

THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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In case you may not have noticed, there is currently a “turf war” going on between cardiologists and electrophysiologists as to which treatment, pharmaceutical drugs or catheter ablation, should be officially pronounced as the first-line treatment for atrial fibrillation. The newest gambit is the finding by a team of cardiologists that treatment with rhythm control drugs such as flecainide and propafenone is superior to treatment with beta-blockers, digoxin, and other rate control drugs when it comes to preventing paroxysmal AF from progressing to persistent or permanent. In contrast, electrophysiologists at the University of Michigan recently reported that a successful catheter ablation virtually eliminates the progression to persistent/permanent AF. This is hardly surprising since, if your AF is cured, there is really no reason why it should progress.

Also in this issue: – Bleeding risk with aspirin revisited, new definition proposed for ablation failure, the link between anxiety, depression and AF episodes, more bad news for dronedarone, fish oil helps prevent AF, and marathon running enlarges the atria.

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

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Thus, the Food and Drug Administration (FDA) in the US has not approved aspirin for primary prevention and European guidelines advise against its use for primary prevention in healthy individuals since the risks (major bleedings and hemorrhagic stroke) outweigh its benefits (protection against stroke and heart attack).

A recent Dutch study involved 27,939 initially healthy women who were randomized to receive either placebos or 100 mg of aspirin every second day. During 10 years of follow-up, 340 major cardiovascular events (heart attack, stroke and cardiovascular death) were observed in the placebo group (0.24%/year) as compared to 312 events (0.22%/year) in the aspirin-treated group. However, aspirin therapy was of no net benefit when taking into account its associated increased risk of major bleeding, in particular, gastrointestinal bleeding. Especially noteworthy was the finding that aspirin treatment of women with a 10% or greater 10-year risk for coronary

Bleeding risk with aspirin therapy

MARIA IMBARO, ITALY. While there is substantial evidence that taking aspirin daily reduces the incidence of heart attack, ischemic stroke, and cardiovascular death amongst people with existing heart disease or a prior stroke (secondary prevention), there is no convincing evidence that the daily “aspirin ritual” reduces the risk of heart attack and stroke in those without cardiovascular disease (primary prevention).

heart disease, as advocated by most guidelines, was not associated with a net benefit.[1]

Another study carried out by researchers at Oxford University involved 95,000 persons with low risk for cardiovascular disease. Amongst participants who took aspirin every day, the incidence of stroke, heart attack, and cardiovascular death was 0.51%/year as compared to 0.57%/year amongst those who did not. On the other hand, 0.10%/year of those on aspirin experienced a major gastrointestinal or intracranial bleed as compared to only 0.07%/year of those not using aspirin. Of particular interest is the finding that aspirin on a daily basis did not reduce the risk of an ischemic or hemorrhagic stroke in those at low average risk for cardiovascular disease.

The Oxford researchers conclude that their observations “do not seem to justify general guidelines advocating the routine use of aspirin in all apparently healthy individuals above a moderate level of risk of coronary heart disease.”[2]

Now a group of Italian researchers report that the daily use of low-dose aspirin (300 mg/day or less) is associated with a significantly increased risk of major gastrointestinal and cerebral bleeding episodes. Their study involved 186,425 individuals being treated with low-dose aspirin and 186,425 matched controls not on aspirin. During an average follow-up of 5.7 years (1.6 million person-years) the incidence of major bleeding events was found to be 0.56%/year in the aspirin group versus 0.36%/year in the control group. This corresponds to a 55% relative risk increase in the aspirin group. The risk increase was similar for major gastrointestinal bleeding and cerebral bleeding.

The following factors were associated with a higher than average incidence of major bleeding amongst aspirin users – female sex, age below 50 years, previous hospitalization for cardiovascular or gastrointestinal problems, and use of oral anticoagulants and other antiplatelet agents. Protective effects were observed from the use of proton pump inhibitors (PPIs) and anti-hypertensive drugs. Multivariate analysis of factors associated with hospitalization for major bleeding events indicated that men were more likely to be hospitalized than women. Other factors associated with an increased risk of hospitalization were the use of aspirin, oral

anticoagulants (warfarin), other antiplatelet agents (clopidogrel), anti-hypertensive medications, and previous hospital admittances for cardiovascular or gastrointestinal problems. A reduced risk of admittance was observed for those on PPIs and statin drugs.

Included in the study group were 56,000 patients with type 2 diabetes of which 27,000 were on daily aspirin. Amongst diabetics not on aspirin the incidence of major bleeding was 0.54%/year as compared to 0.33%/year amongst non-diabetics not on aspirin. Thus, it is clear that diabetes, by itself, is a strong risk factor for major bleedings (61% relative risk increase). However, being on aspirin did not significantly increase the risk of bleeding (0.58%/year). The Italian researchers conclude that daily use of low-dose aspirin is associated with a significantly increased risk of major gastrointestinal or cerebral bleeding episodes in non-diabetics. The use of aspirin was not found to increase the already elevated bleeding risk amongst diabetics.

De Berardis, G, et al. Association of aspirin use with major bleeding in patients with and without diabetes. Journal of the American Medical Association (JAMA), Vol. 307, June 6, 2012, pp. 2286-94

Editor’s comment: Aspirin is often prescribed for stroke prevention in lone atrial fibrillation, even in cases where the patients have few, if any, risk factors for stroke. There is evidence that this approach is actually detrimental. In a 2005 study of 871 low-risk AF patients Japanese researchers conclude that daily aspirin therapy (150-200 mg/day) in this group is neither effective nor safe. They actually observed more cardiovascular deaths, strokes and TIAs in the aspirin group than in the placebo group. In addition, fatal or major bleeding was found to be more frequent in the aspirin group than in the placebo group. Overall, the incidence of strokes, deaths and other adverse events was 42% greater in the aspirin group than in the placebo group. The trial was discontinued prematurely since the probability that aspirin would prove superior to placebo in stroke prevention, if it continued, was deemed to be vanishingly small.[3]

[1] *Dorresteijn, JAN, et al. Aspirin for primary prevention of vascular events in women: individualized prediction of treatment effects. European Heart Journal, Vol. 32, 2011, pp. 2962-69*

[2] *Baaigent, C, et al. Aspirin in the primary and secondary prevention of vascular disease. The Lancet, Vol. 373, May 30, 2009, pp. 1849-60*

Definition of ablation failure

EAST PALO ALTO, CALIFORNIA. The “official” (Heart Rhythm Society) definition of ablation failure is the occurrence of a single arrhythmia (atrial fibrillation, atrial flutter, atrial tachycardia) episode lasting longer than 30 seconds, usually following a post-ablation blanking period of 3 months. This definition is quite arbitrary, and far stricter than the criterion used to define failure of treatment with antiarrhythmic drugs. It is also totally unrealistic from the patient’s point of view.

A group of electrophysiologists at Silicon Valley Cardiology now suggests that a better definition of ablation failure would be an AF burden (episode frequency multiplied by duration) of more than 0.5% when measured over a longer term (7 days of event monitoring, or 1 year of pacemaker interrogation). Their recommendation for the change in ablation failure definition is based on a study carried out to determine the actual incidence of AF in a group of 203 patients who had undergone a successful catheter ablation as defined as being clinically free of AF 1 year after the procedure without the use of antiarrhythmic drugs. An average of 3.1 years following the last ablation, 186 of the patients underwent 7-day event monitoring. The remaining 17 patients had pacemakers, the records of which were analyzed for the most recent year.

The 7-day event monitoring showed that 95.7% of the patients had no AF recurrence at all. Amongst the 8 patients with recurrence, 1 was found to have persistent AF. For the other 7, AF burden varied between 0.0075% (45 seconds/week) and 3.34% (5.6 hours/week) with 3 patients out of 7 having a burden of 0.037% (4 minutes or less/week). In the pacemaker group, 76.5% were totally AF-free

during the 1-year analysis period. The AF burden amongst the 4 patients with recurrence ranged from 0.0037% (22 seconds/week) to 0.16% (16 minutes/week).

The authors conclude that the AF burden (silent and symptomatic) experienced 3 years post-ablation by patients whose last ablation was clinically successful at 1-year post-ablation is very low. They suggest that an AF burden of more than 0.5% on long-term monitoring may be a more realistic definition of ablation failure than a single arrhythmia recurrence lasting longer than 30 seconds. They also noted that the only variable directly correlated with ablation failure was AF duration. In other words, the longer a patient had suffered from AF prior to the ablation, the greater the chance of failure.

Winkle, RA, et al. Atrial arrhythmia burden on long-term monitoring in asymptomatic patients late after atrial fibrillation ablation. American Journal of Cardiology, May 31, 2012 [Epub ahead of print]

Editor’s comment: I wholeheartedly concur with the above conclusion. To suggest that one 31-second arrhythmia episode, following a suitable blanking period, would classify an ablation as a failure is just not realistic in the real world. Most afibbers who have suffered frequent and/or protracted symptomatic episodes prior to their ablation would not consider it a failure, even if they should experience a few short episodes lasting longer than 30 seconds. NOTE: Only 2% of the 203 patients involved in the study actually had an AF burden exceeding 0.5% (50 minutes/week) on long-term monitoring.

Effect of psychological distress on AF severity

CHAPEL HILL, NORTH CAROLINA. Depression and anxiety are common amongst patients with atrial fibrillation (AF). A group of researchers from the University of North Carolina now reports the results of a study aimed at determining how the presence of depression, anxiety, and imagined physical symptoms (somatization disorder) influences the severity of AF symptoms. Their

study included 300 patients with at least 1 documented episode of AF (42% paroxysmal). The average age of the group was 62 years, 66% were male, and most (88.3%) were Caucasian. Most had 1 or more comorbid conditions such as hypertension (56.8%), diabetes (18.7%), coronary artery disease (14.4%), or congestive heart failure (16%).

The study participants completed a total of 7 validated questionnaires designed to quantify the extent of their depression, anxiety, somatization, general health, and AF symptom severity. The following variables were significantly associated with more severe AF symptoms in univariate analysis:

- Younger age
- Female gender
- Being unemployed
- Having less than high school education
- Currently suffering from depression
- Currently suffering from anxiety
- Currently suffering from somatization disorder
- Congestive heart failure
- Smoking

Somewhat surprisingly, AF burden (% of time spent in AF) was not significantly associated with an indication of more severe AF symptoms, whether paroxysmal or persistent. Depression, anxiety, and somatization were all associated with a worsened general health status. In multivariable analysis adjusted for potential confounders (age, gender, ethnicity, working status, education, congestive heart failure, and smoking) increasing severity of depression, anxiety, and somatization symptoms were associated with a worsened general health

status and increasing AF-attributed symptom severity. Increasing severity of depression was associated with more frequent visits to seek medical attention for AF.

The researchers conclude that depression, anxiety, and somatization are associated with worsened general well-being and AF-attributed symptoms severity, but also make the statement – “*However, it is also plausible that AF leads to the development of psychological distress particularly among patients with inadequate knowledge of their condition and ineffective coping strategies. It has been reported that living with the uncertainty and fear of when another episode will occur will increase psychological distress in patients with other supraventricular arrhythmias.*”

Gehi, AK, et al. *Psychopathology and symptoms of atrial fibrillation.* **Journal of Cardiovascular Electrophysiology**, Vol. 23, May 2012, pp. 473-78

Editor’s comment: It would seem a reasonable assumption that none of the researchers involved in this study had AF themselves, or had experienced living with someone affected by AF. If they had, they would likely have concluded that severe AF symptoms bring on depression and anxiety rather than that depression and anxiety results in more severe symptoms.

Dronedaronone (Multaq) – More bad news!

BROOKLYN, NEW YORK. Dronedaronone (Multaq) is a benzofuran derivative similar to amiodaronone but without the iodine moiety, which is believed to be responsible for the toxic effects of amiodaronone, notably on the thyroid and lungs. The US Food and Drug Administration (FDA) has approved dronedaronone for preventing rehospitalisation in patients in sinus rhythm with cardiovascular risk factors. A pretty narrow scope indeed! Nevertheless, 27 trials have been carried out to evaluate the efficacy and safety of using the drug in other populations.

A group of researchers from three American medical centers now report the results of a meta-analysis carried out to determine the safety of dronedaronone across the spectrum of patient populations in which it has been tested. The analysis included 7 randomized, controlled clinical trials involving a total of 10,676 subjects. Six of the trials involved patients with atrial fibrillation (AF),

whilst one (the ANDROMEDA trial) involved patients with heart failure, but no AF. All trials but one used a dose of 400 mg twice daily and follow-up ranged from 3.5 to 21 months. Considering the combined outcome of the 7 trials, there was a trend for increased cardiovascular and all-cause mortality amongst patients randomized to receive dronedaronone. However, when the results of a trial (ATHENA) involving only paroxysmal afibbers (with non-lone AF) were omitted, dronedaronone was associated with a highly significant increase in both cardiovascular and all-cause mortality. Excluding a trial (ANDROMEDA) involving heart failure patients still resulted in dronedaronone use being significantly associated with increased cardiovascular mortality. Similarly, excluding a trial (PALLAS) involving permanent afibbers only from the analysis maintained a statistically significant increase of cardiovascular mortality in the dronedaronone group. However, when limiting the analysis to patients with paroxysmal or persistent AF, dronedaronone use was

associated with a slight decrease in cardiovascular mortality and a decrease in rehospitalisation rate. Cardiovascular and all-cause mortality were independent of the duration of dronedarone use.

The researchers conclude that treatment with dronedarone across a wide spectrum of cardiovascular conditions resulted in a trend toward an increase in mortality. They recommend caution in using dronedarone, especially in patients with cardiovascular risk factors.

Chatterjee, S, et al. Meta-analysis of cardiovascular outcomes with dronedarone in patients with atrial fibrillation or heart failure. American Journal of Cardiology, May 18, 2012 [Epub ahead of print]

Editor's comment: Two trials are of particular interest to lone afibbers. NOTE: Both trials were sponsored by Sanofi-Aventis, the manufacturer of dronedarone.

ADONIS-EURIDIS (2007) – This trial involved 1237 patients with paroxysmal AF of whom 59% had no structural heart disease. The trial found that 400 mg twice daily use of dronedarone significantly decreased the frequency of AF episodes and

reduced the ventricular (pulse) rate during an episode. All-cause mortality in the dronedarone group was 1.0% versus 0.7% in the placebo group over the 12-month follow-up.

DAFNE (2003) – this trial involved 270 patients who had undergone electrical cardioversion for persistent AF. Thirty-five percent of trial participants had valve disease, 20% had coronary artery disease, and 14% had heart failure. A dronedarone dose of 400 mg twice daily significantly extended the time to AF relapse and reduced the ventricular rate at relapse. There was no difference in all-cause mortality between the 800-mg/day dronedarone group and the placebo group over the 6-month follow-up, but 3.9% of dronedarone users discontinued the drug mostly due to gastrointestinal side effects.

Thus, it would seem that, although dronedarone is contraindicated in AF patients with heart failure or other cardiovascular disease, it would be reasonably safe for lone afibbers with paroxysmal or persistent AF.

Marathon runners and atrial enlargement

BERN, SWITZERLAND. Natriuretic peptides are cardiac hormones with diuretic, natriuretic, and vasodilatory properties. Atrial natriuretic peptide (ANP) and its N-terminal prohormone are produced in the atria, whereas brain natriuretic peptide (BNP) is produced in the ventricles. Both hormones are produced in response to stretching of the walls of the heart. The stretching normally comes about through pressure caused by higher than normal fluid (blood) volume; however, in the case of atrial fibrillation (AF), the peptides are released due to the violent contractions of the walls of the atria and ventricles during an episode rather than due to volume overload. ANP is stored as a prohormone within secretory granules in the right and left atria and is secreted as an N-terminal fragment, N-terminal pro-atrial natriuretic peptide (pro-ANP). Pro-ANP levels are elevated in patients with paroxysmal AF and predict the risk for recurrent episodes of AF.

A group of researchers at the University of Bern now suggests that training for and running marathons substantially increase the release of ANP and is associated with atrial enlargement and an increased risk of AF. Their study included 56 men participating in the 2010 Grand Prix of Bern, a

10-mile (16 km) race. The runners were divided into three groups:

- Group A – 22 men who had never run a marathon
- Group B – 16 men who had run 1 to 4 marathons
- Group C – 18 men who had run 5 or more marathons

The average age of the men was 42 years (range of 35 to 49 years), with men in group C tending to be older (average age of 45 years) than men in groups A and B (average age of 40 years). Men in group C had also been in training for long-distance running for a considerably longer period (18.9 years on average) than had men in group A (10.3 years) and group B (13.7 years). None of the participants had cardiovascular disease, hypertension or AF. Not surprisingly, the men in groups B and C had considerably lower average resting heart rates (51 bpm) than those in group A (61 bpm). Both the left and right atria were significantly enlarged in groups B and C with men in group B having an average left atrial volume index of 30 ml/m² and those in group C having a volume index of 34 ml/m² as compared to an average of 25 ml/m² in group A. Defining left

atrial enlargement as a volume index greater than 29 ml/m², 77.8% of group C and 62.5% of group B had enlargement as compared to only 22.7% in group A.

It is also noteworthy that men in group C had substantially more ectopics (PACs and PVCs) on pre-race 24-hour Holter monitoring than did those in group A. Finally, it was observed that the veteran marathon runners in group C had significantly higher blood levels of pro-ANP at baseline than did runners in groups A and B. Pro-ANP increased significantly in every group when measured immediately following the race with group C levels being the highest. In a multiple linear regression model, average weekly endurance training hours and marathon participation contributed independently to left atrial enlargement. Interestingly, pro-ANP levels at baseline and after the race correlated only with right atrial volume, indicating the importance of volume overload of the right atrium during strenuous activities.

The researchers speculate that repetitive episodes of atrial stretching, as measured by increased pro-ANP excretion, is associated with atrial remodelling (enlargement) which, in turn, may cause atrial arrhythmias. They refer to a study involving middle-aged endurance athletes with lifetime training exposure in excess of 4500 hours. In this group, atrial enlargement was observed in 83%, and the prevalence of paroxysmal AF was 9%.

Wilhelm, M, et al. Comparison of pro-atrial natriuretic peptide and atrial remodelling in marathon versus non-marathon runners. American Journal of Cardiology, Vol. 109, No. 7, April 1, 2012, pp. 1060-65

Editor's comment: It is well established that considerable amounts of ANP are released during an AF episode (accounting for the increased frequency of urination often experienced). Thus, it is not too giant a leap of faith to suggest that the repeated stretching of arterial walls experienced during an AF episode, just like marathon running, leads to atrial enlargement and perpetuation of AF – "AF begets AF".

Progression of paroxysmal AF

MAASTRICHT, THE NETHERLANDS. Most afibbers begin their "career" with intermittent (paroxysmal) self-terminating episodes, although some are diagnosed with permanent asymptomatic atrial fibrillation (AF) during a routine visit to the doctor. Unfortunately, left to its own devices, AF tends to progress from paroxysmal to persistent episodes lasting longer than 7 days or requiring cardioversion for termination), and then to permanent (long-standing persistent) where the patient has been in AF for at least a year and cardioversion has proven ineffective. Several studies have been carried out to determine the factors that are associated with progression.

A 2010 study, involving 1219 initially paroxysmal afibbers, reported from the University of Maastricht concluded that hypertension, history of heart failure, chronic obstructive pulmonary disease (COPD), age above 75 years, and a history of stroke or transient ischemic attack (TIA) predicted progression of paroxysmal AF to persistent or permanent. Digoxin, ACE inhibitors, and diuretics speeded up progression, while angiotensin II receptor blockers slowed it down.[1,2]

A 2005 survey of 188 lone afibbers concluded that the risk of progression from paroxysmal to permanent was associated with a family history of

AF, having undergone one or more cardioversion, having developed hypertension, and having an enlarged left atrium.[3]

Now researchers from 532 centers in 21 countries weigh in with a major study to determine the factors involved in progression. The study followed 2137 initially paroxysmal afibbers having experienced a single first episode, or having experienced episodes for a year or less prior to enrolment. During the 12-month follow-up, 318 patients (15%) progressed to persistent (6%) or permanent (9%) AF. Advanced age, elevated diastolic blood pressure, coronary artery disease, a history of TIA or stroke, hypertension, and heart failure were all associated with increased risk of progression, as was a treatment strategy based on rate control only. Multivariable analysis

showed that a history of heart failure (odds ratio=2.2), a history of hypertension (OR=1.5), and the use of rate control rather than rhythm control (OR=3.2) were the only independent variables significantly associated with progression.

The use of class 1C antiarrhythmics (flecainide, propafenone) for rhythm control was associated with a significantly lower risk of progression, whereas the use of digoxin almost tripled the risk. The risk among lone afibbers was significantly lower

than average at 8%/year and very significantly lower than the risks associated with heart failure (24%) and hypertension (16%). The risk of progression was closely related to stroke risk as measured with the CHADS₂ score. A score of 0 was associated with an average 9%/year progression, a score of 1 was associated with an average 14% progression, and a score of 2 with a 19%/year progression. The researchers suggest that an aggressive rhythm control strategy slows electrical remodelling and the resulting progression. *de Vos, CB, et al. Progression of atrial fibrillation in the Registry on Cardiac Rhythm Disorders assessing the control of atrial fibrillation cohort: clinical correlates and the effect of rhythm-control therapy. American Heart Journal, Vol. 163, May 2012, pp. 887-93*

Editor's comment: An earlier study involving 330 paroxysmal afibbers who had a pacemaker implanted to deal with bradycardia concluded that an increasing AF burden (more frequent and/or longer episodes) was associated with a more rapid progression to persistent or permanent AF.[4,5] If increasing AF burden is indeed a universal sign of

progression, then lone afibbers who experience such an increase may wish to consider medication with an angiotensin receptor blocker (losartan, valsartan, irbesartan) in order to slow down remodelling.

- [1] *de Vos, CB, et al. Progression from paroxysmal to persistent atrial fibrillation. Journal of the American College of Cardiology, Vol. 55, No. 8, February 23, 2010, pp. 725-31*
- [2] *Jahangir, A and Murarka, S. Progression from paroxysmal to persistent atrial fibrillation. Journal of the American College of Cardiology, Vol. 55, No. 8, February 23, 2010, pp. 732-34 (editorial comment)*
- [3] *Kerr, CR, et al. Progression to chronic atrial fibrillation after the initial diagnosis of paroxysmal atrial fibrillation. American Heart Journal, Vol. 149, March 2005, pp. 489-96*
- [4] *Saksena, S, et al. Progression of paroxysmal atrial fibrillation to persistent atrial fibrillation in patients with bradyarrhythmias. American Heart Journal, Vol. 154, No. 5, November 2007, pp.884-92*
- [5] *Homoud, MK and Estes, M. Shedding new light on the pathophysiology of conversion of paroxysmal atrial fibrillation into persistent atrial fibrillation. American Heart Journal, Vol. 154, No. 5, November 2007, pp.801-04*

Fish oil helps prevent AF

BOSTON, MASSACHUSETTS. In 2009 Finnish researchers reported that high levels of eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA) in the serum phospholipid phase were associated with a significant decrease in the risk of developing atrial fibrillation (AF). The study involved 2174 men aged 60 years or younger at baseline in 1984. During 18 years of follow-up, 11% of study participants were diagnosed with AF upon admission to hospital (for arrhythmia or other reasons). At baseline, the mean percentages of EPA, DPA and DHA in serum fatty acids were 1.67%, 0.55% and 2.46% respectively. After adjustment for age and other possible confounders the researchers observed that men in the highest quartile of EPA+DPA+DHA concentration (5.3 – 15.6%) had a 35% reduced risk of developing AF when compared to men in the lowest quartile (1.7 – 3.6%). The absolute risk in the lowest quartile group was 13.4% vs 8.7% in the highest quartile group. Further analysis revealed that DHA accounted for the entire risk reduction and that EPA and DPA levels were not associated with risk of developing AF.

Considering only lone afibbers (no heart disease prior to diagnosis of AF) strengthened the association between serum fatty acid concentration

of DHA and AF risk. Men in the lowest quartile had a risk of 10.9%, while those in the highest quartile had a risk of only 5.6% – a relative risk reduction of 49%.

Now researchers from Harvard School of Health and a group of other research centers confirm that high phospholipid levels of EPA, DPA and EPA (the main components of fish oil) also help prevent the development of AF in older men and women. Their study involved 3326 American men and women aged 65 years or older at enrolment in the Cardiovascular Health Study in 1989 to 1990. None of the participants had AF or heart failure at baseline. Blood serum levels of EPA, DPA and DHA were measured at baseline as percentages of total phospholipid fatty acid concentration.

During 31,169 person-years of follow-up, 789 cases of AF were diagnosed either through hospital admission records or routine annual ECG readings. This corresponds to an incidence (new cases diagnosed) of 2.5%/year. A high percentage of EPA+DPA+DHA in the phospholipid phase (average 6.4%), after adjusting for potential confounders, was found to be associated with a 27% relative reduction in the risk of developing AF when compared to an average level of 2.9%. The

risk reduction was almost entirely attributable to DHA which, on its own, was associated with a 23% relative risk reduction when comparing the highest quartile of phospholipid level (4.37%) to the lowest quartile (1.98%). In absolute terms, the risk of developing AF was 1.9%/year in the highest quartile group versus 2.8%/year in the lowest quartile group.

The researchers point out that long-chain n-3 polyunsaturated fatty acids (PUFAs) such as found in fish oil have several important biological effects on a range of cellular functions that may reduce the risk of developing AF. Among these are improvement in myocardial efficiency, and significant anti-inflammatory and anti-fibrotic effects that may reduce long-term atrial remodelling and limit the creation of an "AF-friendly" substrate. There is also evidence that PUFAs directly affect cardiac electrophysiology through modulation of ion channels, potentially increasing myocardial electric stability. The researchers recommend a

randomized trial to test the efficacy of PUFAs (fish oil) for prevention of the development of AF in older adults.

Wu, JHY, et al. Association of plasma phospholipid long-chain omega-3 fatty acids with incident atrial fibrillation in older adults. *Circulation*, Vol. 125, March 6, 2012, pp. 1084-93

Editor's comment: Fish oil has now been shown to have strong anti-inflammatory properties, and to help prevent the development of AF, help reduce ventricular ectopy (PVCs), help prevent AF recurrence following catheter ablation, help prevent atrial mechanical stunning (an important stroke risk) after cardioversion and catheter ablation, help prevent sudden cardiac death, and has many more beneficial effects. I see no need to wait for the results of another clinical trial before embarking on daily fish oil supplementation. To read more about the enormous benefits of fish oil see www.oilofpisces.com

Catheter ablation and progression of paroxysmal AF

ANN ARBOR, MICHIGAN. Atrial fibrillation (AF) tends to progress over time from self-converting paroxysmal (intermittent) to persistent (episodes lasting longer than 7 days or requiring cardioversion) to permanent. A recent study showed a progression rate of 8%/year for paroxysmal, lone afibbers. This rate is significant but not in the same league as the progression rate (16%) observed in afibbers with hypertension or heart failure (24%). Class 1C antiarrhythmic drugs (propafenone, flecainide) cut progression rate in half, but their use is unfortunately contraindicated in many AF patients with underlying heart disease. It is generally believed that progression is associated with remodelling, notably enlargement of the left atrium.

A group of electrophysiologists from the University of Michigan now reports that a successful radio frequency (RF) catheter ablation essentially eliminates progression to persistent/permanent AF during a mean follow-up of 2 years. Their study included 504 paroxysmal afibbers who underwent a RF-powered pulmonary vein isolation (PVI) procedure with additional lesions as required to terminate their AF. The average (mean) age of the patients was 58 years, 67% were men, 47% had hypertension, 10% had coronary artery disease, and 11% had diabetes. The average left atrial diameter was 41 mm (4.1 cm). At follow-up 27

months after the initial procedure, 46% of patients were in normal sinus rhythm (NSR) without the use of antiarrhythmic drugs and 9% were in NSR with the aid of antiarrhythmics.

A total of 193 patients (38%) had one or more repeat procedures with an average of 1.5 procedures per patient. After an average follow-up of 22 months following the most recent procedure, 71% of ablatees were in NSR without the use of antiarrhythmics, while 15% were in NSR with the aid of antiarrhythmics. The remaining 14% either continued to experience paroxysmal AF episodes (9.5%), 1.5% had progressed to persistent AF, and 3% had persistent atrial flutter. The progression to persistent AF occurred in 7 of the 56 patients in whom the ablation procedure had been unsuccessful. Thus, the annual incidence of progression to persistent/permanent AF in the entire group was 0.6% - a very favourable rate when compared to the rates obtained with therapy with pharmaceutical drugs. Age, duration of AF, and diabetes were found to be independent risk factors for progression.

The authors conclude that RF catheter ablation is more effective than pharmaceutical therapy in halting the progression of paroxysmal AF.

Jongnarangsin, K, Morady, F, et al. Effect of catheter ablation on progression of paroxysmal atrial fibrillation.

Editor's comment: It is comforting, but not really surprising, to learn that a successful catheter ablation will halt the progression of paroxysmal AF to the persistent or permanent varieties.

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