THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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Welcome to our end of year holiday issue with this Dec/Jan edition of ***The AFIB Report****.*

Before we begin our brief summary of the topics covered, I want to let all our valued subscribers know that, yet again, this year has brought to my door an unanticipated, and utterly surprising, unwelcomed life event that will require that I take a step back from my duties as editor of The AFIB Report and website, and take a temporary sabbatical.

My dear wife, Magdalena, was diagnosed with kidney cancer this week as an entirely incidental finding from an MRI ordered to search for what was assumed to be garden variety sciatic-like left low back pain that had not resolved under the usual conservative approaches. The potentially complex nature of her diagnosis, and the sudden demand to turn all of my energy, focus and efforts toward her care and well-being, will leave no time for my AFIB-related support efforts, for the time being.

I had finished about ¾ of this issue when the news struck, not yet even a week ago, and it's been a total whirlwind of activity since, as I dive into the world of kidney cancer as I would for the most serious AFIB-related issue here. First, searching for a top tier nephrectomy surgeon and hospital along with all the related minutia and nuance that taking on such a challenge will entail.

Forum stalwarts Jackie Burgess and George Newman, as well as a host of long time regulars will keep the forum humming along without missing a beat, while my wife and I walk down this path where ever it leads to the point where her health and situation stabilizes enough for me to saddle up again here at our wonderful oasis for afibbers everywhere. Many thanks to Hans and Judi too for stepping in here, and interrupting their peaceful retirement this week to help polish off the last couple pages of this issue, and to all of you for your continued support.

This year has been both highly rewarding and challenging for me personally with the stroke and LARIAT leak repair, and now this. I do look forward to perhaps a bit less of a rollercoaster ride in 2015, but most of all, to the return to full health for my lovely Magdalena. Thank you all for your understanding. I'm really not sure how long it will be, but rest assured, when the dust settles and the smoke clears enough and I know that my gal is settled in and well on the mend, I'll be able to rejoin you all more consistently again.

We wrap up this busy year in the world of AFIB and Electrophysiology (EP) with a focus on a handful of important studies conveying real world practical insights that have been of interest and discussion over the course of this year on our active and dynamic forum at http://www.afibbers.net.

In our first three reviews, we look at a few new angles on a very hot topic in EP circles addressing the larger issue of silent cerebral ischemia/events (SCI/SCE) and its association with both AFIB and risk of dementia. We first looked at this topic in detail in a special report in our April/May issue, and now we have even more confirming insights to share, each with a key take home message for all afibbers.

Next up, we take a look at commonly used NSAID anti-inflammatory drugs with a meta-analysis from China underscoring their previously known associations for not only an increased risk of serious bleeding and thromboembolism in AFIB patients (especially for those receiving concomitant anti-coagulation therapy), but also as a direct risk for contributing to AFIB itself.

In a related, and no less important, a set of studies provides more reinforcement for not prescribing low dose aspirin as a general cardiovascular primary prevention medication in most cases. There are specific exceptions where an aspirin may be warranted, but the indications for its use, that not long ago seemed widespread, have shrunk considerably as a wave of new studies in recent years have called into question the wisdom of widespread aspirin use as a daily prophylactic drug for most people with AFIB, and even some other cardiovascular issues. The bleeding risks increasingly seem to outweigh any modest benefit in too many areas that once appeared to be a no-brainer for low dose aspirin use as primary prevention.

Wishing all our readers Happy Holidays and plenty of NSR throughout the coming new year …
Shannon

Meta-Analysis of NSAIDs and Risk of Atrial Fibrillation

PEKING, CHINA. Although the exact mechanism of AFIB is not yet fully understood, inflammation may well be involved at a fundamental level. Naturally then, it makes sense that use of anti-inflammatory drugs, including the popular non-steroidal anti-inflammatory (NSAIDs) agents, might well reduce the incidence and/or severity of AFIB episodes. Such was the premise behind this large meta-analysis out of China, investigating just what potential benefits might be accrued for the AFIB patient from use of NSAIDs such as ibuprofen and COX-2 inhibitor drugs, etc. And to examine any potential association of these agents with respect to possible increased risk of AFIB incidence in this study.

The epidemiologic literature regarding the effect of NSAIDs use on AFIB has been mixed. Yet as noted by the authors, 'any confirmed association between use of NSAIDs and AFIB would have major clinical and public health implications because NSAIDs are commonly prescribed in daily practice to treat pain and inflammatory conditions', and in the US these agents are widely purchased over the counter as well. The idea, here, was to quantify which patients might be at greater risk of AFIB due to use of non-aspirin NSAIDs.

This analysis combined the results of several large epidemiological studies, including five studies that were identified for inclusion in this meta-analysis that met the inclusion criteria, 3 of which additionally reported specifically on the association with a **12%** increased risk for AFIB incidence (RR [relative risk] = 1.12, 95%CI [confidence interval] 1.06 to 1.18) in those using non-aspirin NSAIDS. Surprisingly, the associated increased risk was even higher for new use of the drugs at **53%**. And this added jump in risk was despite the well-known anti-inflammatory effects of this class of drugs.

A potential explanation for these findings is that the use of NSAIDs may increase the risk of AFIB via renal and cardiovascular related actions. The authors noted: 'that both cyclooxygenase (COX) as both COX-1 and COX-2 are expressed in distinct anatomic regions of adult kidney tissue. Inhibition of these enzymes by NSAIDs may result in an increase in blood pressure, left atrial pressure and left atrial stretch due to fluid retention and expansion of plasma volume."

Moreover, electrolyte disturbances (potassium) due to NSAID use can also render the patient more susceptible to the occurrence and development of AFIB … (no doubt this sounds familiar to regular readers of this newsletter and website forum).

The study conclusion hypothesized that the increased risk among new users may be attributable to short-term adverse renal effects of NSAIDs, which subsequently may trigger AFIB. And stratified analysis tends to support that hypothesis. For one, the association between these drugs and AFIB risk was greater among current users, especially new users as noted above, with the risk tending to disappear among recent users no longer taking the drugs. In addition, this view is further supported by the fact that patients with chronic kidney disease had a greater risk of AFIB when starting treatment with NSAIDs.

Thirdly, heart failure (HF) patients who were inherently more sensitive to fluid status and electrolyte imbalances were also found to have a significantly greater risk due to NSAID use and, in addition, this increased AFIB risk was also observed in long-term users.

It was reported that the long-term use of NSAIDs was also in associated with increased risk of cardiovascular events, such as myocardial infarction (MI), and thereby causing an increased risk of HF which, in turn, closes yet another circle leading to higher incidence of new-onset AFIB among NSAID users.

Of note, while the COX-2 inhibitors, as selective NSAIDs, cause fewer overall gastrointestinal adverse events than nonselective NSAIDs, they are still significantly related to an increased risk of AFIB. This is likely due to the fact that COX-2 inhibitors still have similar renal effects to their nonselective brethren causing fluid retention, electrolyte disturbances and blood pressure fluctuations. These effects,

combined with impact of these drugs on a variety of other physiological parameters, may subsequently induce acute renal dysfunction.

In addition, this study highlights other experimental studies indicating that prostaglandin could release into coronary circulation and pericardial fluid as a result of use of these drugs. Moreover, selective depletion of COX-2 results in mouse cardiomyocyte hypertrophy with interstitial and perivascular fibrosis, and thus potentially contribute to enhanced tendency to induce arrhythmo-genesis.

Liu G, et al. ***Meta-Analysis of Non-steroidal Anti-Inflammatory Drug use and Risk of Atrial Fibrillation. Am J. of Cardiology 2014;114:1523-1529*** ***http://dx.doi.org/10.1016/j.amjcard.2014.08.015***

Editors comments: Taken all together, those experimental studies noted in this report on this interesting meta-analysis, support a causal relationship between COX-2 inhibitors and AFIB. And while, as in most such papers, the authors suggest further studies to deepen our insights on such an important topic, the present study, as it is, strongly suggests that physicians everywhere should carefully consider this very real increased risk of new-onset AFIB when thinking of prescribing NSAIDs.

The association, and perhaps even a core relationship, between inflammation and AFIB seems likely, and yet, how we go about lowering such inflammation might make a big difference in both efficacy and safety. Certainly, all afibbers should forgo use of NSAIDs whenever possible. Noting here that even new use or starting again after a long hiatus may predispose one to an even greater short-term risk of an AFIB breakthrough.

Association between AFIB and Silent Cerebral Infarctions

BOSTON, MASS. Over the past few years, a watershed of new studies have been completed that investigate the association and possible role that AFIB and AFIB ablation, as well as other invasive cardiac procedures, may have in the creation of silent cerebral ischemia. In our first look at this increasingly important topic among cardiologists and EP's in a Research Report from our April/May issue, SCI's were defined as small asymptomatic white lesions in the brain of at least ?3mm in size and detected by DWI (diffusion weighted imagining) on high resolution MRI (magnetic resonance imaging). Typically using hi-powered 1.5 tesla MRI machines.

As in most early discoveries like this, initial reports contained significant variability in reported prevalence of SCIs in patients with AFIB. One source of this heterogeneity is likely from the different methods used to diagnosis SCIs in earlier studies, ranging from less consistent autopsy findings to computed tomography (CT scans), and more recently studies have begun to standardize SCI detection and diagnosis around the aforementioned DWI-MRI.

The well-respected Deane Institute for Integrative Research in AFIB and Stroke at Massachusetts General Hospital funded and conducted this systematic review and meta-analysis, with support from Harvard Catalyst and Harvard University. They reviewed all relevant literature to-date in order to estimate the association between AFIB and SCIs, as well as the prevalence of SCI's in patients with AFIB and no history of symptomatic stroke.

Meta-analysis was performed on eleven studies including 5,317 patients with a mean age from 50 to 83.6 years, reporting on the association between AFIB and SCI. After ruling out low quality results from autopsy studies, CT and MRI studies were combined in the meta-analysis. The net results strongly suggest that SCI's are very common, with an SCI detected by MRI in at least 40% of AFIB patients across this meta-analysis. As large as that number is, it's lower than several high quality recent individual studies using DWI MRI diagnosis as well in which SCI prevalence in Afibbers ranges from 60 to a whopping 85%!

In addition, AFIB was associated with a more than a 2-fold increase in the odds of having any SCI's. The overall prevalence of MRI-detected SCI's in the general non-AFIB population ranges between 8% and

28%, but keep in mind that this is less than one half of the estimated prevalence of SCI in the investigated AFIB population.

And while SCI's do not present with stroke-like symptoms, they have now been shown to be associated with a more than 3-fold increased risk for future symptomatic stroke as well as a 2-fold increased risk for dementia.

Keeping in mind that an association does not inherently imply a direct causal relationship, and yet the growing body of associative evidence combined with a plausible physiological connection between increased burden of SCI, AFIB and dementia across the board imply added weight and concern to these sobering statistics.

And interestingly, while only a few of the 11 studies that made up this meta-analysis examined, at all, the prevalence of SCI based on type of AFIB, they did not find a significant distinction in the prevalence of SCIs between paroxysmal and persistent AFIB, though with a slight numerical increase in the persistent category that one might expect. Consequently, it's becoming increasingly clear that a higher prevalence of SCIs found in AFIB patients across all classifications makes increasing our understanding of this association all the more critical, not only due to it being a likely mediating factor in the link between AFIB and cognitive impairment and dementia, but also because SCI's may well predict future symptomatic strokes and disability.

Certainly, additional studies and randomized controlled trials are warranted, and a number are underway now, seeking to identify appropriate preventative and treatment strategies to reduce the incidence of SCI in AFIB patients. Clearly, the very best way to minimize increasing SCI burden is by achieving as robust and consistent NSR in one's life as is possible, by whatever means that may be achieved.

Kalantarian S, et al. ***Association Between Atrial Fibrillation and Silent Cerebral Infarctions: A Systematic Review and Meta-Analysis****. Annals of Internal Medicine 2014;161:650-658 http://dx.doi.org/10.7326/m14-0538*

Editor's comments: It is obvious now that SCI prevalence has become recognized as an unwanted consequence of both living with AFIB directly, as well as a possible asymptomatic complication of certain AFIB ablation procedural steps and from other invasive cardiac procedures, though at a lesser overall risk of occurrence than from long-term untreated AFIB itself. Already, several top centers have identified procedural modifications that can greatly reduce risk of creating SCI during an ablation as we will see shortly in this issue, though more ongoing investigation will surely help reduce the risks even further.

Anticoagulation has been shown to reduce symptomatic strokes associated with AFIB in those who meet the strict guidelines for use of these drugs. And while some will be no doubt be eager to suggest broadening those guidelines to include treating the presence of SCI with anticoagulation as well, we need to be very cautious in making such a leap. Two studies included in this meta-analysis did not report any reduction in incidence of SCIs under anti-coagulation (29,33).

It's much too early to assume efficacy, and an overall positive safety metric of anticoagulation as a preventative of SCI creation, or as protection against future risks resulting from SCI burden in spite of the logical appeal of the premise at first glimpse. At least, not without a battery of solid randomized control trials that better define the true risks and dangers of SCI burden long term, while also demonstrating a clearly positive benefit vs. risk outcome from using these powerful drugs that carry their own well-known risks of use. Such steps are vital before even considering expanding the established guidelines to include presence of SCI as an indication for use.

Long-term Overtreatment with Antiplatelet/Anticoagulant Therapy may Increase Risk of Dementia in AFIB Patients

MURRAY, UTAH. The following report looks at a combination of two overlapping studies by the busy researchers at Intermountain Heart Institute in Utah whose solid work we have featured several times this year in *The AFIB Report*. We look now at the topic of long-term anticoagulation over-use and its associated impact on dementia … a timely pair of studies in light of the above report on SCI and AFIB.

In our April/May issue we examined the case for AFIB's association with future onset of dementia, also by the same Utah group who now report specifically on the potential impact that long term 'out of range' anticoagulation itself might have on developing dementia. Obviously, with long-term anticoagulation use being such a common hallmark of treatment for people with AFIB and heightened stroke risk factors, this topic is of paramount interest.

The mechanisms behind AFIB's association with dementia are not entirely known, though one likely possibility as we explored last spring, is from chronic exposure to microembolism or microbleeds that may result in repetitive cerebral injury which, in turn, manifest over the long haul as cognitive decline. Microemboli might arise more from ongoing AFIB-related thrombo-genesis, while frequent periods of over-anticoagulation could increase microbleeds tendency.

Either way, it's a 'gotcha' when an effective and safer INR anticoagulation status is not maintained consistently within the therapeutic time window. Certainly with warfarin this is the case, and the study in question found a clear association between afibbers who experience a too low '*time within the therapeutic range'* (TTR) on warfarin and subsequent long-term risk of developing dementia.

A total of 2,605 patients (age 73.7 ?10.8 years, 1,408 [54%] male) were studied. The percent TTR averaged 63.1% ± 21.3% with percent INR < 2.0 = 25.6% [± 17.9%] and percent INR >3.0 = 16.2% [± 13.6%]). Dementia was diagnosed in 109 patients or (4.2%) overall, with the senile form at (1.4%); Alzheimer's group at (2.5%); and vascular dementia coming in at (0.3%) of the total.

After adjustment, decreasing categories of percent TTR were associated with increased risk of dementia risk. In other words, as the percentage of total time afibbers on warfarin stayed within the 2.0 to 3.0 therapeutic INR window, the greater the prophylaxis against risk of later dementia. The TTR quartile breakdown for decreasing risk of dementia is as follows: <25%TTR =5.8% incidence of future dementia, 26%-50% TTR = 5.5% risk, 51% -75% = 4.9% risk and >75%TTR = a big improvement at 1.9% risk of late dementia.

Keep in mind that the risk for dementia increases when the time within the 2-3 INR range is excessive on either side of that therapeutic window. Too much time lower than 2 increases ischemic clot risk, while excess time spent over 3.0 increasingly ups the ante for increased bleeding risk, both of which can increase SCI as well as symptomatic stroke risk and dementia over time.

Dementia risks with combined antiplatelet/anticoagulation therapy

In the companion study by EP's Jared Bunch, Pete Weiss, John Day, et al, of the Intermountain group, the same issue of dementia risk was extended to the addition of an antiplatelet drug (aspirin or Plavix/Brilinta) to warfarin in this case, as a dual OAC therapy commonly prescribed for AFIB patients with coronary artery or peripheral vascular disease.

The obvious concern is for the added bleeding risk of the combined therapy potentially leading to even more micro-bleeding risk, and thus may increase not only SCI burden and overt stroke risk, but thereby increase risk of dementia as well.

This arm of the anticoagulation-dementia investigation analyzed retrospectively over a four year study, included 1,031 chronically anti-coagulated patients receiving warfarin and antiplatelet drugs (aspirin in

>90% of cases) with no previous history of stroke, TIA or dementia for up to 10 years while on the drug combination.

From this cohort of AFIB patients on dual antiplatelet/anticoagulation therapy, the researchers expected, and found, that the percent time over-anti-coagulated (INR >3.0) significantly influenced dementia risk. Dementia was diagnosed in 2.7% in those who were in a supra-physiologic >3.0 INR state for <10% of the total therapeutic time. And 5.8% of the total group were diagnosed with dementia who spent >25% of their total treatment time at >3.0 INR. Not surprisingly, those patients with a higher percentage of time above the therapeutic range were more likely to have valvular heart disease, renal failure, and a higher percentage of CHADS-2 scores between 3-6 … and among those who suffered a prior bleed.

One encouraging finding, is that if a patient is well-controlled on warfarin with a stable therapeutic INR the vast majority of the time, the risk of dementia remains very low even when an antiplatelet drug like aspirin or Plavix is required as part of dual therapy.

Conclusions

"The collective findings of these two important studies" (as noted by the authors): "support the strong possibility of repetitive subclinical chronic cerebral injury resulting in an accumulative burden that ultimately is manifest as dementia, and strongly suggests this as a mechanism that underlies the association between AFIB and dementia."

It is clear, too, that anti-coagulation with periods of supra- and sub-therapeutic effects provoke both chronic micro-emboli and micro-bleeds. That this risk association was found with low TTR percentages in those who were chronically under or over anti-coagulated suggests that both chronic micro-emboli and micro-bleeds may well contribute to cognitive decline and dementia.

In an important message from these studies, Dr. Bunch noted in an interview with *Cardiac Rhythm News* (Nov 21, 2014)* that people who are starting to take aspirin need to make sure there is really an indication for its use. "A lot of people take aspirin (whether prescribed or over the counter) assuming that it is good for the heart, but not everybody needs to be on aspirin", he said.

Dr. Bunch also noted: "that clinicians should think that if they are having trouble managing people on warfarin, and notice it is consistently over-effective, either they need to see their patients much more frequently, educate them on the proper use of warfarin (including weekly home testing when appropriate), or perhaps switch them to a NOAC (novel oral anti-coagulant). At least early large-scale marketing-based clinical trials on these new agents indicate a reduction in large brain injuries from strokes and bleed in AFIB, so there is some hope that these outcomes will translate into similar reduction in risks for small micro-events as well."

Jacobs V. ***Time outside of therapeutic range in atrial fibrillation patients is associated with long-term risk of dementia. Heart Rhythm 2014;11:2206-2213*** ***http://dx.doi.org/10.1016/j.hrthm,2014.08.013***

Interview T. Jared Bunch.* ***Long-term overtreatment with antiplatelet/anticoagulation therapy may increase the risk of dementia in atrial fibrillation patients. Cardiac Rhythm News. Nov 21, 2014.* ***http://www.cxvascular.com/crn-latest-news/cardiac-rhythm-news---latest-news/long-term-overtreatment-with-antiplateletanticoagulant-therapy-may-increase-the-risk-of-dementia-in-af-patients-***

Editor's comments: As noted earlier, it bears repeating that, unfortunately, no current studies have looked at dementia risks in afibbers using these NOAC agents, nor have we seen a direct association with their use in reduction of SCIs, as yet. It simply is too early in their history for meaningful results to show up. As such, great caution needs to be exercised in extrapolating any potential benefit of these drugs in reducing micro-cerebral events and SCI's until further rigorous studies demonstrate a clear connection and net benefit for this indication. Lifelong oral anticoagulation needs very careful and consistent management to increase safety not only from symptomatic strokes and hemorrhagic bleeds, but also from such micro-cerebral events that can build up over time toward increased risk of dementia. Hopefully, future improvements and new developments in LAA exclusion devices will increase their

installation and long term safety to the point where they become a more widespread option to replace lifelong anti-coagulation in those who require it now. We aren't there quite yet, and in the meantime those on OAC/NOAC therapy should educate themselves as to how best to manage their anticoagulation status.

Exchanging Catheters over a Single Trans-septal Sheath in Left Atrial Ablation is Associated with a Higher Risks for SCEs

BAD NEUSTADT, GERMANY. Wrapping up our review of the latest reports on the SCI/SCE issue, the heading for this study summarizes the take home message well.

In our initial look at the subject in our April/May newsletter, we noted that the confirmed risks for SCE (silent cerebral events) during an AFIB/Flutter ablation that included a transseptal puncture, could be dramatically reduced by employing the, by now, well-validated continuous anti-coagulation protocol throughout the peri-procedural ablation period. And this, as compared with stopping warfarin, for example, 4 to 5 days before an ablation while bridging with low-molecular weight heparin over those last few days prior to ablation, and then switching to IV Heparin just before transseptal puncture, which showed greater risks of associated procedure-related SCI.

Now, from a modest multicenter investigation from Germany, Italy and Texas, highly experienced operators confirm another independent procedural factor for further reducing SCI creation during an ablation by employing a dual puncture/sheath approach to transseptal access to the left atrium (LA).

A dual puncture/dual sheath approach dedicates a separate sheath for routing both the circular mapping catheter (CMC or Lasso catheter) and ablation catheter, respectively, into the LA. The study findings identified this approach as inherently superior compared to a single puncture/single sheath method in which both catheters must be exchanged two or more times through the single sheath (ExCath), which can result in an increased risk for introducing gas, or thrombotic debris, as micro-emboli from within the sheaths, or lodged on catheter tips, into the LA during such multiple catheter maneuvers in and out of each sheath.

In addition, such multiple exchanges over one sheath may degrade the sheath's valve, leading to introduction of tiny air bubbles into the LA, as well, as another possible mechanism for the increase risk of SCI.

The net results from 88 carefully chosen patients using Irrigated RF catheters (Biosense Webster irrRF), Endoscopic Laser Ablation catheters (Cardio-Focus Heartlight) or Cryo-catheters (ArticFront Medtronic), showed a significantly higher incidence of SCI via DWI-MRI in 40% of patients with catheter exchanges via one sheath, compared to 13% in the group ablated without any catheter/sheath exchanges.

Of note, the peri-procedural anti-coagulation protocol used for all ablations of this study was standardized as interrupted warfarin, enoxaparin (low-molecular weight heparin) and IV heparin. As such, the results do not reflect the further significant overall reduction in SCI achieved by using an uninterrupted anti-coagulation protocol along with dual punctures/sheaths with no catheter exchange.

Deneke T. ***Exchanging Catheters Over a Single Trans-septal Sheath During Left Atrial Ablation is Associated with a Higher Risk for Silent Cerebral Events. Indian Pacing Electrophysiology J. 2014 Oct 6;14(5):240-249***

Editor's Comment: We conclude our recap and update on the important issue of SCI as a consequence of both AFIB itself, as well as from some procedural aspects of AFIB ablations. Previously, having identified use of irrigated RF catheters and uninterrupted anti-coagulation as factors reducing risks of ablation-related SCI, we add use of dual puncture/dual sheath trans-septal access without exchange of catheters as another modifiable step for significantly reducing risk of SCI. In combination,

when all of the above methods are used, they can reduce risk of ablation-related SCI from over 40% to less than 2%.

Keeping in mind that AFIB itself is, by far, the greatest risk for ongoing increase of SCI burden over time, making a wise choice for a skilled ablationist who employs all the best practices for SCI reduction can help lower ones overall risk of both symptomatic strokes as well as these asymptomatic silent events which, as they accumulate over time, may not be so silent long term after all.

A BLAST FROM THE PAST

The AFIB Report – November 2005

Heart rate increase after ablation

COPENHAGEN, DENMARK. Several studies and indeed our own LAF surveys have observed that many afibbers experience an increase in heart rate after a pulmonary vein isolation (PVI) procedure. Electrophysiologists at the Danish Heart Centre now confirm these observations in a study involving 62 patients with paroxysmal or persistent afib. The average age of the patients was 55 years; 29% were women and 63% had hypertension or associated cardiovascular disease. The patients were divided into two groups with one group of 37 undergoing segmental PVI (Haissaguerre method) and the remaining 25 undergoing circumferential PVI (Pappone method). A Lasso catheter was used for mapping in the segmental group, while the CARTO system was used in the circumferential group.

Successful isolation of the pulmonary veins was achieved in 97% of cases; however, a repeat ablation was required in 72% of patients having the circumferential procedure and in 73% of patients in the segmental group. A substantial number of patients (55%) required ablation in areas other than the pulmonary veins with isolation of the superior vena cava (right atrium) being the most common extra procedure (required by 26 patients). The procedure time for the segmental method was somewhat longer than for the circumferential method (166 versus 138 minutes). The procedure times for the second ablations were somewhat shorter at 115 and 99 minutes respectively. During a follow-up of 8.8 months, 35 of the 62 patients (56%) experienced recurrent afib corresponding to an overall success rate of 44%. At the 12-month follow-up point 29% of the study participants were still on antiarrhythmic drugs.

The researchers observed a significant increase in the average heart rate (in sinus rhythm) of the ablatees. One month after the ablation the average rate had increased from 58 bpm at baseline to 67 bpm and further increased to 71 bpm after 3 months; at the final measuring point 12 months after the ablation, the average heart rate was still 70 bpm. Three patients had mean heart rates of 99 bpm going as high as 140 bpm and had to be prescribed a calcium channel blocker and digoxin to reduce their heart rate to a comfortable level. The researchers noted that those patients who did not experience a recurrence of afib had a significantly greater increase in heart rate than did those whose ablations were unsuccessful (13 bpm versus 6 bpm).

Other electrophysiologists have observed increases in heart rate after PVIs, but in most cases these have been transient. The Danish researchers conclude that the increases may not be transient and that up to 5% of ablatees may need long-term medication to control symptoms associated with the uncomfortably high heart rate. They suggest that the reason for the heart rate increase is that they used deeper lesions resulting in a more extensive destruction of vagal nerve fibers and thus partial elimination of the heart's built-in slowdown mechanism. They recommend that patients undergoing PVI should be informed of this possible complication.

Nilsson, B, et al. Increased resting heart rate following radiofrequency catheter ablation for atrial fibrillation. Europace, Vol. 7, September 2005, pp. 415-20

Editor's comment: It is always rewarding to see the findings of our LAF surveys confirmed by other studies. The following is taken from the September 2005 issue of *The AFIB Report*.

"Changes in heart rate after the procedures were quite common as indicated in the table below.

	Complete Success	Partial Success	Failure	Average
Increase in heart rate	58%	59%	20%	44%
No change in rate	34%	27%	52%	40%
Decrease in rate	8%	14%	27%	16%
TOTAL	**100%**	**100%**	**100%**	**100%**

The most frequent change was an increase in heart rate (experienced by 44%). This change was most common among afibbers who had undergone successful procedure(s) (58%) and least common among those whose procedures had failed to cure the afib (20%). Statistically, the difference was very significant (p=0.0015).

The reason for the increase in heart rate after an ablation is that a significant portion of vagal nerve endings are damaged during the RF ablation procedure. Because the vagal nerves imbedded in the myocardium serve as "speed controllers" counteracting the adrenergic influence, a reduction in the number of effective vagal nerves would be expected to lead to an increased heart rate. Thus, it is possible that a more "aggressive" ablation, as indicated by a higher heart rate after the procedure, is more likely to be successful. However, this is speculation on my part and obviously assumes that the "aggression" is directed at the right spots on the atrium walls and pulmonary vein ostia.

The increase in heart rate is usually temporary and abates as the vagal nerve endings heal."

My own heart rate increased to about 95 bpm after my PVI in Bordeaux; it is now, 6 months later, down to 80 bpm and will hopefully return to my normal 60 or 65 bpm within the next 6 months. Dr. Jais suggested that increased physical activity might hasten the process towards normalcy.

Benefits and risks in warfarin therapy

SAN FRANCISCO, CALIFORNIA. A team of researchers from the University of California, the Massachusetts General Hospital and Boston University School of Medicine has just completed a study aimed at determining whether women with afib have a higher risk of ischemic stroke than do men. The study included 13,559 adults with atrial fibrillation. The majority of the study participants had one or more recognized risk factors for stroke, such as hypertension (57.7%), congestive heart failure (26.7%), coronary artery disease (23.9%), or diabetes (14.2%). Only 15.8% of women and 23.8% of men could be classified as non-hypertensive lone afibbers.

The overall incidence of ischemic stroke during 15,494 person years was 2.4%. The annual average rate on warfarin was 1.5% for women and 1.2% for men as compared to 3.5% and 1.8% when not on warfarin. However, the rate among lone afibbers (not on warfarin) with no additional risk factors for stroke was only 0.6% for women and 0.5% for men – in other words, no higher than would be expected in the general population.

The incidence of major hemorrhage (fatal bleeding, blood transfusion requiring two units or more of packed blood cells, or bleeding into a critical anatomical site) was 1.0% a year among warfarin-treated women and 1.1% among men. Of the major hemorrhages 0.36% among women and 0.55% among men were intracranial (hemorrhagic stroke). The authors of the study point out that, "the health consequences of intracranial hemorrhage are worse than those resulting from the ischemic strokes we seek to prevent through anticoagulation."

Fang, MC, et al. Gender differences in the risk of ischemic stroke and peripheral embolism in atrial fibrillation. Circulation, Vol. 112, September 20, 2005, pp. 1687-91

Editor's comment: These recent findings confirm earlier ones that neither men nor women with LONE atrial fibrillation and no other risk factors for stroke benefit from warfarin therapy. As a matter of fact, for this group the risk of major hemorrhage is almost twice as high as the risk of ischemic stroke and the risk of hemorrhagic stroke for men on warfarin is actually higher than the risk of ischemic stroke when not on warfarin. Even for lone afibbers with one additional minor risk factor such as hypertension, diabetes or age over 75 years, the benefits of warfarin therapy are not at all clear-cut. Women with one additional risk factor would have an annual ischemic stroke risk of 1.8% if not on warfarin. On warfarin this risk would be reduced to 0.7%, but would be accompanied by a 1.0% risk of major hemorrhage of which 0.36% would be associated with hemorrhagic stroke. For men the ischemic stroke risk when not on warfarin would be 1.2%. On warfarin this would be reduced to 0.7%, but would be accompanied by a 1.1% risk of major hemorrhage of which 0.55% would involve hemorrhagic stroke – in other words, pretty well a toss-up.

Editor: Shannon W. Dickson

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