THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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Editorial

We have completed phases I and II of the LAF survey. Phase I involved getting the replies back on the questionnaire. We have now received 50 completed questionnaires – thanks for your effort!

Phase II dealt with the rather substantial task of inputting all the collected information into our computer so that we could analyze it.

Phase III, which we begin today, is aimed at reviewing and analyzing the results and getting them back to you.

Phase IV, by far the most complex one, involves analyzing the data using a sophisticated neural network program that will enable us to pick up correlations. For example, do afibbers who take antiarrhythmics have fewer or shorter episodes than afibbers who do not take anything? Do episodes get more frequent with age or the number of years you have had LAF, etc.

So here are the first results of the survey. Stay tuned for more!

Yours in health,
Hans Larsen

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Survey Results – Part I

A total of 50 afibbers completed the survey. Of these 40 were men over the age of 30 years, 3 were men younger than 30 years, and 7 were women. The average age of the whole group was 54 years (range 18-82 years). The average age of the older men was 54 years with 83% of this group being between the ages of 45 and 65 years. The average age of the younger men was 25 years, and the average age of the women was 64 years. Overall 62% of all respondents were between the ages of 45 and 65 years.

The members of our afib group tended to be tall with an average height of 6 feet (183 cm) for the older men, 6 ft. 2 in. (187 cm) for the younger men, and 5 ft. 6 in. (168 cm) for the women. Weight tended to be within normal ranges with an average weight among men of 185 lbs (84 kg) and among women of 150 lbs (69 kg). The average weight for women decreased to 138 lbs (63 kg) when one overweight woman was excluded.

Body mass index (BMI) averaged out at 25 (25 for older men and 24 for both women and younger men). However, there were still a significant number of overweight men in the over 40-age group. Fifty per cent had a body mass index over

25 and 3 or 7.5% had a BMI over 30 thus being classified as obese. In comparison, a recent survey of over 17,000 US army personnel concluded that 54% of these young (75% under the age of 35) supposedly fit people were overweight and 6.2% were obese(1).

The questionnaire respondents are a highly educated group and include 3 MDs, 3 PhDs, 12 people with master's degrees, 13 with bachelor's degrees and 13 with a college degree or at least some college education. In other words, 88% has at least a college education.

The largest percentage (28%) of respondents is retired. This group is closely followed by engineers/scientists at 24%, people involved in business at 22%, lawyers at 8% and MDs at 4%. Perhaps the most interesting conclusion is that 98% of all respondents are, or before retirement were, involved in brainwork.

Interesting observations, but not really conclusive. These demographic data may characterize a group prone to afib, but then again, they may also characterize a group with ready access to the Internet who is motivated to find a solution to their health problems.

Question 9 (dominant personality) is an interesting one. It is obvious that a fair amount of soul-searching took place before answering this one – and even so, the spouse's opinion often carried the day! About 74% of all respondents described themselves as aggressive (tense, up-tight) or ambitious (competitive, tenacious). About 28% (33% among the men over 40) described themselves as being easily upset (sensitive) and 32% as being laid-back (easy-going, calm). Another 14% saw themselves as workaholics (driven, hard working) and 12% were energetic (enthusiastic, restless). Twelve per cent felt one of their main characteristics was that they were friendly, caring, people persons.

So it is certainly not obvious that afibbers are characterized by one particular personality trait. While 74% say they are aggressive or ambitious, 60% are laid-back and easily upset. Please note that many respondents listed more than one trait so the percentages do not add up to 100. Assigning respondents to personality types indicate that 41% are type A (aggressive, ambitious), 22% are type B (calm, laid-back) with the remaining 37% being a mixture of the two types.

Question 10 concerned smoking. Over 50% (54%) of all respondents had never smoked; 34% were former smokers and 12% were occasional smokers at this time. So LAF cannot be blamed on the weed!

Most respondents, 74% to be exact, had received a diagnosis of paroxysmal (intermittent) lone atrial fibrillation. Ten per cent had chronic LAF and the remaining 16% had been diagnosed with LAF, but had some additional risk factors, most commonly high blood pressure.

The average number of years that respondents had suffered from LAF was 8. However, the range was wide. Among older men the range was 1 to 40 years, among younger men 1 to 14 years, and among women 2 to 64 years. Leaving out one woman who had had LAF from childhood (64 years) the range for women changes to 2 to 13 years and the average to 5 years. I guess this data shows that one can live a long time with LAF and, unless we come up with a viable solution, we just may have to!

In the next report we will continue with question 14 – "What triggered the first episode?"

Pharmacological Treatment of LAF

The treatment of atrial fibrillation has two goals – the prevention and the termination of episodes. As pointed out previously (The Afib Report – March 2001) there are no drugs specifically developed for the prevention of LAF. All antiarrhythmic drugs available today were developed for the treatment of arrhythmias arising form cardiovascular disease, heart episodes, and heart surgery. The second fact to remember is that ALL arrhythmias connected with heart disease are adrenergic in nature. As a consequence, there is very little research on the use of antiarrhythmics in the management of vagally mediated LAF.

Prevention of Vagal LAF

The fact that most antiarrhythmics are specifically designed to deal with an excessive adrenergic reaction makes their use somewhat problematical in the prevention of vagally mediated LAF. For example, beta-blockers (atenolol, propranolol, metropolol), which work directly to dampen adrenergic response, are definitely contraindicated for vagal origin LAF(2,3,4). The same goes for digoxin (Lanoxin, digitalis), which actually enhances vagal tone(5). Numerous medical experts have warned against the use of digoxin for vagal LAF and indeed more recently against the use of digoxin for any kind of LAF(2-8). Digoxin tends to increase the number of episodes and causes the condition to become chronic.

Some antiarrhythmics also have beta-blocking properties. Among them, propafenone (Rythmol), amiodarone (Cordarone) and sotalol (Sotacor). So where does this leave us? The optimum would clearly be to use a drug that reduced vagal activity and did not increase adrenergic activity. Among such drugs are quinidine (BiQuin), disopyramide (Rythmodan), procainamide, and flecainide (Tambocor). Quinidine, disopyramide and procainamide all have quite serious side effects and do not seem to be used much for LAF. This leaves flecainide. Is flecainide a good choice for preventing LAF of vagal origin?

Flecainide is highly effective in terminating a LAF episode (of any origin), but this does not mean that it also is effective in preventing episodes. It and many other antiarrhythmics are most effective when the heart is beating fast, that is, when the ion channels in the heart muscle cells are opening and closing rapidly. So it stands to reason that these drugs may not be that effective until the heart actually is beating faster, i.e. is in fibrillation.

Some very preliminary observations from the LAF survey bear this out. I compared a group of vagal afibbers with no other health problems who were not taking antiarrhythmics with a similar group who took flecainide. The groups were small (7 and 6 respondents respectively) and I have not yet corrected for confounding variables. Nevertheless, there was a clear indication that afibbers who do not take preventive drugs have fewer, but significantly longer episodes than do afibbers taking flecainide. In other words, it seems that flecainide may not prevent the initiation of an episode, but does indeed significantly shorten it.

So, if no flecainide means fewer episodes and taking flecainide means shorter episodes, the optimum approach may well be to just take the flecainide when you have an episode. This approach would eliminate the long-term side effects of taking the drug continuously and appears to be safe provided you have no underlying heart problems.

Conversion of Vagal LAF

Once a fibrillation episode has taken hold it ceases to be an autonomic nervous system problem and becomes a heart problem. More specifically, it becomes a problem of an excessive influx of sodium ions and, to a lesser extent, calcium ions into individual heart muscle cells. This, coupled with the suppression of a compensating backflow of potassium and magnesium, is what sets up the rapid, erratic heartbeat unrelieved by periods of rest. The nervous system is essentially shut out of the loop at this stage and maneuvers and drugs or other potions that may help to prevent or abort a LAF episode are now of little use.

Conversion to sinus rhythm can be accomplished in two ways – through a shock or through the action of specific drugs. In a clinical setting the shock is delivered through an electrical current applied to the chest area (cardioversion). Cardioversion is useful in some types of arrhythmia, but LAF unfortunately is not one of them. While it may work in some cases its effect in the case of LAF seems to be relatively short-lived. Static electricity shocks, driving into a pothole or sneezing violently have also been known to stop episodes.

The most effective drugs for conversion to normal sinus rhythm are dofetilide and flecainide. Dofetilide (Tikosyn) is still relatively new and should only be applied in a hospital setting due to the need for very precise dosing and monitoring for potential side effects. Flecainide can certainly also have serious side effects, but considerably more experience in its use is available. Clinical trials have shown that flecainide (2 mg/kg body weight) converts 70-80% of all atrial fibrillation episodes within 8 hours(9,10).

A recent clinical trial found that intravenous flecainide acted quicker than oral flecainide, but at 2 hours and 8 hours after treatment there was no difference in the percentage of patients converted by the two

approaches(10). There is some evidence that it may be important to take converting drugs as quickly as possible after an episode has started. One recent trial of propafenone found that application 24 hours after an episode had started had no beneficial effect at all(11).

A team of German and Italian researchers found that oral doses of approximately 200 mg (3 mg/kg) of flecainide can be safely and effectively used at home to stop episodes of paroxysmal supraventricular tachycardia (a condition somewhat similar to LAF). They observed an 80% success rate within 2 hours, but emphasize that the flecainide tablet should be taken in crushed form within 5 minutes of the start of the episode(12).

So the bottom line is, if you have vagally mediated LAF and are now taking flecainide on a continuous basis, ask your doctor if you could try taking it just when you have an episode. And don't forget to let us all know how it goes!

Of course, if you are not taking any drugs, but are getting to the point where you feel you need something, the best thing to try may be flecainide when you have an episode. Again, be warned though, flecainide is a dangerous drug and is specifically contraindicated for chronic LAF. The first time you try it should be in the hospital, emergency clinic or in your cardiologist's office.

Stay tuned! In our next report we will discuss alternative treatments for vagally mediated LAF.

The Glucose Connection

In an earlier LAF survey report we reported that not one of the 45 respondents who had returned their questionnaire has diabetes (high blood sugar). Now with 50 responses in hand we can state that this is still the case. On the other hand, 22% of all respondents have hypoglycemia (low blood sugar) and an additional 24% report definite symptoms of hypoglycemia. Is this unusual and is it perhaps a clue? Maybe!

It is certainly well established that hypoglycemia can cause palpitations and LAF. I have a hunch, and that's all it is at this time, that many afibbers (LAF in particular) may have either hypoglycemia or a blunted glucose response, i.e. their blood glucose levels are generally low and do not rise very much after eating.

Clinical trials carried out at the University of Illinois during the late 40s and early 50s established the existence of the so-called "flat" glucose tolerance curve in patients suffering from fatigue. These patients had slightly lower than normal fasting glucose levels, but the key difference was that their blood glucose level rose by an average of only 28% one-half hour after ingesting sugar. In contrast, the glucose level of the controls rose by about 73%. Also, after one hour the glucose levels of the controls were still 32% higher than fasting levels while the fatigue patients' levels were only 4% higher. The researchers concluded that flat curves are associated with excessive vagal (parasympathetic) stimulation(13). A more recent study carried out at the University of Montreal showed that a majority (83%) of patients with suspected postprandial hypoglycemia had average glucose levels of 4.3 mmol/liter (76 mg/dL) at the time of their symptoms(14).

So what does this mean? It means that a flat glucose curve is associated with an overactive vagal system and that symptoms of postprandial hypoglycemia can appear at much higher glucose levels than previously thought – and furthermore, that the level at which symptoms occur is highly individual.

Assuming then, as the survey shows, that most afibbers use their brain a lot coupled with the fact that the brain requires at least 20% of the body's energy supply (in the form of glucose), it is conceivable that afibbers could have a problem with low glucose levels or a flat glucose response curve. If the brain runs short of glucose it causes the release of epinephrine and norepinephrine in order to send a message to the liver to release more glucose. If these norepinephrine releases become more frequent than normal (because of generally low blood glucose levels and the constant need to keep the brain supplied with glucose) then it is perhaps possible that an autonomic system dysfunction could develop over the long run involving both the adrenergic and vagal branches. Could this eventually lead to LAF? Maybe!

So far, I have received just 2 sets of glucose levels from afibbers. Fasting glucose levels of 4.5 mmol/L (80 mg/dL) and 4.8 mmol/L (86 mg/dL) respectively, a 71% and 33% increase half an hour after breakfast and a remaining 62% and 27% increase after one hour respectively. So one result is fairly normal, the other indicates a flat curve.

We obviously need more results to check out the glucose angle so if you have your fasting glucose level and a level half an hour and an hour after breakfast please let me know.

This whole idea is clearly just a hypothesis, but if there is something to it would mean that we could perhaps move LAF, at least partially, out of the realm of heart problems and into endocrine or neurological disorders. The solutions might then be a lot simpler and safer!

AFIB News

The heart remembers. Dr. Michael Rosen, MD of Columbia University is convinced that the heart has a memory. He has studied ECGs (electrocardiograms) of both normal beating hearts and hearts in arrhythmia. He observed that the "T" wave on the ECGs is changed markedly in arrhythmia and that the change is evident as much as 28 days after converting to normal sinus rhythm. T waves are a measure of the balance between inward and outward ion currents in ventricular heart cells. Dr. Rosen's findings could explain why many afibbers have great difficulty in reaching the magic number of 30 days free of fibrillation and also why it seems easier to stay in sinus rhythm once one has been episode-free for a month or more.
The Lancet, February 10, 2001, pp. 468-71

Vitamin C affects the heart directly. Researchers at the Boston University Medical Center have found that infusion of vitamin C increases the action of dobutamide (a drug used to increase the heart rate in congestive heart failure patients). This could mean that antioxidants such as vitamin C directly affect the activity of the adrenergic (sympathetic) nervous system – probably increasing adrenergic activity. Other research (animal) has shown that the antioxidant n-acetylcysteine (NAC) definitely increases sympathetic activity.
Circulation, Vol. 103, February 13, 2001, pp. 782-83, 826-30

Amiodarone should be taken with meals. Amiodarone (Cordarone) is a class III antiarrhythmic drug used in the treatment of ventricular tachycardia and fibrillation. Due to its serious side effects it is not generally recommended for LAF patients. Researchers at the Philadelphia School of Pharmacy now report that amiodarone is much better absorbed if taken with meals. Their clinical trial involving 30 healthy male subjects found that it was absorbed 40% quicker when taken with a meal (maximum concentration reached in 4.5 hours versus 7.1 hours when taken without food). They also observed that the total absorption after ingestion of a 600 mg dose was 2.4 times higher when taken with a meal. The researchers recommend that amiodarone be taken consistently with meals.
American Journal of Cardiology, Vol. 87, February 15, 2001, pp. 432-35

Tarantulas to the rescue. Researchers at Georgetown University have isolated a polypeptide GsMtx-4 from tarantula venom. Experiments have shown that GsMtx-4 completely eliminates fibrillation in rabbit hearts. Says the researchers, "We believe that GsMtx-4 could be the first of a new class of antiarrhythmic agents to be directed against the causes rather than the symptoms of fibrillation."
Nature, January 4, 2001, p. 35

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