THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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*Almost 15 years ago Professor Michael D. Ezekowitz, MD of the Veterans Administration made the statement "patients with **lone atrial fibrillation** are not at higher risk for thromboembolism than the general population and can be managed without anticoagulation or anti-platelet therapy". This statement was supported by Rodney Falk, MD of Boston University and by Dr. Stephen L. Kopecky of the Mayo Clinic who in 1987 reported that lone atrial fibrillation patients have an exceptionally low risk of stroke and that this risk varies little whether the fibrillation is paroxysmal or permanent.*

Despite the overwhelming evidence that special stroke prevention measures are unnecessary for lone afibbers with no risk factors for stroke (hypertension, diabetes, congestive heart failure, age over 75 years, and previous stroke/TIA), and no evidence to the contrary, guidelines for the management of AF maintained the recommendation that lone afibbers with no risk factors for stroke should be on aspirin or warfarin for life.

The just-released 2010 European Guidelines for the Management of Atrial Fibrillation finally bring some common sense to this subject with the following two statements:

- *In low-risk patients with no stroke risk factors (essentially lone afibbers below the age of 65 years with a $CHADS_2$ score of 0) no anti-thrombotic therapy is the preferred option.*
- *Patients below the age of 60 years with no evidence of cardiovascular disease (lone afibbers) have a very low risk of stroke estimated at 1.3% over 15 years (cumulative).*

It would seem to me that if the risk of stroke for a 60-year-old lone afibber is 1.3% over the next 15 years, then the risk for a 70-year-old lone afibber must also be exceptionally low.

In summary, lone afibbers with no stroke risk factors are best off avoiding aspirin and warfarin as the risks of taking these drugs on a regular basis outweighs the benefits.

This year-end issue contains a thorough evaluation of these new European guidelines, as well as summaries dealing with factors affecting AF recurrence, AF and quality of life, diabetes and risk of AF, age versus ablation efficacy and risk, and much more.

*If you have not already done so, I encourage you to take a look at my new **AFIB JOURNEYS** section at http://www.afibbers.org/resources/journeys/index.htm. Here you will find the personal stories of afibbers who have dealt with their afib challenges in many different ways – some through successful surgical interventions, others through supplementation or dietary changes – to name just a few. There is a great deal to be learnt from the experiences of your fellow afibbers!*

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

Wishing you good health and lots of NSR,

Hans

Mitral isthmus block and atrial tachycardia

SAN DIEGO, CALIFORNIA. Pulmonary vein isolation (PVI) is now the standard procedure for dealing with paroxysmal and persistent AF. In many cases, a PVI by itself is enough to eliminate AF in paroxysmal patients but in persistent afibbers it is often necessary to include additional lesions in order to achieve success. There are currently two major variants of the PVI procedure.

- **Pulmonary vein antrum isolation (PVAI or Haissaguerre/Natale procedure) –** This procedure involves locating aberrant pathways through electrophysiological mapping (using a multipolar Lasso catheter) and ablating these pathways guided by an ultrasound (ICE) catheter. The ablation is performed as close as possible to the outside edge (antrum) of the junction between the pulmonary veins and the atrial wall. All four pulmonary veins as well as the superior vena cava (if indicated) are isolated during the procedure.

- **Circumferential anatomical pulmonary vein isolation (CAPVI or Pappone procedure) –** 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.

The PVAI yields superior results if performed by an experienced EP, while the CAPVI may enable less experienced EPs to achieve acceptable success rates. However, in order to achieve success with the anatomically-guided procedure in the case of persistent AF, it is necessary to create additional linear lesions in the left atrium. This, in turn, results in a high incidence (up to 30%) of post-procedure symptomatic, sustained atrial tachycardia (AT).

Electrophysiologists at the University of California in San Diego now report that the AT is often due to incomplete mitral isthmus ablation. Their study included 35 paroxysmal and 25 persistent afibbers. Seventy percent of participants had lone AF, 77% were men, and 23% women with an average age of 60 years. All patients underwent a CAPVI using either the CARTO or NavX mapping system, ICE guidance for transseptal puncture, and an 8-mm non-irrigated catheter. Additional left atrial linear lesions were created in the left atrium roof and between the left inferior pulmonary vein and the edge of the mitral valve opening (annulus).

During an average 18 months of follow-up, AT occurred in 25% of the patients. The incidence of AT was 60% in the case of those where complete mitral isthmus block (electrical isolation) had not been demonstrated at completion of the procedure as compared to only 18% (9 patients) among the 50 patients whose mitral isthmus block was documented. Of these 9 patients, 7 underwent a repeat ablation and 2 were able to control the AT with amiodarone or sotalol. Post-procedure electrophysiology studies identified 5 ATs originating from the ridge between the left atrial appendage and the upper left pulmonary vein, 4 originating from the mitral isthmus, and 3 originating from the left atrial roof.

Also during the 18 months of follow-up, 12 patients (20%) had recurrence of AF after a 90-day blanking period. Seven of these underwent a repeat ablation. Complete success rate after an average 1.4 procedures (40% repeat rate) was 85% and partial success rate (sinus rhythm maintained with the help of antiarrhythmic drugs) was 2%.

The authors conclude that failure to achieve bidirectional mitral isthmus block during a CAPVI procedure increases the risk of subsequently developing atrial tachycardia by a factor of 4.
Anousheh, R, et al. Effect of mitral isthmus block on development of atrial tachycardia following ablation for atrial fibrillation. **PACE**, *Vol. 33, April 2010, pp. 460-68*

Editor's comment: This study clearly shows that the circumferential, anatomically-guided PVI procedure is associated with a substantial risk of

post-procedure atrial tachycardia which may need a repeat ablation to fix.

Incidence of late recurrence of AF following PVI

MUNCHEN, GERMANY. Data regarding long-term success for pulmonary vein isolation (PVI) procedures are sparse. Most clinical trials only report success rates for 6 to 12 months post-procedure. A group of German electrophysiologists now reports on the long-term (up to 5 years) AF status of 356 paroxysmal afibbers who underwent a segmental PVI during the period 1998 – 2008.

Early recurrence (after a 90-day blanking period) was observed in 57% of the patients. However, only 6.7% experienced long-term recurrence if they had experienced normal sinus rhythm for a year after the initial PVI. The time to recurrence in this group of 24 patients ranged from 18 to 69 months following the initial PVI. Fourteen of the 24 patients underwent a repeat PVI with 8 patients receiving additional lesions as required. It is interesting that the electrophysiology study performed in the 14 patients showed reconnection between the left atrium and 43 of 48 initially isolated pulmonary veins.

After a further follow-up of 15 months, 71% of the re-ablated patients were in normal sinus rhythm. The authors conclude that very late recurrence (after a year or longer following the initial procedure) is relatively rare and that the success rate of a repeat procedure in this group is high.
Fichtner, S, et al. Very late relapse of atrial fibrillation after pulmonary vein isolation: incidence and results of repeat ablation. **PACE**, *Vol. 33, October 2010, pp. 1258-63*

Editor's comment: The 2009 Ablation/Maze Survey dealt with the long-term recurrence rate of AF episodes following an initially successful PVI procedure. Twenty-seven ablatees did not experience any arrhythmias during the first year following their procedure. At the end of year 4 recurrence rate in this group was 7% - very close to the 6.7% reported by the German group. Thus, it is clear that being arrhythmia-free during the first year post-procedure is an excellent indicator of long-term success. Being arrhythmia-free during the first year is, in turn, almost entirely dependent on the skill and experience of the EP performing the final ablation (p=0.036 in the 2009 Ablation/Maze Survey).

Factors affecting AF recurrence

TRENTO, ITALY. The goal of the GISSI-AF trial was to determine if addition of the angiotensin II-receptor blocker (ARB) valsartan to established medical therapies would reduce the recurrence of AF in patients with cardiovascular disease. The trial enrolled 1442 patients with documented AF and hypertension (85%) and/or coronary artery disease (12%). The average age of the participants was 68 years, 38% were women, 15% had diabetes, and all were in normal sinus rhythm (NSR) at time of enrolment. All patients were provided with a trans-telephonic monitoring device and underwent clinical examination at 2, 4, 8, 24 and 52 weeks following enrolment.

The researchers observed that patients who had experienced 2 or more episodes in the 6-month period prior to enrolment had a 3-fold increased risk of experiencing two or more episodes during the 1-year follow-up. Patients on amiodarone had a significantly lower risk, while those on diuretics had a significantly higher risk of recurrence. Afibbers with a low resting heart rate also had an increased risk of recurrence. There was a trend for aldosterone blockers (spironolactone, eplerenone) to be protective, but none of the other drugs, including class I antiarrhythmics (propafenone, flecainide, disopyramide), beta-blockers, calcium channel blockers, statins, ACE inhibitors, and ARBs had any significant effect on recurrence rate. The authors suggest the following explanations for their findings:

- A low heart rate may reflect parasympathetic (vagal) predominance which, in turn, could be associated with a higher recurrence rate. NOTE: The association with a low heart rate was still significant after adjusting for the use of beta- and calcium channel blockers.
- The use of diuretics can induce hypokalemia (potassium deficiency),

but there was no significant difference in serum potassium levels between patients with recurrence and those without. The researchers suggest that loop diuretics (furosemide – *Lasix*) may stimulate the renin-angiotensin-aldosterone system and subsequent AF recurrence or, alternatively, they may cause alterations in the ionic channel activities of atrial myocytes.

The Italian researchers suggest their finding that diuretic use is associated with an increased risk of AF recurrence may have important clinical implications in view of the widespread use of these drugs in the treatment of AF patients with hypertension and heart failure.

Disertori, M, et al. Clinical predictors of atrial fibrillation recurrence in the GISSI-AF trial. **American Heart Journal**, *Vol. 159, May 2010, pp. 857-63*

Editor's comment: The GISSI-AF study clearly confirms that the use of non-potassium-sparing diuretics [hydrochlorothiazide and furosemide (*Lasix*)] can be detrimental in AF patients treated for hypertension or heart failure. There is no reason to believe that they would not also be detrimental in lone afibbers. Thus, if one needs diuretic treatment it should preferably include a potassium-sparing diuretic such as amiloride or triamterene. NOTE: Serum potassium levels should be closely monitored if supplementation is used in conjunction with potassium-sparing diuretics.

Quality of life and AF

PARIS, FRANCE. There is now ample evidence that patients with symptomatic atrial fibrillation (AF), particularly if paroxysmal (intermittent), experience a broad range of symptoms which adversely affect their quality of life (QoL). A group of French, Belgian and Italian researchers now reports that the QoL of **lone** afibbers can be markedly improved through treatment with controlled-release flecainide acetate (Flec CR).

Their study included 227 patients with symptomatic, paroxysmal AF with an average age of 65 years and 62% being male. Fifty-six percent of the group had ***controlled*** AF, that is, no more than one episode per 6 months prior to enrolment, while the remaining 44% had ***uncontrolled*** AF defined as having experienced two or more symptomatic episodes during the 6 months pre-enrolment. Eighty percent of the patients in the ***controlled*** group were taking regular (non time-release) flecainide at baseline vs. 2% in the ***uncontrolled*** group. A major difference between the two groups was the time since diagnosis which averaged less than one month for 4% in the ***controlled*** group vs. 54% in the ***uncontrolled*** group.

All study participants completed the Medical Outcomes Study 36-Item Short-Form Health Survey (MOS SF-36) at baseline and after 12, 24 and 48 weeks treatment with 100 – 200 mg/day of Flec CR. The MOS SF-36 contains questions concerning:

- Physical functioning
- Role limitations due to physical problems (role physical)
- Bodily pain
- General health
- Vitality
- Role limitations due to emotional problems (role emotional)
- Social functioning
- Mental health

A comparison of scores at baseline showed that ***controlled*** afibbers had a score very similar to that of a matched general population sample except for role emotional and mental health scores which tended to be worse in the controlled group. Baseline scores in the ***uncontrolled*** group, however, were worse in all categories than those for both the reference group and the controlled group. The role physical, role emotional and mental health scores were particularly low in the ***uncontrolled*** group.

After 24 weeks of treatment with Flec CR, the scores in the ***uncontrolled*** group approached those in the ***controlled*** group and by week 48 were essentially equivalent. Thirty-eight percent of patients experienced at least one AF episode during the study period (32.5% in the controlled group vs. 46.9% in the uncontrolled group). However, these episodes were substantially less symptomatic in the ***uncontrolled*** group than those experienced prior to therapy with Flec CR.

Overall, the most frequent symptoms accompanying AF episodes were palpitations (85%), fatigue (31%), breathing problems (21%), and chest pain (12%). Dizziness, weakness and feeling faint were less

common symptoms reported by less than 10% of participants.

The researchers conclude that treatment with controlled-release flecainide acetate improves quality of life scores to the level reported for the general, afib-free population.

Guedon-Moreau, L, et al. Impact of the control of symptomatic paroxysmal atrial fibrillation on health-related quality of life. **Europace**, *Vol. 12, 2010, pp. 634-42*

Editor's comment: This study clearly shows that ***uncontrolled*** AF is associated with a significant deterioration of quality of life and that attainment of a prolonged period of normal sinus rhythm results in a very significant increase in QoL scores.

Diabetes and risk of AF

SEATTLE, WASHINGTON. Diabetes (type 2) is associated with systemic inflammation (high CRP level), left atrial enlargement, obstructive sleep apnea, obesity, and alterations to autonomic nervous system function in the atria. As these conditions are recognized risk factors for atrial fibrillation (AF), it makes sense to ask the question, *Are diabetics at increased risk of developing AF*?

A group of researchers at the University of Washington recently set out to answer this question. Their study involved 1410 patients with newly diagnosed AF and 2203 controls without AF. Type of AF was classified as follows:

- **Transitory** – an episode lasting 7 days or less with no further episodes during the 6 months following diagnosis.
- **Persistent/intermittent** – an episode lasting longer than 7 days or recurring self-terminating episodes during the 6 months following diagnosis.
- **Sustained** – an episode lasting at least 6 months with no evidence of normal sinus rhythm.

The average age of AF patients was 74 years vs. 68 years for controls. Sixty-five percent of AF patients were female vs. 55% in the control group. Hypertension was common in both groups (75%) as was obesity (42%). AF patients were more likely to have heart disease or heart failure than were those in the control group. Of the 1410 cases with AF, 39% had the transitory variety, 45% the persistent/intermittent kind, and 15% sustained.

After adjusting for all potential confounders the researchers conclude that patients with treated diabetes have a 45% increased risk of developing AF when compared to a matched group of non-diabetics. There was no correlation between AF risk and untreated diabetes. The risk increased with years of pharmacologic treatment with patients having undergone treatment for more than 10 years having a 64% increased risk of AF. A higher value for glycosylated hemoglobin (HbA1c), a measure of longer-term glucose exposure, was also associated with increased AF risk. An HbA1c value between 8 and 9 was associated with a 46% increased risk, while a value above 9 was associated with a 96% increased risk.

The authors conclude that treated diabetics who have been on diabetes medications for more than 5 years or have an HbA1c value above 7 are at increased risk for developing AF. They caution that their findings may apply only to obese patients. They also suggest that the reason why untreated diabetics do not have an increased risk of AF is because they are *probably* earlier in the course of the disease or have milder disease.

Dublin, S, et al. Diabetes mellitus, glycemic control, and risk of atrial fibrillation. **Journal of General Internal Medicine**, *Vol. 25, August 2010, pp. 853-58*

Editor's comment: It seems to me the finding that patients undergoing pharmacologic treatment for diabetes have an increased risk of AF could equally well point to the possibility that common diabetes medications increase the risk of developing AF. Particularly in view of the finding that untreated diabetics do not have an increased risk of AF. In any case, the findings of this study are unlikely to be relevant to lone afibbers. An early LAF Survey involving 200 lone afibbers found that only 1% had diabetes, while 25% had hypoglycemia – once again substantiating the conclusion that heart disease-related AF is an entirely different entity than lone AF[1].

[1] Chambers, PW. Lone atrial fibrillation: Pathologic or not? Medical Hypotheses, Vol. 68, No. 2, 2007, pp. 281-87

Age vs. ablation efficacy and risk

LONDON, ONTARIO, CANADA. Current US guidelines for the management of atrial fibrillation (AF) recommend that catheter ablation only be considered after antiarrhythmic therapy has failed. A group of researchers from London Health Sciences and the University of Pennsylvania now suggests that ablation should be considered as first-line therapy in patients younger than 45 years. This suggestion is based on the results of a major study comparing efficacy and complications in various age groups. The study included 1548 consecutive procedures over an 8-year period. The study participants were divided into four groups:

- **Group 1** – 232 patients below the age of 45 years (77% male) undergoing a total of 309 procedures (33% repeat rate)
- **Group 2** – 438 patients between the ages of 45 and 54 years (85% male) undergoing a total of 583 procedures (33% repeat rate)
- **Group 3** – 570 patients between the ages of 55 and 64 years (77% male) undergoing a total of 768 procedures (35% repeat rate)
- **Group 4** – 308 patients age 65 years or older (65% male) undergoing a total of 378 procedures (23% repeat rate).

As expected, members of group 1 were generally healthier than the older members of group 4 and were also more likely to be male (77% vs. 65%) and to have paroxysmal AF (71% vs. 63%). Group 1 members also had a smaller left atrium diameter (4.2 cm vs. 4.5 cm average), a lower $CHADS_2$ score (0.3 vs. 1.1 average), as well as a lower incidence of hypertension (22% vs. 63%), diabetes (3.0% vs. 7.1%), and heart failure (2.2% vs. 9.4%).

All patients underwent an antral pulmonary vein isolation procedure guided by intracardiac echocardiography (Natale protocol) with elimination of non-pulmonary vein triggers as required. Isoproterenol infusions and burst pacing were used to document complete isolation. Patients with a history of right atrial flutter prior to or during the procedure also underwent a cavotricuspid isthmus ablation.

All participants were followed-up through clinical visits and trans-telephonic monitoring. Twenty-eight to 32 months after the last ablation close to 90% of the ablatees had achieved control of their AF as shown below:

	Complete Success(1)	Partial Success(2)	Rare Episodes(3)	Failure
Group 1	76%	7%	4%	13%
Group 2	68%	11%	9%	12%
Group 3	65%	17%	6%	12%
Group 4	53%	23%	6%	18%

(1) no afib, no antiarrhythmics
(2) no afib, but only with the aid of (previously ineffective) antiarrhythmics
(3) 6 or fewer afib episodes during follow-up or a more than 95% reduction in afib burden compared to pre-ablation.

Major complications were defined as stroke/TIA, pulmonary vein stenosis (70% or more), tamponade, atrioesophageal fistula, phrenic nerve injury, retroperitoneal bleeding, and severe anaphylaxis. Other complications included large hematoma, femoral fistula or pseudoaneurysm, asymptomatic stenosis, and deep vein thrombosis. Complication rates were as follows:

	Major	Other
Group 1	0%	0.6%
Group 2	1.7%	2.3%
Group 3	2.0%	2.9%
Group 4	2.6%	4.5%

The only variable affecting success rate was type of AF with persistent afibbers having a 64% greater risk of AF recurrence when compared to paroxysmal afibbers.

The authors point out that most young afibbers would be reluctant to take antiarrhythmics for decades and suggest that catheter ablation should be first-line therapy for afibbers below the age of 45 years as for this age group the outcome is very favorable and complications rare.

In an accompanying editorial, Drs. Hugh Calkins and David Edwards disagree with this conclusion and maintain that antiarrhythmic therapy should be considered first-line treatment in all age groups.

Leong-Sit, P, et al. Efficacy and risk of atrial fibrillation ablation before 45 years of age. **Circulation: Arrhythmia and Electrophysiology**, *Vol. 3, October 2010, pp. 452-57*

Edwards, DN and Calkins, H. Should catheter ablation of atrial fibrillation be a first-line therapy in the young? **Circulation: Arrhythmia and Electrophysiology**, *Vol. 3, October 2010, pp. 425-27*

Editor's comment: The suggestion that catheter ablation should be first-line treatment for afibbers below the age of 45 years is well supported by the data presented in the report. However, there is still no data as to how permanent the effects of a successful ablation are. Is a successfully ablated afibber likely to still be in sinus rhythm 10 years after the procedure? Nobody knows! On the other hand, there is now evidence that antiarrhythmic therapy is less effective than ablation in most cases (52% vs. 77%)[1] and it is also well established that antiarrhythmics, especially amiodarone can have serious long-term adverse effects. Nevertheless, I personally would be reluctant to jump straight to an ablation, even at age 45 years, without having thoroughly explored other options such as those outlined in my 12-step plan. See http://afibbers.org/resources/12stepplan.pdf

The complete success rate for afibbers 65 years or older is clearly inferior to that observed for younger individuals (45 years or younger). However, members of the older group had several disadvantages when compared to the younger group:

- Higher percentage of females (success rates for females are notoriously lower)
- Higher percentage of persistent afibbers
- Higher incidence of hypertension, diabetes and heart failure
- Less use of repeat procedures.

Thus it is quite possible that success rates for older afibbers with paroxysmal AF and without comorbid conditions would be very close to that found for younger individuals if the use of repeat procedures was equal in the two groups.

[1] Calkins, H, et al. Treatment of atrial fibrillation with antiarrhythmic drugs or radiofrequency ablation: two systematic literature reviews and meta-analyses. Circulation: Arrhythmia and Electrophysiology, Vol. 2, 2009, pp. 349-61

NEWS BRIEFS

Canadian Guidelines for the Management of Atrial Fibrillation

The Canadian Cardiovascular Society (CCS) has just released new guidelines for the management of atrial fibrillation. Among the highlights:

- Warfarin or dabigatran should be prescribed for patients with a CHADS2 score of 1 or higher.
- The 150-mg dose of dabigatran is preferred over the 110-mg dose.
- Catheter ablation is recommended for patients "*who remain symptomatic following adequate trials of antiarrhythmic drug therapy and in whom a rhythm-control strategy remains desired*."
- The target of heart rate control should be less than 100 bpm for patients with persistent/permanent atrial fibrillation or atrial flutter.

Interaction between clopidogrel and omeprazole

The FDA has issued a public-health warning about a potentially serious interaction between clopidogrel (Plavix), a popular antiplatelet agent, and omeprazole (Prilosec), an equally popular proton pump inhibitor used to block the production of stomach acid. Apparently omeprazole significantly reduces the ability of clopidogrel to prevent platelet aggregation. Research suggests that pantoprazole (Protonix) or ranitidine (Zantac) may be better alternatives for dealing with gastric problems caused by clopidogrel.

Hiatal hernia increases risk of atrial fibrillation

Researchers at the Mayo Clinic report that the prevalence of AF in men under the age of 55 years with hiatal hernia is 13 times greater than in the age-matched general population. For women (under the age of 55 years) with hiatal hernia, the prevalence of AF was 15 times greater than expected. The lead author of the study, Dr. Komandoor Srivathsan, believes that hiatal hernia acts to cause AF either through the direct mechanical effect of pressing on the left atrium, or through an indirect effect involving activation of the autonomic nervous system or inflammation. He also points out that having both AF and hiatal hernia is a strong predictor of congestive heart failure.

Atrial fibrillation epidemic in Australia

A research team led by Professor Prash Sanders of the University of Adelaide reports that hospital admissions due to AF has more than tripled in Australia over a 15-year period. Says Professor Sanders, "*This study highlights the enormous public health burden of atrial fibrillation on hospitals and the need for not only better treatments for this increasingly common condition, but also preventative strategies to stop it occurring in the first place.*"

Vernakalant study suspended

The FDA has asked the cosponsors of the ACT-5 trial of vernakalant to suspend enrolment in the study. The request was prompted by an AF patient going into cardiac arrest after being given the drug. Vernakalant is approved in the European Union for the rapid conversion of recent-onset AF to sinus rhythm. The drug works by blocking early-activating potassium (K+) channels and frequency-dependent sodium (Na+) channels.

REVIEW

European Guidelines for the Management of Atrial Fibrillation

The European Society of Cardiology (ESC) and the European Heart Rhythm Association (EHRA) have just released their very extensive (60 pages with 200 references) 2010 guidelines for the management of atrial fibrillation. Cardiologists and electrophysiologists from 14 European countries were involved in this very major project. It is estimated that over 6 million Europeans now suffer from atrial fibrillation (AF), the most common cardiac arrhythmia seen in clinical practice. Its "true" prevalence is estimated at 2% and this number is expected to double in the next 50 years. The lifetime risk of developing AF is about 25% in those who have reached the age of 40 years.

Most AF patients are symptomatic, but about one-third are not aware of their arrhythmia (asymptomatic or silent AF). In most patients AF progresses from short, rare paroxysmal episodes to longer and more frequent episodes, and then to persistent and permanent associated with further development of the disease underlying the arrhythmia. The majority of AF cases involve such comorbidities as hypertension, heart failure, valvular heart disease, cardiomyopathy, congenital heart defects, coronary heart disease, thyroid dysfunction, obesity, diabetes, sleep apnea, chronic kidney disease, and chronic obstructive pulmonary disease (COPD). Aging increases the risk of AF primarily because of the increased risk of developing cardiovascular and other disease late in life.

Following are highlights from the guidelines. Please note that the **focus is on AF with underlying heart disease** and other comorbidities. Thus observations and recommendation **may or may not apply to "lone" or "idiopathic" atrial fibrillation (LAF)**.

Types and Severity of AF

First diagnosed – Every patient who presents with AF for the first time falls in this category irrespective of how long he or she has actually had AF.

Paroxysmal – Self-terminating in less than 7 days, most often in less than 48 hours.

Persistent – Lasts longer than 7 days or requires termination by cardioversion.

Long-standing persistent – Persistent AF having lasted longer than one year before a rhythm control strategy is attempted.

Permanent – Is said to exist when the permanent presence of the arrhythmia is accepted by patient and physician and no attempts are made to control rhythm.

The severity of AF is classified as follows:

- EHRA I – No symptoms
- EHRA II – Mild symptoms; normal daily activity not affected
- EHRA III – Severe symptoms; normal daily activity affected
- EHRA IV – Disabling symptoms; normal daily activity discontinued

The authors note that, "*It is also appropriate to inform the patient with lone or idiopathic AF about the good prognosis, once cardiovascular disease has been excluded*".

Management of AF

Management of AF patients is aimed at reducing symptoms and preventing complications, especially ischemic stroke.

A. Stroke Prevention

The main risk factors for stroke are:

- Prior stroke or transient ischemic attack (TIA)
- Hypertension
- Diabetes
- Structural heart disease
- Left ventricular systolic dysfunction (low ejection fraction)
- Age

- Type of AF (paroxysmal, persistent, permanent) does not influence the risk score and the need for stroke protection.
- Patients below the age of 60 years with no evidence of cardiovascular disease (lone afibbers) have a very low risk of stroke estimated at 1.3% over 15 years (cumulative).
- Stroke risk starts to rise after age 65 years and as patients get older stroke prevention therapy with antiplatelet agents (aspirin) becomes much less effective while the effectiveness of oral anticoagulation does not change.
- Uncontrolled hypertension increases stroke risk; however, there is evidence that well-controlled blood pressure is associated with a low risk of stroke and thromboembolism.
- Kidney disease affects stroke risk with a glomerular filtration rate less than 45 mL/min being associated with a 50% increase in stroke risk.
- The $CHADS_2$ stroke risk score is a convenient way of estimating stroke risk in AF patients. A score of 1 is assigned to hypertension, congestive heart failure, diabetes, vascular disease, age 65 to 74 years, and female sex, whereas age of 75 years or older and having suffered a previous stroke or TIA warrants a 2 score.
- The evidence that aspirin protects against ischemic stroke is sparse indeed and for lone afibbers the daily ritual of an aspirin may actually be detrimental. In the Japan Atrial Fibrillation Stroke Trial, **patients with lone AF** were randomized to an aspirin group (aspirin at 150 – 200 mg/day) or a control group without antiplatelet or anticoagulation therapy. The incidence of stroke, TIA and cardiovascular death was 3.1%/year in the aspirin group vs. 2.4% in the control group. The incidence of major bleeding also tended to be higher in the aspirin group (1.6%) than in the control group (0.4%).

- In low-risk patients with no stroke risk factors (essentially lone afibbers below the age of 65 years with a $CHADS_2$ score of 0) no anti-thrombotic therapy is the preferred option. For AF patients with a score of 1 oral anticoagulation (warfarin) or aspirin (75 – 100 mg/daily) may be used with oral anticoagulation being preferred. Aspirin may be preferable in women below the age of 65 years with a $CHADS_2$ score of 1 solely due to their gender. Recommendations for AF also apply to patients with atrial flutter.
- The HAS-BLED score evaluates the risk of bleeding associated with antithrombotic therapy. A score of 1 is assigned for hypertension, previous stroke, previous bleeding, variable INR, age 65 years or older, abnormal kidney function, abnormal liver function, alcohol abuse, and use of aspirin or NSAIDs. A total score of 3 or higher indicates the need for caution in the initiation and follow-up of antithrombotic therapy.
- The recommended INR range for adequate stroke protection is 2.0 – 3.0. Many "real life" studies reveal that patients on warfarin are within this range less than 50% of the time, thus vastly overestimating the benefits of warfarin observed in tightly-controlled clinical trials.
- Self-monitoring of INR may be considered for patients who are physically and cognitively capable of performing the test.
- Cardioversion is associated with an increased risk of stroke. If an episode has lasted longer than 48 hours, 3 weeks of anticoagulation is required prior to cardioversion followed by 4 weeks after cardioversion. The 3-week pre-cardioversion period may be omitted or shortened if a TEE (transesophageal echocardiogram) shows no evidence of thrombi (clots) in the left atrium or left atrial appendage.

B. Acute Rhythm and Rate Control

Although most paroxysmal afibbers convert to normal sinus rhythm (NSR) on their own within 24 – 48 hours, it is sometimes necessary to visit the emergency department to achieve NSR or at least bring the ventricular (pulse) rate down to a tolerable 80 to 100 bpm. Conversion to NSR can be achieved in two ways – pharmacological conversion and electrical cardioversion.

Pharmacological conversion
This is achieved by injection of an antiarrhythmic drug. Flecainide and propafenone are the most effective, but are not recommended for patients with underlying heart disease and abnormal left ventricular function. Ibutilide (Corvert) is effective for both atrial flutter and AF with conversion rates of 50% within 90 minutes. However, it can cause torsades de pointes and a significant increase in QT interval. Conversion with amiodarone occurs several hours later than with flecainide and propafenone with a conversion rate of 80 to 90% at 24 hours. Sotalol, verapamil, metoprolol and digoxin are not useful for pharmacological conversion, but metoprolol and verapamil are effective in slowing the heart rate.

It is also possible to use propafenone and flecainide orally to convert to NSR. In one trial AF terminated in 45% of patients given propafenone within 3 hours as compared to 18% among those given a placebo. Flecainide has a similar effect. Both propafenone (450 – 600 mg) and flecainide (200 – 300 mg) can be used on-demand (pill-in-the-pocket) approach by patients experiencing episodes monthly or less frequently. Both drugs should be taken as soon as possible after the onset of an episode.

Electrical cardioversion
A detailed discussion of electrical cardioversion can be found at www.afibbers.org/resources/cardioversion.pdf. The procedure is associated with a 1 to 2% risk of thromboembolism and ventricular tachycardia and fibrillation may occur in patients on digoxin or those deficient in potassium. Pre-treatment with amiodarone, ibutilide, flecainide, propafenone and sotalol increases the likelihood of successful cardioversion.

C. Long-term management

The long-term management of AF may involve rate control, rhythm control, or a combination of both. In ***rate control*** the patient is prescribed beta-blockers or calcium channel blockers (verapamil or diltiazem) with the goal of maintaining a ventricular rate below 100 bpm, but no attempt is made to convert the patient to NSR. In ***rhythm control*** the patient is treated with an antiarrhythmic drug (amiodarone, flecainide, propafenone, disopyramide, dronedarone or sotalol) with or without the use of rate control drugs.

The commonly held view is that there is no difference in stroke rate, overall mortality and quality of life between rate and rhythm control. This conclusion is mainly based on the results of the AFFIRM trial which, in my opinion, was seriously flawed and not applicable to lone afibbers. The AFFIRM trial involved 4060 patients with persistent AF and a mean age of 70 years. Seventy-one per cent had a history of hypertension, 38% had coronary artery disease, and 26% had impaired left ventricular function. Only 12% had lone AF. Half the patients were randomized to rate control plus anticoagulation, while the other half was randomized to rhythm control plus anticoagulation. After 5 years of follow-up 21.3% of the patients in the rate control group had died as compared to 23.8% in the rhythm control group.

So how do these findings affect lone afibbers, particularly paroxysmal ones? To quote the authors of the study, "*the results probably cannot be generalized to younger patients without risk factors for stroke (i.e. patients with primary, or "lone" atrial fibrillation), particularly those with paroxysmal atrial fibrillation*."

Quite apart from the fact that the study is not particularly applicable to lone afibbers, I believe it has several serious flaws:

- The most "popular" drug used in the trial was digoxin. Over 70% of the people in the rate control group had used this drug at one time or another. Digoxin had been used by 54% of the participants in the rhythm control group as well. So as far as digoxin use is concerned, there was little difference between the two groups.
- Beta-blockers were used liberally in both groups as well – 68% in the rate control group and 50% in the rhythm control group.
- The main antiarrhythmic used was amiodarone (Cordarone). This drug was used by 63% of the patients in the rhythm control group and by 10% in the rate control group.
- The second most popular "antiarrhythmic" used in the rhythm control group was sotalol (Betapace) – this drug was used by 41% of patients despite the fact that it is well known that it does little, if anything, to maintain sinus rhythm, although it may help control the heart rate during an afib episode.
- Propafenone, flecainide and disopyramide had been used by only 4-15% of patients in the rhythm control group. It is impossible to say whether any of these drugs were beneficial or detrimental because of the way the data is reported.

The significant overlap in drug use between the two groups (especially in regards to digoxin) and the low usage of Class I antiarrhythmics do, in my opinion, significantly detract from the value of the AFFIRM study, particularly in the case of lone afibbers.

The authors of the new European guidelines seem to agree that rhythm control is preferable to rate control when it comes to quality of life. They state, "*quality of life is significantly impaired in patients with AF compared with healthy controls, and post-hoc analyses suggest that maintenance of sinus rhythm may improve quality of life and be associated with improved survival."*

Other observations

- Amiodarone should only be used in patients who have failed treatment with other antiarrhythmic drugs or have significant structural heart disease. It should not be used in patients with permanent AF.

- In patients with no or minimal heart disease, beta-blockers represent a logical first attempt to prevent recurrent AF when the arrhythmia is clearly related to mental or physical stress (adrenergic AF). Since beta-blockers are not very effective in many other patients with lone AF, flecainide, propafenone, sotalol, or dronedarone is usually prescribed. Disopyramide, which has marked anticholinergic effects, may be useful in vagally mediated AF.

- Patients with coronary artery disease should not receive flecainide or propafenone. Dronedarone or sotalol should be administered as first-line therapy with amiodarone being the drug of last resort. Sotalol prolongs QT interval, may induce torsades de pointes and should not be used in patients with heart failure or left ventricular hypertrophy.

Left Atrial Catheter Ablation

Catheter ablation is now an accepted alternative to therapy with antiarrhythmics and rate control drugs, but should be reserved for patients who remain symptomatic despite optimal medical therapy. The authors of the guidelines make the following observations:

- Operator experience is an important consideration when contemplating ablation as a treatment option.
- Since amiodarone treatment may be associated with serious and frequent adverse effects, especially during long-term treatment, it is reasonable to consider catheter ablation as an alternative to amiodarone treatment in younger patients.
- Patients with heart failure benefit from ablation as it results in improved ejection fraction and exercise tolerance.
- Ablation of complex fractionated atrial electrograms on its own (without isolation of the pulmonary veins) is not effective in eliminating paroxysmal AF.
- Catheter ablation for AF should include a right atrial flutter ablation if there is any evidence of flutter prior to or during the primary ablation procedure.
- A recent meta-analysis found a 77% average success rate for catheter ablation vs. 52% for medical therapy.

Prevention of AF

Upstream therapy to prevent or delay myocardial remodeling associated with inflammation, hypertension and heart failure may help prevent the development of AF or, once established, may reduce its rate of recurrence or progression to permanent AF.

- Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) may help prevent inflammation and resulting fibrosis, and have been found effective in patients with hypertension and congestive heart failure.
- Patients with primary hyperaldosteronism have a 12-fold increased risk of developing AF. Several trials to evaluate the effects of spironolactone and eplerenone in this patient group and in afibbers with hypertension are underway.
- There is no compelling evidence that statin drugs are effective in preventing the development or recurrence of AF except in the case of AF associated with bypass surgery.
- There is no robust evidence to make any recommendation regarding the possible benefits of fish oil (eicosapentaenoic acid and docosahexaenoic acid) in preventing the establishment and recurrence of AF.
- There is increasing evidence that AF is 2 to 10 times more prevalent in active or former competitive athletes and those performing intense recreational endurance sports.
- Atrial fibrillation is often associated with hyperthyroidism and may disappear if normal thyroid function is attained.

Conclusion

Although the new European guidelines for the management of atrial fibrillation are primarily aimed at afibbers with underlying heart disease, they do contain points of specific interest to lone afibbers.

- Patients below the age of 60 years with no evidence of cardiovascular disease (lone afibbers) have a very low risk of stroke estimated at 1.3% over 15 years (cumulative).

- Uncontrolled hypertension increases stroke risk; however, there is evidence that well-controlled blood pressure is associated with a low risk of stroke and thromboembolism.

- The evidence that aspirin protects against ischemic stroke is sparse indeed and for lone afibbers the daily ritual of an aspirin may actually be detrimental. In the Japan Atrial Fibrillation Stroke Trial, **patients with lone AF** were randomized to an aspirin group (aspirin at 150 – 200 mg/day) or a control group without antiplatelet or anticoagulation therapy. The incidence of stroke, TIA and cardiovascular death was 3.1%/year in the aspirin group vs. 2.4% in the control group. The incidence of major bleeding also tended to be higher in the aspirin group (1.6%) than in the control group (0.4%).

- In low-risk patients with no stroke risk factors (essentially lone afibbers below the age of 65 years with a $CHADS_2$ score of 0) no anti-thrombotic therapy is the preferred option.

- For AF patients with a score of 1 oral anticoagulation (warfarin) or aspirin (75 – 100 mg/daily) may be used with oral anticoagulation being preferred. Aspirin may be preferable in women below the age of 65 years with a $CHADS_2$ score of 1 solely due to their gender. Recommendations for AF also apply to patients with atrial flutter.

- In patients with no or minimal heart disease, beta-blockers represent a logical first attempt to prevent recurrent AF when the arrhythmia is clearly related to mental or physical stress (adrenergic AF). Since beta-blockers are not very effective in many other patients with lone AF, flecainide, propafenone, sotalol, or dronedarone is usually prescribed. Disopyramide, which has marked anticholinergic effects, may be useful in vagally mediated AF.

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