

THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

NUMBER 117

MARCH 2012

12th YEAR



In June 2007 cardiologists at the Mayo Clinic reported the results of a 30-year study carried out to determine the long-term prognosis of lone atrial fibrillation. They concluded that lone afibbers have a very low risk of ischemic stroke and that whatever risk there is (0.2%/year) is due, not to AF as such, but rather to the development of comorbid conditions such as hypertension, diabetes and heart failure. They also concluded that overall survival is not adversely affected by lone AF.

This month a group of cardiologists in Serbia released the results of the Belgrade Atrial Fibrillation Study aimed at determining the long-term prognosis for lone AF. This 12-year study, involving 346 newly diagnosed patients, confirmed that lone afibbers have a very low risk of ischemic stroke (0.2%/year) and excellent survival. However, 27% of originally paroxysmal afibbers did progress to permanent AF.

Also in this issue we report that blood level of brain natriuretic peptide (BNP) is a reliable indicator of how long a patient has been in AF, that a persistent high white blood cell count is a risk factor for the development of AF, that combining radiofrequency ablation with cryoablation substantially reduces the need for repeat procedures, and that the latest trial of dronedarone (Multaq) was halted early due to excess mortality.

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 very much appreciated.

Wishing you good health and lots of NSR,

Hans

Highlights

Chromium associated with AF	p. 3
BNP and safety of cardioversion	p. 3
White blood cell count predicts AF	p. 4
Importance of repeat ablations	p. 5
Success of combined RF & cryoablation	p. 6
Dronedarone (Multaq) fails in clinical trial	p. 6
Long-term efficacy of amiodarone	p. 7

average follow-up of 30 years, 29% of paroxysmal and persistent afibbers had progressed to permanent AF. In most cases the progression to permanent AF occurred within the first 15 years after diagnosis. Survival in the study group at 92% at 15 years and 68% at 30 years was similar to or even slightly better than expected for an age- and sex-matched group of Minnesotans (86% and 57% at 15 and 30 years respectively). The development of congestive heart failure (19% of the group at 30 years follow-up) was not significantly higher than expected (15%).

During the follow-up, 5 strokes (0.2%/person-year) and 12 transient ischemic attacks (0.5%/person-year) occurred in the group . mostly among permanent afibbers. All strokes and TIAs (transient ischemic attacks) occurred in participants who had developed one or more risk factors for stroke during

Long-term prognosis for lone afibbers

BELGRADE, SERBIA. In June 2007 cardiologists at the Mayo Clinic reported the results of a study carried out to determine the long-term prognosis of 76 patients with lone atrial fibrillation (AF). After an

follow-up (hypertension in 12 patients, heart failure in 4, and diabetes in 3). Not a single stroke or TIA occurred among lone afibbers with no risk factors for stroke. This prompted the remark from the researchers . *Our long-term data suggest that the increased risk of stroke in atrial fibrillation is due to "the company it keeps"*. In other words, lone AF as such is not a risk factor for ischemic stroke. The overall conclusion of the study is highly reassuring to lone afibbers . *After >30 years of follow-up of our rigorously defined cohort, findings confirm that overall survival is not affected adversely by lone atrial fibrillation.[1]*

A group of Serbian cardiologists now report on a larger long-term study involving 346 patients with newly diagnosed lone atrial fibrillation (LAF). Their definition of LAF was AF in patients 60 years old or younger with no hypertension, underlying heart disease or other comorbid conditions that could explain the presence of AF. The average age of the study participants at baseline was 43 years (range of 18 to 60 years), 76% were male, and 12% had asymptomatic AF. The majority (70%) had paroxysmal (intermittent) AF at baseline with 22% having persistent and the remaining 8% having permanent AF. Permanent afibbers were significantly more likely to have an enlarged left atrium and asymptomatic AF when compared to paroxysmal afibbers. During the average 12-year follow-up, 35% of the group developed heart disease, 25% hypertension, and 10% diabetes.

During follow-up, 27% of paroxysmal afibbers and 55% of originally persistent afibbers progressed to permanent AF. The average time to progression was 10 years and the average age at which progression was documented was 55 years (range of 24 to 74 years). Older age at diagnosis and development of congestive heart failure were predictors of progression. Somewhat surprisingly, the development of hypertension was associated with a 30% decrease in the risk of progression from paroxysmal to persistent or permanent AF. It is likely that this is due to the fact that therapy with angiotensin II converting enzyme inhibitors was much more common among patients with hypertension (77%) than among those who retained normal blood pressure (5%). NOTE: Hypertension was defined as a blood pressure reading above 140/85 mm on 3 separate occasions.

A newly developed risk score, the so-called HATCH score (1 point each for hypertension, age of 75 years or older, and chronic obstructive pulmonary disease and 2 points each for heart failure and prior

stroke or TIA) was found to accurately predict the risk of progressing from paroxysmal to permanent AF. A score of 0 was associated with a 20% risk of progression, a score of 1 with a 36% risk, and a score of 2 with a 63% risk of progressing to permanent AF.

Thromboembolism was documented in 14 patients (4%) over the 12-year follow-up period. Nine of the 14 patients suffered an ischemic stroke corresponding to an annual stroke incidence of 0.2%. This rate is identical to the one observed in the Mayo Clinic study and, once again, confirms that the risk of stroke associated with one AF is extremely low . actually lower than the rate observed in the general population. Furthermore, it should be noted that 6 of the 14 patients had developed one or more risk factors for thromboembolism (5 patients with hypertension, 1 with coronary artery disease, and 2 with diabetes) by the time they experienced their stroke or other thromboembolic event. It is also of interest to note, that of the 14 patients 8 were taking aspirin, while 6 had no antithrombotic therapy. In multivariate analysis only the development of hypertension and coronary artery disease was significantly associated with thromboembolism.

During follow-up, 14 patients (4%) developed congestive heart failure (CHF) at an average 10 years from diagnosis (range of 0 to 26 years). The only variable independently associated with an increased risk of CHF in multivariate analysis was progression from paroxysmal to permanent AF. The 10-year survival of study participants was 99.6%. It is not clear from the study whether permanent AF increases the risk of CHF, or CHF increases the risk of permanent AF. The former clearly makes more sense.

The Serbian researchers conclude that the prognosis of lone AF is favourable, but becomes less so with increasing age and the development of (new) underlying heart disease.

Potpara, TS, Lip, GYH, et al. A 12-year follow-up study of patients with newly diagnosed lone atrial fibrillation: Implications of arrhythmia progression on prognosis. Chest, Vol. 141, No. 2, 2012, pp. 339-47

Boriani, G, et al. Atrial fibrillation: It is better to be alone than in bad company! Chest, Vol. 141, No. 2, 2012, pp. 290-92

Editor's comment: The Belgrade study clearly confirms the conclusions of the Mayo Clinic study that lone AF is a benign condition with excellent long-term prognosis. The risk of stroke is extremely low even without anticoagulation, and survival rate

is excellent. There is a significant trend though for paroxysmal AF to progress to persistent or permanent AF. It is, however, likely that this trend would have been significantly less pronounced if 36% of paroxysmal and persistent afibbers had not been treated with digoxin. This medicine from hell, for lone afibbers at least, may not only prolong episode duration, but may actually convert paroxysmal AF to permanent.[2,3]

NOTE: I personally do not agree that chronological age should enter into the definition of lone AF. This conviction is supported by the following statement by Dr. Lars Frost of the Aarhus University Hospital in Denmark, *Cardiologists with strong political influence have suggested that a diagnosis of lone atrial fibrillation should be restricted to patients <60 years of age, although there is no evidence of any threshold values by age regarding the risk of stroke*

in patients with atrial fibrillation – or in any other medical condition for that matter.[4]

References

1. Jahangir, A, et al. Long-term progression and outcomes with aging in patients with lone atrial fibrillation. *Circulation*, Vol. 115, June 19, 2007, pp. 3050-56
2. Sticherling, C, et al. Effects of digoxin on acute, atrial fibrillation: Induced changes in atrial refractoriness. *Circulation*, Vol. 102, November 14, 2000, pp. 2503-08
3. Falk, RH. Proarrhythmic responses to atrial antiarrhythmic therapy. In **Atrial Fibrillation: Mechanism and Management**, edited by Rodney H. Falk and Philip J. Podrid, Lippincott-Raven Publishers, Philadelphia, 2nd edition, 1997, p. 386
4. Frost, L. Lone atrial fibrillation: Good, bad or ugly? *Circulation*, Vol. 115, June 19, 2007, pp. 3040-41

Chromium associated with atrial fibrillation

OPOLE, POLAND. Researchers at the Institute of Technology in Opole, Poland have undertaken a project to determine how environmental pollution affects the incidence of common diseases and disorders. They are using the concentration of various elements found in rainwater as an indicator of the degree of environmental pollution. The Opole province has a population of 1 million divided into 12 counties. Regular rainwater sampling and analysis is done in each county and expressed in grams per hectare per year.

The researchers now report a strong correlation between rainwater content of chromium (correlation coefficient = 0.62, $p < 0.05$) and the number of hospital admissions for atrial fibrillation (AF). For example, in the county of Namyslowski the incidence of admission to hospital for AF was 20 per 10,000 inhabitants per year and the rainwater content of chromium was 2.6 grams/hectare/year. In contrast, the county of Strzelecki reported 130

admissions per 10,000 inhabitants and chromium content of 3.5 grams/hectare/year. The rainwater content of cadmium, lead and zinc was also positively correlated with the incidence of AF with correlation coefficients of 0.57, 0.57 and 0.50 respectively at a significance level of $p < 0.05$.

The researchers speculate that the effect of chromium is related to its effect on the autonomic nervous system and the cytotoxic activity of hexavalent chromium. There are also reports suggesting possible relations between cadmium, lead and zinc and increased adrenergic stimulation. Finally, recent research has revealed a positive correlation between zinc content of cardiac cells and AF.

Tubek, S, et al. The content of elements in rainwater and its relation to the frequency of hospitalization for atrial fibrillation in Opole Voivodship, Poland, during 2000 – 2002. Biological Trace Element Research, Vol. 138, 2010, pp. 1-7

BNP and safety of cardioversion

PARIS, FRANCE. BNP (brain natriuretic peptide) is a hormone released by stretching of the walls of the ventricles. Thus, it is not surprising that elevated levels of BNP have been observed in patients with atrial fibrillation (AF). The serum level of BNP has been found to be highest in permanent afibbers and lowest in paroxysmal afibbers, with persistent afibbers falling somewhere in between. The

observation that BNP increases with increasing duration of AF led a group of researchers at the Cochin Hospital to speculate that BNP level may be a useful indicator of how long a patient arriving in emergency has been in AF. As a general rule, cardioversion is not performed immediately if a patient has been in AF for more than 48 hours, unless a transesophageal echocardiogram (TEE)

shows no evidence of thrombi (blood clots) in the left atrium and appendage. If a TEE is not performed, and a patient has been in AF for more than 48 hours, then a 3-week treatment with anticoagulants is required before cardioversion.

The French researchers included 45 patients arriving at the emergency department in AF. AF was paroxysmal in 21 patients, persistent in 6, and permanent in the remaining 18. Average BNP level (measured as NT-proBNP) was 1030 pg/mL for paroxysmal, 3658 pg/mL for persistent, and 4350 pg/mL for permanent (long-standing persistent) afibbers. Eighteen patients (40%) had been in AF for less than 48 hours upon admission (according to their own experience of symptoms, notably palpitations). These patients tended to have a higher average heart rate (136 bpm) than those who had been in AF for more than 48 hours (102 bpm).

Even more significant was the difference in BNP level. Patients who had been in AF for less than 48 hours (presumably all paroxysmal) had an average BNP level of 960 pg/mL, while those who had been in AF for more than 48 hours had an average level

of 3695 pg/mL. No patients with a BNP level less than 304 pg/mL had been in AF for more than 48 hours. A cut-off value of 1328 pg/mL was associated with a sensitivity and a specificity of 74.1% and 72.2% respectively.

The researchers conclude that AF patients presenting with low values of BNP are likely to have been in AF for less than 48 hours and can, therefore, be safely cardioverted. They do point out that their study involved only a small number of patients and that larger studies are needed to confirm their findings and fine-tune the cut-off point. *Meune, C, et al. N-Terminal-proBrain natriuretic peptide measurement at presentation to identify patients with recent onset of atrial fibrillation. International Journal of Cardiology, Vol. 154, January 26, 2012, pp. 208-09*

Editor's comment: Most afibbers present for cardioversion with symptomatic AF so they know well how long they have been fibrillation. It would be very useful if their statement concerning how long they have been in AF could be confirmed with a simple blood test, so as to avoid a 3-week course of anticoagulation prior to cardioversion.

White blood cell count predicts AF

BOSTON, MASSACHUSETTS. Numerous studies have found a clear association between inflammation and atrial fibrillation (AF). Several of these studies measured level of C-reactive protein (CRP), a powerful marker of systemic inflammation, and concluded that CRP levels are elevated in paroxysmal afibbers, and further elevated in persistent and permanent (long-standing persistent) afibbers. What is still not entirely clear is whether the observed correlation means that inflammation is a cause of AF or that AF is a cause of inflammation. Now a group of American, Dutch and German researchers weigh in with new research that supports the hypothesis that inflammation is a cause of AF.

Their study involved 936 participants in the Framingham Heart Study originally enrolled in 1948. At the routine follow-up examination in 1988, the average age of the cohort was 76 years and 61% were women. Ten percent had experienced a prior heart attack, 10% were current smokers, and 54% were on anti-hypertensive medications. The average (median) white blood cell (WBC) count was

$6.4 \times 10^9/L$. An elevated WBC count is the most commonly used marker for systemic inflammation.

During a 5-year follow-up, 82 study participants (9%) developed AF or flutter. The incidence was 5% among participants with a WBC count less than $5.9 \times 10^9/L$ and 15% among those with a WBC count greater than $7.3 \times 10^9/L$. The association between elevated WBC count and increased risk of AF did not change after adjusting for previous heart attack, smoking, heart failure, and known risk factors for AF.

The researchers conclude that an elevated WBC count is associated with an increased future risk of AF and speculate that inflammation causes modification of heart tissue (substrate) through electrical and structural remodeling of the atria. They recommend further studies to confirm their findings and to conclusively determine whether inflammation is a risk factor or a risk marker for AF. *Rienstra, M, et al. White blood cell count and risk of incident atrial fibrillation. American Journal of Cardiology, 2012 [Epub ahead of print]*

Editor's comment: This exploratory study lends credence to the hypothesis that systemic inflammation is associated with an increased risk of developing AF. It does not involve a huge leap of faith to also hypothesize that inflammation is involved in the maintenance and progression of already established AF. Thus, it would seem

prudent for afibbers with elevated WBC or CRP levels to take steps to eliminate, or at least reduce, their systemic inflammation. Powerful natural anti-inflammatories such as fish oils, vitamin C, curcumin, *Zyflamend*, *Boswellia*, beta-sitosterol, and pycnogenol can help achieve this goal.

Importance of repeat ablations

REDWOOD CITY, CALIFORNIA. It is becoming increasingly clear that about 15 to 50% of afibbers undergoing catheter ablation will need two or, in rare cases, more than two procedures in order to achieve lasting freedom from atrial fibrillation (AF). Ablation failure is more common in persistent AF (episodes lasting longer than 7 days or requiring cardioversion) and long-standing persistent AF (permanent) than in paroxysmal (episodes self-converting in less than a week, usually less than 48 hours). An enlarged left atrium, hypertension, diabetes and advanced age are other factors associated with ablation failure. Electrophysiologists at Sequoia Hospital now report that repeat ablations are more successful than initial ablations.

Their study involved 843 patients (72% male) undergoing RF-powered catheter ablations (96% using general anesthesia) during the period October 10, 2003 to December 31, 2009. Thirty-two percent of the study participants had paroxysmal AF, 50% had persistent, and the remaining 18% had permanent AF. Paroxysmal AF was significantly more common among women (43.4%) than among men (27.6%), while permanent AF was more common among males (20.4%) than among females (11.1%). Twenty percent of the group had heart disease, 43% had hypertension, and a sizeable proportion of the group was overweight or obese (average BMI 29).

All patients underwent an initial circumferential pulmonary vein isolation procedure with additional lesion sets as required. The average total procedure and fluoroscopy times were 138 and 71 minutes respectively, and were similar for the initial and repeat procedures. The 1-year AF-free success rates (without antiarrhythmics) after the initial procedure were 66.1% for paroxysmal, 54.5% for persistent and 44.8% for permanent AF. Four-year complete success rates (from Kaplan-Meier curves) were 60.9% for paroxysmal, 42.9% for persistent and 35.2% for permanent AF. Significant

predictors of failure were advanced age, enlarged left atrium, and the presence of coronary artery disease.

Twenty-eight percent of the 843 initial patients underwent one repeat procedure and 21 patients (2.5% underwent two repeat ablations. Complete success rates (no AF, no antiarrhythmics) at 1-year from the repeat ablation(s) were 82.9% for paroxysmal, 69.8% for persistent and 66.3% for permanent AF. Corresponding 4-year rates were 81.1%, 58.5% and 59.1% respectively. Thus, the final success rates after one or more procedures were (at 1-year) 85.1% for paroxysmal, 76% for persistent and 65.6% for permanent AF. Corresponding 4-year success rates were 83.6%, 62.2% and 57.3% respectively. At the final follow-up, an additional 24 paroxysmal (2.9%), 58 persistent (6.9%) and 62 permanent (7.33%) afibbers were afib-free with the aid of antiarrhythmic drug therapy. Procedure-related complications at 3.5% were relatively rare with no deaths, atrial-esophageal fistula or pulmonary vein stenosis requiring intervention.

A total of 138 patients whose initial ablation had been unsuccessful did not undergo repeat procedure(s) before the study's termination on December 31, 2009. Of these, 55 underwent a procedure at a later date, 31 were advised by their physician not to undergo a repeat procedure, and 52 decided on their own to forego further treatment. The Sequoia electrophysiologists estimate that if these 138 patients had all undergone repeat procedures, then the final complete success rates at 4 years would have been 94.5% for paroxysmal, 84.9% for persistent, and 78.5% for permanent afibbers. They conclude that repeat ablations are more successful than initial ablations and recommend that prospective ablation patients be advised that a repeat procedure may be required to eliminate their AF.

Winkle, RA, et al. Long-term results of atrial fibrillation ablation: the importance of all initial ablation failures

undergoing a repeat ablation. *American Heart Journal*, Vol. 162, July 2011, pp. 193-200

Editor's comment: The success rate obtained by the EPs at Sequoia Hospital are indeed impressive and should remind all afibbers of the famous quote "At first you don't succeed, try, try again."

Success of combined radiofrequency and cryoablation

LONDON, UNITED KINGDOM. Initial complete success rates (no AF, no antiarrhythmics) for catheter ablation at high-volume centers average between 50 and 60% at the 1-year follow-up. The main cause of failure is recovery of electrical conduction between the pulmonary veins and the left atrium through the development of gaps in the originally complete lesion rings around the pulmonary veins. The primary aim of repeat procedures is to re-ablate the gaps and doing so can bring success rates to 85% or higher for paroxysmal afibbers. A group of electrophysiologists from St. Bartholomew's Hospital now report that a combination of standard radiofrequency (RF)-powered pulmonary vein isolation and balloon-based cryotherapy may eliminate the need for repeat ablations.

The study involved 25 consecutive paroxysmal afibbers who underwent a first circumferential (wide area) pulmonary vein isolation procedure, 25 paroxysmal afibbers who underwent cryotherapy using a cryo-balloon (88% used a 28-mm balloon) and 25 who were treated with a combination of the two approaches. Follow-up ranged from 1.4 to 2.2 years. Complete success rate at the 1-year follow-up (freedom from symptomatic episodes) was 52% in the RF ablation group, 56% in the cryoablation group, and 80% in the combined group. No

complications were observed in the RF only group, but two phrenic nerve palsies, which recovered by 3 months, and one groin hematoma occurred in the cryo only and combined treatment groups. The total average procedure time was slightly longer in the combined group (229 minutes) than in the RF only group (197 minutes), and the cryo only group (185 minutes). The additional cost involved in the combined procedure was \$3360 US. The British EPs conclude that the combined approach is safe and significantly more effective than stand-alone RF ablation, or stand-alone cryotherapy.

Tayebjee, MH, Schilling, RJ, et al. Pulmonary vein isolation with radiofrequency ablation followed by cryotherapy. Europace, Vol. 13, 2011, pp. 1250-55

Editor's comment: It makes sense that creating two sets of lesions isolating the pulmonary veins from the left atrium is more effective than just one set. However, the study was really just a feasibility study and larger, randomized studies with longer follow-up periods are needed to confirm the superior efficacy of the combined procedure. Nevertheless, substantial cost savings could, no doubt, be realized if the combined approach would eliminate the need for repeat procedures in a significant number of cases.

Dronedaron (Multaq) fails in clinical trial

HAMILTON, ONTARIO, CANADA. In July 2009 the US Food and Drug Administration approved the antiarrhythmic drug dronedarone (Multaq) for the treatment of atrial fibrillation (AF) in patients without severe systolic heart failure. The approval was based on three clinical trials (EURIDIS, ADONIS, ANDROMEDA) involving almost 2000 patients with AF and various comorbidities. The ANDROMEDA trial involving 600 patients with advanced congestive heart failure. In the 2 months the trial lasted, 8% of the patients receiving dronedarone died vs. 3.8% in the placebo group.

Nevertheless, in July 2010, an international group of researchers decided to go ahead with a new trial (PALLAS) designed to determine if treatment with dronedarone (400 mg twice daily) would reduce the rate of major cardiovascular events and associated hospitalizations in high risk patients with permanent AF. In July 2011 a total of 3236 patients had been enrolled. The average age of the patients was 75 years, 64% were male, 41% had coronary artery disease, 85% had hypertension, 35% diabetes, and about two-thirds of them had a history of heart failure. One-third of the patients were on digoxin and 84% received warfarin, but were only within the proper INR range 57% of the time.

On July 15, 2011 when the trial was prematurely halted twice as many patients in the dronedarone group had died or suffered a stroke or heart attack when compared to the placebo group. The rate of unplanned hospitalizations for heart failure and other cardiovascular causes was 31%/year in the dronedarone group and 16%/year in the placebo group. Arrhythmia-related mortality was 3 times higher in the dronedarone group than in the placebo group indicating that dronedarone can cause dangerous ventricular arrhythmias in high-risk permanent afibbers. The use of dronedarone was found to be particularly dangerous in patients with diabetes.

The researchers conclude that dronedarone increases the rate of heart failure, stroke and death from cardiovascular causes in high-risk patients with permanent AF and consequently should not be prescribed for this patient population.

Connolly, SJ, et al. Dronedarone in high-risk permanent atrial fibrillation. New England Journal of Medicine, November 14, 2011 [Epub ahead of print]

Nattel, S. Dronedarone in atrial fibrillation – Jekyll and Hyde? New England Journal of Medicine, November 14, 2011 [Epub ahead of print]

Editor's comment: Unfortunately, this report is not the first pointing to a less than sterling safety profile

for dronedarone. On September 22, 2011 the European Medicines Agency (EMA) issued a bulletin recommending restricting the use of dronedarone to cases where no other drugs had proven effective. This recommendation was partly based on the results of the prematurely-halted PALLAS trial. The EMA recommends that dronedarone use should be restricted to patients with paroxysmal or persistent AF when they are in normal sinus rhythm. It should not be used when patients are in AF, nor in those with permanent AF or heart failure. In any case, patients on the drug should be monitored by a specialist and have their lung, liver and heart rhythm function checked regularly.

Several electrophysiologists have 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. It seems to me that giving paroxysmal afibbers a drug that becomes dangerous whenever they actually experience AF is a less than smart move. I think dronedarone deserves a place, alongside digoxin and sotalol, as the most useless pharmaceutical drug for lone AF patients.

Long-term efficacy of amiodarone

IWATE, JAPAN. It is estimated that 3% of Japanese people over the age of 70 years suffer from atrial fibrillation (AF) and this percentage is expected to increase to 4.5% over the next 20 years. In comparison, the number of people in the USA with AF was estimated at 5 million in 2000 and is expected to increase 2- to 3-fold over the next 50 years. Currently recommended first-line treatment for paroxysmal (intermittent) AF involves the use of antiarrhythmic drugs such as flecainide, propafenone, disopyramide, sotalol and amiodarone. Class I drugs (flecainide and propafenone) are contraindicated in patients with heart disease and low left ventricular ejection fraction (< 40%). A group of Japanese researchers now report the results of a study carried out to determine the efficacy of amiodarone (Cordarone) in the treatment of paroxysmal AF patients who had received no benefit from treatment with other antiarrhythmic drugs.

The study included 49 men and 22 women (average age of 68 years) with paroxysmal AF (52% had

underlying heart disease) who had proven refractory to therapy with at least two antiarrhythmic drugs other than amiodarone. The study participants were hospitalized for 2 weeks during which time they were given a loading dose of 400 mg/day of amiodarone. The dose was subsequently reduced to 200 mg/day (maintenance dose) and further adjusted downwards (minimum dose was 50 mg/day) if no recurrence was observed for 6 or 12 months.

After an average follow-up of 4 years, 54% of patients had experienced AF recurrence. Patients who experienced recurrence were significantly more likely to have asymptomatic AF (24% vs 3%), less likely to be on RAAS inhibitors (ACE inhibitors, angiotensin II receptor blockers or aldosterone antagonists) (29% vs 64%), and more likely to have normal/high left ventricular ejection fraction (LVEF). It was also clear that amiodarone therapy was significantly less effective in patients with mixed (neither purely vagal nor purely adrenergic) AF. Multivariate analysis confirmed that amiodarone

was more effective in patients with symptomatic AF, lower LVEF, and either vagal or adrenergic AF.

The researchers speculate that mixed AF is less related to a dysfunction of the autonomic nervous system, but more related to the influence of degeneration or fibrosis of atrial tissue. The progression to permanent AF over the follow-up period was 31%. Patients with diabetes, asymptomatic AF, and normal/high LVEF and those not on RAAS inhibitors were more likely to progress to permanent AF; however, multivariate analysis showed that only asymptomatic AF was a statistically significant predictor of progression to permanent AF. The incidence of pulmonary toxicity among the study participants was 1.4%/year.

The researchers conclude that amiodarone is most effective in maintaining sinus rhythm in patients with impaired LVEF and least effective in those with

asymptomatic or mixed AF. They surmise that amiodarone is less effective in the case of asymptomatic AD because this type of AF is likely to have been present for much longer prior to official diagnosis and thus have allowed time for extensive remodeling.

Komatsu, T, et al. Long-term efficacy of amiodarone therapy for the prevention of recurrence of paroxysmal atrial fibrillation. International Heart Journal, Vol. 52, July 2011, pp. 212-17

Editor's comment: It is interesting that amiodarone was found to be significantly less effective for mixed afibbers. An early LAF survey carried out about 10 years ago concluded that amiodarone actually increased the frequency and duration of AF episodes in mixed afibbers. The finding that amiodarone is most effective in patients with impaired heart function supports the view that this drug is a last resort for lone afibbers.

THE AFIB REPORT is published 10 times a year 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>

Copyright 2012 by Hans R. Larsen

THE AFIB REPORT does not provide medical advice. Do not attempt self-diagnosis or self-medication based on our reports. Please consult your healthcare provider if you are interested in following up on the information presented.