THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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I receive numerous messages every month, some describing personal experiences, others asking questions about various aspects of LAF. I believe many of these communications are of interest to readers of The AFIB Report, so beginning with this issue we will feature a new section "Letters to the Editor".

The evaluation of the results of the 5th LAF survey is continuing and in this issue we discuss the findings regarding episode severity as measured by frequency, duration and intensity. I have also taken a second look at my conclusion that taking preventive drugs during the first year of LAF may be detrimental. Additional data support the suggestion that preventive drugs, particularly beta-blockers, digoxin and sotalol may well increase episode frequency and should not be started without evidence that episodes are abnormally frequent or intolerable.

Finally, the third and final installment of Patrick Chambers' review of the importance of magnesium and potassium.

Just a reminder - if you haven't already done so, don't forget to get your copy of my recent book "Lone Atrial Fibrillation: Towards A Cure" at www.afibbers.org/lafbook.htm - it provides a wealth of information on dealing with LAF.

Enjoy!

Wishing you lots of sinus rhythm,
Hans Larsen

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LETTERS TO THE EDITOR

On re-reading some of the back issues of The AFIB Report I came across an afibber mentioning that an episode of AF is accompanied with the "big pee syndrome". I could not find any further reference to this. Is there a connection of any urinary problems with AF? I have developed such a condition that this so aptly describes and which I am about to have investigated.

GC, AUSTRALIA

Editor: *About 64% of all afibbers experience frequent urination in the early stage of an afib episode. This is caused by the release of a diuretic hormone, ANP (atrial natriuretic peptide) from the walls of the heart when it is beating "violently". The phenomenon has nothing whatsoever to do with urinary system problems.*

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The other day I was in afib and atrial flutter for hours. Having read your book, I decided to stay at home and sit it out. Yippee! I reverted on my own – no drips, extra medication or cardioversion!! Soon I may consider giving up medication and taking flecainide only when in afib. I only go into afib in the

early hours of the morning whilst sleeping. I am a vagal afibber. Thanks for your excellent book. At least I feel more in control of this annoying disorder.

MR, NZ

Editor: *Thank you very much for sharing your experience with your latest afib episode. Most "veteran" afibbers do indeed just stay home during an episode and wait it out. The fact that you also have atrial flutter though may complicate things as far as the on-demand flecainide approach is concerned. Flecainide (and propafenone) can, in some cases, convert a tolerable 2:1 or 4:1 atrial flutter transfer ratio to 1:1 meaning that the ventricular rate equals the atrial rate, which can reach 300 bpm or more (see page 26 of my book). This is very uncomfortable and dangerous. So if your episodes are relatively short (24 hours or less) and your heart rate is 100 bpm or less, you may be better off just taking verapamil or Cardizem to slow the heart rate whilst you wait it out. Anyway, in your case I would very definitely consult with a competent cardiologist before making any medication changes.*

Evaluation of Survey Results

Number of Episodes During First Year – Revisited

In the May issue I concluded that afibbers who took preventive drugs (antiarrhythmics or beta-blockers) during their first year of afib had significantly more episodes (median = 6) than did those who did not take drugs (median = 2). From this response I further concluded that taking these drugs during the first year is detrimental. I surmised that this could well be because the first choice in drugs is often digoxin, sotalol or beta-blockers. All are directly detrimental to vagal afibbers and of dubious value to mixed and adrenergic afibbers.

Several afibbers pointed out that the data could also be interpreted to mean that afibbers with frequent episodes are more likely to be prescribed drugs. Of course, this is correct. In order to attempt to settle the question of the effect of drugs during the first year I sent another questionnaire to the 72 afibbers who had indicated that they had taken drugs during their first year of afib. The questions were:

1) Did you start therapy with antiarrhythmics, beta-blockers or digoxin immediately after your first or second episode or did you only begin therapy after it became clear that you had an abnormally high frequency of episodes?
2) Which drug(s) did you take during your first year?

Thirty-seven (51%) of the 72 original respondents answered the second questionnaire. There was no statistically significant difference between the number of episodes experienced in the two groups within the first year. Thus the responses from the second group can be considered representative of the whole group.

An evaluation of the results of the second questionnaire produced the following results:

- 87% of all respondents were prescribed drugs after their first or second episode; in other words, they were not prescribed drugs because it had been established that they had frequent episodes.
- 81% were prescribed either digoxin, beta-blockers or sotalol after their first or second episode.
- 75% of vagal afibbers took digoxin, beta-blockers or sotalol after their first or second episode. These drugs are clearly contraindicated for vagal afibbers. The average (mean) number of episodes for this group was 12.0 (median = 6.5).
- 49% of all afibbers took beta-blockers either alone or in combination with digoxin during their first year. The average (mean) number of episodes for this group was 16.6 (median = 12).
- 38% of all afibbers took digoxin either alone or in combination with beta-blockers. The average (mean) number of episodes for this group during the first year was 20.0 (median = 8).
- 19% of all afibbers took sotalol. The average (mean) number of episodes for this group during the first year was 12.7 (median = 8).

- Only four out of 37 (11%) of survey respondents had taken antiarrhythmics as their sole medication during their first year. The average (mean) number of episodes for this small group was 2.0 (median = 2). Although the small data set precludes any firm conclusions it would appear that properly prescribed antiarrhythmics (flecainide, disopyramide, propafenone and amiodarone) on their own may be beneficial, neutral or at least not detrimental during the first year.

Considering that the average (mean) number of episodes for those not taking any drugs during their first year was 4.7 (median = 2) it is probably fair to say that digoxin, beta-blockers, and sotalol during the first year are generally not helpful and may indeed be detrimental. It is, of course, impossible to say if the people who took drugs during their first year would have been better off if they had not done so. However, the evidence from the survey certainly indicates that they might have been.

In conclusion, I believe it would be prudent to follow the advice given in the 2001 Guidelines for the Management of Patients with Atrial fibrillation[1]:

"Prophylactic drug treatment is seldom indicated in case of a first-detected episode of AF and can also be avoided in patients with infrequent and well-tolerated paroxysmal AF".

In other words, don't begin drug treatment until it is clear that your episodes are frequent or intolerable. It is also prudent to postpone drug treatment until you are reasonably sure which type of AF you have (adrenergic, mixed or vagal). Digoxin should be avoided by all afibbers and beta-blockers and sotalol should be avoided by vagal afibbers. Properly prescribed antiarrhythmics, on their own, may be helpful in dealing with frequent or intolerable episodes during the first year.

[1] ACC/AHA/ESC Guidelines for the Management of Patients with Atrial Fibrillation: Executive Summary. Journal of the American College of Cardiology, Vol. 38, No. 4, 2001

Severity of LAF

The severity of paroxysmal (intermittent) LAF is measured by four parameters – episode frequency over a 6-month period, average duration of episodes, total time spent in fibrillation over a 6-month period, and intensity of episodes (extent of discomfort). A total of 255 paroxysmal afibbers (33 adrenergic, 94 mixed and 128 vagal) supplied data regarding episode frequency and duration and 148 supplied information about intensity.

A preliminary review of the data revealed that the sample population was far from homogenous. It was clear that there was a distinct group of "heavy hitters" who had far more frequent or far longer lasting episodes than did the majority of the afibbers. The presence of this group led to a significant skewing of results and could result in erroneous conclusions being drawn regarding correlations with other variables. The "heavy hitter" group consisted of 25 afibbers (1 adrenergic, 14 mixed and 10 vagal) or 10% of the total sample. The members of this group fulfilled one or more of the following criteria:

- Number of episodes greater than total group mean plus two standard deviations;
- Average episode duration longer than 168 hours (1 week);
- Total time spent in fibrillation longer than total group mean plus two standard deviations.

The mean values for episode frequency, episode duration, and time spent in fibrillation differed significantly between the "heavy hitter" group and the group containing the remaining 230 afibbers (main group).

The following statistical analyses were carried out on both of these groups individually as well as on the total group of 255 paroxysmal afibbers.

I. EPISODE FREQUENCY

The median number of episodes experienced by the main group over a 6-month period was 5. Further analysis produced the following results:

	Participants	Mean	Median	Range
Whole Group	255	17	6.0	0-180
Adrenergic	33	9	4.0	0-68
Mixed	94	22	9.0	0-176
Vagal	128	16	5.0	0-180
Males	206	17	6.0	0-180
Females	49	18	8.0	0-180
Main Group	230	10	5.0	0-70
Adrenergic	32	7	4.0	0-68
Mixed	80	12	6.0	0-70
Vagal	118	10	4.0	0-70
Males	187	11	5.0	0-70
Females	43	8	5.5	0-25
Heavy Hitters	25	81	84.0	6-180

Episode frequency was significantly different between adrenergic and mixed afibbers in the whole group, but not between adrenergic and vagal or between mixed and vagal. The difference between adrenergic and mixed was no longer statistically significant when considering only the main group (omitting the “heavy hitters”).

In conclusion then, for the main group the median number of episodes over a 6-month period is 5 with a mean of 10 and a range of 0-70. There is no statistically significant difference in the frequency of episodes between adrenergic, mixed and vagal afibbers when ignoring the heavy hitters. No statistically significant difference was found in episode frequency between men and women neither in the whole group nor in the main group considered by itself.

Correlations

- 55% of respondents were taking one or more drugs in an attempt to manage their afib while 45% were not taking any preventive drugs. There was no difference in episode frequency between the two groups. The effectiveness of drugs will be covered in considerably more detail in a future issue.

- Somewhat surprisingly, no correlation was observed between frequency of episodes and age or number of years since first diagnosed. However, when only drug-free afibbers were considered there was a moderate positive correlation between age and increased frequency of episodes. No correlation was observed with number of years since diagnosis.

- Afibbers whose episodes occurred at regular intervals tended to have more episodes than those whose episodes occurred irregularly (median of 16 episodes versus 6 episodes per 6 months).

- There was a modest negative correlation for mixed afibbers only between the frequency of episodes and a high heart rate during an episode. This can either mean that mixed afibbers with less frequent episodes tend to have higher heart rates during their episodes or that those with a high heart rate during their episodes tend to have fewer episodes.

- There was a moderate to strong positive correlation for vagal afibbers only to have a higher episode frequency with a high intake of elemental magnesium. This is certainly an unexpected finding and clearly needs to be investigated further.

II. EPISODE DURATION

The median duration of episodes experienced by the main group was 6 hours. Further analysis produced the following results:

	Participants	Mean (hrs)	Median (hrs)	Range
Whole Group	255	14	6	0-168
Adrenergic	33	16	8	0-72
Mixed	94	15	6	0-168
Vagal	128	12	6	0-168
Males	206	15	6	0-168
Females	49	7	4	0-48
Main Group	230	11	6	0-84
Adrenergic	32	15	8	0-72
Mixed	80	10	5	0-48
Vagal	118	10	6	0-84
Males	187	12	6	0-84
Females	43	6	4	0-48
Heavy Hitters	25	40	12	0-168

The difference in episode duration between adrenergic, mixed and vagal was not significant in the whole group or in the main group. The difference in episode duration between male and female afibbers was, however, highly significant with men tending to have longer episodes than did women.

Correlations

- There was no significant difference in the whole group in episodes duration between afibbers taking preventive drugs and drug-free afibbers. The effectiveness of drugs will be covered in considerably more detail in a future issue.

- There was a modest, but statistically highly significant correlation between exposure to pesticides and solvents and duration of episodes with afibbers who had been exposed having longer episodes. This correlation was most apparent in the main group where afibbers with no solvent exposure had a median episode duration of 6 hours as compared to 15 hours for exposed afibbers. This finding raises the intriguing possibility that afibbers with long lasting episodes may benefit from a detoxification program.

- Adrenergic afibbers who were able to terminate their episodes with rest tended to have significantly shorter episodes.

- There was a modest positive correlation for vagal afibbers between the amount of elemental calcium absorbed and duration of episodes. This confirms earlier findings indicating that supplementation with large amounts of calcium may be detrimental to vagal afibbers.

III. TIME SPENT IN FIBRILLATION

The median time spent in atrial fibrillation for the main group was 30 hours over a 6-month period. Further analysis produced the following results:

	Participants	Mean (hrs)	Median (hrs)	Range
Whole Group	255	261	45	0-3960
Adrenergic	33	201	24	0-3300
Mixed	94	400	45	0-3960
Vagal	128	175	47	0-1920
Males	206	270	48	0-3960
Females	49)	222	24	0-3888
Main Group	230	123	30	0-1428
Adrenergic	32	105	24	0-1224
Mixed	80	139	29	0-1200
Vagal	118	119	36	0-1428
Males	187	139	36	0-1428
Females	43	57	22	0-399
Heavy Hitters	25	1526	1144	10-3960

The differences in time spent in fibrillation between adrenergic, mixed and vagal was not statistically significant in the whole group or in the main group. The difference observed between male and female afibbers was barely significant in the main group, but not significant in the whole group.

Correlations

- There was no significant difference in the whole group in time spent in fibrillation between afibbers taking preventive drugs and drug-free afibbers. The effectiveness of drugs will be covered in considerably more detail in a future issue.

- Not surprisingly, there was a strong, extremely significant correlation within all groups between episode frequency and time spent in fibrillation and between episode duration and time spent in fibrillation.

- There was a strong, positive significant correlation between time spent in afib and previous exposure to solvents or pesticides in both the main and whole groups.

- Afibbers whose episodes occurred at regular intervals tended to spend considerably longer in afib than did those whose episodes occurred at irregular intervals (150 hours versus 48 hours over a 6-month period).

IV. INTENSITY OF EPISODES

Episode intensity was judged subjectively by 148 respondents (18 adrenergic, 52 mixed and 78 vagal). Intensity was rated on a scale from 1 to 5 where 1 is barely noticeable while 5 is akin to World War III erupting in the chest area. The average (median) intensity for the whole group was 2.5. Specific values were as follows:

	Participants	Mean	Median	Range
Whole Group	148	2.6	2.5	1-5
Adrenergic	18	2.0	2.0	1-4
Mixed	52	2.7	3.0	1-4.5
Vagal	78	2.7	2.75	1-5

Adrenergic afibbers judged their episodes to be significantly less intense than did mixed and vagal afibbers. There was no significant difference between mixed and vagal afibbers as far as intensity is concerned.

Sixty-seven (47%) of 143 respondents felt their episodes had decreased in intensity over time, 55 (38%) reported no change, and 21 (15%) felt they had increased in intensity over time. So the good news is that episode intensity is likely to decrease over time or at least remain constant. Adrenergic afibbers showed the largest decrease in intensity.

Correlations

- There was a highly significant negative correlation between intensity of episodes and present age confirming the earlier observation that intensity lessens with age. This effect is independent of how many years afib has been present indicating that aging, as such, is what tends to lessen episode severity.

- There was a modest, but highly significant positive correlation between intensity and maximum heart rate during an episode, indicating that a rapid heart beat contributes significantly to the feeling of discomfort during an episode.

- Surprisingly, no correlation was observed between reported intensity and the use of a calcium channel or beta-blocker during the episode.

Magnesium & Potassium in Lone Atrial Fibrillation – Part III

by Patrick Chambers, MD

ABNORMAL ELECTROPHYSIOLOGY OF LAF

How does Mg (and K) deficiency actually cause AF? Muscle cells (skeletal, smooth and cardiac) contract during depolarization (excitation phase) and relax during repolarization. During a portion of the relaxation phase, the cell is immune to further stimulation (refractory period)(75). AF requires a shortened atrial effective refractory period (AERP), enhanced atrial dispersion of refractoriness, slow conduction velocity and a trigger (increased PACs)(78). Dispersion of refractoriness is nothing more than a measure of how much variability in AERP exists between atrial muscle cells. Greater variability in AERP from cell to cell implies greater dispersion. The mechanism of AF is based on the now proven Moe wavelet theory (1959)(74), which requires both reentry and automaticity. Reentry occurs when the advancing wavefront of depolarization (and contraction) encounters refractory tissue in such a way that it reenters its own path, creating a wavelet (circular wave). The lack of AERP uniformity between cells can force some unusual paths of conduction (colorfully called circus movements), making creation of these wavelets or closed circuits a real possibility. Wavelets are described by the equation:

wavelength = (conduction velocity) x (AERP)(75,76).

Atrial conduction velocity (via normal pathway) is about 1m/s and AERP<50 ms results in AF 80% of the time. Therefore, a micro reentrant wavelet is something around 5 mm in circumference(73). In addition to reentry, there must be automaticity, whereby a single atrial focus fires repeatedly (PACs). The number of PACs is inversely proportional to intracellular K and Mg and directly proportional to intracellular Ca(80,81). The SA and AV nodes and the rest of the His Purkinje conduction system have innate pacemaking properties (automaticity). Catecholamines can cause automaticity in cells not so disposed (foci of ectopics)(76). Since PACs arise outside the normal conduction system of the heart, the impulse travels via an alternate less efficient pathway with slower conduction velocity. This further contributes to shortening of the wavelength and dispersion of refractoriness (see above equation). These simultaneously occurring conditions (PACs, slow velocity, shortened AERP and enhanced dispersion) lead to AF by fragmentation of the propagating wavefront of depolarization. Multiple reentrant wavelets (six wavelets or involvement of about 75% of atrial tissue constitute critical mass for sustaining AF)(73,76) are created. The dispersion of refractoriness allows the wavelets to meander around the

atrium forming a moving barrier against any successful wave of contraction. Instead, additional wavelets are created from these unsuccessful attempts. Hence, there is no P wave, unlike in atrial flutter.

Autonomic tone (especially vagal but also sympathetic) can shorten AERP(75) and increase atrial dispersion. Hypokalemia and hypomagnesemia can also increase atrial dispersion(79). Inhomogeneous distribution of vagal nerve endings will increase dispersion of refractoriness(77). Atrial dispersion is also a function of atrial electrical remodeling (increased intracellular Ca)(76). Electrical remodeling causes loss of physiologic rate adaptation, i.e., the AERP fails to adapt to the heart rate, especially during bradycardia(74), when it should lengthen. There is also structural remodeling (increase in atrial size) as well as ultrastructural or contractile remodeling (76,77). When the conduction velocity increases, the wavelets begin to disappear or fuse because the advancing wavelet front of depolarization catches up to its trailing tail of refractory tissue. The wavelets are forced to enlarge or coalesce, but then they are more likely to bump into others, canceling themselves. At some point their numbers dip below critical mass and AF is terminated. Increasing sympathetic tone causes an increase in conduction velocity (dromotropism) (74). This latter is instrumental in terminating VMAF episodes.

MAGNESIUM THERAPY

Mg Water

In view of the growing problem of inadequate Mg intake, several Mg rich drinking waters have become quite popular. These are mineral waters or their approximations. They include Unique Water (Australia, 120 mg Mg/liter), Noah's California Spring Water (120 mg Mg/liter) and Waller Water (developed by Erling Waller and containing 150 mg of Mg/liter). All have pHs well over 8 and have the potential to cause urinary K wasting, due to bicarbonaturia (see GERD discussion). This also causes urinary Mg loss(104). However, a generous squeeze from a fresh lemon addresses nicely not only this concern but also adds a touch of taste. Hexahydrated Mg is otherwise especially beneficial, because it provides more bioavailable Mg. This results in not only enhanced GI absorption but also more biologically active ionized Mg. If the concentrations of ionized magnesium falls 25 to 40 percent below normal—irrespective of the total amount of magnesium present—magnesium-dependent enzymes no longer function properly(1).

There are also some Mg preparations that dissolve in water (Natural Calm with magnesium citrate). Oral Mg supplementation in tablet form enjoys considerable popularity and success. Herbert Mansmann, M.D., Director of the Magnesium Research Laboratory at Thomas Jefferson Medical College, has developed an effective magnesium dosing regimen that exploits nighttime absorption(40). However, whichever route one chooses, the maximum tolerated dose (MTD) should be approached carefully. Once exceeded, the K and Mg loss in loose stool is regressive and may easily trigger a breakthrough episode of LAF. Many factors help or hinder Mg absorption and directly impact the efficacy of oral supplementation.

HEART RATE VARIABILITY (HRV)

Finally, heart rate variability (HRV) is a measure of the small variation in heart rate from beat to beat. It is a direct measure of autonomic tone and decreases with age. Elevated HRV implies greater vagal tone and has always been an independent prognosticator of longevity(108). Greater vagal tone translates to longer life, all else being equal. Perhaps the "defective substrate" of VMAF is nothing more than the combination of many years of poor diet, skipped meals and poor hydration along with excessive exercise in individuals already possessing a slow heart rate. But it's never too late to change. Increased dietary Mg and regular moderate exercise with plenty of hydration will increase ANP(38,53), the antialdosterone hormone. This will help flush out excess Na and oppose the deleterious effects of RAAS. It will enable glucagon to help moderate glucose levels and it will promote proper balance within the ANS. All this should help keep LAF at bay. Besides that you'll sleep better (more serotonin and melatonin) as well, because Mg is required for the synthesis of both(94).

*******For references please see Part 1*******

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