

# THE AFIB REPORT

*Your Premier Information Resource for Lone Atrial Fibrillation!*

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*Atrial fibrillation has now reached the status of “epidemic”. Mayo Clinic researchers estimate that about 6 million Americans are afflicted by the condition. Clearly, the only rational and sane way to deal with an epidemic is to determine the cause(s) and deal with it. Unfortunately, I have seen so evidence that any major, organized effort is underway to do so. Considerable sums of money are being fed into research projects aimed at developing new drugs and catheterization/surgical procedures for managing or curing the condition, but are these efforts enough? At best, antiarrhythmics are effective in 30-50% of cases and, while dietary changes and supplementation have helped some afibbers, it is unrealistic to expect these measures to have much impact simply due to the difficulty in communicating these approaches to the general afib population. This leaves ablation and surgery as the main and best hopes for a cure.*

*In recent years about 25,000 afib ablation procedures have been performed annually in the United States. Considering that many were repeat procedures, and the overall success rate (no afib, no antiarrhythmics) is no better than 50% leads to the sobering conclusion that only about 10,000 patients are cured every year in the US. So, unless techniques improve to an unprecedented degree, it will take about 600 years to deal with just today’s afib patients – clearly an untenable situation!*

*The problems with current catheter ablation techniques are that they require highly skilled electrophysiologists if a reasonable rate of success is to be achieved and they take far too long to perform. What is needed is a procedure that can routinely be performed by any EP in less than an hour. Could a robot help out? At least two companies, Stereotaxis and Hansen Medical, are betting that they could. The Stereotaxis Niobe system is a magnetically-guided, remotely-controlled system for performing radiofrequency (RF) ablation. It is usually combined with the CartoMerge system and a CT scan to provide accurate mapping and precise catheter location. The main advantages of the system are the substantially improved mapping accuracy, greater flexibility of the catheter enabling its tip to reach areas in the left atrium which may be difficult to reach with a manually-guided catheter, and the fact that the catheter movement can be controlled remotely, thus substantially reducing radiation exposure to the operator. It is expected that the use of the Stereotaxis system will significantly improve the outcome of RF ablations, even if carried out by relatively inexperienced electrophysiologists.*

*In this issue we report on two recent trials of the system – one involving a case of atrial tachycardia and the other involving 26 patients with right atrial flutter. The immediate (acute) success rates for the procedures were impressive, but data concerning long-term success of the Stereotaxis procedure are still awaited. Also in this issue we report on the long-term success of pulmonary vein isolation, the role of fibrosis in atrial fibrillation, exercise capacity after a PVI, gamma-tocopherol for stroke prevention, and more.*

*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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## Long-term success of circumferential PVI

SYDNEY, AUSTRALIA. Circumferential anatomical pulmonary vein isolation (CAPVI or Pappone method) is an increasingly popular approach to curing AF via radiofrequency ablation. In this procedure anatomical mapping (CARTO) is used to establish the exact location of the pulmonary veins. Two rings of lesions are then created in the left atrium – one completely encircling the left pulmonary veins and another completely encircling the right pulmonary veins; the two rings are usually joined by a linear lesion.

Researchers at the University of Sydney now report on the long-term success of the procedure in persistent and permanent afibbers. Their study involved 45 (80%) male afibbers and 11 female with either persistent (69.6%) or permanent (30.4%) afib who had failed an average of 2 antiarrhythmic drugs. The mean age of the patients was 56 years and they had suffered from afib from 1 to 12 years (average of 6.4 years). Nine patients (16.1%) had structural heart disease, 3.6% had coronary artery disease, 66.1% had hypertension, and 10% had impaired left ventricular systolic function.

All patients underwent a circumferential PVI guided by the CARTO electroanatomical mapping system with a merged, three-dimensional CT image of the heart. Lesions were positioned about one centimetre from the edge (ostia) of the pulmonary veins where they join the left atrium. The endpoint of the ablation was electrical isolation (from the left

atrium) of all the pulmonary veins as measured with a Lasso mapping catheter. A linear ablation (roof line) was added in 57% of patients and 25% also underwent a right atrial flutter ablation. Antiarrhythmics were continued for the first month after the procedure and then discontinued if there were no afib recurrences. Repeat procedures were common with 28.6% undergoing two procedures, 8.9% undergoing 3 procedures, and 1.8% undergoing 4 procedures. Four major complications, one each – stroke, TIA, tamponade, and atrio-esophageal fistula – were observed during the 86 procedures.

After a follow-up of 13 to 30 months (average of 21.6 months), 53.6% of the ablated patients were in normal sinus rhythm (NSR) without the use of antiarrhythmics, 32.1% were in NSR with the aid of antiarrhythmics, and the remaining 14.3% still experienced afib episodes; thus, according to our usual way of grading success, 53.6% of the procedures (including repeats) were complete successes, 32.1% were partial successes, and 14.3% were failures.

Early recurrence (symptomatic episodes within the first 90 days following the procedure) was quite common after the initial procedure (46.4%) as was late recurrence (symptomatic episodes more than 90 days post-procedure), which was experienced by 69.6%. Ten percent developed flutter after the initial PVI and required an extra procedure to correct this. After the final procedure 23.3% had an early recurrence, and 46.4% had a late recurrence. Most late recurrences occurred within 12 months of the procedure. The researchers observed that female afibbers and those with afib of long standing were more likely to experience recurrences. They also noted that experiencing late recurrence was not precluded by the absence of early recurrences.

*Seow, SC, et al. Efficacy and late recurrences with wide electrical pulmonary vein isolation for persistent and permanent atrial fibrillation. Europace, Vol. 9, 2007, pp. 1129-33*

**Editor's comment:** A final complete success rate (after repeat ablations) at 53.6% is not impressive, but probably about average for other than top-ranked institutions/EPs.

## Successful application of Stereotaxis system

HOUSTON, TEXAS. The *Stereotaxis Niobe* system is a magnetically-guided, remotely-controlled system for performing radiofrequency (RF) ablation. It is usually combined with the CartoMerge system and a CT scan to provide accurate mapping and precise catheter location. The main advantages of the system are the substantially improved mapping accuracy, greater flexibility of the catheter enabling its tip to reach areas in the left atrium which may be difficult to reach with a manually-guided catheter, and the fact that the catheter movement can be controlled remotely, thus substantially reducing radiation exposure to the operator. It is expected that the use of the *Stereotaxis* system will significantly improve the outcome of RF ablations, even if carried out by relatively inexperienced electrophysiologists.

EPs at the Ohio State University Medical Center and the University of Texas now report on the case of a 72-year-old man experiencing daily episodes of atrial tachycardia causing palpitations and shortness of breath. The patients underwent a RF ablation using the *Stereotaxis* system with a 4-mm tip *Navistar-RMT* catheter. The operators located the source of the tachycardia and isolated it with 5 lesions (burns). The total procedure time was close

to 5 hours (275 minutes) with a fluoroscopy time of 29 minutes. After the ablation it was no longer possible to induce the tachycardia. The authors of the report conclude that, "*From our experience in general, and this case in particular (where the entire mapping and ablation procedure was performed safely, effectively, and efficiently with remote navigation), we feel that Stereotaxis Niobe MNS potentially has wide applicability in the area of interventional ablation therapy of complex cardiac arrhythmias.*"

*Mehta, R, et al. Successful ablation of focal left atrial tachycardia using Stereotaxis Niobe remote magnetic navigation system. Europace, Vol. 10, 2008, pp. 280-83*

**Editor's comment:** Although one large study undertaken at the Cleveland Clinic found significant shortcomings with the *Stereotaxis* system when used in pulmonary vein isolation, it is expected that these shortcomings (inadequate lesion depth and charring at catheter tip) have been overcome through the development of an irrigated catheter. Other studies have confirmed the advantages of the system in achieving immediate success in eliminating arrhythmias, but a definitive study of the long-term success rate of the system for PVI is still awaited.

## Flutter ablation with Stereotaxis system

LEIPZIG, GERMANY. Radiofrequency (RF) catheter ablation of common right atrial flutter (cavotricuspid isthmus-dependent – CTI) is a comparatively simple procedure with a success rate of about 95%. Because the location of the electrical circuit involved in the flutter is so well-established, this procedure lends itself particularly well to the use of electroanatomical (CARTO) mapping. German researchers now report on their evaluation of a new system combining the CART-RMT mapping system with the Stereotaxis NIOBE II remote magnetic navigation system. The Stereotaxis system makes use of two stationary magnets (one of each side of the patient) that controls the movement of a magnetically-tipped RF ablation catheter. The system is operated remotely so the operator's exposure to x-ray radiation from fluoroscopy is minimized. An earlier version of the NIOBE II system used a 4-mm catheter, but the German researchers used a new, flexible-tip, 8-mm (non-irrigated) catheter.

The clinical trial involved 26 patients (23 men, mean age of 65 years). At the time of the ablation, 20 were in flutter (19 counter-clockwise and 1 clockwise), and the remaining 6 were in sinus rhythm. In the case of one patient, a conventional ablation had to be performed because of technical difficulties with the NIOBE system. Among the remaining 25 patients, 24 were successfully ablated (acute success rate of 95%). One patient had to be ablated with a conventional catheter before complete isthmus block could be achieved. The procedure, RF application, and fluoroscopy times were 80 minutes, 31 minutes, and 11 minutes respectively in the first group of 14 patients. In the remaining patients, the corresponding times were 45 minutes, 20 minutes, and 7.2 minutes respectively indicating a steep learning curve – in other words, the new technique is relatively easy to learn.

Compared to the conventional RF flutter ablation procedure, the fluoroscopy time was reduced by

43%, but overall procedure time did not change. There were no major complications in the group of 26 patients treated with the new system; however, significant charring was observed in 19% of patients. The researchers conclude that ablation of right atrial flutter with the NIOBE II/CARTOMERGE system is safe, feasible, and effective. However, they do make the following qualifying statement, "This study was conducted to assess the acute results of RF catheter ablation using remote MNS and an 8-mm tip magnetic catheter. Therefore, no comment on the long-term outcome of this system for the ablation of AFL can be made."

Arya, A, et al. Initial clinical experience with a remote magnetic catheter navigation system for ablation of cavotricuspid isthmus-dependent right atrial flutter. *PACE*, Vol. 31, May 2008, pp. 597603

**Editor's comment:** The combined Stereotaxis/CartoMerge system has now undergone at least 9 trials that I am aware of. All, but one, have shown good safety and impressive results as

far as **acute** success is concerned. However, somewhat curiously, I am not aware of any trials that have reported on the long-term success of the procedure. Dr. Carlo Pappone and colleagues in Milan, Italy performed the first trial of the system in atrial fibrillation patients more than 2 years ago. The acute success rate, as measured by the lack of electrical conduction between the pulmonary veins and the left atrium shortly after placing the last ablation lesion, was an impressive 95%. However, as far as I know, long-term follow-up has not yet been reported, although there has been ample time to do so. Several studies have shown that **acute** success does by no means guarantee **long-term** success. As a matter of fact, long-term success (6 months or longer) may be as low as 50% even with a 95% acute success rate. Even though the Stereotaxis/CartoMerge system certainly looks like a winner, long-term data are still required to prove its ultimate efficacy.

## Long-term success of pulmonary vein isolation

ATHENS, GREECE. Pulmonary vein isolation (PVI) is now a well-established procedure for "curing" atrial fibrillation. Acute success rates (elimination of electrical potentials between pulmonary veins and the left atrium), measured shortly after lesion completion, are indeed impressive and often quoted as between 90 and 100%. Unfortunately, this does not mean that 90-100% of afibbers undergoing a PVI are free of afib for the remainder of their life, or even for the first 6 months after the procedure. A team of American and Greek researchers now provide the first evidence that long-term (over 3 years) success rates are substantially less than generally believed.

Their study involved 39 patients (average age of 52 years, 87% male) with symptomatic paroxysmal atrial fibrillation (about 30% with LAF and 50% with hypertension). All patients underwent a first segmental PVI (antral in 4 cases) and were then followed for an average 3.5 years (minimum of 3 years). Total pulmonary vein isolation was verified in all cases before catheter withdrawal. During the follow-up, the team made the following observations:

- Ninety-two percent of all patients experienced at least one AF recurrence within 3 to 42 months of the initial procedure (first 2 months were

considered a blanking period); 22% of these episodes were within the third month, 22% between months 3 and 12, and the remaining 56% occurred more than 12 months after the first procedure. This equates to a complete long-term success rate of 8% after just one ablation.

- Twenty-five of the 36 patients with recurrence (69%) underwent a second ablation. Among these, 10 patients (40%) experienced no relapse, while the remaining 15 (60%) were either classified as failures (60%), or went on to undergo a third ablation which was successful in 67% of cases. (NOTE: 80% of patients undergoing the third ablation had the circumferential procedure).
- Overall, the long-term (longer than 3 years) success rates were 21.4% for patients undergoing just one procedure, 52.6% for those undergoing two, and 66.7% for those who underwent 3 procedures. However, symptomatic improvement was reported in 67% of all patients.

The team concludes that, 3.5 years (on average, but minimum 3 years) after the initial procedure, 46% of study participants were free of afib, while 67% experienced symptomatic improvement. To accomplish this, almost half of the patients had a second procedure, and 15% underwent a third.

*Katritsis, D, et al. Long-term follow-up after radiofrequency catheter ablation for atrial fibrillation. Europace, Vol. 10, 2008, pp. 419-24*

**Editor's comment:** The long-term success rates found in this study are indeed sobering. It should be kept in mind though that the ablations were not performed at top-ranked institutions where success rates would be expected to be significantly higher. Nevertheless, the study clearly shows that follow-up ablations may be the norm rather than the exception, and also makes it abundantly clear that acute success is in no way related to long-term success.

## Role of fibrosis in atrial fibrillation

MONTREAL, CANADA. According to the late Professor Philippe Coumel, three conditions must be met in order for atrial fibrillation to occur:

1. The myocardium (heart tissue) must be capable of being triggered into and sustaining an episode. In other words, it must provide an electrophysiological substrate that is suitable for AF initiation and maintenance.
2. The autonomic nervous system must be out of balance.
3. A trigger or precipitating event capable of initiating an episode must be present.

Researchers at the Montreal Heart Institute believe that cardiac fibrosis (formation of scar tissue in response to injury) is an important feature in the development of an "afib friendly" substrate. Tissue fibrosis results from an accumulation of fibrillar collagen deposits which themselves are formed in a repair process aimed at replacing degenerating myocardial tissue. Fibrosis is associated with aging, dilated cardiomyopathy, mitral valve disease, and possibly myocardial ischemia (angina).

However, fibrosis and increased collagen deposition have also been observed in lone afibbers. Fibrosis interferes with the normal progression of the sine wave from the sinoatrial node to the atrioventricular node by impairing the transfer of the impulse from myocyte (heart muscle cell) to myocyte. The researchers point out that the renin-angiotensin-aldosterone system (RAAS) is involved in the formation of myocardial fibrosis and that patients with primary hyperaldosteronism (Conn's syndrome) have a significantly increased incidence of atrial fibrillation. They also point out that locally produced angiotensin II is associated with the formation of collagen deposits and fibrosis.

Mechanical stretch of cardiac muscle fibers induces collagen synthesis and increased angiotensin II

production, thus creating structural remodeling that further promotes afib (AF begets AF). The researchers reason that, if the production of collagen deposits and fibrosis could be slowed or even reversed, then it may be possible to eliminate or at least control AF. They suggest that ACE inhibitors (lisinopril, enalapril, ramipril), angiotensin II type 1 receptor blockers (valsartan, irbesartan, losartan), and aldosterone antagonists (spironolactone, eplerenone, canrenone) may be useful in preventing fibrosis and thus denying the atria the electrophysiological substrate necessary for initiating and sustaining an AF episode.

*Burstein, B and Nattel, S. Atrial fibrosis: mechanisms and clinical relevance in atrial fibrillation. Journal of the American College of Cardiology, Vol. 51, No. 8, February 26, 2008, pp. 802-09*

**Editor's comment:** Although the observation that angiotensin II is involved in cardiac fibrosis is not new, the finding that patients with primary hyperaldosteronism have a substantially increased incidence of atrial fibrillation is certainly of considerable interest. I was eventually (after 14 years of afib) diagnosed with primary hyperaldosteronism (see <http://www.afibbers.org/conference/session26.pdf> for details), but my attempts to reverse the resulting fibrosis with spironolactone were not successful. Now, after reading the article by Burstein and Nattel, I cannot help wondering if earlier intervention with an ACE inhibitor, angiotensin II receptor blocker, or aldosterone antagonist might have saved me a lot of trouble. Certainly, I would strongly recommend that all new-onset afibbers include an aldosterone:renin ratio test, or even just a renin measurement in their initial evaluation. An abnormally high ratio, or an abnormally low renin level should alert the patient and their physician to the possible presence of primary hyperaldosteronism. If primary hyperaldosteronism is indeed diagnosed, then treatment with an ACE inhibitor, angiotensin II receptor blocker, or

aldosterone antagonist may well be worth trying before embarking on stronger measures, especially for newly diagnosed afibbers. NOTE: Primary hyperaldosteronism results in potassium wasting, so

supplementation with potassium may also be necessary. However, combining ACE inhibitors, etc. with potassium should only be undertaken in close cooperation with a physician.

## Exercise capacity after PVI

MILAN, ITALY. According to the Italian National Eligibility Guidelines for Continuing Sport Participation, patients with symptomatic atrial fibrillation and those on anticoagulation are prohibited from participating in competitive sports. Thus, it is of considerable interest to establish whether competitive athletes with afib can meet eligibility requirements after a successful pulmonary vein ablation (PVI). Researchers at the University of Milan now report on a clinical trial to determine this.

The trial involved 20 male athletes (average age of 44 years) who, after participating in competitive sports (cycling, long-distance running, soccer, and skiing) for an average of 25 years, had been disqualified because of symptomatic lone AF. Fourteen (70%) of the athletes experienced paroxysmal LAF, while the remaining 6 had the persistent variety. The study participants had suffered from afib for an average of 3 years and had failed 3 or 4 antiarrhythmic drugs (quinidine, flecainide, propafenone, and sotalol). They often experienced episodes during training. The impact of afib on the physical performance of the athletes was assessed by comparing pre-ablation maximal exercise performance (MEP) with post-ablation MEP, as well as with the average MEP measured in a group of matched athletes without AF.

All study participants underwent a segmental PVI accompanied by a flutter ablation, if indicated. At least 3 months after the first procedure, all participants underwent a planned second electrophysiology study and re-isolation of veins that had regained conductivity. The researchers noted that 81% of 77 veins isolated during the first procedure had regained some conductivity. Five patients (25%) needed a third procedure to achieve complete isolation. During a 3-year follow-up, 90% of the group were free of afib without the use of antiarrhythmics, and the remaining 2 patients were still experiencing infrequent, short episodes. All study participants were able to resume full training and met eligibility requirements 6 months after their final procedure.

The athletes underwent stress testing pre- and post-ablation. Prior to the first ablation the average MEP was 183 W with athletes experiencing afib during the stress test having a lower MEP (176 W) than those remaining in normal sinus rhythm (207 W). After the final ablation the average MEP in the group was 218 W, still somewhat lower than the average 231 W recorded among matched athletes who had never experienced AF. It is of interest to note that 65% of study participants went into afib during training indicating adrenergic dominance, while at the same time 78% experienced episodes at night indicating vagal dominance.

In an accompanying editorial, Dr. Rachel Lampert of the Yale University School of Medicine gives an elegant explanation for this seeming paradox. Says Dr. Lampert,

*“Data have also shown that sympathetic stimulation decreases atrial effective refractory period. Most relevant to the situation of the trained athlete are studies demonstrating that sympathetic activation acts synergistically with vagal stimulation to shorten the atrial refractory period further than either branch of the autonomic nervous system acting alone.”*

*“These findings imply that while both adrenergic and vagal activity can induce AF, the interaction between high levels of sympathetic and parasympathetic activity is particularly arrhythmogenic, a situation analogous to intense exercise in the trained athlete.”*

*Furlanello, F, et al. Radiofrequency catheter ablation of atrial fibrillation in athletes referred for disabling symptoms preventing usual training schedule and sport competition. Journal of Cardiovascular Electrophysiology, published online, February 8, 2008*  
*Lampert, R. Atrial fibrillation in athletes: toward more effective therapy and better understanding. Journal of*

**Editor's comment:** It is clearly of great comfort to competitive athletes that it is possible to restore their ability to compete through extensive pulmonary vein isolation. Whether they will achieve their full pre-afib capacity is open to question since the average MEP after ablation was still only 218 W as compared to the 231 W measured in a group of matched non-afib athletes. The observation that intense exercise increases activation of both the

sympathetic (adrenergic) and parasympathetic (vagal) nervous system resulting in a shortened atrial refractory period is of particular interest in explaining why competing athletes are more prone to developing lone afib than are less intense exercisers. Finally, the finding that 81% of ablated veins had regained some conductivity after the initial ablation goes a long way toward explaining the now quite common need for a "touch-up" ablation.

## Gamma-tocopherol in stroke prevention

MELBOURNE, AUSTRALIA. Natural vitamin E is not a single compound but a complex of at least four tocopherols (*alpha*, *beta*, *delta*, and *gamma*) and four tocotrienols (*alpha*, *beta*, *delta*, and *gamma*). *Alpha*-tocopherol is the predominant form found in human blood, while *gamma*-tocopherol is the predominant form found in food. Based on the finding that *alpha*-tocopherol is the most abundant form in blood, scientists concluded that it was also the most active and beneficial form. This led to the formulation of vitamin supplements based solely on *alpha*-tocopherol, and later to the synthesis and marketing of synthetic (*dl*-) *alpha*-tocopheryl acetate. *Dl*-*alpha*-tocopheryl acetate also quickly became the preferred form used in clinical trials aimed at evaluating the benefits of vitamin E, particularly in regard to cardiovascular disease.

A team of Australian and Chinese researchers now suggests that *gamma*-tocopherol may be significantly more effective than *alpha*-tocopherol and may be particularly beneficial in stroke prevention. Their clinical trial included 39 healthy volunteers (19 men and 20 women) between the ages of 20 and 40 years. The participants were randomly assigned to supplement with a placebo, or 100 mg/day or 200 mg/day of pure *gamma*-tocopherol. Blood samples were drawn for analysis at the beginning and end of the 5-week trial. Supplementation clearly increased *gamma*-tocopherol concentrations in blood serum from 5.3 to 16.8 mg/mL in the case of the 100-mg/day dose, and from 5.4 to 30.1 mg/mL in the case of the 200-mg/day dose. The serum concentration of *alpha*-tocopherol did not change significantly during the trial.

The researchers also noted a significant decrease in platelet activation, LDL cholesterol level, platelet

aggregation, and mean platelet volume. They also made the following interesting observations:

- "Several independent investigations have demonstrated that the blood concentration of *gamma*-tocopherol, not *alpha*-tocopherol, was negatively correlated to the incidence of coronary heart disease."
- "Supplementation with large amounts of *alpha*-tocopherol was shown to increase the breakdown and decrease blood concentrations of *gamma*-tocopherol."
- Both natural and synthetic *alpha*-tocopherol suppresses serum *gamma*-tocopherol. The resulting imbalance between *alpha*- and *gamma*-tocopherol may have significant health consequences.

The researchers conclude that the results of their study suggest, "that the daily consumption of small amounts of *gamma*-tocopherol, in conjunction with usual dietary intake from mixed food sources may provide protection from oxidative damage and prevent thrombosis."

Singh, I, et al. Effects of *gamma*-tocopherol supplementation on thrombotic risk factors. **Asia Pacific Journal of Clinical Nutrition**, Vol. 16, No. 3, 2007, pp. 422-28

**Editor's comment:** The results of this study support my own long-held belief that supplements, especially vitamins and antioxidants, should always be taken in a formulation that mimics, as close as possible, the way the vitamin/antioxidant is found in nature. Thus, vitamin C should always be taken

with the bioflavonoids with which it is associated in nature. B vitamins should always be taken as the whole complex, as should vitamin E with emphasis on natural *gamma*-tocopherol. The finding that

*gamma*-tocopherol helps prevent thrombosis logically leads to the conclusion that it may also be effective in preventing transient ischemic attacks (TIAs) and ischemic stroke.

## New drug for conversion of AF

MONTREAL, CANADA. Although most atrial fibrillation (AF) episodes experienced by lone afibbers are self-terminating, some do require medical intervention in order to convert to normal sinus rhythm (NSR). Electrical cardioversion has an immediate success rate of about 90%. But only 25-50% of patients remain in NSR for a year. The efficacy is improved if patients are replete in potassium when the conversion is attempted and is very much decreased if the patient is on digoxin (Lanoxin) at the time of the cardioversion.

Pharmacologic conversion is also used and employs intravenous infusions of such drugs as ibutilide (Corvert), flecainide (Tambocor), and propafenone (Rythmol). Although these drugs result in conversion in 30-60% of cases, they must be used with caution as they can cause dangerous ventricular arrhythmias and serious hypotension. A group of researchers from Canada, Scandinavia and the United States recently completed a phase III clinical trial to evaluate the safety and effectiveness of vernakalant hydrochloride (RSD1235). Vernakalant is an atrium-selective potassium and sodium channel blocker and has, in animal studies, been found to prolong the atrial refractory period.

The clinical trial involved 336 patients enrolled at 44 different centers. The patients were divided into two groups. Group I (220 patients) consisted of AF patients who had been in afib for 3 hours to 7 days, while Group II (116 patients) was made up of those who had been in afib for 8 to 45 days. None of the patients had heart failure (class IV), had experienced a heart attack, or had previously failed electrical cardioversion. They were randomized to receive a 10-minute infusion of vernakalant (3.0 mg/kg) or placebo followed by a 15-minute observation period. If conversion to NSR was not achieved, an additional dose of vernakalant (2.0 mg/kg) or placebo was administered. Patients were then observed in the hospital for a minimum of 8 hours.

Successful conversion was defined as converting to NSR for at least one minute within 90 minutes of the

initiation of drug infusion. In Group I (short-duration AF), 51.7% of patients were successfully converted as compared to 4% in the placebo group. Most (76%) of those who converted with vernakalant did so with a single dose and within a median time of 11 minutes. All but one of the 75 patients who converted remained in NSR for more than 24 hours. The success rate in Group II was much lower at 7.9% among vernakalant-infused patients, and 0% among those receiving placebo.

There was a clear trend for the procedure to be more successful the shorter time the patient had been in afib. Thus, those who were treated no more than 48 hours from the onset of their episode experienced a 62.1% conversion rate versus 4.9% with placebo. Overall, 83 of the 221 patients (37.6%) given vernakalant successfully converted versus 2.6% in the placebo group. There were no reports of torsade de pointes or ventricular fibrillation during the first 24 hours after infusion; however, three patients did develop serious adverse events (hypotension and heart block) probably related to vernakalant administration. Minor adverse effects included impaired sense of taste experienced by almost 30% of patients treated with vernakalant, sneezing experienced by 16%, nausea by 9%, and hypotension by 6.3%.

The researchers conclude that vernakalant is safe and effective for conversion of short-duration atrial fibrillation. NOTE: This study was sponsored by the manufacturer of vernakalant, and 8 of the 13 authors had received financial compensation from the manufacturer and/or other pharmaceutical companies.

Roy, D, et al. Vernakalant hydrochloride for rapid conversion of atrial fibrillation. *Circulation*, Vol. 117, March 25, 2008, pp. 1518-25

**Editor's comment:** Vernakalant would appear to be a useful drug for intravenous, pharmacological conversion of short-duration afib. However, it does require a trip to the ER so most lone afibbers would likely be better off using the pill-in-the-pocket approach (with flecainide or propafenone), which has a conversion effectiveness around 90%.



## PACs and coughing

WAKEFIELD, RHODE ISLAND. Dr. Neil Brandon, a cardiologist in Rhode Island, reports on the case of 3 patients who were observed to have a single premature atrial contraction (PAC) immediately preceding a cough. In discussing his findings with colleagues, he found that several physicians had noted a similar association including two cardiologists who had experienced it themselves. Dr. Brandon speculates that a PAC arising in the

atrium near the phrenic nerve may trigger the cough reflex in susceptible patients and points out that patients sometime cough during an atrial fibrillation procedure. He also suggests that otherwise unexplained coughing may be due to asymptomatic PACs.

*Brandon, N. Premature atrial contraction as an etiology for cough. Chest, Vol. 133, 2008, p. 828*

## **Elimination/Reduction Protocol**

### **Case No. 661**

**Male** afibber – **52 years** of age with **vagal AF** of **4 years standing**; no underlying heart disease

No. of episodes in 6 months prior to starting protocol: **7 (including one lasting 2.5 months)**

Afib burden in 6 months prior to starting protocol: **Average 7 hours/episode except for one lasting 2.5 mos.**

No. of episodes in most recent 6 months after starting protocol: **0**

Afib burden in most recent 6 months after starting protocol: **NONE**

Time on protocol: **43 months**

Episodes since protocol implementation: **4 episodes (3 of 0.7 hrs, 1 of 20 hrs)**

Still need to avoid triggers?: **No**

#### **Main components of effective protocol**

Trigger avoidance: **None**

Diet changes: **None**

Supplementation: **Magnesium, potassium, taurine**

Drug therapy: **Pill-in-pocket flecainide**

Stress management: **None**

Approaches to shorten episodes: **Pill-in-pocket flecainide**

Approaches to reduce ectopics: **Supplementation with magnesium, potassium and taurine**

#### **Background and details of protocol**

I am a vagal afibber and a life-long exerciser. I am sufficiently fit to compete annually in a 13-mile race up Pike's Peak (14,100', 4,300m elevation, 7850' elevation gain). In the summer of 2004 several days after a long training day on a 14'er, I woke up with a rapid, irregular heart beat and was subsequently diagnosed with lone atrial fibrillation. During the next 2 months I experienced 5 more classically vagal episodes starting around 3 AM. These either converted on their own or converted with exercise after about 7 hours. The next episode, however, lasted 2.5 months, but I was eventually able to convert it by taking 300 mg of flecainide (conversion took 20 hours).

Early on, I found the LAF Bulletin Board and purchased Hans' first book. I looked at low potassium (hypokalemia) as a potential issue. Prior to afib, I'd had two annual blood tests with serum potassium levels at the low end of normal - 3.5 mmol/l. The day of my first episode, my level was 3.2 in the ER. Five days later it was 4.2 in the doctor's office.

My conclusion was that I had intermittent hypokalemia. I set out to design a supplement program that would keep my serum K above 4.2. This program includes 3 grams of potassium as citrate, 0.8 grams magnesium as glycinate and 4 grams of taurine per day. All doses are divided and taken morning and evening around meal time. I proposed to my EP that I use on-demand flecainide as a back-up in case the supplements failed. He agreed.

After ending the 2.5 month episode, I started supplements. Here are the subsequent episodes:

1. 1 month – 3 AM episode, converted 20 hours after taking 300 mg flecainide
2. 4.5 months – midnight episode, converted 20 minutes after taking 300 mg flecainide
3. 5.5 months – 3 AM episode, converted 20 minutes after taking 300 mg flecainide
4. 2.5 years – 11 PM episode, in vagal period after sexual climax. Converted 50 minutes after taking 300 mg flecainide. .... Cont'd

**Notes** – prior to episodes 2 & 3, I'd run out of taurine and not bothered to replace it. Episode 4 occurred, 3 days after ceasing all supplements. This was evidence that all three supplements are essential for me. Episode 2 was a bit unusual, as I'd snow-shoed for 4 hours through heavy snow with a 75-pound pack and then spent 6 hours of hard work constructing a snow cave. It came on after I'd gone to bed. Normally I would crush the flecainide in warm water, however all I had was partially frozen water bottle. I chewed the flecainide tablets and washed them down with near freezing water – still effective.

When I started the supplement program, I also started a monitoring program with a Polar S810 heart rate monitor and a FreezeFramer heart rate monitor. Using them I was able to count PAC and PVC rates/hour. PAC's typically run 0-2/hr and PVC's 0-20/hr. My monitoring concept is that an increase in ectopic rates will foreshadow afib. The results could also be used to "tweak" the supplement program.

For anyone copying this program, I recommend BUN and creatinine tests to make sure your kidneys are OK. Also start slowly with the supplements and gradually increase dosages.

A couple of other, perhaps unrelated notes. When I was out of rhythm for 2.5 months, I gained 20 lbs (9.1 kg). I decided a good approach to losing weight would be to keep my blood sugar low and level. I purchased the most accurate home glucometer I could find – Bayer Ascencia Contour. I sampled my blood sugar 45 minutes (usually maximum spike) after eating and would modify my meals such that I'd keep this spike to around 100 or 110 mg/dL (6.1 mmol/l) or less. This allowed me to drop the excess weight in around 2 months. This did not have any bearing on my success at keeping afib in remission, I only include it for general information.

The reason I stopped all supplements prior to episode 4 is that I thought I might be allergic to the fillers in the pills. I subsequently underwent an Elisa IgE/IgG test and determined that I was allergic to wheat, dairy, eggs, soy, almonds, grapes ... These were the source of my allergy, not the pills.

I have had a regular meditation habit for many years (before and after I ended up with afib). I have not seen any effect afib by meditation.

In summary, I'm very happy with my program. I am still very active, exercising on the excessive side of moderate. However I no longer train for endurance activities and try to keep my heart rate under 130 BPM during daily exercise (in fact, a lot of my exercise is in the 100 to 110 BPM range). However, I have done long hard days of exercise with high HR without adverse effect. I just try not to make it too regular a habit and limit them to FUN activities – not training. I do pay attention to my early morning resting HR. If it is elevated by 10 BPM or more, it is a sign that: 1) I've over done it the day before, or 2) I'm coming down with some illness. In either case, I take it very easy.

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