THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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In this issue we feature the afib journey of Suzi E. She experienced her first episode in February 2006 and her last 4 years later. Suzi's story is a remarkable one and clearly shows the huge impact of unrelenting stress on the initiation and continuation of AF. One of our early LAF surveys found that 26% of respondents attributed their first episode to emotional or work-related stress. Subsequent episodes were deemed to be stress-related in 50% of cases. Suzi's story also illustrates the long-term effects of growing up in a dysfunctional home. LAF Survey IV revealed that 25% of the 104 respondents had been brought up in a dysfunctional family environment. These afibbers were more likely to be women, more likely to smoke, have a bowel disorder, have been on valium, and have a high C-reactive protein level. Quite a legacy!

Is there any rational explanation for the connection between AF and a dysfunctional childhood? Yes indeed, at least two studies have found that frequent stressful conditions in childhood, resulting in elevated cortisol levels, may contribute to low levels in adulthood, and that these low cortisol levels may make one hypersensitive to stress and thus a good candidate for AF.

Also in this issue we report that post-ablation arrhythmia recurrence is strongly related to elevated levels of BNP (brain natriuretic peptide), and is not affected long-term by antiarrhythmic therapy during the fist six weeks following the ablation. Lone afibbers have elevated levels of parathyroid hormone, warfarin induces calcification of coronary arteries, and researchers in Iceland confirm that AF has reached epidemic proportions and is set to overwhelm health care systems by 2050.

And finally, if you need to restock your supplements, please remember that by ordering through my on-line vitamin store you will be helping to defray the cost of maintaining the web site and bulletin board. You can find the store at http://www.afibbers.org/vitamins.htm - your continuing support is truly appreciated.

Wishing you lots of NSR,

Hans

Highlights

Post-ablation antiarrhythmics and AF recurrence

PHILADELPHIA, PENNSYLVANIA. Early recurrence of atrial arrhythmias (atrial fibrillation, flutter or tachycardia) is common following a pulmonary vein isolation (PVI) procedure, but does not necessarily indicate failure of the procedure. Nevertheless, such recurrences are disturbing to the patient and may result in the need for cardioversion and hospitalization. Some electrophysiologists (EPs) prescribe antiarrhythmics to be taken for a certain period following the ablation, while other just prescribe beta- or calcium channel blockers (AV node blocking agents) or no drugs at all.

In 2009 EPs at the University of Pennsylvania reported that ablatees on antiarrhythmics post-ablation were significantly less likely to experience a prolonged arrhythmia recurrence during the first 6

weeks than were patients on AV node blocking agents only (13% vs. 28%). The Pennsylvania group now reports the results of a further 20-week follow-up, bringing the total follow-up time to 6 months.

The experimental group consisted of 110 paroxysmal afibbers (71% men) aged between 46 and 64 years. They had suffered from AF for an average of 6.5 years; 50% had hypertension, and 12% had coronary artery disease. After undergoing a pulmonary vein antrum isolation procedure (Natale protocol), the participants were randomized to receive an antiarrhythmic + AV node blocking agent, or just an AV node blocking agent for a 6-week period immediately following the procedure. Thirty-four percent of members of the antiarrhythmic group were prescribed flecainide, 26% propafenone, 36% sotalol, and 4% dofetilide (Tikosyn).

Ignoring arrhythmias during the first 6 weeks (blanking period), 72% of patients in the antiarrhythmic group were AF-free at the 6-month follow-up (no recurrence during the period 6 to 26 weeks post-ablation) as compared to 68% in the group receiving beta- or calcium Channel blockers only. This difference is not statistically significant indicating that antiarrhythmic therapy during a 6-week period post-ablation does not prevent arrhythmia recurrence at 6 months. However, there was a strong correlation between lack of recurrence during the 6-week blanking period and AF-free status at 6 months. In the group with no recurrence during the blanking period, 84% were AF-free at 6 months as compared to only 38% who experienced early recurrence.

The researchers conclude that, although short-term antiarrhythmic therapy decreases early recurrence, it does not prevent arrhythmia recurrence after the blanking period. They speculate that the main factor determining recurrence is electrical reconnection between isolated veins and the left atrium – a progression which would not be affected by antiarrhythmic therapy.

Leong-Sit, P, Gerstenfeld, EP, et al. Antiarrhythmics after ablation of atrial fibrillation – six-month follow-up study. **Circulation: Arrhythmia and Electrophysiology**, *Vol. 4, February 2011, pp. 11-14*

Editor's comment: The absence of early recurrence is clearly of huge importance in determining medium- and long-term outcome. The 2009 Ablation/Maze Survey found that ablatees who had experienced no recurrence in the last 6 months of the 12-month period following ablation had a 93% chance of being afib-free at 4 years, while the chance for those who experienced recurrences was only 50%.

Role of BNP in post-ablation recurrence

CLEVELAND, OHIO. Brain natriuretic peptide (BNP), a cousin of atrial natriuretic peptide (ANP), is a hormone released from the walls of the ventricles when stretched such as during unusually strenuous activity. It is stored as a prohormone within secretory granules in the ventricles and is secreted as an N-terminal fragment, N-terminal pro-brain natriuretic peptide (nt-pro-BNP), and the smaller active hormone BNP. BNP has effects similar to those of ANP, that is, it decreases sodium reabsorption rate, renin release, and aldosterone release; it also increases vagal (parasympathetic) tone and decreases adrenergic (sympathetic) tone. Because nt-pro-BNP is easier to measure than BNP it is often used as a marker for BNP.

It is well established that BNP and nt-pro-BNP levels are elevated in heart failure and that the degree of elevation is directly proportional to the seriousness of the failure. However, researchers at the Massachusetts General Hospital have reported that lone afibbers also have elevated nt-pro-BNP values even when in sinus rhythm.

Now researchers at the Cleveland Clinic report that an elevated BNP level is a strong predictor of the recurrence of atrial arrhythmia (atrial fibrillation, flutter or tachycardia) after pulmonary vein isolation (PVI). Their study involved 726 lone afibbers undergoing their first PVI. The average age of the patients was 57 years, 71% were male, and 78% had paroxysmal AF. All study participants underwent a thorough medical examination to exclude known causes of AF and had their BNP level determined on the day of the procedure (median value 52 pg/mL). An elevated BNP level was found to be associated with older age, longer duration of AF, non-paroxysmal (persistent or permanent) AF, and larger left atrial size.

Over a median follow-up of 26 months, excluding a 2-month blanking period, 78.8% of ablatees

remained arrhythmia-free. The following variables independently predicted arrhythmia recurrence:

- Higher body mass index (BMI)
- Non-paroxysmal AF
- Longer duration of AF
- Lower left ventricular ejection fraction
- Larger left atrial size.

However, the most important predictor of ablation failure was an elevated BNP level. Afibbers with a pre-ablation BNP level above 126 pg/mL had a 6 times greater risk of recurrence than did those with a BNP level of less than 31 pg/mL.

The Cleveland researchers speculate that in lone afibbers, the source of BNP, typically secreted by the ventricles, is actually the atria and may reflect intrinsic atrial disease such as inflammation, fibrosis or even subclinical atrial myocardial ischemia.
Hussein, AA, Wazni, OM, et al. Plasma B-type natriuretic peptide levels and recurrent arrhythmia after successful ablation of lone atrial fibrillation. **Circulation**, *Vol. 123, May 17, 2011, pp. 2077-82*

Editor's comment: The role of BNP in atrial fibrillation was discussed in detail in an earlier research report. (See URL for further information - http://www.afibbers.org/resources/BNP.pdf). The conclusion of this report was that BNP is an important hormone released from the walls of the ventricles and, to some extent, the atria when stretched. It is well established that a high BNP level is associated with heart failure, but it is now also clear that elevated BNP levels are closely associated with atrial fibrillation including lone AF. BNP levels are higher in afibbers than in non-afibbers and those in permanent afibbers are higher than those in paroxysmal afibbers. A high BNP level is associated with a lower probability that cardioversion will be successful and also predicts a poor outcome of catheter ablation. There is also evidence that an elevated BNP level in paroxysmal afibbers is associated with a quicker progression to the permanent state. Finally, some very recent research provides convincing evidence that an elevated BNP level is strongly associated with the risk of developing AF over a 10-year period following the baseline BNP determination. It is to be hoped that electrophysiologists will soon include a measurement of BNP or nt-pro-BNP in their initial evaluation of all afibbers and their relatives.

Bleeding risk with dabigatran (Pradaxa)

HAMILTON, ONTARIO, CANADA. Although there is no evidence that otherwise healthy lone afibbers have an increased risk of ischemic stroke, it is clear that atrial fibrillation (AF) patients with heart failure, diabetes or hypertension have a significantly increased risk and this risk is further magnified if the patient has already suffered a heart attack or stroke. To date, oral anticoagulation with vitamin K antagonists such as warfarin (Coumadin) is still considered to be the best preventive therapy for patients at risk for stroke. Unfortunately, warfarin interacts with many foods and drugs and treatment requires constant, costly monitoring. Its use also substantially increases the risk of hemorrhagic stroke and major internal bleeding, particularly in older people, a group that, ironically, is also most at risk for an ischemic stroke.

Warfarin acts by inhibiting the activation of the vitamin K-dependent coagulation factors V, VII, and X in the extrinsic and common pathways of the coagulation cascade. Research aimed at replacing warfarin has focused on developing new pharmaceutical drugs which will inhibit specific coagulation factors. The most promising of these new drugs is the direct thrombin inhibitor dabigatran etexilate (Pradaxa).

Dabigatran was evaluated in a very large clinical trial (RE-LY) involving over 18,000 atrial fibrillation patients with one or more risk factors for stroke (average $CHADS_2$ score was 2.1). NOTE: 79% of the participants had hypertension, 32% had heart failure, 20% had experienced a prior heart attack or stroke, and 23% had diabetes. The patients were randomly allocated to receive 110 or 150 mg of dabigatran twice daily, or standard warfarin therapy (INR range aim of 2.0 to 3.0). After two years of follow-up, the researchers conducting the RE-LY trial concluded that low-dose dabigatran (110 mg twice daily) is associated with an ischemic stroke rate similar to that obtained with warfarin, but results in a lower incidence of hemorrhagic stroke and major bleeding. High-dose dabigatran (150 mg twice daily) is superior to warfarin when it comes to preventing ischemic and hemorrhagic stroke, but has a similar rate of major hemorrhage.

Now the researchers (a group of scientists from 9 different countries) report on a follow-up study of

the RE-LY data aimed at evaluating bleeding risk with dabigatran therapy. They specifically looked at the effect of age and kidney impairment on intracranial (intracerebral, hemorrhagic stroke) and extracranial (mainly gastrointestinal) bleeding. They conclude that low-dose dabigatran therapy (110 mg twice daily) compared with warfarin is associated with a 20% lower risk of major bleeding (2.87%/year vs. 3.57%/year), and a 70% reduced risk of intracranial bleeding (0.23%/year vs. 0.76%/year) with no significant difference in extracranial bleeding. There was no significant difference in the incidence of ischemic stroke between low-dose dabigatran and warfarin. The incidence of major bleeding in patients under the age of 75 years was significantly lower in the dabigatran group, but no difference was observed in the 75 years or older group. The incidence of intracranial bleeding was substantially lower in the dabigatran group irrespective of age, whereas the incidence of gastrointestinal bleeding was substantially higher among patients aged 75 years or older (2.19%/year for dabigatran vs. 1.59%/year for warfarin).

High-dose dabigatran therapy (150 mg twice daily) was associated with a major bleeding risk similar to that of warfarin (3.31%.year vs. 3.57%/year) and a 58% reduced risk of intracranial bleeding (0.32%/year vs. 0.76%/year) with no difference in extracranial bleeding. The incidence of ischemic stroke in the high-dose dabigatran group was significantly lower than in the warfarin group (1.69%/year vs. 1.10%/year) irrespective of age.

However, the incidence of gastrointestinal bleeding was substantially higher among patients aged 75 years or older (2.80%/year for dabigatran vs. 1.59%/year for warfarin). The researchers observed that the risk of major bleeding increased with the concomitant use of aspirin. They also found that renal impairment (kidney dysfunction) was a strong risk factor for bleeding with a creatinine clearance of less than 50 mL/min associated with a 2-fold higher risk of major bleeding than if creatinine clearance was more than 80 mL/min. The researchers speculate that renal impairment may be a major cause of the increased tendency for gastrointestinal bleeding observed with dabigatran therapy in elderly patients (dabigatran is renally excreted so a kidney dysfunction may result in higher blood concentrations of the drug).

The RE-LY investigators conclude that "*both doses of dabigatran compared with warfarin provide substantial safety benefits in patients with AF and at least 1 additional risk factor for stroke. At ages <75 years, the higher dabigatran dose seems preferable because of the lower risk of stroke without any increase risk of bleeding, whereas at higher ages, the lower dabigatran dose might be considered a means to reduce the risk of bleeding in selected patients who are at high risk of bleeding.*"
Eikelboom, JW, Yusuf, S, et al. Risk of bleeding with 2 doses of dabigatran compared with warfarin in older and younger patients with atrial fibrillation. **Circulation**, *Vol. 123, May 31, 2011, pp. 2363-72*

Editor's comment: A recent report from France http://www.theheart.org/article/1260157/print.do reveals the cases of two elderly, frail women who suffered massive bleeding (one fatal) on the 110 mg twice daily dabigatran dose. It is likely that renal impairment was a contributing factor in these incidents and that a dabigatran dose of 75 mg twice daily may be more appropriate for elderly patients with renal impairment. Nevertheless, dabigatran (Pradaxa) would appear to be a satisfactory replacement for warfarin in the treatment of AF patients with one or more risk factors for stroke. There is, however, no evidence whatsoever that lone afibbers with no stroke risk factors would achieve an overall benefit by taking this drug.

Is an AF epidemic looming?

REYKJAVIK, ICELAND. There seems to be no question that the incidence (new cases per 1000 person-years) and prevalence (% of a given population having AF at any given point in time) of atrial fibrillation (AF) is on the rise, at least in first world countries. American researchers believe that between 2.3 million and 5.1 million Americans were suffering from AF in the year 2000, and that this number could rise to 5.6 million or even 15.9 million in 2050. A recent major study involving 21 million Americans concluded that 3 million people in the USA were struggling with AF in 2005 and that this number would rise to 7.6 million by 2050. Chinese researchers have estimated that 8 million Chinese suffer from AF with 22% of cases being classified as lone AF. A Dutch study involving 6400 citizens of Rotterdam found an overall prevalence of AF of 5.5% in 1990 increasing to 8.3% by January 2000.

Now a team of researchers from the National University Hospital of Iceland reports that the incidence and prevalence of AF is also increasing dramatically in Iceland (2008 population of 229,000). During the period 1991 to 2008 the age- and sex-standardized incidence of AF increased from 2.1% to 2.4% (as determined from AF-related admissions to hospital, emergency rooms, and outpatient clinics). The age- and sex-standardized prevalence of AF rose from 1.5% to 1.9% in the period 1998 to 2008 (2.3% for men and 1.5% for women). The prevalence increase was most pronounce (5.1%) in men aged 85 to 99 years. Taking into account increases in life expectancy and population, it is estimated that the prevalence of AF will rise from 2.0% in 2008 to 3.0% in 2020, and 4.3% in 2050. This corresponds to an increase of over 200% in the number of adult Icelanders having AF by 2050.

Applying the numbers for Iceland to all of Europe would lead to the conclusion that about 10 million Europeans currently have AF and that by 2050 this number could rise to a staggering 25 to 30 million – clearly a very serious burden on health care systems. By far, the majority (probably around 80%) of AF cases are associated with comorbid conditions such as hypertension, heart disease, diabetes, and obesity. In an accompanying editorial, Danish and British cardiologists suggest that the way to stem the AF epidemic is an increased emphasis on prevention of the above modifiable risk factors through exercise and diet changes.

Stefansdottir, H, Arnar, DO, et al. Trends in the incidence and prevalence of atrial fibrillation in Iceland and future projections. **Europace**, *Vol. 13, 2001, pp. 1110-17*
Olesen, JB, et al. An epidemic of atrial fibrillation? **Europace**, *Vol. 13, 2001, pp. 1059-60*

Editor's comment: This newest estimate of the present and expected AF burden in Europe is indeed sobering and most likely underestimated. Although two-thirds of the population of Iceland lives in Reykjavik and there is only one hospital there, it is highly likely that some cases of AF were missed either because they were asymptomatic or because they were managed by general practitioners without involving hospital admissions.

LAF and elevated parathyroid hormone level

BOSTON, MASSACHUSETTS. The parathyroid glands are four or more small glands, each about the size of a grain of rice, located on the backside of the thyroid gland. They are named for their proximity to the thyroid, but serve a completely different role. While the thyroid gland is involved in regulating metabolism, the major function of the parathyroid glands is to maintain the body's calcium level within a very narrow range so that the nervous and muscular systems can function properly. The parathyroid glands perform their function by releasing a hormone, parathyroid hormone (also known as parathormone or PTH), in response to a low blood level of calcium. The glands have sensors for measuring calcium level in the blood and, if found to be low, the release of PTH will result in removal of calcium from the bones (resorption) and/or the conversion of 25-hydroxy vitamin D (cholecalciferol) to its active form 1,25 dihydroxycholecalciferol (calcitriol), which will increase intestinal calcium absorption.

The parathyroid gland also releases PTH if it senses a magnesium deficiency and, somewhat paradoxically, magnesium is also required for the synthesis and secretion of PTH. Finally, there is some indication from animal experiments that vitamin K2 can counteract an increase in PTH by stimulating renal calcium absorption. In addition to its direct effects on calcium homeostasis, PTH also acts as a cardiac hormone. It accelerates heart rate and increases the force of heart contractions. There is also evidence of an association between PTH and hypertension, disturbances in the RAAS (renin-angiotensin-aldosterone system), left ventricular hypertrophy, and heart failure. The normal level of PTH is 10-55 pg/mL.

A group of researchers at the Massachusetts General Hospital now report an association between elevated PTH levels and lone atrial fibrillation (AF). Their study included 230 lone afibbers and 150 controls. The mean age of the participants was 56 years, 80% were male, and 88% had paroxysmal AF. About a third (37%) of the lone afibbers had hypertension. All participants had blood samples drawn for PTH measurement and underwent a physical examination as well as electrocardiography and echocardiography at entry to the study. The PTH level was higher in afibbers than in the control group (56 pg/mL vs. 50 pg/mL) and higher in afibbers with hypertension than in

those without (59 pg/mL vs. 54 pg/mL). PTH levels were also higher in permanent afibbers than in paroxysmal ones (61 pg/mL vs. 55 pg/mL).

At the time of the blood draw, 164 afibbers were in sinus rhythm and 50 were in AF. PTH levels were substantially higher in those not in normal sinus rhythm (64 pg/mL vs. 54 pg/mL) and the difference in PTH level between afibbers in sinus rhythm and the controls was statistically non-significant.

The researchers conclude that PTH levels are higher in lone afibbers than in controls. The difference was particularly marked in afibbers actually experiencing AF at the time of blood sampling, in permanent afibbers, and in afibbers with hypertension. They also observed that a higher PTH level was associated with a larger left atrium. They suggest that their observations support the hypothesis that AF causes an increase in PTH, but concede that the possibility that an elevated PTH level causes AF cannot be excluded.
Rienstra, M, Ellinor, PT, et al. Elevation of parathyroid hormone levels in atrial fibrillation. **Journal of the American College of Cardiology**, *Vol. 57, No. 25, June 21, 2011, pp. 2542-43*

Editor's comment: The finding that atrial fibrillation and PTH levels are associated confirms an earlier report by Israeli researchers. The team from Tel Aviv University found that PTH levels were significantly elevated during a bout of paroxysmal AF. They also observed a direct correlation between blood glucose level and duration of an AF episode. The higher the glucose level, the longer it took to convert to normal sinus rhythm[1].

Assuming that AF causes the release of PTH rather than vice versa, it would be interesting to speculate as to why AF would increase PTH. In my 2003 report "Aldosterone: Villain of the Peace", I suggested that the wildly beating heart would release substantial amounts of ANP (atrial natriuretic peptide) and, to a lesser extent, BNP (brain natriuretic peptide). Inasmuch as ANP and BNP are strong diuretics, their release would be accompanied by copious urination (the big pee) which, in turn, would cause a substantial loss of sodium and, a somewhat lesser loss, of calcium, magnesium and phosphorous. The disproportional loss of sodium would rebalance the potassium/sodium ratio and eventually terminate the AF episode. The loss of calcium would result in a lowering of its concentration in the blood which would cause the release of PTH in order to correct the imbalance by drawing calcium from the bones[2,3].

So what do these findings mean, in practical terms, to afibbers?

- The release of PTH is normally associated with low levels of calcium in the blood and serves to restore normal levels by causing the release of calcium from the bones (resorption). Presumably, PTH release associated with AF would have the same effect, and thus be a risk factor for osteopenia and osteoporosis, especially in the case of permanent afibbers.

- If PTH released via AF has the same effect as PTH released due to low calcium levels than AF-related PTH release could presumably cause the common symptoms of hypercalcemia, including kidney stones, hypertension, development of cardiac structure abnormalities, myocardial calcification, and disturbances to the RAAS (renin-angiotensin-aldosterone system).

- The observation that an AF episode lasts longer at high levels of blood glucose would lead to the conclusion that consuming high glycemic index foods during or immediately prior to an AF episode is a bad idea. Thus attempting to stop an episode by eating a banana or drinking orange juice is clearly not recommended.

While there is, as far as I know, no clinical data proving that AF-related PTH release could lead to the above complications, it would seem prudent to take steps to reduce PTH levels. Fortunately, this can easily be accomplished by supplementing with vitamin D. A recent study by Japanese researchers found that daily supplementation with 800 – 1200 IU of vitamin D3 reduced PTH levels by an average of 5.6 pg/mL in a group of 107 subjects without disorders affecting vitamin D metabolism. The increase in blood levels of vitamin D and the decline in PTH was accompanied by a slight increase in circulating calcium from 9.5 mg/dL (2.33 mmol/L) to 9.6 mg/dL (2.35 mmol/L)[4]. Another group of Japanese researchers has reported that vitamin K2 also retards an increase in PTH level and the resulting bone resorption[5].

Thus it would seem prudent for afibbers to ensure an adequate intake of vitamin D and K2. Inasmuch as PTH can also be released as a result of a magnesium deficiency, continued magnesium supplementation would also be in order.

[1] Shor, R, et al. Serum parathyroid hormone-related protein levels before and after paroxysmal atrial fibrillation. American Journal of Emergency Medicine, Vol. 26, March 2008, pp. 361-63

[2] Larsen, HR. Aldosterone: Villain of the Peace? www.afibbers.org/resources/aldosterone.pdf

[3] Richards, AM, et al. Renal, haemodynamic, and hormonal effects of human alpha atrial natriuretic peptide in healthy volunteers. The Lancet, Vol. 1, No. 8428, March 9, 1985, pp. 545-49

[4] Okazaki, R, et al. Vitamin D insufficiency defined by serum 25-hydroxyvitamin D and parathyroid hormone before and after oral vitamin D_3 load in Japanese subjects. Journal of Bone and Mineral Metabolism, Vol. 29, 2011, pp. 103-10

[5] Iwamoto, J, et al. Effects of vitamin K_2 on the development of osteopenia in rats as the models of osteoporosis. Yonsei Medical Journal, Vol. 47, No. 2, 2006, pp. 157-66

Warfarin and coronary calcification

MAASTRICHT, THE NETHERLANDS. Arterial calcification is commonly associated with atherosclerosis and involves the deposition of calcium phosphate (hydroxyapatite) on artery walls. Atherosclerosis is a major risk factor for ischemic stroke so it is indeed ironic that warfarin has been implicated in the formation of arterial calcification. Australian researchers have reported that rats treated with warfarin develop extensive arterial calcification and concluded that, "It is likely that humans on long-term warfarin treatment have extrahepatic vitamin K deficiency and hence are potentially at increased risk of developing arterial calcification."[1] US doctors recently reported the case of an otherwise healthy man who developed extensive calcification of the coronary arteries after long-term warfarin treatment. They conclude "that physicians prescribing long-term warfarin treatment should consider arterial calcification as one of its potential consequences."[2] Dutch researchers have confirmed that a vitamin K deficiency, such as would be induced by warfarin treatment, increases the risk of arterial calcification and conclude that the current RDA for vitamin K is too low.[3]

Unfortunately, the common advice given by physicians to their warfarin-treated patients is to avoid dark green leafy vegetables (the major dietary source of vitamin K) and to strictly avoid vitamin K-containing supplements – thus guaranteeing a vitamin K deficiency.

A group of cardiologists from the University of Maastricht now report that otherwise healthy afibbers treated, often unnecessarily, with warfarin also develop coronary calcification. Their study included 157 atrial fibrillation (AF) patients (69% male) with an average age of 57 years. All participants had a low risk of cardiovascular disease as defined as no hypertension, no diabetes, normal cholesterol levels, age below 70 years, no history of coronary artery disease or stroke, normal kidney function, no cancer, thyroid or pulmonary disease, and no congestive heart failure. Perhaps most significant, none of the study participants had evidence of structural heart disease, so would be classified as lone afibbers. All participants underwent echocardiography and had a 64-slice coronary calcium scan. The Agatston score was used to quantify the degree of calcification as shown in the table below.

Degree of Calcification	Agatston Score
None	0
Minimal	1 – 10
Mild	11 – 100
Moderate	101 – 400
Severe	> 400

Out of the total of 157 patients, 79 had an Agatston score above zero, while the remaining 78 patients did not have any detectable calcium in the coronary blood vessels (Agatston score of 0). The authors of the study noted that 71 (45%) of the patients were on warfarin even though their CHA_2DS_2-VASc score was zero (55 patients) or 1 (all because of female gender). The remaining 86 patients had never been on warfarin. Among patients with an Agatston score of 0, only 32% were on warfarin as compared

to 58% in the group with an Agatston score greater than 0. The average Agatston score increased significantly with duration of warfarin use.

The average score among non-users was 53 as compared to 90 for 6 to 60 months of use, and 236 for greater than 60 months of use. In multivariate analysis, older age and duration of warfarin were independent predictors of increased coronary calcium score. The Dutch researchers conclude that many low-risk AF patients are overtreated with warfarin and that such overtreatment should be avoided, especially in young, low-risk afibbers facing a lifelong career as warfarin users.

Weijs, B, Crijns, HJGM, et al. Patients using vitamin K antagonists show increased levels of coronary calcification: an observational study in low-risk atrial fibrillation patients. **European Heart Journal,** *July 20, 2011 [Epub ahead of print]*

Editor's comment: The lesson to be learned from this study is that overtreatment with warfarin is common and should be avoided in order to prevent coronary calcification and the many other adverse effects associated with warfarin usage. See http://www.afibbers.org/resources/warfarin.pdf for details. Fortunately, another group of researchers from Maastricht University has reported that a high intake of vitamin K2 (menaquinone) is associated with a significantly reduced risk of arterial calcification and coronary heart disease.[4] Furthermore, other studies have reported that warfarin has little effect on the activity of vitamin K2 and that a vitamin K2 intake of 100 micrograms/day has very little effect on INR.[5,6]

Considering the above findings it is tempting to conclude that daily supplementation with menaquinone (100 micrograms/day of the MK-7 form of vitamin K2) would be highly beneficial in reducing arterial calcification (whether warfarin-induced or not), coronary heart disease, and overall mortality without impacting on warfarin's role in reducing the level of coagulation factors. In other words, supplementing with moderate amounts of vitamin K2 should not affect INR levels. Clinical trials, of course, should and hopefully will be carried out to substantiate or negate this hypothesis.

[1] Howe, AM and Webster, WS. Warfarin exposure and calcification of the arterial system in the rat. Int J Exp Pathol., Vol. 81, No. 1, February 2000, pp. 51-56

[2] Schori, TR and Stungis, GE Long-term warfarin treatment may induce arterial calcification in humans: case report. Clin Invest Med., Vol. 27, No. 2, April 2004, pp. 107-09

[3] Schurgers, LJ, et al. Role of vitamin K and vitamin K-dependent proteins in vascular calcification. Z Kardiol., Vol. 90, Suppl. 3, 2001, pp. 57-63

[4] Geleijnse, JM, et al. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. Journal of Nutrition, Vol. 134, 2004, pp. 3100-05

[5] Sconce, E, et al. Patients with unstable control have a poorer dietary intake of vitamin K compared to patients with stable control of anticoagulation. Thrombosis and Haemostasis, Vol. 93, May 2005, pp. 872-75

[6] Reedstrom, CK and Suttie, JW. Comparative distribution, metabolism, and utilization of phylloquinone and menaquinon-9 in rat liver. Proc Soc Exp Biol Med., Vol. 209, No. 4, September 1995, pp. 403-09

Complications associated with RF ablation

ANN ARBOR, MICHIGAN. Although radiofrequency (RF) ablation for atrial fibrillation (AF) has a very low mortality (comparable to that associated with a cataract operation), complications can and do arise during the procedure. Electrophysiologists at the University of Michigan now report on the rate of perioperative complications (complications occurring during the period between hospital admission and discharge) observed during 1642 RF ablation procedures, including 634 (39%) repeats, carried out on 1295 consecutive AF patients during the period January 2007 to January 2010. The mean age of the patients was 60 years, 74% were men, 53% had paroxysmal AF, and the remaining 47% had the persistent variety. Only 16% had heart disease, so the group essentially consisted of lone afibbers.

The overall incidence of perioperative complications was 3.5% with vascular access (initial insertion of the catheters in the femoral vein) being the most common at 1.9% (31 patients), followed by pericardial tamponade (fluid accumulation in the pericardium due to procedure-related rupture of the heart wall) in 20 patients (1.2%). The incidence of other complications was negligible and included 4 patients (0.2%) experiencing a TIA or ischemic stroke, 1 patient experiencing deep vein thrombosis, and 1 patient diagnosed with pulmonary vein stenosis. There were no procedure-related deaths, and no incidence of phrenic nerve palsy or atrioesophageal fistula. The vascular complications (1.9%) involved 12 patients with a major hematoma requiring blood transfusion, 17 patients with an arteriovenous fistula (abnormal

connection between an artery and a vein), and 2 patients with a pseudoaneurysm (enlargement of an artery due to trauma) of the femoral artery. Successful surgical repair was performed in 9 of the 19 patients with arteriovenous fistula or pseudoaneurysm.

An analysis of various variables that could possible affect the incidence of vascular complications revealed that females had a 4-fold (OR=4.40) increased risk of experiencing this complication, possibly due to the fact that women have a significantly shorter common femoral vein than do men. Patients who had been on clopidogrel prior to the procedure had an almost 5-fold (OR=4.70) greater risk of vascular complications, while patients whose procedure was performed in July or August had an almost 3-fold (OR=2.71) increase in risk. This later observation is explained by the fact that physicians who had just started their internship in a teaching hospital are often entrusted with the initial catheter insertion. The only variable affecting the risk of pericardial tamponade was having undergone a previous RF ablation (OR=3.32). There was no evidence that ablation strategy, case volume, total procedure time, or total duration of radiofrequency energy application had any influence on complication rates.

Baman, TS, Oral, H, et al. Prevalence and predictors of complications of radiofrequency catheter ablation for atrial fibrillation. **Journal of Cardiovascular Electrophysiology**, *Vol. 22, June 2011, pp. 626-31*

Editor's comment: This large study again underscores the fact that a radiofrequency ablation for AF is very safe if carried out at a high-volume center. It may be advisable though to avoid having the procedure during July or August if it is to be performed at a teaching hospital.

Repeat ablation – the sooner the better

SHANGHAI, CHINA. It is becoming increasingly clear that as many as 30 to 50% of afibbers undergoing a radiofrequency catheter ablation will need a repeat procedure. What is not clear is the optimal timing of the second procedure. Should it be performed as soon as possible after the initial procedure, or should there be a wait time to see if the post-procedure arrhythmias will settle down on their own? A group of electrophysiologists from Shanghai Chest Hospital now suggest that having the repeat ablation approximately 1 month after the initial procedure is optimum.

Their trial involved 375 patients with paroxysmal atrial fibrillation (PAF) who were treated at the hospital during the period July 2008 to February 2009. The average age of the patients was 53 years, 62% were male, and all had been unsuccessfully treated with at least one antiarrhythmic drug during the 6 months preceding their first circumferential pulmonary vein isolation (CPVI) procedure. All patients were discharged after 1 week in hospital and then underwent frequent electrocardiography and Holter monitoring for the 21-month trial duration.

A total of 117 (31.2%) of ablatees experienced early recurrences of atrial tachyarrhythmia (AF, atrial flutter, atrial tachycardia lasting longer than 30 seconds) during the first 2 weeks following their initial procedure. They were randomized into two groups – an early re-ablation group (ERA) with 57 patients, and a later re-ablation group (LRA) with 60 patients. Recurrences occurred an average of 6.7 days (2 to 22 days) from the initial ablation in the ERA group. They had gradually subsided within one month in 17 patients leaving 40 who underwent a repeat ablation approximately 28 days (24 to 42 days) after their first procedure. Pulmonary vein reconnection was observed in 36 (80%) of the 40 patients and the gaps were re-ablated and focal and linear ablation performed as necessary. At the end of the 6.5-month follow-up from the second procedure, 47 patients (82.5%) in the ERA group were free of arrhythmias, with 5 (10.6%) achieving this status with the aid of previously ineffective antiarrhythmics.

In the LRA group recurrences occurred an average of 8.2 days (1 to 29 days) from the initial ablation. They had gradually subsided within one month in 20 patients, leaving 40 who underwent a repeat ablation approximately 98 days (90 to 122 days) after their first procedure. Pulmonary vein reconnection was observed in 29 (72.5%) of the 40 patients and the gaps were re-ablated and focal and linear ablation performed as necessary. At the end of the 15.2-month follow-up from the second procedure, 51 patients (85%) in the LRA group were free of arrhythmias with 6 (11.8%) achieving this status with the aid of previously ineffective antiarrhythmics.

The Shanghai EPs conclude that there is no advantage in postponing a repeat ablation for patients whose early recurrences of atrial tachyarrhythmias do not subside within one month following their initial procedure. They suggest that doing the second procedure about a month following the first one would be optimum. They also point out that a reduction in the number of weekly AF episodes during the first month is a reliable indicator that episodes will have subsided by the end of the month.

Wang, X, Zhou, L, et al. Early recurrences after paroxysmal atrial fibrillation ablation: when is the proper timing for reablation? **PACE**, *Vol. 34, June 2011, pp. 709-16*

Editor's comment: Undergoing a follow-up ablation sooner rather than later, if post-procedure arrhythmias persist, would make sense, especially if the recurrences are frequent, long or severe. It is interesting to note that the complete success rate (no AF, no antiarrhythmics) was 74% for the ERA group and 75% for the LRA group. Corresponding numbers for partial success (no AF, but still on antiarrhythmics) were 8% and 10% respectively.

AFIB No More

by Suzi E.
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AFIB knocked on my door or, better said, hijacked my heart in February of 2006. It was in the morning at around 9AM. I was sitting on the floor surrounded by receipts from my art studio, trying to organize them for my accountant to prepare taxes. I had been working about an hour and a half, fueled only by strong coffee. I was 61 years old at the time, in good health, slim and active.

I began to feel hungry, and started to make breakfast, when I suddenly felt very dizzy. I could feel my heart racing, but attributed it to the coffee. I didn't have a blood pressure cuff, but I did have an exercise monitor. I put it on and my pulse read 190 bpm!

My normal BP is 100/70 and pulse 60. I checked it several times, but the readings were the same. A neighbor took me to the hospital, and I was admitted and diagnosed with AFIB and tachycardia. The attending cardiologist put me on a beta-blocker and Coumadin. "How long will I have to take this?" I asked, as I knew I did not feel comfortable with this protocol. "For the rest of your life", he answered.

A little background here, I've been a health "foodie" since before it became fashionable, and I take very little medication – antibiotics when needed, an occasional sleeping pill, but nothing like warfarin. I think my afib was mixed. Often when resting I experienced lots of ectopics after meals, especially heavy meals. I remember waking up at night once with an episode, driving in the car, but never really after exercise.

I made an appointment with the top electrophysiologist in my area, a Harvard medical school graduate. He had me continue the Coumadin, and try another beta-blocker, which he assured me was very mild. I felt horrible, like I had the flu. My resting pulse was in the 40's or 50's. I could barely get out of bed.

I began to Google desperately, and found the www.afibbers.org website. I'd never heard of afib, and wanted to educate myself. A RN friend recommended Dr. Jamnadas, an Interventional Cardiologist in Orlando. He took me off the Coumadin, had me take lots of fish oil and nattokinase, and controlled the arrhythmia with low doses of propranolol. This was tolerable, but I still had daily, sometimes disturbing, bouts of PACs and PVCs. My daily propranolol dose was anywhere between 20-60 mgs. At higher does, I felt very tired and lethargic.

I read Hans' books, frequented the afibbers.org bulletin board, e-mailed Jackie and other members, and tried everything to find natural ways to control my arrhythmia with taurine, l-arginine, magnesium. I cut out caffeine, most carbs and sweets. Nothing seemed to make any difference.

It's important now that I relate a bit about the circumstances of my life, as ultimately my physical health and AFIB

were completely intertwined with my emotional well being. At sixty, I found myself single, having recently ended an eight-year relationship with an alcoholic man. My lifelong relationship history had been with artistic men, with no money and substance abuse problems. This all stemmed, I came to understand, from my relationship with my wealthy, abusive, controlling, narcissistic father.

Ever since early childhood, my father had rarely been pleased with me, and the stronger his displeasure, the stronger my need to please. My mother was distant, meek, and emotionally battered herself. As is so often the case, she always sided with my father. I was alone to defend myself. On the outside, our family looked prominent and successful, but the interpersonal relationships were destructive, and I was definitely the scapegoat.

Although my father was forthcoming with financial gifts, the lifelong criticism and belittling made it hard for me to hear my own inner voice. His questioning of my every decision, made me doubt myself.

In 2007, my father then in his eighties got very sick. He developed aspiration pneumonia, and was in and out of the ICU. Ever the dutiful daughter, I frequently made the drive from Orlando to West Palm Beach, to help in any way I could. I remember one instance when I was pushing my Dad in a wheelchair around an assisted living faculty that he wanted to visit, as he barked orders. All the time, I was popping propranolol to keep my afib at bay. Always looking for that approval, minimizing my own needs. Interesting, although I was victimized, my fighting spirit made me believe that I was OK. It all felt normal – just the way things were.

In November of 2009, my father died. I was filled with a tremendous sense of relief, both for him and for myself. His last years had been miserable. He suffered horribly in the hospital on life support and feeding tubes. All the while, I was there to help him and my mother.

After he passed I sold my house in Orlando and moved to West Palm Beach, to be close to the ocean, and to my mother. I made an appointment with Dr. Sergio Pinski at the Cleveland Clinic in Weston, Florida. My arrhythmia had become intolerable, and I was considering an ablation. Dr. Pinski, upon reviewing my charts, did not seem alarmed at all. From all the tests, my heart was perfectly normal and healthy. I have always exercised, and have done yoga since the 1970's. There was no physiological reason for my erratic heartbeat.

As I adjusted to life in West Palm, I began to notice that my afib was absent, and the PACs and PVCs were becoming less and less. My father's death had lifted a huge burden form my heart. No more abusive phone calls, no more constant belittling, no more making me doubt the power of my own inner wisdom, no more guilt trips. I felt free and light!

Over the last almost two years there has been no afib, and I haven't taken a propranolol in months. I never realized that I was under stress. What I rationalized in my mind as "normal", my heart knew as danger. When the emotional abuse stopped, so did my afib. My father's death removed a huge stressor from my life. It was this stress, and the constant pressure that I felt, as I tried to please someone who I never could, that had caused the racing erratic heart.

I hope that my story gives hope to others.

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