

# THE AFIB REPORT

*Your Premier Information Resource for Lone Atrial Fibrillation!*

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11<sup>th</sup> YEAR



*Welcome to the first issue of a new year – our 11<sup>th</sup> year of publication! Catheter ablation for atrial fibrillation has become hugely popular since Profs. Haissaguerre and Jais (Bordeaux group) discovered in 1998 that the majority of rogue cells triggering AF were located in the pulmonary veins – at least in the case of paroxysmal (intermittent) AF. Since then, tens of thousands of catheter ablations have been performed and the technology involved in doing them has advanced with astonishing speed. Immediate and even one year success rates of 80% or higher are now reported from high-volume centers (2 or more procedures a day). What has been lacking until now is evidence concerning the longevity of these procedures.*

*Our 2009 Ablation/Maze Survey evaluated the long-term prognosis for afibbers who had undergone one or more catheter ablation procedures for the purpose of curing their AF. Eighty-six percent of those who experienced no AF episodes during the index period (the last 6 months of the 12 months following their last procedure) were still AF-free without the use of antiarrhythmics 5 years later. This excellent success rate was, unfortunately, reduced to 33% if AF episodes had been experienced during the index period.*

*Australian researchers recently confirmed the importance of having no AF episodes by the end of the first 12 months following the last procedure and quoted a success rate (with or without antiarrhythmics) of 80% at 4 years for a group of highly symptomatic paroxysmal afibbers. Success rates quoted by the Bordeaux group are 81% at 2 years and 63% at 5 years for a group of paroxysmal, persistent and permanent afibbers having undergone a median of two procedures. However, the failure criterion used by the Bordeaux group (one episode of AF, atrial flutter or atrial tachycardia lasting more than 30 seconds anytime after the completion of the ablation) is, in my opinion, unrealistically strict.*

*Also in this issue we report that Polish researchers confirm my 2003 hypothesis that aldosterone is a major player in AF and that its detrimental effect can largely be counteracted by treatment with spironolactone or eplerenone. Japanese researchers have found that corticosteroid treatment immediately following ablation markedly reduces the risk of recurrence, and finally, a group of university-associated American cardiologists reports that Lovaza (a synthetic fish oil derivative) is ineffective in preventing AF recurrence.*

*All this and more in the first 2011 blockbuster issue!*

*And finally, 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> - your continuing support is truly appreciated.*

*Wishing you good health and lots of NSR,*

**Hans**

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## Prescription fish oil does not prevent AF recurrence

WYNNEWOOD, PENNSYLVANIA. Fish oils (notably eicosapentaenoic acid and docosahexaenoic acid) have potent electrophysiological, autonomic nervous system modulating, and anti-inflammatory effects in atrial and ventricular tissue. Several trials have shown fish oil consumption to have beneficial effects on heart rate variability and to reduce sudden cardiac death in patients having experienced a heart attack. There is also substantial evidence that fish oil consumption helps reduce inflammation and plays an important role in preventing atherosclerosis, heart attack and ischemic stroke. Several smaller trials have also found that supplementation with from 1 to 1.7 grams/day of natural fish oil reduces AF recurrence in patients having undergone coronary bypass surgery, patients having undergone electrical cardioversion, and those with dual chamber pacemakers. The reduction in AF recurrence rate ranged from about 30% to about 60%.

Now a group of university-associated American cardiologists reports that prescription omega-3 fatty acid esters (Lovaza) is ineffective in preventing AF recurrence in paroxysmal and persistent afibbers. Their 6-month trial included 663 afibbers with confirmed paroxysmal (n=542) or persistent (n=121) AF and no substantial structural heart disease at time of enrolment from November 2006 to July 2009. The average age of the participants was 60 years, 56% were male, 90% were white Caucasians, and a large proportion of the group were obese (average BMI of 30.7). Almost half of the entire group (45%) were on statin drugs, 13% were taking an antiarrhythmic, and 39% were on ACE inhibitors or angiotensin II receptor blockers. All patients were in normal sinus rhythm at enrolment.

After randomization, study participants were assigned to receive a placebo (corn oil) or Lovaza. Each 1-gram capsule of Lovaza contained approximately 465 mg of eicosapentaenoic acid and 375 mg of docosahexaenoic acid. Dosage was 8 grams/day of Lovaza or corn oil (placebo) for the first 7 days and then 4 grams/day thereafter through week 24.

At the end of 24 weeks, 48% of the paroxysmal afibbers in the placebo group had experienced one or more documented symptomatic atrial flutter or atrial fibrillation events. The corresponding number in the Lovaza group was 52%. In the persistent AF group, 33% of the placebo group experienced event(s) versus 50% in the Lovaza group. None of these differences were statistically significant. The researchers noted that the average heart rate during an episode was about 7 bpm lower in the Lovaza group than in the placebo group. They also observed an 11.5% larger drop in triglyceride levels and an 11.4% larger drop in the level of very low-density lipoprotein in the Lovaza group as compared to the placebo group at the end of the 24-week trial period.

Of particular interest is their comment that nearly half of the AF and flutter events occurred during the first 2 weeks of follow-up, suggesting that the effect of fish oil supplementation may not have rapid effects, even with high-loading doses. They conclude that Lovaza does not reduce recurrence rate among paroxysmal afibbers when given for a period of 24 weeks.

*Kowey, PR, et al. Efficacy and safety of prescription omega-3 fatty acids for the prevention of recurrent symptomatic atrial fibrillation. Journal of the American Medical Association, Vol. 304, No. 21, December 1, 2010, pp. 2363-72*

**Editor's comment:** First it should be kept in mind that Lovaza is a synthetic product formed by reacting fish oils (eicosapentaenoic acid and docosahexaenoic acid) with ethyl alcohol to form omega-3-acid ethyl esters. It is by no means certain that the ester of an acid will have the same properties as the acid itself. A good example is nitroglycerine, which has very different properties from its parent compounds – nitric acid and glycerine. Thus it may well be that eicosapentaenoic acid may behave quite differently from its ethyl ester. The fact that at least half a dozen studies have shown a beneficial effect of fish oils on atrial fibrillation recurrence ([www.oilofpisces.com/arrhythmias.html](http://www.oilofpisces.com/arrhythmias.html)) would tend to support the idea that fish oils can be effective in

preventing AF, whereas Lovaza obviously is not. It should also be noted that the triglyceride-lowering

effect of Lovaza is not superior to that of pharmaceutical grade, natural, unmodified fish oil.

## Five-year success of catheter ablation

BORDEAUX, FRANCE. Although there is ample evidence that catheter ablation can be highly effective in eliminating atrial fibrillation (AF) in the short term, there is, except for our 2009 Ablation/Maze Survey, no published data regarding the long term durability of the procedure. Electrophysiologists at the Hopital Cardiologique du Haut-Leveque have now remedied this shortcoming. Their study involved 100 patients resident in France who underwent catheter ablation for AF during the period January 2001 to April 2002. During these early years of pulmonary vein isolation procedures (PVI), the Bordeaux group was already performing an average of two procedures five days a week.

The patients involved in the study were predominantly male (86%) with an average age of 56 years and the average length of time they had suffered from AF was six years. Most (64%) had paroxysmal AF, 22% had persistent AF, and the remaining 14% were in permanent AF (long-standing persistent). None of the patients had undergone prior ablation or surgery to deal with their condition, and all experienced at least one hour a week (average) of AF.

The patients all underwent an initial segmental PVI procedure as well as cavotricuspid isthmus ablation (ablation for right atrial flutter). Seventy-five per cent also had linear ablation (left isthmus and/or roofline) during the first procedure. During the first six months following the procedure, about 50% of the patients had at least one arrhythmia episode – defined as an AF, flutter or tachycardia episode lasting 30 seconds or longer. Arrhythmia-free survival rates (from Kaplan-Meier curves) after a single procedure were 40% at the end of the first year, 37% at the end of the second year, and 29% at the end of the fifth year.

Fifty-one patients underwent one or more repeat procedures to reconnect gaps that had appeared in pulmonary veins or linear lesions. Afib-free survival one year after the final procedure was 87% and 81% and 63% respectively at two and five years after a median of two procedures. The major predictors of arrhythmia recurrence were permanent AF (odds ratio of 2.6), valvular heart disease (odds

ratio of 5.2), and non-ischemic dilated cardiomyopathy (odds ratio of 34.0). Thus, it seems likely that an otherwise healthy paroxysmal afibber could expect a significantly better long-term, afib-free survival rate than indicated by the figures presented above.

The authors of the study make the interesting observation that none of the patients with paroxysmal AF at the start of the study progressed to persistent or permanent AF during the follow-up, and also emphasize that there were no procedure-related deaths.

*Weerasooriya, R, et al. Catheter ablation for atrial fibrillation: are results maintained at 5 years of follow-up? Journal of the American College of Cardiology, Vol. 57, No. 2, January 11, 2011, pp. 160-66*

**Editor's comment:** The Bordeaux study is a most welcome addition to our sparse data and evidence concerning the longevity of a catheter ablation for the purpose of curing AF. The quoted rates for afib-free survival does, however, in my opinion, paint a too pessimistic picture of single procedure success rates. It is well known that atrial arrhythmias are common during the first six months following a catheter ablation and indeed in this study, 56% of participants reported arrhythmias lasting more than 30 seconds during this period. These patients were presumably counted as failures, thus resulting in arrhythmia-free survival rates as low as 40%, 37% and 29% after one, two and five years. The success rates would obviously have been substantially higher if the first six months had been counted as a blanking period rather than as part of the follow-up.

Our 2009 Ablation/Maze Survey involved 88 AF patients who had undergone their last catheter ablation more than four years ago (53 had only one procedure). The long-term success rate (no atrial arrhythmia and no use of antiarrhythmic drugs) was found to be highly dependent on whether or not the patients had experienced atrial arrhythmias during the last six months of the 12-month period following their last procedure (Index Period). Those who had not experienced arrhythmias during their index period had success rates of 84% at year two, and 86% at year five. In contrast, those patients who did experience arrhythmias during the index period

had success rates of only 33% at years two and five. Thus, absence of atrial arrhythmias during the index period is clearly a very important predictor of long-term success. Being a persistent or permanent afibber prior to the procedure was found to be associated with a 5% lower success rate at five years (87% for paroxysmal and 82% for persistent and permanent).

In judging the long-term success of catheter ablation for AF, it should also be kept in mind that the failure criteria of one episode lasting 30 seconds

or more, is very strict and not really that relevant to an individual AF patient. In our survey we found that at the end of year four, 27% of respondents were still experiencing AF episodes. However, their frequency was down by 95% from pre-procedure levels and the total time spent in AF was down from 7% to 0.2% for paroxysmal afibbers. The reduction in AF burden from pre-procedure days to year four was 97%, and this decline was pretty well universal with only 1 in 16 respondents reporting an increase in burden.

## AF recurrence after PVI – Prevention

TSUKUBA, JAPAN. There is ample evidence that any procedure involving damage to the myocardium (middle muscular layer of the heart wall) results in an inflammatory response. Thus, catheter ablation is associated with post-procedure inflammation. Since there is a close relationship between inflammation and atrial fibrillation (AF), it is reasonable to pose the question – Would attenuating or eliminating the post-PVI inflammation result in greater freedom from AF recurrence? A group of physicians from the University of Tsukuba now report the results of a study designed to provide an answer to this question.

A total of 125 paroxysmal afibbers with no underlying structural heart disease with an average age of 61 years (80% male) and an average duration of AF of seven years underwent a pulmonary vein isolation procedure using the double Lasso technique. Linear lesions were added as needed and all patients were also ablated to prevent right atrial flutter (cavotricuspid ablation). Upon completion of the procedure, the study participants were randomized into two groups. The corticosteroid group had a saline hydrocortisone solution administered intravenously immediately after the procedure and then received oral prednisone (0.5 mg/kg/day) for the following three days. The control (placebo) group received a saline solution administered intravenously immediately after the procedure and then received a placebo (lactose) orally for the next three days.

During the first month following the procedure, 27% of the members of the corticosteroid group experienced AF recurrence of which 7% occurred within the first four days (immediate recurrence), and the remaining 20% occurred between four and thirty days after the procedure (early recurrence).

In the control group, 49% experienced recurrence within the first month with 31% being immediate and 18% being early. Thus, the incidence of immediate recurrence was substantially less in the corticosteroid group.

Fourteen months after the PVI, 85% of the members of the corticosteroid group were afib-free without the use of antiarrhythmics as compared to 71% in the placebo group. The Japanese researchers also made the following interesting observations:

- A high body temperature and an elevated level of the inflammatory marker, C-reactive protein (CRP), were significantly associated with an increased risk of experiencing immediate, but no early recurrence.
- Frequent ectopics (premature atrial complexes or PACs) and episodes of non-sustained AF were associated with an increased risk of experiencing early, but not immediate recurrence.

The researchers conclude that post-procedure corticosteroid therapy decreases the recurrence risk at 14 months by preventing immediate AF recurrence caused by inflammatory responses. They suggest that the transient use of small amounts of corticosteroids shortly after a PVI procedure may be effective in preventing both immediate and medium term (14 months) AF recurrences.

*Koyama, T, et al. Prevention of atrial fibrillation recurrence with corticosteroids after radiofrequency catheter ablation. Journal of the American College of Cardiology, Vol. 56, No. 18, October 26, 2010, pp. 1463-72*

**Editor's comment:** The 85% recurrence-free rate at 14 months (no antiarrhythmics) experienced by patients assigned to the corticosteroid group is indeed impressive considering that repeat ablations were not allowed in the study. It would thus seem that reducing post-procedure inflammatory response is an important part of ensuring long-term

success. Hopefully, this approach to inflammation control will become standard practice, but until it does, natural anti-inflammatories may be helpful. For further information on this see the Post Ablation Care protocol at [www.afibbers.org/resources/postablationcare.pdf](http://www.afibbers.org/resources/postablationcare.pdf)

## Spirolactone helps prevent AF recurrence

### Background

In March 2003 I published a report "Aldosterone: Villain of the Peace?" in which I suggested that elevated aldosterone levels could be a trigger for AF episodes and that the aldosterone antagonist spironolactone might be helpful in lengthening the interval between paroxysmal atrial fibrillation episodes. To quote from the March 2003 issue of *The AFIB Report*:

*"Spirolactone, a potassium-sparing diuretic, is highly effective in blocking MC-receptors. By doing so, it rebalances the ANS (increase parasympathetic activity and decreases sympathetic activity), decreases the risk of stroke, prevents hypokalemia, reduces fibrosis, improves endothelial function, and helps prevent hypertension (by blocking MC-receptors in the brain)[1,2]. Could spironolactone help extend the period between LAF episodes or prevent them altogether? Clearly it is a possibility, but one that only a clinical trial can confirm or deny.*

*Spirolactone, unfortunately, has several nasty side effects, especially breast enlargement and impotence. It is therefore not likely to be a viable long-term solution for LAF prevention. However, a "cousin" of spironolactone, eplerenone, has recently been developed and shows great promise in initial trials. Eplerenone is significantly more effective than spironolactone and animal experiments have shown that it protects the heart, brain and kidneys, especially against stroke and vascular injury[1,2]. Eplerenone does not cause breast enlargement or impotence. Could this new drug help prevent episodes? If the hypothesis is correct, it is certainly a very real possibility, but of course only a clinical trial will tell."*

That long wished for clinical trial has now been completed.

[1] Kolb, C, et al. *Modes of initiation of paroxysmal atrial fibrillation from analysis of spontaneously occurring episodes using a 12-lead Holter monitoring system. American Journal of Cardiology, Vol. 88, No. 8, October 15, 2001, pp. 853-57*

[2] Pitt, B, et al. *New insights into the role of aldosterone in cardiorenal disease and the clinical implications. www.medscape.com/viewprogram/1004\_pnt*

### Abstract

WARSAW, POLAND. Angiotensin II and aldosterone are key factors in the structural and neuro-hormonal remodeling of the atria and ventricles in patients with AF. A group of Polish researchers now report that the aldosterone antagonist (blocker) spironolactone is effective in lengthening the interval between episodes among paroxysmal afibbers with no underlying heart disease. Their prospective, randomized clinical trial involved 164 consecutive symptomatic, paroxysmal AF patients of which 53% were male. Average age of all patients was 66 years, 73% had hypertension, 41% had metabolic syndrome, 27% had coronary artery disease, and 59% were on statin drugs – so not exactly a healthy group.

The patients were randomized into receiving for different combinations of spironolactone, enalapril (an angiotensin II receptor blocker) and beta-blocker (propranolol, metoprolol or bisoprolol) as follows:

- Group A – spironolactone + enalapril + beta-blocker
- Group B – spironolactone + beta-blocker
- Group C – enalapril + beta-blocker
- Group D – beta-blocker (control group)

The daily spironolactone dose was 25 mg, the mean dose of enalapril was 12.5 mg/day, and the

beta-blocker dosage was adjusted to achieve a resting heart rate (in sinus rhythm) between 60 and 70 bpm. In patients with hypertension, blood pressure was controlled to achieve a level below

130/80 mm Hg. The number of AF episodes (documented with ECG) over four separate 3-month periods was compared as shown below:

|                | <u>Group A</u> | <u>Group B</u> | <u>Group C</u> | <u>Group D</u> |
|----------------|----------------|----------------|----------------|----------------|
| Baseline       | 4.0            | 3.5            | 2.9            | 3.6            |
| 0 to 3 months  | 1.0            | 1.5            | 1.1            | 2.5            |
| 4 to 6 months  | 0.7            | 0.7            | 1.5            | 3.1            |
| 7 to 9 months  | 0.6            | 0.7            | 1.7            | 3.3            |
| 9 to 12 months | 0.6            | 0.5            | 1.5            | 2.6            |

The total cumulative incidence of AF episodes in the one-year follow-up period was 2.9 for group A (13 episodes less than baseline), 3.4 for group B (11 episodes less than baseline), 5.8 for group C (5.8 episodes less than baseline), and 11.5 for group D (2.9 episodes less than baseline). Only the improvement noted for groups A and B were statistically significant indicating that only spironolactone, but not enalapril or beta-blocker, is effective in AF prevention.

The researchers conclude that spironolactone + beta-blocker (group B) treatment might be a simple and valuable option in preventing paroxysmal AF episodes. They also comment that eplerenone might be a good alternative since it does not have the side effects of spironolactone, especially gynecomastia.

*Dabrowski, R, et al. Effect of combined spironolactone-beta-blocker with or without enalapril treatment on occurrence of symptomatic atrial fibrillation. American Journal of Cardiology, Vol. 106, 2010, pp. 1609-14*

**Editor’s comment:** It is indeed gratifying to see my 8-year-old hypothesis regarding the role of

aldosterone and spironolactone confirmed in a clinical trial. The following sentence in the Polish report is also of particular interest:

*“Goette et al. demonstrated that AF occurrence results in an increase in aldosterone concentrations and that 2 days after cardioversion, its level has decreased, with a reduction of the aldosterone-renin index and mean heart rate.”*

In February 2003 I had my aldosterone and renin levels measured 2 days after an episode and 1 day before the next episode. Aldosterone levels were 34 nmol/day (24-hour urine test) 2 days after the episode and 51 nmol/day just before the next episode, while renin levels were 0.04 ng per liter per second after the episode and an undetectable 0.00 prior to the next episode. These results ([www.afibbers.org/results.pdf](http://www.afibbers.org/results.pdf)) clearly confirm Goette’s observations and again demonstrate the desirability of afibbers having their aldosterone:renin ratio determined, particularly if episodes are of a cyclical nature.

## Success rates for the Cox maze IV procedure

SAINT LOUIS, MISSOURI. The Cox maze procedure for the purpose of curing atrial fibrillation (AF) has been performed since 1987. It has gone through several iterations from the use of a cut-and-sew protocol to create the lesion set to the now prevalent use of ablation catheters or clamps powered by radiofrequency or cryo energy. The last cut-and-sew version, the Cox maze III, had a complete success rate (no AF, no antiarrhythmics) of 70% and a partial success rate of 27% (no AF, but still on antiarrhythmics) after a mean follow-up of 5 years.

Cardiothoracic surgeons at the University of Washington Medical School (Dr. Damiano’s group)

now report on the success of the Cox maze IV procedure. This procedure still involves open heart surgery and the use of a heart/lung machine, but now uses bipolar radiofrequency-powered clamps (Atricure or Medtronic) to create the main lesions (on both the left and right atrium). At the tricuspid and mitral valve openings cryoablation is generally used. A study was recently completed to establish the one-year success rate of the Cox maze IV procedure.

The study involved 282 patients (63% men) of which 42% had paroxysmal AF, 10% had the persistent variety, and 48% were in long-standing persistent (permanent) AF. The median duration

was 3.7 years. The majority (66%) of patients had other reasons than the presence of AF for undergoing the maze procedure, 28% underwent mitral valve replacement, 20% had coronary bypass surgery with or without valve replacement, and another 18% had various other indications for the surgery. The remaining 34% had AF as the only indication for the procedure.

The study participants underwent the Cox maze IV between January 2002 and December 2009 and were followed up to 3, 6, 9 and 12 months post-procedure with 24-hour Holter monitoring. In procedures done since 2005, a second superior connecting lesion was added (the box lesion set) to anatomically isolate the entire posterior left atrium. All participants were on antiarrhythmics at discharge but these were discontinued if the patients were afib-free at two months. Anticoagulation was usually stopped after three months.

Complete success was defined as being free of atrial tachyarrhythmias (AF, atrial flutter and atrial tachycardia) lasting longer than 30 seconds without the use of antiarrhythmics. Complete success rates were 63%, 79%, and 78% at 3, 6 and 12 months respectively. Partial success rates (arrhythmia-free, but still on antiarrhythmics) were 26%, 14%, and 20% respectively, giving overall afib-free rates (with or without antiarrhythmics) of 89%, 93%, and 89% respectively. There was no difference in success rates for paroxysmal versus persistent and permanent AF.

Early post-operative atrial arrhythmias were quite common (53% of patients), but usually resolved over the first month following the procedure. Postoperative mortality was 1% among patients with AF only and 3% among those with concomitant valve or other problems. Eleven percent of patients had major procedure-related complications including serious bleeding, renal failure, and stroke. The median length of hospital stay was 9 days with a range of 4 to 73 days. The major factors associated with failure were early atrial arrhythmias

(OR=3.0), and larger left atrial diameter (OR=1.4). Having completed the box set lesions around the pulmonary veins were significantly associated with improved outcome (OR=0.38)

The authors conclude that the Cox maze IV procedure has a high success rate at one year even with improved follow-up and stricter definition of failure.

*Damiano, RJ, et al. The Cox maze IV procedure: predictors of late recurrence. Journal of Thoracic and Cardiovascular Surgery, Vol. 141, No. 1, January 2011, pp. 113-21*

**Editor's comment:** The Washington School of Medicine is one of the world's most successful centers for the performance of the Cox maze. Thus, it is reasonable to compare their results with such catheter ablation centers as the Cleveland Clinic (during Dr. Natale's tenure), the California Pacific Medical Center, and the Bordeaux group at Hopital Cardiologique du Haut-Leveque. The 2008 Ablation/Maze Survey included 165 lone afibbers treated at these three institutions. Complete success rate (no AF, no antiarrhythmics) for the three institutions combined was 71% and the partial success rate was 5%, giving an overall success rate of 76% after an average of 1.3 procedures. No procedure-related deaths were reported from any of the institutions.

Thus, the Cox maze IV is clearly more successful than even the best catheter ablation. However, it is a substantially more complicated procedure, has a substantially higher mortality and rate of serious complications, and a longer recovery period. It also involves the use of a heart/lung machine, which in itself can cause problems, especially of a cognitive nature. Finally, it would appear that only arrhythmia incidences happening at the 3, 6, 9 and 12 months follow-ups were counted. It would seem very unlikely that episodes would not have occurred outside of these four 24-hour monitoring periods. My opinion has not changed – a full Cox maze procedure is “overkill” for a paroxysmal lone afibber.

## Timing essential in ablation for persistent AF

TOKYO, JAPAN. Persistent atrial fibrillation (AF) is defined as episodes needing cardioversion to achieve termination or episodes lasting longer than seven days but amenable to cardioversion to normal sinus rhythm. Persistent AF is notoriously

more difficult to eliminate than is paroxysmal (intermittent) AF because the foci precipitating the fibrillation are not exclusively or almost exclusively located in the pulmonary veins as is the case in paroxysmal AF.

A group of researchers from the Tokyo Medical University recently treated a group of persistent afibbers and observed that the chance of a successful outcome was substantially higher the shorter the time the patients had suffered from persistent AF. In other words, if an afibber develops the persistent variety, an early ablation would be in order. The study included 93 patients (85% male) with an average age of 58 years and the median duration of persistent AF being one year. Average left ventricular ejection fraction was 60%, and 85% of participants had lone AF (no underlying heart disease).

The first procedure included anatomically-guided pulmonary vein isolation (PVI), electrogram-based ablation in the left atrium and coronary sinus, left atrium linear ablation, superior vena cava (SVC) isolation, and cavotricuspid isthmus linear ablation (right atrial flutter ablation). The pulmonary veins were isolated in all patients, but this part of the procedure only terminated the AF in two patients, clearly indicating that the triggers for persistent AF are not primarily located in the pulmonary veins. Following ablation of other targets, AF was terminated in 25 patients (27%), while the remaining 68 patients (73%) had their arrhythmia terminated by cardioversion.

After a mean follow-up of 1.8 years, only 38% of patients remained in normal sinus rhythm (NSR), 33% had experienced recurrence of AF, while the remaining 29% were found to have atrial tachycardia (AT). Twenty-eight of the 31 patients who had recurrence of AF (21 persistent and 7 paroxysmal) underwent a second procedure involving re-isolation of the pulmonary veins and

electrogram-based ablation. This terminated AF in two patients. Further ablation in the right atrium added another five patients to the AF-free group. All of the patients with AT after the first procedure underwent a second procedure specifically aimed at curing the AT. This was successful in 66% of cases. Finally, 19 patients underwent a third procedure – 6 patients for AF and 13 for AT.

After an average 1.3 years from the last procedure, 76 patients (82%) were in NSR, but five of them (5%) only with the aid of antiarrhythmics. Patients who had only had their persistent AF for a relatively short time were significantly more likely to have a successful outcome as were those whose arrhythmia stopped on its own during the first ablation. The researchers also observed substantial benefits of having an extensive right atrium ablation. Of the 26 patients who underwent this additional procedure, 62% achieved NSR.

The researchers speculate that the fibrillatory substrate progressively extends from the left atrium to the right atrium over time, and conclude that right atrial ablation may improve outcome in patients whose left atrial ablation was unsuccessful. They also point out that patients with shorter duration of persistent AF are more likely to have a successful left atrial ablation.

*Takahashi, Y, et al. Clinical characteristics of patients with persistent atrial fibrillation successfully treated by left atrial ablation. Circulation Arrhythmia and Electrophysiology, Vol. 3, October 2010, pp. 465-71*

**Editor's comment:** The take-home message of this study is not to wait too long to undergo an ablation once it is established that the AF is of the persistent nature.

## Long-term ablation outcomes in Australia

MELBOURNE, AUSTRALIA. A fortunate trend seems to be emerging, namely that of reporting long-term outcomes of catheter ablation. The Bordeaux group (Profs. Haissaguerre and Jais at Hopital Cardiologique du Haut-Leveque) recently reported a 5-year AF-free survival rate of 63% in a group of 100 patients with paroxysmal (64%), persistent (22%) or permanent (14%) atrial fibrillation.

Now electrophysiologists at the Royal Melbourne Hospital report their results for a group of 100 consecutive patients with highly symptomatic

paroxysmal atrial fibrillation (AF) who had undergone one or more circumferential pulmonary vein antral isolation (PVAI) procedures. The average age of the patients was 54 years (44 to 64 years) and 79% were men. None had structural heart disease, but 27% had hypertension and 6% had coronary artery disease. The average duration of AF was six years.

Interestingly enough, the Australian researchers also report on the episode frequency and severity prior to ablation. A total of 34% of the study participants experienced AF episodes at least once



a week, 27% had at least one episode a month, and the remaining 39% went more than a month between episodes. The episode duration was commonly between 1 and 24 hours (76%), but 10% reported episode duration of less than an hour and 14% reported duration of more than 24 hours. A severity score was also developed with scores from 1 to 10 with 10 indicating more severe symptoms. A composite score of episode frequency, duration and severity was also developed (ranging from 3 to 30) and named "Total AF Burden Score".

All patients underwent a PVAI using a combination of electrophysiological and anatomical guidance and employing a radiofrequency-powered 4 mm irrigated catheter. The endpoint of the procedure was electrical isolation (from the left atrium) of all four pulmonary veins through the placement of two wide circular lesions of ipsilateral veins. The procedure was performed under general anaesthesia and was free of major complications. Patients were followed up at 3, 6, 9 and 12 months and then at least every six months thereafter. Holter monitoring or 7-day monitoring was also performed at any hint of symptoms of possible recurrence.

After an average follow-up of 39 months since the initial PVAI, 49% of patients were in normal sinus rhythm without the use of antiarrhythmics. Twenty-two patients underwent a repeat procedure during which it was found that all had recurrent conduction across previously isolated pulmonary vein-left atrium junctions. After an average 1.2 procedures, 57% of patients were in sinus rhythm after 39 months, while another 25% were in sinus rhythm aided by previously ineffective antiarrhythmics. Thirteen patients continued to have paroxysmal episodes, but their Total AF Burden Score declined from an average of 17 to 10. Thirty-seven patients experienced at least one episode of AF or atrial tachycardia after a 1-month blanking period, and

86% of these patients developed recurrent arrhythmia within 12 months of their procedure. In contrast, only 14% of patients had recurrence after having been AF-free for 12 months or more. Kaplan-Meier curves predicted freedom from AF (no AF with or without antiarrhythmics) after the final procedure of 87% at 12 months post-PVAI and 80% at 4 years post-PVAI.

The researchers conclude that the majority of patients who are free of AF at 1-year post-ablation can be reassured that the risk of later recurrence is relatively small, although antiarrhythmics may be required to maintain normal sinus rhythm.

*Medi, C, et al. Pulmonary vein antral isolation for paroxysmal atrial fibrillation: results from long-term follow-up. Journal of Cardiovascular Electrophysiology, August 31, 2010 [Epub ahead of print]*

**Editor's comment:** It is of interest to compare some of the Australian findings to those reported in our 2009 Ablation/Maze Survey. The Australian researchers reported that 57% of patients were in sinus rhythm without the use of antiarrhythmics at the 3-year mark (39 months). Another 25% were AF-free with the use of antiarrhythmics. In our survey 69% were in sinus rhythm in year 3-4 without the use of antiarrhythmics, while another 6% were AF-free with the aid of antiarrhythmics. As found in the Australian study, the major determinant of an AF-free existence at 3 years was the absence of AF at 12 months post-ablation. In our survey, absence of AF at 12 months post-ablation was associated with an 80% complete success rate and a partial success rate of 4% at year 3-4. Having experienced episodes during the last 6 months of the 12-month period following the procedure was associated with a 29% complete success rate and a 12% partial success rate. This is a clear vindication of the conclusion that AF-free status during the first year post-ablation (excluding a suitable blanking period) is crucial for long-term success.

## WARNING

SILVER SPRING, MD. The US Food and Drug Administration (FDA) have issued a "drug safety communication" warning that the use of the antiarrhythmic drug dronedarone (Multaq) may cause severe liver injury. The makers of the drug, Sanofi-Aventis, recommend that healthcare professionals consider periodic liver-function tests in patients taking dronedarone. The warning was prompted by the incidence of acute liver failure followed by liver transplants in two women without previous liver problems who had been on the drug for 4 to 6 months.

## REVIEW

### 2011 ACCF/AHA/HRS Update of 2006 Guidelines for Management of Atrial Fibrillation

The American College of Cardiology/ American Heart Association guidelines for the management of patients with atrial fibrillation was last issued in 2006 (<http://circ.ahajournals.org/cgi/reprint/114/7/e257>). Since then several important new developments have been reported which warrant changes to the 2006 guidelines. Hence this so-called “focused update”, expected to become a regular feature in order to keep guidelines up-to-date. The focused update was written by a writing committee of 12 experts – the majority being university professors with 6 having financial or other relationships with relevant industries. The focused update document was peer-reviewed by 30 experts of which 20 (67%) had ties to the pharmaceutical and/or medical devices industry.

This update contains seven recommendations which replace or add to the 2006 guidelines.

- Treatment to achieve strict control of heart rate (< 80 bpm at rest or 110 bpm during a 6-minute walk) is not superior to achieving a resting heart rate less than 110 bpm in patients with persistent AF who have stable ventricular function (left ventricular ejection fraction greater than 40%).
- The addition of clopidogrel (Plavix) to aspirin to reduce the risk of major vascular events, including stroke, might be considered in patients with AF and an average of 2 stroke risk factors in whom oral anticoagulation with warfarin is considered unsuitable. The ACTIVE-W trial observed an annual rate of vascular events (first ischemic stroke, non-central nervous system systemic embolism, heart attack or vascular death) of 3.9% in patients on warfarin and a rate of 5.6% in patients on aspirin + clopidogrel. Major hemorrhages occurred in 2.1% of patients on warfarin and in 2.4% of those on clopidogrel + aspirin.
- Dronedarone (Multaq) may be useful for decreasing the need for hospitalization in patients with paroxysmal AF, or after conversion of persistent AF. Dronedarone can be initiated on an out-patient basis.
- Catheter ablation performed in experienced centers is useful in maintaining sinus rhythm in selected patients with significantly symptomatic, paroxysmal AF who have failed treatment with an antiarrhythmic drug and have normal or mildly dilated left atria, normal or mildly reduced left ventricular function, and no severe pulmonary disease. NOTE: An experienced catheter ablation center is defined as one performing more than 50 procedures a year.
- Catheter ablation is reasonable to treat symptomatic persistent AF.
- Catheter ablation may be reasonable to treat symptomatic paroxysmal AF in patients with significant left atrial dilatation or with significant left ventricular dysfunction.
- Initiation of therapy with propafenone or flecainide can be beneficial on an out-patient basis in those without structural or coronary heart disease who are in normal sinus rhythm at the time of drug initiation.

Wann, LS, et al. 2011 ACCF/AHA/HRS focused update on the management of patient with atrial fibrillation (updating the 2006 guidelines). *Heart Rhythm*, Vol. 8, January 2011, pp. 157-76

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