THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

NUMBER 120 **JUNE/JULY 2012** **12th YEAR**

Welcome to this our 120th issue!! Our inaugural issue was published in January 2001 and among other news, we highlighted the following:

Researchers at the Johns Hopkins University School of Medicine have just released a major study aimed at determining the effectiveness of heart drugs in converting atrial fibrillation to sinus rhythm and in maintaining sinus rhythm in AF patients. They looked at the results of 36 major clinical trials and reached the conclusion that ibutilide/dofetilide and flecainide (Tambocor) are the most effective drugs when it comes to converting AF to sinus rhythm. Ibutilide/dofetilide was 29 times more effective than placebo and flecainide 25 times more effective. Verapamil, diltiazem (Cardizem) and digoxin (Lanoxin) were all found to be essentially useless; that is, no better than placebo. So while these drugs may be helpful in slowing the heartbeat, they are ineffective in converting it to normal sinus rhythm. Propafenone (Rythmol) and quinidine (Biquin) were much less effective and sotalol (Sotacor, Betapace) actually had a negative effect. None of the drugs evaluated were particularly effective in maintaining sinus rhythm; that is, preventing another attack. Quinidine, disopyramide (Rythmodan), flecainide, propafenone, and sotalol all showed some positive effect while verapamil, diltiazem and digoxin had no beneficial effects.

In this issue we report on the latest findings regarding the factors determining the outcome of chemical and electrical cardioversion and the complications commonly associated with these procedures. We also report that catheter ablation with uninterrupted warfarin therapy is safer and more successful than the current warfarin/heparin protocol, that alcohol is an important trigger for the first and subsequent AF episodes, that the chance of a successful ablation outcome declines the more antiarrhythmics a patient has tried prior to the ablation, that there are new concerns about the WATCHMAN device for stroke prevention, and that a Norwegian study discovers new risk factors for AF and lone AF.

Enjoy!!

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

Wishing you good health and lots of NSR,

Hans

Highlights

Continuous use of warfarin during catheter ablation

AUSTIN, TEXAS. Catheter ablation for atrial fibrillation (AF) is associated with an approximately 1% risk of procedure-related ischemic stroke. The risk arises from the formation of blood clots (thrombi) on catheters and sheaths as well as from the stagnation of blood in the left atrial appendage. It is also possible that char formed on catheters due

to overheating may be dislodged and carried to the small arteries in the brain where they, like the above-mentioned thrombi, may cause a stroke.

In order to prevent a procedure-related stroke, prospective ablation patients are placed on warfarin (INR 2.0-3.0) for two months prior to the procedure. Warfarin is usually discontinued a day or two before the ablation and replaced with heparin, which is also infused during the procedure. After a couple of days "bridging" with heparin, warfarin therapy is reintroduced and the patients are maintained on this for 3 to 6 months post-procedure.

A group of electrophysiologists headed by Dr. Andrea Natale now report that discontinuing warfarin immediately before and during the ablation procedure may be a bad idea. Their meta-analysis included 9 studies which compared the standard anticoagulation protocol (DW) in which warfarin is discontinued a day or two prior to the ablation and replaced by heparin which is also infused during the procedure and for a couple of days following with a new protocol (CW) where warfarin therapy (INR between 2.0 and 3.5) is maintained without interruption from 2 months before the procedure to 2 or 3 months after. The patients in both the DW group (21,002 patients) and the CW group (6400 patients) underwent pulmonary vein isolation with additional lesions as required. Intravenous unfractionated heparin was administered to all patients, although with different doses and at different stage of the procedure. Irrigated ablation catheters were used in all but two of the studies, and navigation guidance with an ICE (intracardiac echocardiography) catheter was used in 5 studies.

Overall, procedure-related death was 0.09%. The incidence of procedure-related thromboembolic events (ischemic stroke and TIA) was 16 times higher in the DW group (0.94%) than in the CW group (0.06%). A total of 4 strokes occurred in the CW group. One of these occurred in a patient who had only been on warfarin for 3 days prior to the procedure, while another occurred in a patient whose INR was below 1.8.

Major bleeding requiring medical intervention or blood transfusion occurred among 1.25% of patients in the DW group vs. 0.55% in the CW group. The majority of major bleeding complications was due to cardiac tamponade (fluid build-up in the sac enclosing the heart caused by puncture of the heart wall) which occurred in 0.29% of patients in the CW group and in 1.10% in the DW group. Minor bleeding complications occurred in 4.5% of patients in the CW group and in 18.6% of those in the DW group. This increase in minor bleeding was strongly associated with the use of low-molecular-weight heparin in pre-procedural bridging. A combination of CW and the use of ICE guidance was highly successful in reducing major bleeding complications.

The researchers conclude that continuous warfarin treatment (CW protocol), especially if used in conjunction with ICE imaging, materially reduces stroke/TIA risk and risk of bleeding when compared to the current standard DW protocol, which discontinues warfarin immediately before, during, and immediately following the ablation procedure. They do point out though that the studies involved procedures carried out in highly experienced AF ablation centers. They finish off with the following comment – *whether the benefit and safety of CW also extend to low-volume centers merits further investigation.*

Santangeli, P, Natale, A, et al. Ablation of atrial fibrillation under therapeutic warfarin reduces periprocedural complications. **Circulation: Arrhythmia and Electrophysiology**, *Vol. 5, 2012, pp. 302-11*

Editor's comment: This highly encouraging study provides convincing evidence that the risk of bleeding complications and stroke/TIA can be very significantly reduced by replacing the current DW protocol involving discontinuation of warfarin with the new CW protocol based on continuous warfarin therapy. However, whether the success of the CW protocol can be reproduced by less experienced EPs remains, at least in my mind, a question. Dr. Natale and colleagues not only have an outstanding success rate, but also an equally remarkable safety record. I would think this plays a large part in the success of the CW approach, which was primarily used by Dr. Natale and colleagues.

Alcohol and vagal activation as AF trigger

SAN FRANCISCO, CALIFORNIA. There is evidence that alcohol consumption, especially binge drinking, often precedes that very first atrial fibrillation (AF) episode. Two studies specifically surveying paroxysmal afibbers found that 22% to 34% reported that alcohol consumption preceded

their first episode. The question naturally arises is alcohol consumption also a trigger for future episodes? A group of electrophysiologists (EPs) at the University of California now confirms that alcohol consumption is indeed a trigger, especially in younger afibbers with the vagal variety of AF.

Their study included 133 participants with documented, mostly lone, paroxysmal atrial fibrillation (PAF) and 90 controls with various documented forms of supraventricular tachycardia (SVT) with 56% having atrioventricular nodal re-entrant tachycardia (AVNRT), 27% having atrioventricular re-entrant tachycardia (AVRT), and 16% having atrial tachycardia (AT). One hundred and ten patients with PAF (83% of a total AF sample) and 68 patients with SVT (76% of total SVT sample) answered questions as to how frequently alcohol provoked their episodes. After adjusting for potential confounders, the researchers concluded that PAF patients were 4.4 times more likely to report alcohol as a trigger than were those with SVT. Seven percent of afibbers reported that alcohol always or often triggered an episode, while only 1% in the SVT group reported an association. By far, the worst offender was beer.

The California EPs also investigated the association between activation of the vagal (parasympathetic) arm of the autonomic nervous system and the triggering of an AF or SVT episode. Overall, 50% of the 221 respondents reported that vagal activities (resting, sleeping, eating, and symptoms that terminated with exercise) precipitated their episodes. However, vagal activation was twice as likely to trigger episodes in PAF patients than in SVT patients. Younger age and a family history of AF were markedly associated with having vagal triggers. There was a strong correlation between having alcohol and vagal activities as triggers, with afibbers reporting alcohol as a trigger also reporting vagal activities as a trigger. The researchers speculate that alcohol may trigger AF through vagal activation or that the electrophysiologic effects (shortening of action potential duration and refractory period) of alcohol consumption and vagal activation are similar.

Activation of the adrenergic (sympathetic) arm of the autonomic nervous system (physical overexertion, emotional stress and caffeine consumption) was associated with the triggering of arrhythmias in 40% of cases, with no significant difference between PAF and SVT patients.

Mandyam, MC, et al. Alcohol and vagal tone as triggers for paroxysmal atrial fibrillation. **American Journal of Cardiology**, *April 20, 2012 [Epub ahead of print]*

Editor's comment: Our very first LAF Survey (February 2001) identified the following important triggers of AF episodes:

Emotional or work-related stress	50%
Physical overexertion	24%
Alcohol consumption	22%
Resting	22%
Heavy meals	18%
Caffeine consumption	16%

Later surveys associated the initiation of vagal episodes with alcohol consumption (33%), resting/sleeping (33%), heavy meals (28%), and fatigue and lack of sleep (36%). The most important triggers for adrenergic episodes were stress and anxiety (94%), exercise (44%), specific foods and food additives (38%), and caffeine (31%).

Ablation success and prior use of antiarrhythmics

REDWOOD CITY, CALIFORNIA. Most guidelines for the management of atrial fibrillation (AF) specify that patients should not be considered for a catheter ablation unless treatment with at least one antiarrhythmic drug (AAD) has proven ineffective in controlling their condition. The 2010 European guidelines suggested that paroxysmal afibbers could proceed directly to ablation without having tried AADs, if they are symptomatic even with rate control and have no underlying heart disease. Similarly, the 2011 Canadian guidelines allow for first-line ablation for symptom relief in highly selected patients with paroxysmal AF. Now a group of electrophysiologists (EPs) from Sequoia Hospital and Silicon Valley Cardiology suggests that the outcome of an ablation becomes less favourable

the more antiarrhythmics the patient tries prior to having the ablation.

Their study involved 1125 AF patients who had undergone a total of 1504 catheter ablation (average of 1.3 procedures per patient) during the period 2003 to 2010. Most patients (53%) in this particular group had persistent AF, 31% had the paroxysmal variety, and the remaining 16% had permanent AF. The average age of the patients was 62 years and 29% were female. Four hundred patients had tried one AAD, 231 had tried two, 115 had tried 3 or more, and the remaining 195 had never been on any AAD prior to their initial ablation. A significant proportion of the group had coronary artery disease (14%), hypertension (47%), dilated cardiomyopathy (8%), or had suffered a stroke or TIA (7%). So, it was not a terribly healthy group of patients and certainly not comparable in characteristics to a group of otherwise healthy afibbers.

The researchers observed that patients who failed several AADs were older, had been suffering from AF longer, were more likely to be female, and were more likely to have persistent rather than paroxysmal AF. They also noted that the extent of drug failure was directly related to an increase in the need for repeat ablations. The overall complete success rate (no AF, no ADDs after a 3-month blanking period) at one year from the initial ablation was 68.9% for patients who had never been on AADs vs. 42.8% for those who had failed 3 or more AADs (paroxysmal and persistent afibbers combined). Corresponding numbers at the 4-year mark (from Kaplan-Meier curves) was 61.3% and 29.4%. Other statistically significant predictors of initial ablation failure were an enlarged left atrium, female gender, and persistent AF. The number of pre-ablation failed AADs did not affect the outcome of ablations in permanent afibbers.

Major procedure-related complications occurred in 1.6% of procedures with pericardial tamponade being the most common. There were no procedure-related deaths, PV stenosis requiring intervention, or atrial-esophageal fistulae. The researchers speculate that the additional time elapsed during the trial of one or more AADs allows for disease progression from paroxysmal to more persistent AF and thus reduces the chance of a successful ablation outcome. They suggest that EPs should not actively discourage patients from having an ablation if they do not wish to try AADs first.

Winkle, RA, et al. Prior antiarrhythmic drug use and the outcome of atrial fibrillation ablation. **Europace**, *Vol. 14, 2012, pp. 646-52*

Editor's comment: I believe this report carries two important messages:

1. Don't wait for your left atrium to enlarge beyond about 4 cm (40 mm) in diameter before undergoing an ablation.
2. Go for an ablation as first-line treatment, or if you have failed one antiarrhythmic. Chances are that a different AAD won't work either, and that postponing an ablation will result in a poorer outcome.

Real-world cardioversion results

MAASTRICHT, THE NETHERLANDS. Cardioversion is used to convert a patient experiencing highly symptomatic or persistent atrial fibrillation (AF) to normal sinus rhythm (NSR). Conversion can be achieved by oral administration of antiarrhythmic drugs like amiodarone or propafenone, or by the infusion of drugs like ibutilide (Covert), dofetilide (Tikosyn) or flecainide (Tambocor) in a hospital setting (chemical conversion). Chemical conversion is most effective if started within a couple of hours of the onset of the episode and becomes less effective as time goes by. In cases where an episode has lasted longer than 7 days drug-induced conversion is not effective and electrical conversion (cardioversion) must be used to regain NSR, either alone or in combination with antiarrhythmic drugs. Cardioversion is also sometimes used instead of drugs in an attempt to convert an AF patient who has just arrived in hospital if the patient suffers severely (fainting, dizziness, breathlessness, etc).

Electrical cardioversion (also known as direct-current or DC cardioversion) is a procedure whereby a synchronized electrical current (shock) is delivered through the chest wall to the heart through special electrodes or paddles that are applied to the skin of the chest and back. The purpose of the cardioversion is to interrupt the abnormal electrical circuit(s) in the heart and to restore a normal heartbeat. The delivered shock causes all the heart cells to contract simultaneously, thereby interrupting

and terminating the flutter or AF without damaging the heart. The heart's electrical system then restores a normal heartbeat controlled by the sinus node.

Skin burns and ischemic stroke are the most common adverse effects accompanying the procedure. Patients with a low blood serum level of potassium or a toxic level of digoxin may experience life-threatening ventricular fibrillations when undergoing cardioversion. Thus potassium levels should always be checked prior to cardioversion and corrected if necessary.

Cardiologists/electrophysiologists at Maastricht University Medical Center now report the results of a study aimed at determining the immediate and medium-term (1 year) outcome of cardioversion in a group of 1800 AF patients who underwent cardioversion prior to enrolment in the Euro Heart Survey on AF. The patients included in the study were generally not in good health with 64% having hypertension, 31% having coronary artery disease, and 25% having valvular heart disease or heart failure. The average age of the patients was 64 years, 59% were male, and the average length of time that the participants had been suffering from AF was relatively short ranging from 4 days (24%) to 11 months (21%). For 27% of patients cardioversion was for their first episode, while 35% had previously been diagnosed with paroxysmal AF and 37% with persistent AF.

Forty percent of patients (primarily persistent afibbers) underwent electrical cardioversion (ECV), 36% (primarily paroxysmal afibbers or those experiencing their first episode) were treated with intravenously administered antiarrhythmic drugs (63% with amiodarone and 13% with propafenone), and the remaining 24% (primarily paroxysmal afibbers or those experiencing their first episode) underwent oral administration of antiarrhythmic drugs (mainly amiodarone and flecainide) or non-antiarrhythmics (digitalis, beta-blocker, verapamil, diltiazem). Acute success of chemical conversion was defined as restoration of sinus rhythm within 24 hours after the onset of pharmacological treatment. Acute success of ECV was defined as maintaining NSR for at least 10 minutes after the final shock.

Outcomes and complication rates for the three cardioversion approaches are summarized below.

	Electrical	**Intravenous**	**Oral**
Acute success	88%	71%	75%
NSR at 1-year *	70%	72%	64%
Major complications	4.3%	5%	5%

*** NOTE: 63% of study participants used an antiarrhythmic drug during follow-up**

The most common complications in the chemical conversion groups were transient ischemic attack (TIA) at 1.3% and heart failure at 1.0%, while the most common complications in the ECV group were heart failure at 1.1% and ventricular tachycardia at 0.8%. No patients died prior to discharge from hospital. The main factors predicting acute success of ECV were:

- Absence of chronic obstructive pulmonary disease (COPD)
- Paroxysmal AF
- Use of biphasic defibrillator.

Factors predicting acute success of intravenous administration of antiarrhythmics were:

- Paroxysmal AF
- Absence of valvular heart disease
- Absence of heart failure
- Presence of hypertension
- Presence of coronary artery disease.

Paroxysmal AF and a smaller left atrial diameter favourably influenced the results of cardioversion with orally administered drugs.

The following factors were predictive of being in NSR at the one-year follow-up:

- Paroxysmal AF
- Shorter total AF history
- Use of amiodarone or Class 1C antiarrhythmics during follow-up
- Absence of COPD
- Younger age
- Smaller left atrial diameter.

The researchers noted that a significant number of patients treated with non-antiarrhythmics converted to NSR within 24 hours and ascribe this to the known phenomenon of spontaneous conversion.

They conclude that, "Contemporary conversion of AF is routinely successful and safely performed with a high proportion of patients in NSR at 1-year follow-up".

In an accompanying editorial Drs. Rene Tavernier and Mattias Duytschaever of the University Hospital Ghent take issue with the conclusion that a major complication rate of 4.5% can be considered a safe procedure. They also question that 70% of study participants really were in NSR at the 1-year follow-up since this conclusion was based on just a single ECG. Most other studies have found a success rate of 50% or less. Finally, they suggest that cardioversion be delayed a reasonable amount of time to allow spontaneous cardioversion to occur.

Pisters, R, et al. Clinical correlates of immediate success and outcome at 1-year follow-up of real-world cardioversion of atrial fibrillation. **Europace***, Vol. 14, 2012, pp. 666-74*
Tavernier, R and Duytschaever, M. Cardioversion for atrial fibrillation in the real world: there is room for improvement. **Europace***, Vol. 14, 2012, pp. 617-18*

Editor's comment: I agree with the Belgian editorialists that a 1-year cardioversion success rate of 70% is unrealistic. My own study of electrical cardioversion revealed that a typical 1-year success rate is more like 40% or less. It is interesting that the Maastricht group measured serum potassium levels of all patients and took steps to correct low levels prior to proceeding with electrical cardioversion.

Increased stroke risk for older women

MONTREAL, CANADA. Atrial fibrillation (AF), on its own, does not increase the risk of suffering a stroke. However, about 80% of patients with AF also have hypertension, heart disease, diabetes, or other comorbid conditions that substantially increase the risk of stroke. For example, hypertension by itself increases stroke risk by a factor of 4 to 6, while long-term diabetes is associated with a 3-fold increase in stroke. It seems to be firmly engrained in medical minds that AF patients have a 5-fold increase in the risk of stroke compared to the general population. While this may be true for an 80-year-old afibber with heart disease, diabetes, and hypertension, it is patently untrue for a middle-aged, otherwise healthy lone afibber. Nevertheless, the pressure is on to have all afibbers, irrespective of the absence or presence of comorbid conditions, be on warfarin, or one of the newly-developed anticoagulants, for life.

Stroke risk is usually assessed using the $CHADS_2$ scoring system which assigns 1 point each to the presence of congestive heart failure, hypertension, diabetes, age of 75 years or older, and 2 points for a history of stroke or transient ischemic attack (TIA).

A new scoring system, CHA_2DS_2-VASc, has recently come to the fore. This score assigns 1 point each to the presence of congestive heart failure, hypertension, diabetes, vascular disease, age 65 to 74 years, female gender, and 2 points for a history of thromboembolism and age 75 years or older. Thus, according to this new system, an otherwise healthy 65-year-old female afibber with no comorbid conditions supposedly has the same risk as an afibbers who has already suffered a stroke and must be on warfarin for the rest of her life.

Now a group of researchers from three Canadian universities reports that older women with recently diagnosed AF have a significantly higher risk of stroke than do older men. Their study included 39,398 men and 44,115 women admitted to hospital with AF as a primary diagnosis (24%) or with coronary artery disease, valvular heart disease, heart attack, chronic kidney disease, or high cholesterol as the primary diagnosis and AF as the secondary diagnosis (76%). The average age of the male study participants was 77 years and that of the female participants was 80 years. The average $CHADS_2$ score for men was 1.7 vs 2.0 for women. Components of the $CHADS_2$ score were:

	Women	**Men**
Congestive heart failure	27.8%	28.9%
Hypertension	63.9%	51.3%
Age 75 years or older	74.2%	61.4%
Diabetes	22.1%	24.6%
History of stroke	8.0%	6.9%

Warfarin was prescribed at discharge from hospital for 60.6% of women and 58.2% of men. The study participants were followed for 1 year during which a total of 2570 stroke (2.02%/year) occurred among the women and 1696 (1.61%/year) occurred among the men. NOTE: Stroke was defined as ischemic stroke (cerebral thrombosis), embolism, artery occlusion, transient ischemic stroke, or retinal infarction. The rates of hemorrhagic stroke (intracerebral hemorrhage) were 1.42% among the men and 1.33% among the women.

Stroke risk was found to increase significantly with age, rising from 1.05%/year among women aged 65 to 69 years (corresponding figure for men was 1.17%/year) to 2.38%/year for women aged 75 years or older (corresponding figure for men was 1.95%/year). Not surprisingly, stroke risk also increased significantly with increasing $CHADS_2$ score from 1.03%/year for women with a score of 0 (corresponding number for men was 0.86%/year) to 4.91%/year for women with a score of 5 (corresponding number for men was 4.88%/year). NOTE: Only 0.17% of the total patient population had a $CHADS_2$ score of 5 or higher, so it would seem to be gross exaggeration to claim that all AF patients have a 5-fold increased risk of stroke.

As shown below, it is clear that women aged 75 years or older have a higher risk of stroke than do age-matched men, and that this excess risk is reduced by the use of warfarin.

Incidence of Stroke

	Below age of 75 years		**At or above 75 years**	
	No warfarin	**Warfarin**	**No warfarin**	**Warfarin**
Women	1.47%/year	1.10%/year	2.91%/year	2.05%/year
Men	1.48%/year	1.04%/year	2.20%/year	1.78%/year

The authors conclude that the risk of stroke among older women with recently diagnosed AF is greater than that of age-matched men irrespective of whether warfarin therapy is implemented.
Avgil Tsadok, M, et al. Sex differences in stroke risk among older patients with recently diagnosed atrial fibrillation. **Journal of the American Medical Association***, Vol. 307, No. 18, May 9, 2012, pp. 1952-58*

Editor's comment: It is unfortunate that the authors of the Montreal report did not provide details of the distribution of hemorrhagic strokes other than to say that most of them occurred in patients on warfarin. However, based on results from similar studies, it is likely that about two-thirds of hemorrhagic strokes occurred in the warfarin group. Thus, the incidence of hemorrhagic stroke would be 0.44%/year in women not on warfarin and 0.89%/year for women on warfarin. The corresponding numbers for men would be 0.47%/year and 0.95%/year.

It is now well established that the benefits of warfarin are, often to a considerable extent, reduced by its inherent propensity to cause intracranial bleeding (hemorrhagic stroke). Two recent studies have used the concept of Net Clinical Benefit (NCB) to determine the real, overall benefit of warfarin therapy.[1,2] NCB considers both the benefit (reduction in ischemic stroke) and harm (increase in hemorrhagic stroke) in administering the drug. NCB is defined as:

NCB = (TE rate off warfarin – TE rate on warfarin) – W x (ICH rate on warfarin – ICH rate off warfarin)

- TE rate is the annualized rate of thromboembolic events (ischemic stroke and systemic emboli).
- W is a weighting factor designed to reflect the fact that the consequences of a hemorrhagic stroke (intracranial bleeding) are far more serious than that of an ischemic stroke. W is usually assumed to be 1.5.
- ICH rate is the annualized rate of intracranial bleeding (incl. hemorrhagic stroke).

Using the above formula, and assuming that hemorrhagic stroke incidence is independent of age, the following NCBs can be calculated.

NCB of Warfarin Therapy

	Age 75 years or younger	Age 75 years or older
Women	- 0.31%/year	+ 0.18%/year
Men	- 0.24%/year	- 0.26%/year

The above calculation shows that the average NCB of warfarin therapy in recently diagnosed female afibbers, at or above the age of 75 years, is indeed slightly beneficial at 0.18%/year. It would appear to be detrimental for men at all ages, and for women below the age of 75 years. Of course, these numbers are average and whether or not warfarin therapy would be beneficial for an individual afibber would clearly depend on his or her age and $CHADS_2$ score. Thus, warfarin therapy would likely be beneficial for an older woman (age 75 years or older) with a $CHADS_2$ score of 3 or higher, but would almost certainly be detrimental for women with a $CHADS_2$ score below 3 unless the reason for their $CHADS_2$ score of 2 was a history of stroke or TIA. The same cut-off points would apply to men.

[1] Singer, DE, et al. The net clinical benefit of warfarin anticoagulation in atrial fibrillation. Annals of Internal Medicine, Vol. 151, September 1, 2009, pp. 297-305, pp. 355-56

[2] Olesen, JB, et al. Risks of thromboembolism and bleeding with thromboprophylaxis in patients with atrial fibrillation: a net clinical benefit analysis using a "real world" nationwide cohort study. Thrombosis and Haemostasis, Vol. 106, No. 4, October 2011, pp. 739-49

New concerns about the WATCHMAN device

AUSTIN, TEXAS. The formation of cardiac emboli (blood clots) in the left atrium and left atrial appendage (LAA) is a major cause of ischemic stroke in atrial fibrillation (AF) patients with risk factors for stroke. It is estimated that 90% of these emboli are formed in the LAA due to poor circulation in and out of this small pouch attached to the left atrium. Thus it is not surprising that electrophysiologists (EPs) and cardiovascular surgeons have been experimenting with either removing or closing off the LAA.

The latest entry in the market for devices used to close off the LAA is the WATCHMAN device. This is a nitinol (nickel-titanium alloy) cage covered with a polyethylene membrane and having barbs for anchoring it to the inside of the LAA. The device is inserted with a special catheter entering the left atrium through the femoral vein – a procedure similar to that used in pulmonary vein ablation procedures. The first trial of the device involved 66 patients with AF and one or more risk factors for ischemic stroke; it was performed at the Mayo Clinic. After 45 days, 93% of participants had achieved satisfactory sealing of the LAA and 92% were able to discontinue warfarin.

Preliminary results of a larger trial indicated that 87% of patients were able to discontinue warfarin after 45 days and the Mayo Clinic researchers concluded that the WATCHMAN device is "non-inferior" to warfarin treatment as far as the risk of stroke and bleeding is concerned. This despite the fact that 5% of the trial participants required intervention to deal with pericardial effusion occurring during the procedure. NOTE: Both the Mayo Clinic and the authors of the article have a direct financial interest in Atritech, the manufacturer of the WATCHMAN device.[1]

Researchers at McMaster University in Canada question the conclusion that the WATCHMAN device will eliminate the need for warfarin therapy. They state, "*No conclusive evidence exists to demonstrate that LA exclusion reduces stroke in AF patients*". They also point out that there is evidence that removing or isolating the LAA may decrease cardiac function, impair hemodynamic response to volume and pressure changes, impede thirst, and promote heart failure. Thus, it is by no means certain that eliminating LAA function is a benign procedure. Some studies involving surgical closure of the LAA have shown that stroke risk can actually increase if the LAA is not completely isolated.

Now a group of EPs at St. David's Medical Center reports that gaps may develop between the edge of the WATCHMAN device and the wall of the LAA thus allowing blood from the LAA to seep into the left atrium and (presumably) vice versa. Their study involved 58 AF patients who had a WATCHMAN device implanted at St. David's between November 2008 and June 2010. The average age of the patients was 74 years, 64% were male, and 74%

had a $CHADS_2$ score of 2 or higher – in other words, of intermediate risk for stroke. Transesophageal echocardiography (TEE) was used to guide the initial placement of the device. TEE was also used to check its position and look for gaps 45 days and 12 months after implantation. All patients were maintained on warfarin (INR between 2.0 and 3.0) for the first 45 days, after which, 55 (95%) discontinued anticoagulation.

Although TEE at the end of the insertion procedure showed tight closure and no gaps in 72% of patients, notable gaps were observed in the remaining 28%. At the 45-day TEE an additional 12% had developed new gaps, but some of these had closed and others had opened at the 12-month TEE examination. All told, at the 12-month follow-up, 65% of patients had no visible gaps, while the remaining 35% had one or more. During 26 months of follow-up, 1 patient (1.7%) had a stroke (4.7 months after the implantation). No device dislodgement occurred during follow-up. The authors conclude that incomplete LAA closure with gaps between the WATCHMAN device surface and the LAA wall is relatively common. They recommend further trials to determine whether the presence, persistence or variation in size of gaps is related to stroke risk.

Bai, R, Natale, A, et al. Intraprocedural and long-term incomplete occlusion of the left atrial appendage following placement of the WATCHMAN device. **Journal of Cardiovascular Electrophysiology***, Vol. 23, May 2012, pp. 455-61*

Editor's comment: It would seem that there are still questions about the viability of LAA occlusion with a WATCHMAN device as an alternative to anticoagulation with warfarin. It should also be kept in mind that the LAA serves a useful function and that its "elimination" may have unintended consequences. For more on this see www.afibbers.org/resources/LAA.pdf. Fortunately, this is largely irrelevant to lone afibbers with no risk factors for stroke since they do not have an increased risk of stroke and would not benefit from either long-term warfarin therapy or LAA isolation or removal.

[1] *Holmes, DR and Schwartz, RS. Does left atrial appendage occlusion eliminate the need for warfarin? Left atrial appendage occlusion eliminates the need for warfarin. Circulation, Vol. 120, November 10, 2009, pp. 1919-26*

Quality of life following catheter ablation

MUNICH, GERMANY. Several studies have reported that the quality of life (QoL) of atrial fibrillation (AF) patients is significantly reduced compared to that of age-matched healthy control subjects. Doctors at the German Heart Center now report that QoL shows substantial improvement after a catheter ablation. Their study involved 133 patients who underwent catheter ablation at the Center between July 2004 and August 2006. The average age of the patients was 57 years, 74% were men, and 65% had paroxysmal AF. Valvular heart disease was fairly common among the study participants at 29%. Fourteen percent had coronary artery disease or had suffered a heart attack, and 51% had hypertension.

All patients underwent a pulmonary vein isolation (PVI) procedure with additional lesions as required. After a 3-month blanking period, 65% of patients with paroxysmal AF and 46% of those with persistent AF were in normal sinus rhythm without the use of antiarrhythmic drugs. Thirty-nine percent of patients underwent a repeat procedure because of arrhythmia recurrence after a mean follow-up of 11 months. At the last follow-up (a median of 4.3 years after the initial procedure), 66% of paroxysmal afibbers and 50% of persistent afibbers were in normal sinus rhythm without the use of antiarrhythmics. Oral anticoagulation was discontinued after 6 months in all patients without AF recurrence provided their $CHADS_2$ score was below 2.

Prior to the ablation, all patients filled out 7 detailed questionnaires designed to provide a quantitative estimate of their baseline QoL. Three of the questionnaires were specific to AF and covered such aspects as symptoms, severity of episodes, and self-perceived impact of AF. The other 4 questionnaires were generic in nature and dealt with such QoL factors as depression, energy level, sleep quality, mood and general interest. The questionnaires were repeated 3 months and an average of 4.3 years after the initial ablation procedure. After 3 months, all patients regardless of AF type and ablation outcome, showed significant improvement on all 4 generic questionnaires and in 2 of the AF specific questionnaires (changes in self-perceived impact of AF were not statistically significant).

Not surprisingly, QoL improvement was more pronounced among patients with a successful ablation than among those with an unsuccessful one. The improvement in QoL continued to be statistically highly significant at 4.3 years, irrespective of AF type and ablation outcome. However, patients with a successful ablation had significantly greater improvement in QoL than did those with an unsuccessful procedure, especially in regard to depression, AF symptoms, and AF severity.

The authors conclude that, "*Ablation for AF significantly improves QoL irrespective of ablation success during short- and long-term follow-up. The degree of QoL improvement is significantly correlated with ablation success during long-term follow-up in the questionnaires especially designed for AF and in the depression questionnaire. Thus, the longevity of QoL improvement after catheter ablation potentially strengthens the argument for ablation in patients with symptomatic AF*."
Fichtner, S, et al. Prospective assessment of short- and long-term quality of life after ablation for atrial fibrillation. **Journal of Cardiovascular Electrophysiology***, Vol. 23, February 2012, pp. 121-27*

Editor's comment: The results of the German Heart Center QoL survey confirm the findings of our 2007 Ablation/Maze Survey as per the following excerpt:

Although the main concern of the medical profession when it comes to lone atrial fibrillation is stroke risk, the overwhelming concern of the patient is quality of life. As all afibbers know, being in permanent afib, or awaiting the next episode in a state of anxiety, has a devastating effect on one's quality of life and radically changes the life of those nearest and dearest to us.

Considering quality of life improvement rather than strictly success or failure of RF ablation procedures, it becomes clear that even a failed ablation may improve life quality. The average complete success rate found in this survey (after an average 1.3 procedures) is 54%. Adding to this partial success (where afib is kept at bay with antiarrhythmics) brings the percentage of afibbers whose lives have been improved through RF ablation to 65%. Further, considering that about 70% of ablatees, whose procedure failed, still reduced their afib burden by at least 50%, brings one to the conclusion that RF ablation, whether successful or not, is likely to improve quality of life in close to 90% of those undergoing the procedure. A significant portion of the remaining 10% may, however, see a worsening of their condition, or may experience a serious adverse event.

Palpitations can predict future atrial fibrillation

TROMSOE, NORWAY. A team of researchers from the University of Tromsoe reports the results of an 11-year study aimed at determining major risk factors for the development of atrial fibrillation (AF). The 22,815 participants, for whom the necessary data was available, were part of the Tromsoe Study started in 1974 to determine risk factors for, and incidence of, cardiovascular disease in the municipality of Tromsoe. During the period 1994 to 1995 the all the participants (aged 25 to 96 years) underwent a thorough medical examination and answered a comprehensive questionnaire. One of the questions asked was, have you noticed sudden changes in your heart rate or heart rhythm in the past year? During the mean follow-up of 11.1 years, 361 women (3.0%) and 461 men (4.2%) were diagnosed with AF documented on an electrocardiogram. This corresponds to an incidence rate of 0.27%.year in women and 0.39%/year in men. At the end of the follow-up, further examinations were made to determine if the participants had developed, or still had, coronary artery disease, congestive heart failure, valvular heart disease, and enlarged atria. Participants with AF who were free from heart disease, hypertension and diabetes, and who were under the age of 65 years at the time of AF diagnosis were considered to have lone atrial fibrillation (LAF). Only 49 participants met this rather strict definition, indicating that 6% of the entire AF population of 361 had LAF. Considering the entire study population, only 0.21% developed LAF during the 11-year follow-up.

The main risk factors for developing AF are listed below (percent relative risk increase associated with the indicated risk factor when compared to the group without AF):

Risk Factor	Women	Men
Age	434%	406%
Height	NS	33%
BMI	16%	47%
Total cholesterol[1]	NS	-11%
HDL cholesterol[1]	12%	16%
Hypertension[2]	98%	40%
Palpitations	62%	91%
Diabetes	61%	NS
Coronary heart disease	43%	61%

NS means statistically non-significant

[1] Per one standard deviation increase from average
[2] Hypertension was defined as blood pressure above 140/90, or the use of antihypertensive drugs

The main risk factors for women were thus, advancing age, hypertension, palpitations, diabetes, and coronary artery disease, while for men they were, advancing age, palpitations, coronary artery disease, elevated BMI (body mass index) and hypertension. In the case of LAF, the main risk factors were as follows:

Risk Factor	Women	Men
Age	232%	190%
Height	NS	249%
BMI	NS	213%
Systolic blood pressure	-72%	-79%
Palpitations	274%	NS

Higher systolic blood pressure was associated with a reduced risk of LAF. The researchers have no explanation for this. They noted no association between the development of AF and smoking, low physical activity, coffee consumption, or the use of alcohol. They conclude that age, palpitations, hypertension, coronary artery disease, and elevated BMI are risk factors for AF in both men and women. Apart from aging, elevated body height and BMI were the main risk factors for LAF in men, while palpitations were the main LAF risk factor for women.

Nyrnes, A, et al. Palpitations are predictive of future atrial fibrillation. **European Journal of Preventive Cardiology**, *April 5, 2012 [Epub ahead of print]*

Editor's comment: It is interesting that the strong association between height and risk of LAF was initially reported by Patrick Chambers, MD in his article "Lone Atrial Fibrillation: Pathologic or not?" published in 2007 in *Medical Hypotheses*. Dr. Chamber's article was based on the results of our LAF Survey 11 undertaken in 2007.

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