

THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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With the advent of quick and relatively inexpensive tests, more research is focused on determining gene variations relating to atrial fibrillation. Researchers at Vanderbilt University have discovered a strong connection between variations in the ACE (angiotensin-converting enzyme) gene and the response to common antiarrhythmics like flecainide, propafenone, and sotalol. It would seem that some afibbers, possibly as many as 30%, would not experience any benefit from these drugs simply because of their genetic make-up. In a similar vein, researchers at the Utah School of Medicine report that the response to warfarin also may have a significant genetic component.

As many afibbers can attest to, tachycardia (rapid heart beat) and flutter are not uncommon after-effects of otherwise successful ablations. It is now clear that these tachycardias are also fairly common after Cox maze procedures. Fortunately, most of them are short-lived, but if they continue for two months or more they will need a follow-up ablation, which is usually successful.

Other news in this month's issue is that vitamin C protects against stroke, the progression to persistent/permanent afib is not inevitable, new evidence is presented concerning the dangers of digoxin, and a clinical trial supports the benefit of pre-procedure fish oil supplementation in avoiding surgery-induced afib.

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

Wishing you good health with lots of NSR,

Hans

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lower than this increase the risk of ischemic stroke (stroke caused by blockage of small arteries), while values above about 4.0 increase the risk of serious internal bleeding and hemorrhagic stroke (stroke caused by rupture of small arteries). It is estimated that the target range of 2.0 to 3.0 is only achieved in about 50% of all patients at any one time. Not surprisingly, warfarin is the second most common drug implicated in emergency room visits for adverse drug reactions.

Genetic testing for patients on warfarin

SALT LAKE CITY, UTAH. Patients on warfarin need to be monitored regularly to ensure that the INR (International Normalized Ratio) of their blood is within the therapeutic range of 2.0 to 3.0. Values

It is clear that any protocol that would increase the time patients spend within the therapeutic range would be most welcome. Preliminary studies have shown that certain gene variations significantly affect the rate at which warfarin is metabolized and thus the INR. The FDA recently approved a new genetic test designed to determine the presence or absence of three genes affecting warfarin

metabolism [CYP2C9 *2, CYP2C9 *3, and VKORC1(C1173T)].

Researchers at the University of Utah School of Medicine now report on the first trial of genotype-guided warfarin dosing. Two hundred patients starting on warfarin were randomized into a standard treatment arm and the genotype-guided arm. Patients in the standard arm were given 10 mg/day of warfarin for the first two days, 5 mg/day for the third day, and then an adjusted dosage based on their day 3 INR value. Patients in the genotype-guided arm were given an initial dose of from 2 to 16 mg/day for two days as determined by an algorithm taking into account age, weight, gender, and the presence or absence of the variant genotypes. Dosage was halved on day 3 and then adjusted according to INR. The adjustment was calculated as the ratio of the estimated individual weekly maintenance dose determined with the algorithm to the standard weekly dose. INR measurements were made on days 0, 3, 5, 8, 21, 60, and 90.

Somewhat surprisingly, the use of the genotype algorithm did not reduce the time patients had an INR outside the therapeutic range. In both cases, patients were outside the range about 30% of the time pretty evenly split between being too high and too low. It should be pointed out that the study participants were hospitalized, so likely received better care and follow-up than if they had been outpatients. The researchers did notice that

patients in the genotype arm required slightly fewer dose adjustments than did those in the standard arm. They also observed that patients who carried both the CYP2C9 and the VKORC1 variants had a greater risk of experiencing an INR greater than 4 than did those without these two gene variants. They recommend further, much larger (at least 2000 patients) trials to further evaluate their findings.

Anderson, JL, et al. Randomized trial of genotype-guided versus standard warfarin dosing in patients initiating oral anticoagulation. Circulation, Vol. 116, November 27, 2007, pp. 2563-70

Editor's comment: This study clearly shows that genotype-guided warfarin therapy does not reduce the time spent outside the recommended INR range of 2.0 to 3.0. It is possible that identifying carriers of both the gene variants may avoid some cases of overdosing, but this particular study did not have the statistical power to prove this. Says the lead investigator of the study, Dr. Jeffrey Anderson, "I think this approach has a lot of promise for the future, but it's maybe not ready for right now." Dr. Raymond Gibbons of the Mayo Clinic shares this view, "I definitely do not think doctors should rush out there and start giving genetic tests to all the patients they want to put on warfarin at the moment. Maybe one day this will happen, and yes, it does make sense, but we need evidence that it will have a real benefit, and that's not there yet."

<http://www.theheart.org/printArticle.do?primaryKey=826363>

Vitamin C protects against stroke

CAMBRIDGE, UNITED KINGDOM. Researchers at Cambridge University have confirmed that high blood levels of vitamin C (ascorbic acid) protect against stroke. Their study involved 20,649 men and women between the ages of 40 and 79 years when enrolled during the period 1993-1997. None of the participants had suffered a prior stroke. Blood samples were drawn and analyzed for ascorbic acid content at baseline and participants were then followed for an average of 10 years. During this time a total of 448 strokes occurred corresponding to an average annual stroke rate of 0.2%.

After adjusting for the possible effects of gender, age, smoking, BMI, blood pressure, cholesterol, physical activity, diabetes, heart attack, social class, alcohol consumption, and supplement use the

researchers conclude that study participants whose blood plasma levels of vitamin C were above 66 micromol/L had a 42% lower risk of stroke than did those whose levels were below 41 micromol/L. They also observed a 17% reduction in stroke for every 20-micromol/L increase in plasma vitamin C concentration. A 20-micromol/L increase in plasma vitamin C concentration can be achieved by adding one additional serving of fruit and vegetables daily.

It is also of interest to note that six times as many study participants in the high plasma vitamin C group were supplementing with vitamin C as compared to those in the low plasma vitamin C group (10.5% vs 1.9%).

Myint, PK, et al. Plasma vitamin C concentrations predict risk of incident stroke over 10 years in 20,649 participants of the European Prospective Investigation into Cancer.

American Journal of Clinical Nutrition, Vol. 87, January 1, 2008, pp. 64-69

Editor's comment: An average reduction in stroke risk of 42% is indeed impressive and compares favourably with the 25-30% relative risk reduction often quoted for aspirin, and the 50-55% reduction attributed to warfarin, especially since increasing

one's vitamin C intake is not associated with any adverse effects. The Cambridge researchers point out that vitamin C has a very short half-life in the blood (about 30 minutes), so spreading one's intake (whether through foods or supplements) throughout the day is essential.

Metabolism in atrial fibrillation

LONDON/CAMBRIDGE, UNITED KINGDOM. While much research has been done to analyze and describe the mechanism of the disorganized electrical activity underlying atrial fibrillation, the possibility of a dysfunctional metabolism playing a major role seems to have been overlooked. This may now change with some exciting new discoveries made by a group of researchers from the University of Cambridge and King's College, London. The researchers used two very powerful techniques (proteomics and metabolomics) to determine the impact of cardiac metabolism on the initiation and persistence of atrial fibrillation. Their very recent paper (February 2008) is highly technical and to understand their findings it is necessary to bone up on a few definitions.

Metabolism is the set of chemical reactions that occur in living organisms in order to maintain life. These reactions are catalyzed and regulated by enzymes and can be divided into two major categories: - *catabolism* which involves the breakdown of large molecules and produces energy, and *anabolism* which uses energy to produce component of cells such as proteins and nucleic acids.

Glycolysis is the initial process in the breakdown (catabolism) of larger carbohydrate molecules into smaller units. It results in the production of pyruvate for the citric acid cycle (Krebs cycle, TCA cycle) of energy production and ATP (adenosine 5'-triphosphate), the body's main energy transporter.

Ketone bodies (acetoacetate, acetone, and beta-hydroxybutyrate) are produced when fatty acids are broken down in the liver and kidney to produce energy for use in the heart and brain.

Proteomics is the study of the function and structure of proteins. It uses highly sophisticated methods such as gel electrophoresis and mass spectrometry to separate and analyze the proteins and their structure.

Metabolomics is the study and identification of small-molecule metabolites generated by specific cellular processes (such as atrial fibrillation).

The British researchers compared metabolic variables in three groups of patients.

- Group SR – Patients in normal sinus rhythm prior to undergoing valve (nonrheumatic) surgery
- Group AF – Patients in permanent afib prior to undergoing valve surgery.
- Group SR-AF – Patients who developed afib after coronary artery bypass surgery.

The researchers extracted cardiac tissue from all three groups during surgery and then looked for differences in protein and enzyme expression using proteomics and metabolomics. When comparing group SR with group AF they noted that heart tissue from group AF had higher levels of beta-hydroxybutyrate (a ketone body) and the ketogenic amino acids tyrosine and leucine. Group AF also had a significantly higher level of glycine and a higher fumarate/succinate ratio. Structural damage inflicted by prolonged AF was also evident as was depletion of the antioxidant protein peroxiredoxin 1 and a reduced level of ANP (atrial natriuretic peptide) precursor.

Looking at heart tissue from patients who developed afib after bypass surgery, the researchers observed that these patients had significantly reduced levels of glucose, beta-hydroxybutyrate, and acetate (a ketone body). They also noted that those who developed AF after surgery (bypass or valve) had a reduced glucose/acetate ratio and that their ratio of glycolytic end products (alanine, lactate) to lipid metabolism end products (acetate) correlated positively with time of onset of post-operative AF (the lower the ratio, the earlier the onset of AF).

There is evidence that AF is associated with a high-energy demand and that this may explain many of the permanent changes in the atria resulting from permanent AF. There is also evidence that ketone bodies may be a main source of this energy during permanent AF.

The researchers conclude that ketone bodies play an important role in atrial fibrillation and that a discordant regulation of energy metabolites precedes the onset of AF after surgery.

Mayr, M, et al. *Combined metabolomic and proteomic analysis of human atrial fibrillation. Journal of the American College of Cardiology, Vol. 51, No. 5, February 5, 2008, pp. 585-94*

Editor's comment: While these findings are most interesting and exciting, it is not at all clear how to interpret and take advantage of them. Most important, there is obviously no evidence that they apply to lone afibbers since all participants had

underlying heart disease. The finding that bypass surgery patients who go into afib after their surgery are very low in ketone bodies (fatty acid breakdown products) during surgery ties in with recent findings that giving these patients fish oil supplements prior to the operation markedly reduce the risk of afib development.

The observation that valve surgery patients in permanent afib had a higher level of ketone bodies (during surgery) than did those in normal sinus rhythm support the hypothesis that the heart's energy demand is substantially increased during permanent afib and that much of this demand is met by burning fatty acids rather than glucose. This intriguing and most welcome research raises many important questions, but most of all, is hopefully the beginning of a trend to look for the causes of atrial fibrillation.

Safety of digoxin questioned

OSLO, NORWAY. Digoxin (digitalis, Lanoxin) is widely used in the treatment of heart failure in order to increase the force of heart muscle contractions (positive inotropic effect) and reduce heart rate (ventricular rate). This results in an increase in exercise capacity, but digoxin treatment has no effect on overall survival in heart failure patients. This raises the question, "Are the beneficial inotropic benefits of the drug counterbalanced by serious adverse effects?"

A team of American, Norwegian and Swedish researchers now provides a preliminary answer to this question. Their study involved 7329 participants in the SPORTIF III and IV trials aimed at comparing the effectiveness of the anticoagulants warfarin (Coumadin) and ximelagatran in afib patients. About 53% of participants were on digoxin throughout the study.

The researchers found a higher mortality (6.5%) in the digoxin group than in the group not using

digoxin (4.1%). After adjusting for confounding variables, they conclude that digoxin users have a 53% (relative) higher mortality than do non-users. They suggest that in heart failure patients the adverse effects are counterbalanced by the positive inotropic effect, whereas in AF patients, who do not benefit from the inotropic effect, the adverse effects of digoxin dominate and lead to the 53% relative increase in mortality among users.

Gjesdal, K, et al. *Digitalis: a dangerous drug in atrial fibrillation? Heart, Vol. 94, 2008, pp. 191-96*

Editor's comment: In my 2001 book *Lone Atrial Fibrillation: Towards A Cure* I called digoxin "the medicine from hell" and warned that it should never be used by lone afibbers as it has been found to increase episode frequency and promote the conversion of paroxysmal afib to the permanent version. The above finding that digoxin also increases mortality among afibbers only strengthens my conviction that this is indeed a drug to be avoided.

Atrial flutter after ablation

ANN ARBOR, MICHIGAN. Left atrial flutter and supraventricular tachycardia are not uncommon complications of otherwise successful pulmonary vein isolations (PVIs). The incidence of these

tachycardias is highly dependent on the protocol used in the ablation procedure. Thus, about 3% of patients treated with the Haissaguerre method (segmental pulmonary vein isolation) can expect to

develop a left atrial tachycardia (LAT). In contrast, 20-30% of patients undergoing a circumferential anatomical pulmonary vein isolation (Pappone method) with widely encircling PV lines plus mitral and roof lines may develop LAT.

Electrophysiologists at the University of Michigan report on their investigation of 78 patients who underwent an ablation for LAT after having undergone a circumferential anatomical PVI using the 3-dimensional CARTO mapping system. The researchers mapped a total of 155 LATs and found that 88% were the re-entry type, while 12% were of focal origin. They also noted that 96% of the re-entrant LATs were associated with gaps in ablation lines created during the original PVI. Repeated catheter ablations were successful in eliminating the LATs in 85% of the 78 patients with the most common ablation targets being the mitral isthmus, the left atrial roof, and the septum separating the right and left atrium.

At the 13-month follow-up 77% of the 78 patients were free of afib and LATs without the use of

antiarrhythmics. The Michigan EPs conclude that it should be possible to reduce the incidence of LATs by ensuring complete isolation of the pulmonary veins, limiting the number of linear lesions, and ensuring the absence of gaps.

Chae, S, et al. Atrial tachycardia after circumferential pulmonary vein ablation of atrial fibrillation. Journal of the American College of Cardiology, Vol. 50, No. 18, October 30, 2007, pp. 1781-87

Daubert, JP. Iatrogenic left atrial tachycardias. Journal of the American College of Cardiology, Vol. 50, No. 18, October 30, 2007, pp. 1788-90

Editor's comment: The "revelation" that 20-30% of patients undergoing a circumferential PVI may develop a post-procedure left atrial tachycardia (flutter or SVT) is indeed discouraging and again emphasizes the need of carefully considering one's options and choosing a highly skilled EP for the procedure. NOTE: Both Dr. Natale and Profs. Haissaguerre and Jais use the segmental procedure, which is associated with the lowest incidence of LATs.

Genetic connection with response to antiarrhythmic drugs

NASHVILLE, TENNESSEE. There is increasing evidence that the renin-angiotensin-aldosterone system (RAAS) is involved in atrial fibrillation. (NOTE: This has been discussed in the Conference Room – Sessions 2 and 26). There is also recent evidence that the angiotensin-converting enzyme (ACE) has at least three common genetic variations (DD, II and ID) that can affect its blood level and activity. Thus, the DD variation increases ACE activity by 50%, while the ID variation increases it by 25%. This increase in activity has been associated with an elevated risk of experiencing a heart attack or suffering cardiac arrest.

Researchers at Vanderbilt University recently set out to determine if variations in the ACE gene could account for some of the differences experienced by afibbers in response to treatment with common antiarrhythmic drugs. Their study included 213 AF patients (34% were lone afibbers and 41% had hypertension). All patients measured their symptomatic afib burden (duration x frequency x score for severity) before and after being treated with an antiarrhythmic. If their burden decreased by 75% or more, then they were classified as responders. If their burden did not change or reduced by less than 75%, then they were classified

as non-responders, and another drug was tried. The frequency of the three polymorphisms of the ACE gene was 25% for the DD mutation, 30% for the II variation, and 45% for the ID variation. Thus, at least 60% of the study participants had one or two D alleles (gene versions) corresponding to higher levels and increased activity of the ACE when compared to the activity of II ACE.

The response to common class I and III antiarrhythmics (flecainide, propafenone, sotalol) in lone afibbers was 95% in patients with the II allele, 59% in those with the ID allele, and 53% in those with the DD genotype (amiodarone efficacy was not affected by genotype). Put it another way, 31% of study participants did not derive benefit because of an unfavourable variation in their ACE gene. So it is clear that in a fair number of cases a lone afibber will not be able to find an antiarrhythmic that works for them simply because of their genetic make-up. The researchers speculate that patients with one or two D alleles might benefit from adding an ACE inhibitor to their antiarrhythmic in order to compensate for the increased activity of their ACE gene.

Darbar, D, et al. ACE I/D polymorphism modulates symptomatic response to antiarrhythmic drug therapy in

patients with lone atrial fibrillation. **Heart Rhythm**, Vol. 4, June 2007, pp: 743-49

Editor's comment: It is indeed welcome to see the continuing interest in linking the RAAS to lone atrial fibrillation. I am personally convinced that there is a strong link for many afibbers (including myself). However, until it is sorted out afibbers who have experienced no luck with propafenone (Rythmol) or flecainide (Tambocor) may consider asking their

prescribing physician if they could run a trial with an ACE inhibitor in addition to their antiarrhythmic – lisinopril (Zestril, Prinivil) at 10 mg/day may be a good start. Of course, an even better approach would be to be tested for the ACE gene variations before adding an inhibitor, but for most afibbers this would probably be difficult to arrange.

<http://www.afibbers.org/conference/session2.pdf>
<http://www.afibbers.org/conference/session26.pdf>

Case studies with the experts

BOSTON, MASSACHUSETTS. A special satellite symposium was held during the 2007 Heart Rhythm Society meeting. During the symposium 5 experts (Eric Prystowsky MD, Pierre Jais MD, Peter Kowey MD, Stanley Nattel MD, and Jeremy Ruskin MD) discussed various aspects of atrial fibrillation (NOTE: Their comments are not specifically aimed at lone AF). Following are some highlights from the discussion.

- **Re: Aspirin vs. warfarin for stroke prevention**

Comment: *“Of course, you have the discussion with the patients and the patients do generally make the right decision, but I think there is a tendency among many physicians to be somewhat aggressive in many cases and decide to prescribe warfarin just to be on the safe side. That’s not fair either.”*

- **Re: Damage to atrium due to long-term AF**

Summary: The atrial rate is increased about 10-fold in persistent afib. This causes a calcium overload which the body compensates for by inactivating calcium channels. This results in a shortening of the refractory period (AERP) making it more likely that afib will persist. Animal experiments have

also shown that persistent/permanent afib increases fibrosis and collagen expression in the heart.

- **Re: Choice of antiarrhythmic drugs**

Comments: *“In people with minimal or no structural heart disease, drugs with minimal organ toxicity are preferred, such as flecainide, propafenone, and sotalol; amiodarone and dofetilide are second-line choices.”*

“We talked about cardiac risks, but we can’t forget extracardiac risks, and beta blockers, propafenone, sotalol, and dofetilide are all pretty much equivalent and fairly low. Amiodarone is by far the worst. So in the AF management guidelines, there’s a pretty simple general rule. The rule is that amiodarone is kept in reserve because of its significant risk of extracardiac toxicity, particularly with longer term therapy, so it’s not a first-line drug unless the risks of the alternatives are too high.”

Prystowsky, EN, et al. Case studies with the experts: Management decisions in atrial fibrillation. **Journal of Cardiovascular Electrophysiology**, Vol. 19, Suppl. 1, 2008, pp. S1-S12

Tachycardia after Cox maze

BIRMINGHAM, ALABAMA. The development of right or left atrial flutter/tachycardia after an otherwise successful PVI (pulmonary vein isolation) procedure is not uncommon. Most of these arrhythmias disappear on their own, but some

persist and require a follow-up ablation. Surgeons at the University of Alabama now report that post-procedural tachycardias are also fairly common after Cox III maze procedures. Their study included

143 patients who had undergone the procedure during the period 1996 to 2005.

All patients were checked for arrhythmias at 2 and 8 weeks postoperatively; those experiencing palpitations at the 8-week check-up were monitored intensively with Holter monitors or event recorders and, if the tachyarrhythmia persisted, they underwent an electrophysiologic study and catheter ablation. A total of 22 patients (15%) were found to have developed a tachycardia that persisted for more than 8 weeks. Another 10 (7%) developed atrial fibrillation that was treated with medication. The electrophysiologic study of the 22 patients showed the presence of a total of 25 arrhythmias – 15 in the right atrium and 10 in the left atrium. The right atrial arrhythmias were evenly divided between the common counterclockwise right atrial flutter and macroreentrant right atrial arrhythmias that did not involve the cavotricuspid isthmus. Three of the left atrial tachycardias involved reentry around the mitral valve annulus, and the remaining 7 were

mapped to the roof of the left atrium. It is of interest that the lesions around the mitral valve annulus were created with cryoablation. All post-operative flutter/tachycardias were successfully treated with standard catheter ablation and the patients have now been arrhythmia-free for over 3 years.

The Alabama surgeons conclude that the occurrence of post-operative flutter/tachycardia after a maze procedure is related to gaps in lesions lines either in the line itself or at the end of a line where it abuts an anatomic boundary.

McElderry, HT, et al. Proarrhythmic aspects of atrial fibrillation surgery. Circulation, Vol. 117, January 15, 2008, pp. 155-62

Editor's comment: It would appear that tachycardia/flutter may occur fairly often (10-30%) following both Cox maze procedures and PVLs. Fortunately, most of these arrhythmias disappear on their own, but some may require follow-up ablations which are usually successful.

Progression of paroxysmal AF

FLORENCE, ITALY. Paroxysmal (intermittent, self-terminating) atrial fibrillation may over time progress to persistent or permanent afib (episodes lasting 7 days or longer). It is not clear why some paroxysmal afibbers progress to the persistent variety, while other remain paroxysmal for decades. A group of American and Italian researchers now provide at least a partial answer to this question.

Their study involved 330 patients with a history of paroxysmal AF (mean age of 70 years, 61% male) who had had a pacemaker implanted to deal with bradycardia (slow heart beat). Most study participants had underlying heart disease, but 21% were lone afibbers. The pacemaker (Medtronic AT501) automatically recorded the daily burden (duration) of afib and tachycardia for an average of 400 days. After a mean interval of 147 days, 24% of the patients progressed to persistent afib. The researchers made the following interesting observations.

- The prevalence of lone atrial fibrillation (LAF) did not differ between the group that remained in paroxysmal afib and the one that progressed to persistent afib.

- Patients with congestive heart failure were significantly more likely to progress to persistent AF.
- Patients destined to progress to persistent AF experienced a higher daily afib burden and a higher probability of experiencing afib on any given day than those in the paroxysmal group.
- The mean daily afib burden in the group destined for progression to persistent AF increased by about 14 seconds/day, while it stayed relatively constant in the group that remained paroxysmal.
- Lone afibbers experienced significantly more PACs (premature atrial beats, ectopics) than did patients with CVD. However, the incidence of these ectopics decreased over time.
- The conversion to persistent afib occurred suddenly and was often preceded by a period of normal sinus rhythm.

- It is possible that treatment with ACE inhibitors or angiotensin receptor blockers (ARBs) may slow down the remodeling that underlies progression to persistent AF.

The researchers conclude that, "Our results suggest that functional electrical remodeling may not impact all patients or inevitably lead to increasing AT/AF burden and persistent AF. In fact, a large

proportion of patients may not increase their AT/AF burden, particularly in the absence of CVD."

Saksena, S, et al. Progression of paroxysmal atrial fibrillation to persistent atrial fibrillation in patients with bradyarrhythmias. American Heart Journal, Vol. 154, November 2007, pp. 884-92

Editor's comment: This study indicates that a steady progression of afib burden (longer and more frequent episodes) may lead to persistent afib. Thus, if such a trend is noted, it may be worth trying an ACE inhibitor or an ARB.

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Improved cardioversion results

Persistent afib can be converted to normal sinus rhythm (NSR) by electrical cardioversion. Unfortunately, the bliss of NSR is often short-lived. Italian researchers now report that flecainide and a combination of amiodarone and flecainide are safe and effective in maintaining NSR after cardioversion in patients with persistent afib and hypertension. Their trial showed that flecainide on its own maintained NSR in 88% of patients, while the combination maintained it in 80% at the 6-month check-up. In comparison, only 33% of patients on sotalol or amiodarone alone were still in NSR at the 6-month follow-up. The researchers also found that adding an angiotensin II receptor blocker (losartan, valsartan, irbesartan, candesartan) to the medication regimen was highly effective in maintaining NSR.

Abstract 11.3, p. S23 and Abstract 11.5, p. S24

Vagal denervation may cure afib

The atrial fibrillation epidemic is clearly not confined to North America and Western Europe. It would seem that Russian EPs/cardiologists are also very active in the field of AF research. A team from the State Research Institute of Circulation Pathology in Novosibirsk reports that vagal denervation (destruction of vagal nerve endings) in the left atrium may be as effective as pulmonary vein isolation in curing AF. Vagal nerve endings are highly concentrated in the four ganglionated plexi (fat pads) found in the left atrium. (NOTE: There are three ganglionated plexi in the right atrium). The clinical trial involved 58 patients with drug-

refractory afib of which 36% had the permanent variety. All patients underwent ablation of the four ganglionated plexi in the left atrium with no attempt to isolate the pulmonary veins. An average of 7 months after the procedure, 86% of the patients were free of afib without medications. The researchers observed a significant increase in resting heart rate after the procedure and also noted that heart rate variability parameters had changed with an increase in the sympathetic/parasympathetic ratio being quite evident.

Abstract 16.1, p. S36

Improvements in cryoablation

Cryoablation uses a nitrogen-cooled, rather than an electrically-heated, catheter to create ablation lesions in or around the pulmonary veins. The advantage of cryoablation is that the danger of pulmonary vein stenosis and atrioesophageal fistula is eliminated. A possible disadvantage is that cryo lesions may be less durable than those created via the application of radiofrequency energy. German researchers treated 94 afibbers (including 41 one afibbers) with cryoablation using a newly developed 23 or 28 mm balloon catheter. NOTE: The advantage of a balloon catheter is that it produces a continuous ring-shaped lesion with just one or two applications. After a mean follow-up of 6 months (including 8 touch-ups), 77% of patients were free of afib. However, 4 patients (4%) developed phrenic nerve palsy, which disappeared over a 6-month period.

Abstract 16.7, p. S39

Early recurrence of AF not a good sign

It is generally believed that early recurrence of afib following a pulmonary vein isolation (PVI) procedure is not necessarily indicative of long-term failure. Arrhythmia specialists in Rio de Janeiro, Brazil, however, question this belief. Their clinical trial involved 121 afibbers (72% lone) who underwent PV antrum isolation guided by ICE (Natale method). Thirty percent of patients experienced one or more afib episodes during the first 6 weeks following their PVI. The late recurrence (after 21 months of follow-up) in this group was 51% as compared to only 7% in the groups of 91 patients who had not experienced episodes in the 6 weeks following their PVI.

Abstract 17.4, p. S41

PUFAs reduce surgery-induced AF

Atrial fibrillation is a common complication of coronary bypass-graft surgery (CABG). Polyunsaturated fatty acids (PUFAs), notably fish oils, have significant anti-inflammatory, anti-arrhythmic, and anti-thrombotic properties. Slovakian researchers recently completed a clinical trial to see if pre-treatment with PUFAs would reduce the incidence of post-CABG atrial fibrillation. Their study involved 44 patients undergoing CABG. Half of them received 2 grams/day of PUFA for 5 days prior to surgery until discharge from hospital. In this group 18% developed post-procedure afib as compared to 50% in the group not receiving PUFA treatment. There was also a significant difference in the average duration of hospitalization between the two groups – 9.3 days for the PUFA group vs 11.5 days for the non-PUFA group.

Abstract 24.5, p. S59

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Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@afibbers.org World Wide Web: <http://www.afibbers.org>

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