THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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Welcome to our summer issue! I hope you will enjoy Michael Coleman's description of his afib journey as much as I did – truly a poignant and thought-provoking story that all afibbers can relate to. Thanks you Michael, for sharing it!

A question facing many afibbers on warfarin is, "Is it safe to supplement with fish oil as well?" There is very little medical literature relating to this subject, but on the whole, it would appear that it is indeed safe to take them together and that the effect of fish oil supplementation on INR is zero to minimal – at least with daily intakes of 1 gram or less. You can read more about this in my Research Report "Fish Oils and Warfarin".

Also in this issue we report that anticoagulation guidelines are poorly adhered to in Europe and many lone afibbers are being prescribed warfarin even though they should not be, that paroxetine (Paxil) may be beneficial, at least short-term, for some afibbers, there is more evidence that a successful ablation helps remodel the left atrium and reduces the level of natriuretic peptides, and finally, there is new evidence that an increased intake of potassium is highly beneficial for the cardiovascular system.

As most of you will know by now, this month also marks the release of my latest book "Lone Atrial Fibrillation: Toward A Cure – Volume III". This 220-page book contains all the information published in the 2005 issues of "The AFIB Report" arranged in logical sections. The comprehensive subject index makes it easy to locate that elusive, but important piece of information you know is there - somewhere.

Volume III covers subjects ranging from the latest ablation procedures, their outcome and potential complications, to the safety and efficacy of antiarrhythmic drugs. The latest insights into the mechanism of atrial fibrillation as well as important information about stroke risk and prevention are also covered. The results of LAF Survey 9, a comprehensive evaluation of the outcomes of almost 300 ablation and mini-maze procedures, and the personal stories of a number of afibbers who have cured or at least managed to control their condition round out this book -- a worthy companion to the original "Lone Atrial Fibrillation: Towards A Cure" and Volume II.

You can order your copy of Volume III at http://www.afibbers.org/volume3.htm

Wishing you a healthy and happy summer with lots of NSR,

Hans

Highlights

Adherence to guidelines for anticoagulation

MAASTRICT, THE NETHERLANDS. The Euro Heart Survey enrolled 5333 atrial fibrillation patients in 35 countries in 2003 and 2004. Patients were enrolled in 182 university, non-university, and hospitals with cardiology clinics. Patients seen by individual cardiologists were not included. One of the aims of the survey was to evaluate how well the participating institutions adhered to the AHA guidelines for the management of atrial fibrillation (2001) in their prescription practices for oral anticoagulants (warfarin). The overall conclusion was that prescription patterns are generally not tailored to the patient's stroke risk profile. The major reason for prescribing oral anticoagulants (OACs) was valvular heart disease. A prior stroke/TIA, hypertension, age over 75 years, and coronary artery disease (CAD) were not associated with a higher level of OAC prescriptions, but antiplatelet agents (aspirin, clopidogrel) were frequently prescribed for coronary heart disease. The absence of a local clinic for measuring INR was closely related to fewer prescriptions for oral anticoagulants.

About 90% of the study participants had one or more underlying risk factors for stroke with the remaining being lone afibbers with no risk factors. In this group 40-50% were prescribed OACs despite the fact that neither the AHA guidelines, the ACCP guidelines, the $CHAD_2$ scheme, nor the Framingham stroke risk score call for this. The authors of the survey report concluded:

> "*Treatment needs to be tailored according to the patient's risk profile. In low-risk patients, OAC provides a minimal benefit in preventing thrombo-embolic strokes when compared with aspirin, which is largely offset by a higher risk of bleeding with OAC."*

> *"Of concern, this survey shows that OAC prescription for AF was quite high throughout all risk categories, irrespective of the stroke risk stratification scheme used, meaning that a large proportion of low-risk patients is at an avoidable increased hazard for bleeding and troubled with the inconvenience of constant INR monitoring with little chance of benefit."*

The authors also conclude that the type of AF (paroxysmal, persistent, permanent) should not influence the decision to prescribe OACs, but rather, the decision should be based strictly on the presence or absence of recognized stroke factors. They also found that the prescription of OACs prior to pharmaceutical or electrical cardioversion was somewhat haphazard, but OAC prescription around a catheter ablation (PVI) was quite high at 80-90%.
Nieuwlaat, R, et al. Antithrombotic treatment in real-life atrial fibrillation patients: a report from the Euro Heart Survey on Atrial Fibrillation. **European Heart Journal** *advanced access published May 26, 2006*

Editor's comment: The main conclusion of interest to lone afibbers is that 40-50% of afibbers with no stroke risk factors were prescribed oral anticoagulants (warfarin) even though they should not have been according to the guidelines. There is no reason to believe that a similar situation would not exist in Canada and the US. Thus, it is clearly incumbent on each of us to familiarize ourselves with the guidelines and tactfully (more or less) remind our physician that we would like to be treated according to the guidelines, or at least ask for a valid explanation for why we should not be. The guidelines can be found at http://circ.ahajournals.org/cgi/reprint/104/17/2118

Paroxetine (Paxil) may help some afibbers

KYOTO, JAPAN. Japanese researchers have found that taking 10 mg/day of the antidepressant paroxetine (Paxil) alone or in combination with antiarrhythmics may help prevent afib episodes. Their small clinical trial involved 9 men who were still experiencing frequent paroxysmal episodes despite having tried several antiarrhythmics, beta-blockers, and calcium channel blockers. None of the study participants had underlying heart disease and only one had hypertension. The men had all experienced episodes at least twice a week for the past 3 months and were suffering from depression associated with their afib condition.

After beginning the paroxetine treatment the men all experienced a dramatic decline in episode frequency and PACs virtually ceased to occur. Three patients experienced complete resolution of

their afib and 3 were able to reduce their daily dose of antiarrhythmics by 33-50%. Overall, the average number of episodes a month went from 12 prior to paroxetine to 1 after. Although the researchers did not distinguish between adrenergic, mixed and vagal afib as such, they did comment that, "most of our patients did not show clear nocturnal patterns of arrhythmia, and the daily profiles of arrhythmia were not related to the efficacy of paroxetine." They conclude that their preliminary results "suggest that paroxetine could be a choice in the pharmacologic treatment of paroxysmal AF."
Shirayama, T, et al. Usefulness of paroxetine in depressed men with paroxysmal atrial fibrillation. **American Journal of Cardiology**, *Vol. 97, June 15, 2006, pp. 1749-51*

Editor's comment: I tried paroxetine for my afib almost 8 years ago (October 1998). At this time, about 60% of my episodes occurred during daytime so were likely to be adrenergically mediated – probably stress related. The average interval between episodes was about 22 days and episode duration was between 11 and 18 hours. After starting on paroxetine (20 mg/day) I went 55 days before I experienced a 17-hour episode. After another 37 days I had a 20-hour episode, and then went an amazing 76 days before the next episode. However, this episode was an extremely unpleasant 108 hours. Another 40 afib-free days elapsed before another episode, but this time it involved bradycardia (about 40 bpm) which was very unsettling and lasted for 58 hours. In June 1999 my episode frequency increased to once every 2 to 7 days so I discontinued the paroxetine. I later found two articles describing an association between paroxetine and bradycardia.

Based on my own experience, I would say that paroxetine might be helpful – for a time – for some afibbers – a conclusion supported by the Japanese findings. However, paroxetine is a powerful drug and can have some nasty side effects. It can also be difficult to wean off, although I did not experience any problems in doing so. Should you try it? This clearly is a very individual decision. However, if you have no contraindications to SSRIs, it may be worth trying 10 mg/day for 2-4 weeks. But please – read the fine print before embarking on this approach.

Potassium and exercise testing

ROCHESTER, MN. Extremely elevated potassium levels are associated with an increased risk of ventricular fibrillation, which can be fatal. Researchers at the Mayo Clinic recently completed a study aimed at determining if exercise testing increases the risk of cardiac arrhythmias in patients with potassium levels outside the normal range. Their study included 10,272 exercise tests performed on 9,084 patients. All patients had their serum level of potassium measured less than 48 hours before the test. The majority (88%) was found to have a level between 3.6 – 4.8 mmol/L. Three per cent were hypokalemic (2.4 – 3.5 mmol/L), and the remaining 9% were hyperkalemic (4.9 – 6.1 mmol/L).

Most patients had one or more disease conditions (63% elevated cholesterol, 50% hypertension, 11% diabetes, 42% with a family history of coronary artery disease, and 54% with a history of smoking). Both ventricular and supraventricular (atrial) ectopy were common during exercise, but their frequency was not significantly different in the 3 groups. PVCs (premature ventricular complexes) occurred in about 42% of cases irrespective of potassium status, while PACs (premature atrial complexes) occurred in about 32% of cases. New onset atrial fibrillation and flutter were relatively uncommon at about 0.6%. NOTE: Patients who had already been diagnosed with afib or flutter were not counted as having had afib or flutter initiated by the testing.

Supraventricular tachycardia occurred in about 3% of cases and non-sustained ventricular tachycardia also occurred in about 3% of cases. Only one patient went into sustained ventricular tachycardia (potassium level of 4.9 mmol/L). This patient had a history of heart attack and angioplasty. It is interesting that 45% of the patients in the hypokalemic group were on a diuretic. Older, male patients with valvular regurgitation, poor ejection fraction, and/or coronary artery disease were at highest risk of developing atrial fibrillation or flutter during the test. Potassium status did not affect the risk. The researchers conclude that mild to moderate hypokalemia or hyperkalemia should not be a contraindication to exercise testing.
Modesto, KM, et al. Safety of exercise stress testing in patients with abnormal concentrations of serum potassium. **American Journal of Cardiology**, *Vol. 97, 2006, pp. 1247-49*

Editor's comment: It is unfortunate that the study did not include the measurement of intracellular

potassium concentration. It is well established that intracellular concentration is far more indicative of the potential for arrhythmia than is serum concentration (only about 2% of the body's potassium stores are found in blood serum).

Left atrium remodeling after ablation

LEIDEN, THE NETHERLANDS. There is substantial evidence that the left atrium tends to enlarge with the presence of afib. Now Dutch EPs report that this enlargement regresses after a successful PVI (pulmonary vein ablation), but continues if the ablation is unsuccessful. Their study involved 45 male and 12 female afibbers with an average age of 53 years (range of 45-61 years). The study participants had experienced afib for an average of 6 years (range of 1-11 years). Most (61%) had the paroxysmal variety, while 32% had persistent and 7% had permanent. The PVI was carried out using the CARTO electroanatomical mapping system (Pappone method) and a 4 mm irrigated ablation catheter. Lesion lines were placed outside the ostia of the pulmonary veins with additional lines drawn between the mitral annulus and the left inferior pulmonary vein (mitral isthmus line) and between the ostia of the left and right superior pulmonary veins (roof line). This procedure achieved immediate success in all patients, but 3 (5%) did suffer mild pericardial effusion.

After 3 months 68% of the patients were still in sinus rhythm, while still on antiarrhythmic drugs. It is of considerable interest to note that while 77% of the paroxysmal afibbers were in sinus rhythm after 3 months, only 28% of persistent and permanent afibbers had achieved this enviable state.

The Dutch researchers performed two-dimensional echocardiography 2 days prior to the procedure and at the 3-month follow-up visit. The LA anteroposterior diameter decreased from an average of 45 mm to an average of 42 mm in the group that was in sinus rhythm, but increased from 45 mm to 48 mm in the group whose ablation had been unsuccessful. Furthermore, both the LA end-systolic and end-diastolic volumes decreased significantly (from 59 mL to 50 mL and from 37 mL to 31 mL respectively) in the successful group, but tended to increase in the group still in afib. The researchers conclude that the size of the left atrium decreases after a successful ablation, but increases with continuing afib.

Tops, L, et al. Effect of radiofrequency catheter ablation for atrial fibrillation on left atrial cavity size. **American Journal of Cardiology**, *Vol. 97, 2006, pp. 1220-22*

Editor's comment: The overall success rate of 68% is not impressive particularly considering that all the study participants remained on antiarrhythmics for the 3 months following their procedure. The fact that only 28% of persistent and permanent afibbers achieved a cure confirms my own belief that the electroanatomical (Pappone) approach is not appropriate for persistent and permanent afibbers.

Ablation normalizes ANP and BNP levels

NAGOYA, JAPAN. It has been reported that afibbers tend to have higher blood levels of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) than non-afibbers. There is also evidence that the levels are reduced after cardioversion or a successful maze procedure. Japanese researchers recently set out to see if elevated ANP/BNP levels would decline after pulmonary vein ablation (PVI). Their study involved 66 (54 men) paroxysmal afibbers with no underlying heart disease (lone afibbers). The average age of the study participants was 61 years (range of 51-71 years); they had suffered from afib for 1-7 years, had failed 2-4 class I or class II antiarrhythmic drugs, and experienced episodes that self-converted in less than 24 hours. Their average left atrial diameter was 35 mm (range of 25-45 mm).

The participants all underwent a segmental, ostial PVI targeting all 4 pulmonary veins and were followed up for 3 months after their last ablation. The follow-up included monthly 24-hour Holter recordings and ANP and BNP determination at baseline and 3 months. Three months after the initial PVI, only 53% of the study participants were still in normal sinus rhythm without the use of antiarrhythmic drugs. Nine (14%) of the unsuccessfully ablated patients underwent second

and third procedures. Five became afib-free after the second procedure, and two achieved continuous normal sinus rhythm (NSR) after the third procedure.

The Japanese researchers made the following observations:

- At baseline, both ANP and BNP levels were elevated in 14 patients (21%) and in the remaining 52 patients (79%) only BNP level was elevated.
- There were no significant correlations between episode frequency and duration and ANP/BNP levels or left ventricular (LV) ejection fraction.
- There was a significant, but weak correlation between ANP and BNP levels and afib burden (episode frequency x duration) prior to the PVI.
- BNP level was positively correlated with left atrial dimension.
- Patients with elevated ANP levels tended to experience more episodes and a higher afib burden than those with normal levels.
- Both ANP and BNP levels decreased significantly after the first PVI whether ultimately successful or not (ANP from an average of 69 to 25 pg/mL and BNP from 58 to 23 pg/mL).
- In patients with elevated ANP only (at baseline) the ANP concentration returned to normal after the initial PVI.
- Average BNP levels decreased from 55.7 to 12.3 pg/mL in the 35 patients whose first PVI was successful. In contrast, it decreased significantly less in the 7 patients who required additional PVIs (from 66.8 to 42.8 pg/mL)
- An enlarged left atrium at baseline was associated with a greater chance of the PVI being unsuccessful.
- No association was observed between ANP/BNP level at baseline and the outcome of the PVI.
- The decrease in afib burden post-PVI was proportional to the decrease in BNP, which eventually returned to normal level after a successful PVI.
- No asymptomatic afib episodes were observed during the Holter recordings.

The researchers conclude that ANP/BNP levels are elevated in paroxysmal afibbers even if they don't have structural heart disease. Both ANP and BNP levels decrease significantly after a PVI and a return to normal of BNP post-ablation is a good indication that the PVI was successful.

Yamada, T, et al. Plasma atrial natriuretic peptide and brain natriuretic peptide levels after radiofrequency catheter ablation of atrial fibrillation. **American Journal of Cardiology**, *Vol. 97*, *June 15, 2006, pp. 1741-44*

Editor's comment: It is interesting that the procedural success rate was only 53% after the first PVI. This seems to be about the norm in other than top-rated institutions. It is to be hoped that more research will be done on the correlations between PVI success and BNP decrease. For example, if a BNP decrease to normal levels within the first month after the PVI would indicate ultimate success, this would go a long way toward answering the question, "was my ablation successful?" without having to wait the requisite 3 months.

Potassium-enriched salt lowers mortality

TAIPEI, TAIWAN. There is ample evidence that a high intake of sodium chloride (table salt) is associated with an increased risk of hypertension (high blood pressure), especially among elderly people. Taiwanese researchers now report that using a potassium-enriched salt instead of plain table salt in meal preparation can materially reduce death from cardiovascular disease. Their clinical trial included 1981 World War II veterans with an average age of 75 years. The veterans were randomized into two groups – Group 1 (768 men) used a potassium-enriched salt (49% sodium

chloride, 49% potassium chloride and 2% other salts) in meal preparation, while Group 2 (control group of 1213 men) used standard table salt (99.6% sodium chloride). The average daily intake of sodium was 5.2 grams in the control group and 3.8 grams in the experimental group (Group 1). The total extra intake of potassium chloride (from the enriched salt) in Group 1 varied between 1.3 and 2.5 grams/day (0.7 – 1.2 grams/day of elemental potassium).

The study participants were followed for an average of 2.6 years during which 504 died. This corresponds to an overall mortality rate of 9815 per 100,000 person years. Of these deaths, 15% were from cancer, 18% from cardiovascular disease (CVD), and about 10% from pneumonia. There was a significant difference in the CVD mortality between Group 1 (potassium salt) and Group 2 (control group, normal table salt). In Group 1 the mortality was 1310 per 100,000 person years as compared to 2140 per 100,000 person years in the control group, or a reduction of about 60% in CVD mortality in Group 1. The mortality from cerebral vascular disease was twice as high in the regular salt group as compared to the potassium salt group, and the mortality from heart failure was 3.3 times higher in the regular salt group. Veterans in Group 1 also tended to live longer than those in the control group and needed significantly less medical care than did the participants of the control group.

The researchers conclude that the beneficial effects observed in the study were likely due to a major increase in potassium intake and a moderate decrease in sodium intake.

Chang, HY, et al. Effect of potassium-enriched salt on cardiovascular mortality and medical expenses of elderly men. **American Journal of Clinical Nutrition**, Vol. 83, 2006, pp. 1289-96

Editor's comment: This study certainly confirms the beneficial effects of an increased potassium intake. A moderately increased potassium intake (about 10 mmol or 390 mg/day) has also been found to decrease stroke mortality by 40% and many afibbers have found potassium supplementation to be highly effective in reducing PACs, PVCs, and even afib episodes.

Effect of PVI on left atrial function

CLEVELAND, OHIO. A study carried out at the University of Michigan concluded that circumferential pulmonary vein ablation (Pappone protocol) in paroxysmal afibbers is associated with a marked decline in left atrium (LA) ejection fraction. This could be of concern if this impairment of LA function, despite reversion to sinus rhythm, is severe enough to predispose to the formation of blood clots.

A team of EPs from the Cleveland Clinic and the Marin County General Hospital now report the good news that segmental pulmonary vein ablation (Haissaguerre and Natale protocol) does not result in a deterioration of LA function, but rather tends to improve it. Their clinical trial involved 125 consecutive patients with paroxysmal (60%) or persistent (40%) afib. NOTE: Permanent afibbers were excluded due to the impossibility of measuring their LA function in sinus rhythm prior to the ablation procedure.

The study participants, 73% of whom were men, had suffered from afib for an average of 6 years; 31% were hypertensive, 19% had coronary artery disease, and 15% had valvular hear disease. The participants all underwent pulmonary vein antrum isolation (PVAI) and 92% of these were successful (no afib, no medications after 2 months). After excluding patients where imaging could not be carried out because of inability to image in sinus rhythm or the presence of AF symptoms, 67 patients were included in the final study. These patients underwent either TEE (at Cleveland Clinic) or EBCT (at Marin County) immediately prior to the PVAI and 6 months later. They also underwent Holter monitoring immediately following the procedure and at 3- and 6-month follow-up visits.

Transesophageal echocardiography (TEE)

Echocardiography uses ultrasound to evaluate the structure and function of the heart. The ultrasound transducer is usually applied over the heart region of the chest with the patient in the supine position. This technique, known as ***transthoracic echocardiography (TTE)***, can give a good indication of the size of the heart chambers, its ability to pump blood, and will show any valve abnormalities and other structural defects.

Transesophageal echocardiography (TEE) is similar to TTE except that the ultrasound transducer is shaped like a narrow cylinder and is swallowed during the procedure. Because the esophagus is right next to the heart TEE provides much clearer images than does TTE. It is particularly effective in spotting blood clots in the left atrium and left atrial appendage, and is also sometimes used during pulmonary vein ablation to prevent the accidental creation of an atrio-esophageal fistula (a hole between the heart and the esophagus). The most important parameters measured with TEE are:

- Left atrial diameter (LAD)
- Left atrial systolic area
- Left atrial diastolic area
- Blood flow through the mitral valve (TMP)
- Blood flow through the left atrial appendage (LAA)
- Blood flow through the pulmonary veins (PVF)

The important Peak A velocity measures the blood flow across the mitral valve (connecting the left atrium and the left ventricle) and can be taken as a measure of the strength of the atrium's contraction.

Cine electron-beam computed tomography (EBCT)

Computed tomography is an x-ray technique that uses multiple two-dimensional images to produce a three-dimensional representation of the body and its parts. It was developed in the early 1970s and has since undergone many improvements. One of the shortcomings of early CT scans was their inability to accurately depict moving organs such as the heart. This has now been overcome in the latest generation of CT scanners. While early scanners took 20-60 seconds to obtain a scan, the new EBCT scanners only require 50-100 milliseconds to "get the picture". This has made it possible to obtain clear pictures of the moving heart using an injected contrast medium (x-ray dye). Among the most important parameters measurable on an EBCT scan are:

- Left atrial systolic area and volume
- Left atrial diastolic area and volume
- Left atrial ejection fraction (%)

At the 6-month follow-up visit there was a clear, statistically significant decrease in left atrium diameter and area (both by TEE and EBCT) indicating that successful structural remodeling had taken place. Peak A velocity (measured by TEE) increased, on average, from 43 cm/sec pre-ablation to 62 cm/sec post-ablation indicating that the contractile force of the left atrium had improved as a result of the procedure. These improvements were more noticeable in persistent than in paroxysmal afibbers. The observed improvement in left atrial function was further supported by the finding that the left atrial ejection fraction, as measured with EBCT, increased from an average of 16.7% to 22.1%.

The researchers conclude that extensive ablation performed during a PVAI does not cause

deterioration in LA function and may actually result in long-term improvement, especially in persistent afibbers.

David Callans, MD of the University of Philadelphia comments that it is possible that more extensive ablation (such as done in the circumferential or Pappone method) may reduce LA function to a greater extent. He also suggests that the left atrial ejection fraction, although improved after PVAI, may still be well below that found in a normal, afib-free population.

Verma, A, et al. Extensive ablation during pulmonary vein antrum isolation has no adverse impact on left atrial function. **Journal of Cardiovascular Electrophysiology**, *Vol. 17, July 2006, pp. 741-46*

Callans, DJ. The effect of catheter ablation of atrial fibrillation on left atrial transport function. **Journal of Cardiovascular Electrophysiology**, *Vol. 17, July 2006, pp. 747-48*

Editor's comment: It is indeed encouraging to learn that the segmental pulmonary vein isolation procedure (Haissaguerre and Natale protocol) using electrophysiological mapping does not harm the left atrium to the point of interfering with its function of acting as a "booster pump" for the left ventricle. It even appears from this latest study that LA function may actually improve after a PVI or PVAI. It is somewhat unfortunate that the authors of the study did not provide normal LA ejection fraction values as measured with ECBT. I have been unable to find such comparable values in a search of current medical literature.

RESEARCH REPORT

Fish Oils and Warfarin

by Hans R. Larsen

Background

An increased intake of oily fish and long-chain polyunsaturated omega-3 fatty acids (fish oils) is generally beneficial and reduces the risk of ischemic stroke. For people on warfarin it is clearly important to know if it is safe to take both fish oils and warfarin.

Warfarin works by inhibiting the activation of vitamin K-dependent coagulation Factors V, VII and X in the extrinsic and common pathways of the coagulation cascade. Fish oil works primarily by inhibiting platelet aggregation, stabilizing atherosclerotic plaque, and reducing fibrinogen level, but there is some evidence that it also reduces Factors V and VII in both men and women and Factor X in women.[1,2]

There is no evidence that fish oil causes hemorrhagic stroke or internal bleeding, while there is abundant evidence that warfarin does.[3-7] Warfarin was originally developed as a rat poison and has two effects – it damages the integrity of blood vessel walls and inhibits the normal blood clotting action which would prevent the rat from bleeding to death. It would seem that a similar mechanism operates in humans.

The purpose of anticoagulants like warfarin and fish oil is to prevent blood from forming a clot or at least significantly increase the length of time it takes before a clot is formed in response to trauma or stagnation. There are several different tests for measuring clotting tendency, and it is somewhat unfortunate that the test in general use today, the prothrombin time (INR), is not an absolute measure of the blood's tendency to form a clot (thrombus), but rather a measure of the blood level of those coagulation factors that depend on vitamin K for their synthesis and the factors they, in turn, activate. In other words, the universal test today is primarily designed to measure blood level of warfarin. Aspirin, vitamin E, garlic and other natural antiplatelet/anticoagulant agents generally have no or very little effect on INR – and yet, these substances all have proven preventive effects against thrombus formation.

The problem is that the INR test only measures blood coagulation time in the extrinsic and common pathways. Retardation of the coagulation sequence by antiplatelet aggregation medications (aspirin, clopidogrel, ticlopidine), for example, will not affect INR because the sequence is halted in the intrinsic pathway before

vitamin K-dependent coagulation factors become involved. Similarly, if the coagulation process is initiated via the intrinsic pathway and prekallikrein, Factor VIII or von Willebrand Factor are blocked, the thrombus formation sequence will not proceed either, but the INR test, because it bypasses the intrinsic pathway, will not show that you are protected even though you clearly are.

It is clear that both fish oil and warfarin are effective anticoagulants and it is thus likely that taking both would be superior to either agent alone in preventing ischemic stroke. The question is, "Would taking both increase the risk of hemorrhagic stroke and internal bleeding?" As far as I know only three studies have investigated the possible interaction between warfarin and fish oil.

Clinical Studies

A group of Norwegian medical researchers found that fish oil supplementation did not increase the bleeding tendency in heart disease patients receiving aspirin or warfarin. The study involved 511 patients who had undergone coronary artery bypass surgery. On the second day after the operation half the patients were assigned in a random fashion to receive 4 grams of fish oil per day (providing 2 g/day of eicosapentaenoic acid, 1.3 g/day of docosahexaenoic acid, and 14.8 mg/day of vitamin E). At the same time the patients were also randomized to receive either 300 mg of aspirin per day or warfarin aimed at achieving an INR of 2.5-4.2. The patients were evaluated every 3 months and questioned about bleeding episodes for the duration of the 9-month study.

The researchers concluded that fish oil supplementation did not result in a statistically significant increase in bleeding episodes in either the aspirin group or in the warfarin group. Nosebleeds were somewhat more common in the fish oil + warfarin group, while gastrointestinal bleeding was more common in the warfarin group. None of the differences were statistically significant. They also found no significant long-term effects of fish oil on common parameters of coagulation and fibrinolysis – including bleeding time. They noted that the blood levels (serum phospholipid levels) of eicosapentaenoic acid and docosahexaenoic acid increased by 140% and 14% respectively in the patients taking fish oil. The serum triglyceride levels decreased by 19.1% in the fish oil group while no significant change was observed in the remainder of the patients.[8]

Researchers at the University of Texas Health Sciences Center have addressed the question, "Does fish oil supplementation change INR in patients on warfarin?" Their placebo-controlled, randomized, double-blind study included 11 patients with prosthetic heart valves, cardiomyopathy or deep vein thrombosis who were taking warfarin and had achieved stable INR values for at least 4 weeks. The participants were assigned to receive a placebo, 3 grams/day of fish oil (*MaxEPA*), or 6 grams/day of fish oil for a 4-week period. Their INR was measured twice weekly during the study period. INR values remained steady in all groups and there were no significant differences in INR values between the groups during the trial. The researchers conclude that, "there does not appear to be a clinically significant interaction between warfarin and up to 6 grams/day of the fish oil supplement *MaxEPA* in terms of INR changes and bleeding incidence."[9]

Mitchell Buckley and colleagues at the Shawnee Mission Medical Center in Kansas recently reported the case of a 67-year-old woman whose INR increased significantly after she increased her daily dose of fish oil from 1 gram to 2 grams. The woman had serious health problems (TIAs, hypothyroidism, hyperlipemia, osteopenia, and coronary artery disease) and had experienced a heart attack necessitating angioplasty. She was taking several medications including warfarin, aspirin, levothyroxine, atorvastatin, bisoprolol, lisinopril, and conjugated estrogens. She was also supplementing with 400 IU a day of vitamin E and 1 gram a day of fish oil. The patient had been stable for a 5-month period at an INR of between 2 and 3 taking 1.5 mg a day of warfarin. In March 2002 she increased her fish oil dosage to 2 grams a day and a week later her INR measured 4.1. Upon returning to 1 gram a day of fish oil her INR dropped to 1.6. The researchers conclude that the higher dose of fish oil could have provided additional anticoagulation as expressed in a higher INR. There was no indication that the INR was affected by 1 gram a day of fish oil.[10]

Conclusion

There is no evidence that taking both warfarin and fish oil increases the incidence of bleeding. However, there is no clear consensus as to whether fish oil affects INR. One small study found that 3 and 6 grams a day of fish oil had no significant effect on INR, whereas a single case study found that 2 grams a day increased INR

significantly. Thus, it would appear that supplementing with 1 gram a day of fish oil while on warfarin is safe and does not affect INR.

It is not clear whether higher fish oil intakes may affect INR, so it is advisable to increase INR monitoring frequency when changing one's daily fish oil intake. It is possible, but certainly not proven, that taking fish oil and warfarin together may reduce the amount of warfarin required to keep the INR in the therapeutic range.

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How Suffering and Curing Atrial Fibrillation Changed My Life

by Michael Coleman

The two visits for my Executive Health Check, one in September 2002, and the next September 2003, could not have presented more surprising or contrasting advice on my heart function.

Having maintained a regular diet/exercise regime all my adult life, including competing in long "community" running events and ocean swims, I watched on with near smugness as my doctor tore off the cardiogram, knowingly surveyed the pattern and would pronounce, year after year "this Michael, is a heart that functions in the top 5% for your age, you have been blessed with a "Ferrari of an engine"!

In September of 2003 at the age of 42 all this veered wildly onto a totally unfamiliar road. After feeling uncharacteristically light-headed and fatigued following several exercise sessions, my vigilant gym manager suggested that I promptly see my doctor. The same doctor's cardiogram revealed that my heart was in atrial fibrillation…I needed to see a cardiologist fast!!

The early days with AF were a mixture of disbelief that my previously bullet proof heart function had gone awry, with general confidence that a cure would be quickly found, and life as usual, would return.

The "cure" presented to me by my cardiologist was to medicate the heart into finding it's former silky rhythm. I was given a 60% chance that the prescribed beta-blocker would fix the AF. When, after 3 weeks, this medication had no effect, I had an electro cardioversion, which held me in normal sinus rhythm for just 2 days. I was also told from this point that I needed to try other medications and that there could be some side effects.

Though every body is different, in my case I was hit hard by the drug protocol, and in hindsight should have listened much more carefully to my protesting body… instead I embarked on an increasingly desperate quest to

find normal sinus rhythm, with drugs as my only "hope" for a cure. This quest saw me anxiously consuming increasingly high doses of Sotalol, Amiodarone, Tambocor, Quinidine, Metoprolol, Isoptin, and Rythmodan.

Daily life began to become more challenging, with the combination of an average 5 hrs/day in AF, as well as a constant run of side effects from the medications. Lethargy would descend over me, insomnia, headaches, weight loss, and most debilitating of all, depression, littered my life.

My former rigorous exercise regime was pared back to shuffling my local streets… wondering "why me"?

After 12 months (August 2004) I underwent a flutter ablation in Sydney. This, combined with a huge (450 mg) daily dose of Tambocor, kept me in NSR for about 1 month. The resumption of AF coincided with the sad passing of my dear Dad. I can't help think, in hindsight, that the "heartbreak" I felt at the time translated literally to my physiology.

When we are sick or suffering disease, every person has, in trying to rebalance their health, a threshold of questioning whether their path is correct. The turning point for me was sitting, half asleep in front of my family doctor, desperately seeking yet one more medication solution. "We can try something experimental, he offered. You can take 2 different anti-arrhythmic drugs, as well as a beta-blocker. This should cover ALL electrical paths, and stop the AF". I pondered this strategy, quietly desperate, "What's the worst case scenario doc?" I asked. "Heart block", he replied, "where you heart stops and you lose consciousness". I thanked him for his time and walked out of his surgery. Knowing that he was recommending I experiment out of desperation with even more drugs – effectively putting my hand up and saying. "Body I have no respect for your myriad of miraculous healing systems, and opt to become a western medicine junkie". I knew this was just a "band aid" approach, and vowed to start looking at more natural alternatives.

About this time, I discovered Hans Larsen's research, and was extremely impressed by his drive to assist others dealing with AF. I subscribed to his newsletter, made contact with nutrient specialist Dr Michael Lam in California, and commenced a new "hope inspiring" nutrient protocol, in concert with visits to an excellent Sydney-based naturopath, Catherine Pritchard.

Sadly, solving the AF riddle with nutrients alone was never possible in my case, for every time I reduced the drug dosage, my AF would "spike", and I never had the nerve to withstand 24/7 AF, while waiting to see if the nutrients alone would cure me.

In the background, my Sydney cardiologist, a caring guy with a big reputation, Dr David Whalley, was increasingly blunt about my best possibility of a cure. He was suggesting pulmonary vein ablation (with about a 40% chance of a cure, [ie. no AF, no drugs, 6 months after procedure]).

It was Hans' research into global PVI success rates that convinced me to finally try and get off the medication merry go round, and have the ablation procedure– in France. My confidence was further buoyed, when Hans reported on his web site that he had travelled to France for a completely successful cure.

I booked my PVI and flights for my wife and 2 children, just days later, in May 2005. Every aspect of my dealing with the Hospital Haut Leveque, Bordeaux, was impressive. The French have constructed a formidably efficient, professional healing system.

During the 7 months waiting time, I admit trying desperately, to find an alternative cure, which would allow me to defer or avoid what I had convinced myself was "playing my last card". I was still telling friends as close as 2 weeks from departure for France, that I thought I was "stable" enough to delay the procedure. A positive aspect of my nutrient protocol was that I was so full of vitamins that my immune system had been failsafe, for 24 months I had no illness of any sort. Interestingly, the mounting stress of the journey, as a family, "into the French unknown", crashed into me just 1 week prior to departure, when I contracted a nasty respiratory virus spending the first 4 days in years in bed. I recall corresponding 2 days before leaving Australia, with Dr Pierre Jais (who replied patiently to a stream of my emails over 6 months) at the Bordeaux Hospital, and telling him of my concern for undergoing surgery, after being belted by a virus…"You should come, Mr. Coleman, we can wait until your chance of success is best".

In reality, the PVI procedure is now so regularly performed in Bordeaux, that significant risk of injury/mortality has practically been eliminated. The “last card” I had imagined, was a classic case of patient anxiety.

Prof Michel Haissaguerre had been “talked up” to legendary status by Hans Larsen and even my own Australian cardiologist, but meeting him and witnessing the total passion and confidence with which he operates, took my estimation to a new level. He is an exceptional electrophysiologist. I noticed very soon after my first meeting with Michel, that he moved at most times around the hospital with a small army of supporters, all seeming to hang on every word of his medical judgment and experience.

For my first procedure, December 12, 2005, I was surprised at the resources involved – 5 EPs, (including three professors of cardiology and 2 nurses). The procedure consisted of a PVI of all 4 veins. An ablation line was performed at the roof of the left atrium connecting both superior pulmonary veins and terminating AF.

I was carefully monitored for several days in Bordeaux, which has some of the best post-operative care for this procedure, worldwide. Just as well, as in my case, one of the 4 veins had become conductive…. and this necessitated a second procedure 3 days after the first. I was naturally quite apprehensive about needing a second procedure so soon after the first, but Prof Michel soon allayed my fears with his absolute conviction that my history of numerous 24 hr+ episodes of AF, pre-determined that I would be a “difficult” case to cure.

The second procedure consisted of a second line performed at the left isthmus between the left inferior pulmonary vein and mitral annulus resulting in a complete bi-directional block. All in all, in Prof Haissaguerre’s words, “The ablation equivalent of the surgical maze procedure…”

The care shown by all at Haut Leveque was exceptional. I felt like I was being treated as though I was “family” to Prof Haissaguerre and his team. I had my own young family with me (my beloved Jacqueline refused point blank to have it any other way), and an abiding memory of Prof Michel, is the way in which he reacted to meeting my 9-year-old son, Callum.

Cal was clearly overwhelmed by the sight of me returning from the first procedure, a little pale and lethargic. Prof Haissaguerre quickly assumed the role of ‘surrogate dad’, put a comforting arm around my son, and led him quietly to the telemetry station, to show and explain to him the new sinus rhythm of my heart. This man is a completely empathetic, dedicated practitioner!

The day after the second procedure, Prof Michel confidently informed my wife that I may well have small episodes of AF and extra “ectopic” beats for the next months as the scar tissue formed new electrical pathways, but … “he is cured”. He said this with such confident emphasis that I remember feeling quietly elated that my suffering would soon be over.

Two other doctors deserve special mention, being Dr Pierre Jais, and Prof Prash Sanders. They were completely involved in thoroughly addressing my myriad of questions pre and post procedures, and struck me as both being “at the top of their game”.

Haissaguerre’s prediction of slight AF and ectopic beats was very accurate. I had several 15-min AF episodes during the ensuing 3 weeks. In addition, extra beats have occurred spasmodically right up until the last few days. As any doctor will advise, “ectopic” heartbeats are quite normal.

However, it is now over 4.5 months since I have experienced an AF episode, and following an extremely slow medication withdrawal, I am practically “drug free” (1.25mg bisoprolol/day) I am also back in training for a 10km community fun run in 8 weeks time.

My life has changed irrevocably to being far more mindful of “living in the moment”. Mainly, I have discovered this simple joy through the practice of daily relaxation meditation. I am a more compassionate, and grateful, human being than ever. I have never felt physically or mentally tougher in my entire life. I have a new depth of love and respect for my wife Jacqueline and children Kaitlin and Callum. We did it as a team!

The journey through AF has given me all of these insights. If I can help alleviate the torment of just one person's AF through this story, I will be content. I sincerely hope that my story provides further belief to those who need it.

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