing ablations, particularly less experienced ones. I suspect that the "top guns" in the ablation field have an innate capability to sense CF and, based on the thousands of ablations they have done, know exactly how long to apply RF energy in order to achieve an optimum FTI.

Novel ablation technique shows promise

SHANGHAI, CHINA. Prof. Haissaguerre and colleagues in Bordeaux, France discovered in 1998 that paroxysmal atrial fibrillation (PAF) was triggered by ectopic activity in the pulmonary veins. Since then catheter ablation aimed at isolating the pulmonary veins from

the left atrium has been the preferred non-drug approach for dealing with PAF. Pulmonary vein isolation (PVI) may be performed using electrophysiological mapping (using a multipolar Lasso catheter) or anatomical mapping (CARTO) to establish the exact location of the pulmonary veins.

More recently procedures have emerged that target the atrium walls (substrate) where the aberrant impulses from the pulmonary veins (PVs) organize themselves to initiate and sustain atrial fibrillation. Chief among these are the strategy targeting complex fractionated atrial electrograms developed by Dr. Koonlawee Nademanee and the FIRM procedure targeting electric rotors and focal impulses developed by Dr. Sanjiv M. Narayan.

A group of researchers from the Second Military Medical University in Shanghai now reports preliminary results of a new ablation procedure which, rather than encircling the pulmonary veins, creates three short radial lines of lesion emanating from each pulmonary vein and extending into the left atrium (to the point where no PV potentials are present).

The clinical trial of the new procedure involved 86 patients with PAF who were randomized to receive the new pulmonary antrum radial-linear (PAR) ablation procedure (42 patients) or a standard PVI procedure (44 patients) at one of 4 ablation centers in Shanghai. The average total procedure time in the PAR group was 161 minutes vs. 199 minutes in the PVI group. Fluoroscopy time was 25 and 32 minutes respectively. NOTE: PVI was not performed in the PAR patients and none of them demonstrated complete isolation of the PVs. The average age of the patients was 64 years and 63% were men. None of the patients had heart disease, but 45% had hypertension and 17% had diabetes. Left atrium diameter varied from 43 mm to 49 mm (those having a left atrium diameter greater than 50 mm were excluded from the trial) and average left ventricular ejection fraction was 71%.

Follow-up included electrocardiograms, 3-day event recording every 3 months, and 24-hour Holter monitoring 6 months after the procedure and at the final follow-up visit. At 14 months following a single ablation procedure, 74% of the patients in the PAR group were free of atrial fibrillation, atrial flutter, and atrial tachycardia (no episodes lasting longer than 30 seconds) without the use of antiarrhythmic drugs (86% AF-free with the use of drugs). Corresponding percentages for patients in the PVI group were 50% and 59%. No major adverse events were observed during the trial. The researchers noted a significant post-procedural decrease in left atrium diameter in the PAR group. They conclude that the PAR procedure is simple, safe and effective in patients with paroxysmal AF and warrants further large scale trials.

Zhao, X, et al. Pulmonary antrum radial-linear ablation for paroxysmal atrial fibrillation. **Circulation Arrhythmia and Electrophysiology**, *Vol. 6, April 2013, pp. 310-17*

Calkins, H. Has the time come to abandon the concept that "pulmonary vein isolation is the cornerstone of atrial fibrillation ablation"? **Circulation Arrhythmia and Electrophysiology**, *Vol. 6, April 2013, pp. 241-42*

Editor's comment: The PAR procedure certainly looks promising but obviously needs to be evaluated in large-scale trials before it can attain "mainstream" status.

Early recurrence following ablation and long-term outcome

PHILADELPHIA, PENNSYLVANIA. It is quite common to experience atrial fibrillation (AF) episodes or episodes of atrial flutter or supraventricular tachycardia following a catheter ablation. Most studies ignore such episodes occurring during the first 3 months post-ablation (blanking period) when judging final outcome since it is by no means certain that they are an indication of long-term failure. However, what if episodes recur 6 months or 12 months post-ablation? Is that a portent of failure? A group of electrophysiologists from the University of Pennsylvania now provides an answer to that question.

Their study included 1188 patients with AF who underwent an initial catheter ablation between 2004 and 2008. During a follow-up of about 4 years, 439 patients experienced recurrence while the remaining 749 patients (63%) maintained normal sinus rhythm (NSR). The 439 patients were divided into 3 groups:

Group E	245 patients	Early recurrence	3-6 months after ablation
Group L	118 patients	Late recurrence	6-12 months after ablation
Group VL	76 patients	Very late recurrence	More than 12 months after ablation

The average age of the patients was 57 years, 76% were male, 53% had hypertension, 11% had structural heart disease, and 11% had coronary artery disease. They had lived with AF for an average of 6 years and 58% had the paroxysmal variety. The mean follow-up after the initial ablation was 50 months and the mean follow-up after the first recurrence was 41 months.

Patients were typically restarted on previously ineffective antiarrhythmic drugs (AADs) prior to discharge. AAD usage was usually discontinued after 6 to 12 weeks in paroxysmal afibbers and after 6 months in persistent ones. Follow-up included at least 3 outpatient visits, transthoracic echo cardiograms and transtelephonic monitoring. Recurrence was defined as any organized atrial arrhythmia lasting more than 30 seconds. However, in order to provide a more realistic analysis of outcome, the authors defined AF control (rare recurrence) as having no more than two AF episodes and no more than one cardioversion in any 6-month follow-up period.

During the blanking period, 306 of 439 patients (70%) experienced arrhythmia episodes with 82% in group E, 54% in group L, and 54% in group VL doing so. At the time of recurrence after the blanking period, 59% of patients in group E were still on AADs as compared to 31% in group L and 7% in group VL. In 42 patients (9.5%) the recurrence was atrial flutter or tachycardia. During the subsequent 41 months (average) follow-up only 9% of group E members achieved AF control (rare episodes) as compared to 47% in group L and 68% in group VL. There was no significant difference in subsequent AF control between those who required electrocardioversion for initial recurrence and those who did not; nor was there any significant difference between paroxysmal and persistent afibbers.

Treatment with antiarrhythmic drugs was tried in 44% of group E members, 55% of group L, and 42% of group VL following the first procedure. Patients in the VL group were far more likely to respond to AAD therapy than were those in the E and L groups. Positive response was achieved in 72% of the VL group vs 58% in the L group and 19% in the E group.

A total of 290 patients underwent repeat ablation (75% in group E, 59% in group L, and 46% in group VL) and were followed for at least a year. Patients in the VL group had the highest rate of AF control; 89% had no or only rare episodes vs 72% in the L group and 49% in the E group. The authors conclude that the time to first AF recurrence after the blanking period dramatically influences long-term outcome – the longer the time to AF recurrence, the better AF control, response to AADs, and outcome of repeat ablation.
Gaztanaga, L, Marchlinski, FE, et al. Time to recurrence of atrial fibrillation influences outcome following catheter ablation. **Heart Rhythm**, *Vol. 10, January 2013, pp. 2-9*

Editor's comment: Our 2009 Ablation/Maze Survey found that having no AF episodes during the period 6-12 months from final ablation was associated with an 83% probability of being AF-free 4 years after the initial ablation. NOTE: 82% of these ablations were performed by Prof. Haissaguerre, Prof. Jais or Dr. Natale. On the other hand, experiencing AF episodes during the 6- to 12-month period was associated with only a 29% probability of being AF-free at year 4. See www.afibbers.org/resources/2009ablationsurvey.pdf

New risk factor for lone atrial fibrillation

COPENHAGEN, DENMARK. The QT interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. It is measured with a standard 12-lead electrocardiogram (ECG) and represents one ventricular "beat", i.e. the time it takes for one complete cycle of electrical depolarization (contraction) and repolarization (recovery) of the right and left ventricles. The QT interval is obviously dependent on the heart rate (the faster the heart rate, the shorter the QT interval) and most studies report a corrected QT interval (QTc interval) rather than just the QT interval in order to provide more meaningful and comparable results. For more on this, see "Heart Rhythm 101" at www.afibbers.org/resources/heartbeat101.pdf. NOTE: In this study the authors used the Framingham formula to correct for heart rate. A prolonged QT interval is a risk factor for ventricular tachyarrhythmias and sudden cardiac death.

Now a group of Danish researchers reports that both an abnormally short and abnormally long QTc interval are significant risk factors for the development of atrial fibrillation (AF) and, in particular, for the development of lone atrial fibrillation (LAF). NOTE: In this study lone AF is defined as the occurrence of AF before the age of 65 years in the absence of hypertension, heart failure, heart attack, valvular heart disease, diabetes, and hyperthyroidism. The study involved 281,277 people living in Copenhagen who had one or more ECGs during the period 2001 to 2010. The average age of the study subjects was 54 years (41 to 65 years), 56% were women and only 16% had hypertension, while 3% had heart failure or had suffered a heart attack. Average heart rate was 69 bpm (62 to 78 bpm).

During the average follow-up of 5.7 years (1,614,832 person-years), 10,766 subjects developed AF corresponding to an annual incidence of 0.7%/year. The risk of being diagnosed with AF was 44% higher in subjects with a QTc interval at or above 464 ms when compared to the reference group (QTc interval between 411 and 419 ms). Similarly, subjects with an abnormally short QTc interval were found to have a 45% increased risk of AF when compared to the reference group.

A subgroup (LAF group) of 175,738 participants below the age of 65 years without hypertension, heart failure, previous heart attack, valvular heart disease, diabetes and hyperthyroidism was followed for a median of 4.7 years (816,322 person-years). During this time, 1467 persons (0.2%/year) were diagnosed with lone AF. The risk of being diagnosed with LAF was more than twice as high (Hazard Ratio = 2.32) among persons with a QTc interval of 464 ms or longer when compared to the reference group (384 to 397 ms).

The researchers conclude that there is a clear J-shaped association between QTc interval duration and development of AF. The risk associated with a prolonged QTc interval is significantly greater in the case of LAF.

Nielsen, JB, et al. J-shaped association between QTc interval duration and the risk of atrial fibrillation. **Journal of the American College of Cardiology**, *Vol. 61, No. 25, June 25, 2013, pp. 2557-64*

Editor's comment: The incidence of new onset LAF was low at 0.18%/year or 27% of all new AF cases. It is interesting that the risk of AF associated with an elevated QTc interval (at or above 464 ms) was lower (36%) in a subgroup of patients with cardiovascular disease than in the subgroup without (LAF group). This could, according to the authors, indicate that LAF is not associated with undetected cardiovascular disease, but rather with some unknown inherent characteristics or remodelling of cardiac electrophysiology (fibrosis??). It is interesting that potassium and magnesium deficiencies are associated with long QT syndrome (inherited long QT interval). Thus, ensuring adequate potassium and magnesium status would seem to be an absolute must for anyone diagnosed with long QT interval on an ECG.

THE AFIB REPORT is published by Hans R. Larsen, MSc ChE
1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@afibbers.org World Wide Web: http://www.afibbers.org