THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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In this month's issue we present the second part of Jackie Burgess' excellent summary of the proceedings of the Cleveland Clinic Foundation's summit on atrial fibrillation in October 2005. This part covers the use of surgical procedures such as the maze and mini-maze, and also delves into the role of genetic factors and elevated aldosterone levels in AF. The final discussion on the challenges still remaining in the ablation field is particularly interesting.

Also in this issue we report that Mayo Clinic researchers confirm lone atrial fibrillation as such does not increase the risk of ischemic stroke and make the very encouraging observation that the mortality among lone afibbers is half that of the general population. The Bordeaux group provides evidence that the duration of individual afib episodes, left atrium size, and extent of left ventricular hypertrophy can predict the probability of success of a PVI. British, Greek and German researchers all zero in on the association between inflammation, high CRP levels and afib, and German researchers tackle the problem of asymptomatic episodes after a seemingly successful ablation.

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Yours in NSR,
Hans

Highlights

Predicting ablation success

BORDEAUX, FRANCE. Electrical isolation of the pulmonary veins (PVI) is now standard practice in ablation procedures aimed at curing atrial fibrillation. In many cases, a PVI is sufficient to lead to complete abolition of future afib episodes, but in other cases, this unfortunately is not so. Studies have shown that the chance of ultimate success is much higher if afib cannot be induced after the PVI. However, in cases where afib is inducible (by pacing at the mid-coronary sinus, or at the right or left appendage), it is often possible to effect a cure by creating linear lesions at the mitral isthmus or at the roof of the left atrium joining the two superior pulmonary veins. Clearly, it would be highly desirable to be able to predict whether a simple PVI would be likely to cure a patient, or whether further ablation is likely to be required – or, in other words, to predict the likelihood of pacing after the PVI being able to induce afib.

Researchers at the Hopital Cardiologique du Haut-Leveque have now developed a protocol for estimating whether an afibber is likely to need more extensive ablation. Their study involved 181 afibbers (85% male with an average age of 54 years) who had suffered from paroxysmal atrial fibrillation (AF) for an average of 6 years prior to their procedure. The patients all underwent radiofrequency PVI (while in afib) and cavotricuspid isthmus ablation (to prevent right atrial flutter). Total

procedure time was 2.4 hours with fluoroscopy time of 39 minutes and radiofrequency exposure of 49 minutes. After completion of the PVI it was possible to induce sustained AF (longer than 10-minute episode) in 54% of the patients. These patients were then treated with additional linear lesions increasing average procedure time to 3.6 hours, fluoroscopy exposure to 66 minutes, and radiofrequency exposure to 69 minutes.

The Bordeaux researchers compared age, gender, body weight, height, BMI, time since first afib episode, duration of longest episode, presence or absence of structural heart disease, hypertension, left ventricular ejection fraction, and extent of hypertrophy and left atrium size in the group where afib could not be induced after the PVI with those in the group where afib could be induced. They found that the duration of the largest (symptomatic) episode, left ventricular hypertrophy (septum thickness greater than 12 mm in parasternal long-axis view), and longitudinal left atrium diameter (greater than 57 mm) were independent predictors of the likelihood that AF could be induced after a PVI. Not having experienced afib episodes lasting longer than 12 hours was associated with an 86% probability that sustained afib could not be induced after the standard PVI (86% sensitivity, 78% specificity). On the other hand, having experienced episodes longer than 48 hours made it a near certainty (97% probability) that sustained afib could be induced after the PVI, thus necessitating further ablation. The absence of left ventricular hypertrophy was associated with a 96% probability that sustained afib could not be induced, and a left atrium diameter (longitudinal) of less than 57 mm predicted that fib could not be induced with a 75% probability.

The researchers conclude that measuring left atrium diameter, the extent of left atrial hypertrophy, and enquiring about the duration of the longest episode experienced by a patient prior to ablation will assist in better planning of the procedure and a more realistic estimate of the chances of ultimate procedural success.

Rotter, M., et al. Clinical predictors of noninducibility of sustained atrial fibrillation after pulmonary vein isolation. **Journal of Cardiovascular Electrophysiology**, *Vol. 16, December 2005, pp. 1298-1303*

Editor's comment: This Bordeaux study underscores that all afibbers are not created equal, and also goes a long way toward explaining why a simple PVI is often not sufficient to effect a permanent cure.

Inflammation and atrial fibrillation

BIRMINGHAM, UNITED KINGDOM. British researchers present a thorough review of the current knowledge regarding an association between systemic inflammation and atrial fibrillation. Please note that the review does not distinguish between lone AF and atrial fibrillation with underlying heart disease. Thus the conclusions presented may or may not apply to lone afib.

The researchers point out that it is generally accepted that afib results in both electrical and structural remodeling of the atria. The main features of the electrical remodeling are shortening of the atrial refractory period (the rest period following a contraction of the heart muscle. The cell [myocyte] does not respond to stimulation during this period), prolongation of atrial conductivity, and the loss of rate adaptation. Another feature of the electrical remodeling is the accumulation of calcium within atrial myocytes leading to a further shortening of the atrial refractory period. The main features of the mechanical remodeling are enlargement of the left atrium and increasing atrial fibrosis (deposition of connective tissue between individual myocytes). These electrical and structural changes increase the likelihood of further afib episodes (afib begets afib).

There is now also increasing evidence that atrial fibrillation is linked to a systemic inflammation. Atrial biopsies have demonstrated the presence of inflamed tissue in both lone and non-lone afibbers. Measurements of blood levels of the inflammatory marker C-reactive protein (hs-CRP) have shown that levels tend to be higher among people with afib than among normal controls. There is also evidence that levels are higher among persistent afibbers than among paroxysmal afibbers, and finally, studies have shown that high hs-CRP levels are associated with an increased risk of developing new onset AF.

Several drugs and supplements have anti-inflammatory properties and have been found to reduce the risk of developing afib and/or reduce the number of episodes. Four studies have shown that statin drugs may have a role in the prevention of afib in humans, and animal studies have shown that statins may also reduce the frequency of episodes.

Methyl prednisolone, a steroid anti-inflammatory drug, has been found to reduce recurrence of afib episodes when taken together with propafenone. There is evidence that both ACE inhibitors and angiotensin-receptor blockers (ARBs) have significant anti-inflammatory properties and may help prevent both the development and recurrence of AF – at least in patients with hypertension or heart disease. Fish oils also have significant anti-inflammatory properties and may be beneficial in preventing ventricular arrhythmias and AF occurring after bypass surgery. However, there is no convincing evidence that fish oils help prevent lone AF. Vitamin C has also been found to reduce the incidence of post-surgery afib and may help reduce the risk of early recurrence after cardioversion.

The researchers conclude that there is ample evidence of a link between inflammation and afib, and that anti-inflammatory drugs or supplements may play a role in preventing atrial fibrillation and its recurrence.

Boos, CJ, et al. Is atrial fibrillation an inflammatory disorder? **European Heart Journal**, *Vol. 27, 2006, pp. 136-149*

Editor's comment: As is, unfortunately, often the case in articles dealing with AF, no attempt was made here to distinguish between lone afib and afib with underlying heart disease. This is perhaps understandable since lone afibbers are a distinct minority (perhaps 20% of all afibbers). Nevertheless, recent work by Patrick Chambers, MD (*The AFIB Report*, February 2006) points to the very real possibility that lone AF may be a condition distinctly different from AF related to heart disease. Thus, the findings of the review may be only partly applicable to lone atrial fibrillation.

Statin drug may help prevent AF

MYTILINI, GREECE. There is considerable evidence that a systemic inflammation may be involved in atrial fibrillation. There is also evidence that high blood levels of the inflammation marker C-reactive protein (CRP) are associated with an increased risk of developing afib and experiencing recurring episodes. C-reactive protein levels can be effectively reduced with statin drugs (and many natural compounds), and there is some indication that doing so may reduce the risk of recurrent afib episodes after a successful cardioversion. Now Greek researchers report that the cholesterol-lowering drug atorvastatin (Lipitor) is effective in reducing the number of episodes in paroxysmal afibbers. Their study involved 80 patients who had documented asymptomatic afib episodes on a 48-hour Holter monitoring prior to beginning treatment. The patients (55 men and 25 women) were between the ages of 29 and 85 years (median 52 years). Their baseline CRP level ranged from 0.8 to 13 mg/L (0.08 – 1.3 mg/dL) with a median of 5.9 mg/L (0.6 mg/dL). NOTE: The normal range is considered to be 0 – 5 mg/L. Half the patients were assigned to receive a placebo, while the other half received 20 mg/day of atorvastatin (increased to a maximum of 40 mg/day if a 20% reduction of CRP was not achieved by 6 weeks) for the duration of the 4-6 month study period. Holter monitors were used at the beginning and end of the study to ascertain the number and duration of episodes experienced over a 48-hour period.

The researchers, not too surprisingly, found that members of the atorvastatin group experienced a significant drop in total and low-density cholesterol. They also observed that average CRP levels in the atorvastatin group dropped from 5.8 mg/L to 2.8 mg/L over the study period. The average number of afib episodes (all asymptomatic) decreased from 9 in the baseline 48-hour monitoring to 0 in the end-of-study monitoring in the atorvastatin group, while it declined from 13 to 12 in the placebo group. The researchers conclude that atorvastatin may be useful in reducing CRP levels and the frequency of afib episodes in afibbers with the paroxysmal variety.

*Dernellis, J and M. Panaretou. Effect of C-reactive protein reduction on paroxysmal atrial fibrillation***.** **American Heart Journal**, *Vol. 150, November 2005, pp. 1064-69*

Editor's comment: Although intriguing, I am not certain just how much hope these findings hold for the average paroxysmal afibber. The group involved in the study was somewhat unusual in that its members had mild or no symptoms during daily life and did not report any symptoms during the two monitoring sessions. They also tended to have elevated CRP levels, which does not seem to be common among the lone afibbers I have surveyed (my own level during my worst period of afib was less than 0.3 mg/L). So would atorvastatin or CRP-lowering as such help an afibber with highly symptomatic episodes? I don't know, but I am somewhat skeptical that the claims made by the

Greek researchers would apply to the majority of afibbers. However, having a high CRP level is detrimental in many ways so reducing it can certainly do no harm. Successful reduction can be achieved by supplementing with beta-sitosterol, Moducare, Zyflamend or boswellia. Statin drugs will also do the trick, but should always be taken accompanied by at least 100 mg/day of coenzyme Q10.

Warfarin interactions

HEIDELBERG, GERMANY. Warfarin (Coumadin) is widely prescribed for afib patients for the prevention of ischemic stroke. Its purported benefits are, however, to a large degree, offset by its tendency to cause internal bleeding and hemorrhagic stroke. For lone afibbers with no other risk factors for stroke the negative effects of warfarin therapy generally outweigh the benefits.

A team of researchers from Germany, Sweden and Switzerland has just concluded a study aimed at determining if the bleeding risks associated with warfarin usage are increased in patients taking other pharmaceutical drugs as well. Their study involved 4152 afib patients (aged between 40 and 84 years) who were on warfarin for non-valvular AF. During follow-up (for an average of 11 months) 133 patients died from internal bleeding and another 432 were hospitalized with serious bleeding. This corresponds to a warfarin-associated mortality rate of 3.5% a year and a serious bleeding rate of 12% a year. The researchers observed that 58% of all patients on warfarin had also been prescribed one or more of 88 specific drugs that are known to interact with warfarin. They also found that patients who were taking potentially interacting drugs experienced a 3.4-fold increased risk of serious bleeding. The use of a combination of warfarin and aspirin (75-325 mg/day) was associated with a 4.5-fold risk increase, while the concomitant use of acetaminophen (Tylenol, Paracetamol) was associated with a 3.8-fold increased risk at doses between 885-2900 mg/day taken for at least 4 weeks. Other particularly detrimental drugs were allopurinol (Zyloprim), amiodarone (Cordarone), levothyroxine (Synthroid), Metronidazole, Miconazole, and omeprazole (Prilosec). Taking Metronidazole or Miconazole during warfarin therapy was associated with a 40-fold increase in the risk of a serious bleeding event.

The researchers conclude that drug interactions are an independent risk factor for serious bleeding in patients on long-term warfarin therapy. They also point out that the practice of prescribing potentially interacting drugs is widespread.

Gasse, C, et al. Drug interactions and risk of acute bleeding leading to hospitalisation or death in patients with chronic atrial fibrillation treated with warfarin. **Thrombosis and Haemostatis**, *Vol. 94, September 2005, pp. 537-43*

Early recurrence of afib after PVI

BAD NAUHEIM, GERMANY. Several studies have shown that the average success rate (absence of afib with no medications) of pulmonary vein isolation (PVI) is about 50% with some specialized centers like Cleveland and Bordeaux doing much better and other centers doing significantly worse. There is, unfortunately, no agreement as to how success should be measured. Is it the total absence of symptomatic episodes observed by the patients after the PVI? Is it the absence of afib on occasional Holter recordings or ECGs performed after the PVI? How long should an afib episode last to be considered significant – more than 30 seconds or more than 2 minutes? Is a PVI a success if the patient's quality of life improves, or is strict absence of afib the only measure of success? No agreement exists on these points and this, of course, is bound to influence the success rates reported by various institutions.

German cardiologists recently reported on the outcome of 100 consecutive PVIs performed at the Kerckhoff-Klinik. Most (90%) of the 100 patients involved had no underlying structural heart disease with 85% having paroxysmal and 15% having persistent afib; 62% were men and the average age was 54 years (45-63 years). Radiofrequency (RF) ablation was used in the case of 63 patients, while the remaining 37 patients underwent a hybrid cryotherapy/RF ablation.

Early recurrence of afib (ERAF) was documented (with a portable recorder) in 30% of RF-treated patients and 25% reported symptomatic episodes. Corresponding numbers for the patients treated with the hybrid method were 43% and 35% respectively. The researchers found that patients with early recurrence who experienced a total of more than 6 hours of afib during the first 3 months after the PVI had a 100% probability of experiencing further episodes in the future – ie. of not being cured. In contrast, patients who experienced no ERAF during the 3 months following the PVI had a 65% probability of being completely afib-free and an 86% probability of their improvement remaining stable.

The overall probability of freedom from any symptomatic afib episodes over a 2-year period following the PVI was 50% for the RF group and 39% for the hybrid group. About 16% of RF procedure patients (19% of hybrid patients) experienced asymptomatic episodes after the first 3 months; however, these episodes generally lasted only between 1 and 6 hours and thus should not be a cause for concern as far as stroke risk is concerned. Quality of life scores improved significantly for patients who had undergone a completely successful procedure or whose afib burden (total time spent in afib over a 3-month period) was less than 12 hours. However, patients with an afib burden greater than 12 hours (per 3 months) experienced no improvement in quality of life score as compared to their score prior to the PVI.

The researchers conclude that an afib burden greater than 12 hours is an indication of failure as far as quality of life is concerned. They also suggest that symptomatic ERAF (episodes during first 3 months post-PVI) is highly predictive of late recurrence and should be used as an indicator for a repeat ablation.

Berkowitsch, A, et al. Usefulness of atrial fibrillation burden as a predictor for success of pulmonary vein isolation. **PACE**, *Vol. 28, December 2005, pp. 1292-1301*

Editor's comment: The findings of the German researchers are in accordance with the findings of our LAF Survey 9. In this survey we found that afibbers who experienced no episodes during the first 3 months after their PVI had a 63% probability of being completely afib-free (the German researchers corresponding number is 65%).

LAF does not increase stroke risk

ROCHESTER, MINNESOTA. Researchers at the Mayo Clinic have published a very important study regarding the correlation between lone atrial fibrillation (LAF) and stroke risk and overall mortality. The study is remarkable in that it followed the participants for 30 years and thus gives a good indication of the long-term prognosis for untreated LAF. The study involved 46 residents of Olmsted County who were diagnosed with LAF at an average age of 45.8 years (range of 34-58 years). None of the participants had coronary artery disease, hypertension, diabetes, mitral valve prolapse, congestive heart failure, or any other condition that would increase their risk of ischemic stroke (cerebral infarction). None of the participants were treated with warfarin. They were followed until death or July 1, 2002. At time of last follow-up the average age was 74 years (range of 63-85 years). At the beginning of the study 76% of participants had paroxysmal afib and 24% had the persistent variety; this changed to 59% paroxysmal and 41% persistent by the end of the study period. All participants were Caucasians and 83% were men.

The Mayo researchers made the following important observations:

1. The observed mortality rate among the afibbers over a 25-year period was substantially lower (15.9%) than the mortality expected in a group of age- and sex-matched white Minnesotans (32.5%).

2. The incidence of ischemic stroke (cerebral infarction) in the afib group was no greater (0.5%/person-year) than in the general population. The researchers conclude that, "This observation indicated that the pathophysiological mechanisms responsible for the development of a cerebrovascular event were unrelated to the continued presence of AF." In other words, LAF as such is not associated with an increased risk of stroke.

3. The volume of the left atrium (LAV) is an important indicator of the risk of adverse events such as stroke, heart attack (myocardial infarction), and congestive

heart failure. A LAV (indexed for age and body mass) equal to or greater than 32 mL/m^2 was associated with a 4.46-fold increase in the probability of experiencing an adverse event.

4. All cerebral infarctions occurred in participants whose LAV prior to the incident was greater than 32 mL/m^2.

5. No correlation between age or the number of years afib had been present (duration) and LAV was observed; however, there was a highly significant correlation between persistent afib and enlarged LAV.

6. The average age at which a stroke occurred in the LAF group was 77 years, not significantly different from that observed in the general population.

7. Eighteen participants died during the study; 9 of cardiovascular disease, 4 of cancer, and 4 of a respiratory tract infection.

The researchers conclude that LAV is an important predictor of the likelihood that lone afibbers will suffer adverse events (stroke, heart attack, etc) during their lifetime. It is far more important than age and left ventricular ejection fraction. They suggest that only afibbers with a LAV less than 32 mL/m^2 should be classified as "lone". These afibbers had a benign clinical course during follow-up, while afibbers with an elevated LAV at diagnosis or later during follow-up experienced adverse events.

Osranek, M, et al. Left atrial volume predicts cardiovascular events in patients originally diagnosed with lone atrial fibrillation: three-decade follow-up. **European Heart Journal**, *Vol. 26, 2005, pp. 2556-61*

Editor's comment: The findings of the Mayo study are indeed encouraging. They confirm my long-held conviction that otherwise healthy lone afibbers are at no greater risk of stroke than is the general population and therefore does not warrant warfarin therapy. It is encouraging that the mortality among lone afibbers over 25 years of the study was less than half that found in the general population. The observation that left atrial volume (LAV) is an important predictor of future adverse events is intriguing. Hopefully, it will eventually lead to LAV being measured as part of the routine examination of afibbers.

Cardioversion success and CRP level

ROCHESTER, MINNESOTA. Electrical cardioversion is a common procedure for converting atrial flutter and persistent afib to normal sinus rhythm (NSR). Persistent afib is defined as afib lasting longer than 7 days without converting spontaneously to NSR. Unfortunately, in as much as two thirds of cases the conversion does not hold and afib or flutter recurs within one month of cardioversion.

Researchers at the Mayo Clinic now report that a high blood level of C-reactive protein (CRP), a marker of systemic inflammation, prior to cardioversion is associated with a greater probability of afib recurrence within one month. The researchers studied 17 patients with atrial flutter and 50 patients with persistent afib. They measured CRP level just prior to cardioversion and observed that the average level in patients who remained in sinus rhythm after cardioversion (6.0 mg/L) was significantly lower than the level (10.7 mg/L) in patients who reverted to afib or flutter within one month after cardioversion. They conclude that high CRP levels prior to conversion double the risk that the cardioversion will not result in maintenance of NSR beyond the first month (after adjusting for other relevant factors such as age, gender, and medications used prior to cardioversion). About two thirds of the patients cardioverted had no recurrence within the first month. The researchers conclude that anti-inflammatory medications may help retain NSR after cardioversion and that measuring CRP prior to cardioversion may provide valuable information as to the likelihood of the cardioversion being successful beyond the first month.

Malouf, JF, et al. High sensitivity C-reactive protein: a novel predictor for recurrence of atrial fibrillation after successful cardioversion. **Journal of the American College of Cardiology**, *Vol. 46, October 4, 2005, pp. 1284-87*

Editor's comment: There is usually a 6-week waiting period between establishing the need for cardioversion and actually carrying out the procedure. During this period warfarin is administered to prevent blood clotting and a potential ischemic stroke immediately following the procedure. It would seem prudent to use this 6-

week period to reduce the CRP level using such natural anti-inflammatories as Moducare or beta-sitosterol. There is also evidence that a low level of potassium is associated with poorer outcome of cardioversion, so supplementing fairly heavily with potassium and magnesium prior to the procedure may also be beneficial.

Real success rates for PVIs

LEIPZIG, GERMANY. Pulmonary vein isolation (PVI) is now the standard procedure for the curative treatment of atrial fibrillation. Success rates (no afib, no medication) as high as 95% have been reported, but most centers report cure rates of about 50-70%. Unfortunately, there is no common agreement as to how success should be measured. Does absence of symptomatic episodes constitute success, or is it necessary to document the absence of afib via periodic Holter recordings or transtelephonic ECGs?

German researchers recently set out to answer this question in a study of 30 consecutive, highly symptomatic afibbers who underwent an electro-anatomically guided (Pappone) PVI procedure. The study participants (25 men and 5 women) with an average age of 56 years had suffered from AF for an average of 5 years and 37% of them had lone afib, while 50% had a history of hypertension, and 17% had coronary artery disease.

All participants underwent 7-day Holter recordings prior to the procedure, immediately after the procedure, and 3 and 6 months after the procedure. They were also equipped with a monitor that automatically transmitted a 12-lead electrocardiogram to a monitoring service every 2 days throughout the 6-month monitoring period and whenever the patient activated the recorder because of a symptomatic afib episode. Holter monitoring produced the following results:

	Percentage of Patients with AF Episodes	
	Total Documented	Asymptomatic
Prior to ablation	93%	10%
After ablation	80%	50%
After 3 months	58%	46%
After 6 months	54%	53%

Thus, according to the Holter monitoring only 46% of ablated patients were actually totally free of documented afib 6 months after the procedure. However, at the 6-month check-up about 70% of the group were free of afib if only symptomatic episodes were considered. About 31% of all afibbers who experienced episodes were completely asymptomatic. The mean episode duration among afibbers still experiencing episodes showed a gradual decline from an average of 31 hours prior to ablation to 22 hours post-ablation to 16 hours after 3 months and 5 hours after 6 months. A total of 2600 transtelephonic ECGs were recorded in the 30 patients. A total of 216 episodes were documented during 157 days with 25% of them being asymptomatic.

The German researchers conclude that the success rate of the PVI was about 70% if only symptomatic episodes are considered, but only about 50% if asymptomatic episodes were included as well. The high incidence of completely asymptomatic episodes is of concern in regard to the need for continued stroke prevention measures. However, the duration of asymptomatic episodes tended to be quite short (average of 2 hours at the 6-month check-up), so blood clotting may not be a problem in the majority of cases.

Piorkowski, C, et al. Value of different follow-up strategies to assess the efficacy of circumferential pulmonary vein ablation for the curative treatment of atrial fibrillation. **Journal of Cardiovascular Electrophysiology**, *Vol. 16, December 2005, pp. 1286-92*

CLEVELAND CLINIC FOUNDATION ATRIAL FIBRILLATION SUMMIT

October 14-15, 2005
Intercontinental Hotel MNBA Conference Center
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SUMMARY REPORT & OBSERVATIONS – PART II

by Jackie Burgess, RDH

"THE ORIGIN OF SURGICAL ABLATION and WHERE WE ARE TODAY"

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[Clarification - many patients who have opted for a surgical ablation procedure also had concomitant surgery, as in mitral valve repair].

Dr. Jim Cox performed the first Maze procedure in 1987. Cox Maze III procedure is what he settled on which involves a myriad of surgical incisions in the right and left atrium. The theory being, this would block signals, but he ended up isolating all PV and the entire back of the LA felt to be responsible for AF back in the 80's which has shown, in time, to be extremely important in preventing AF.

We have learned the Maze III full maze lesion set for whatever reason seems to be effective in restoring sinus rhythm and is particularly effective in preventing stroke. Summary follow up report of the cut-and-sew method and long-term efficacy indicates what they experienced at Washington U (that is - 200 patients with a median follow up for 5 year and some, for 14years which was the lone maze at 14 years,) 92% had freedom from AF. Pretty spectacular results. In concomitant maze procedure (mitral or coronary surgery) 10 years – 97% AF free.

Why not just keep doing this? Only 80% in the lone maze were actually afib free and medication free and I think most patients would not view as complete success unless off medications. Some of the concomitant surgical patients (about 25%) were still on antiarrhythmic drugs.

In the lone maze, there has been only one late stroke in entire group (was in NSR at the time) – pretty remarkable and has been verified by other institutions across the country as well – average follow 5-1/2 years and 200 patients. We now use the Maze IV procedure using ablation devices with two simple incisions, with whole array; bipolar radio frequency is very quick…less than a minute. Still use cryo lesion at the annulus.

What we don't know: No one knows the significance of each individual lesion of the Cox Maze procedure. It appears bi- atrial is more effective than single atrial procedure, but both are more effective than PVI.

One problem in surgeries is we do not know the mechanism of AF in each individual, and that does not allow us to tailor a procedure for each patient as Dr. Morady does and has made tremendous progress with his tailored electrophysiology approach. To get 100% success for lone AF, probably we need to have better understanding of the mechanisms of AF in order to develop that procedure and this will take development and refinement of clinical diagnostic technology - tremendous progress is being made along that line as you have seen with the pre op mapping. We should continue with limited lesion sets which are working and do a better job of risk stratifying of patient's report atrial diameter, duration of actual AF duration; and carefully state the exact procedure rather than a Maze or Mini-maze – whatever that is. There are lots of types and we need to be careful with reporting results.

In conclusion, looking back on my 20 years experience with atrial fibrillation, it could be said…. "The more you learn about atrial fibrillation, the less you are likely to know." There is a diverse group of patients with a spectrum of complex arrhythmias AF and one procedure probably isn't applicable for all.

Randall K. Wolf, MD
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He began with a video of a live heart, in an open chest cavity, beating in atrial fibrillation, and commented that many allied health people outside of surgery don't have the opportunity to view the chaotic arrhythmia but cardiac surgeons see it every day. He said it was clear why patients are so symptomatic. [For me, it was sad to view that heart and it brought back vivid memories of how badly I felt so many times and for so long while in afib. It's difficult to imagine that it isn't fatal.]

Dr. Wolf said when they interview patients, they describe all the options including the least invasive – catheter ablation – and says the Cox Maze has the best results. Dr. Wolf has worked with Dr. Jackman and agrees with the approach of partial cardiac denervation and the genesis of afib. By focusing on ganglia plexii, high frequency stimulation of fat pads is routine in every case. They use a standard EP catheter; do transmural lesions in veins and find the ganglia plexii. His mapping is very similar to mapping done by Dr. Jackman's at U of Oklahoma.

He said it is very important to divide the Ligament of Marshal (LoM) and is leery of right-side-only 'minimally invasive' approaches that don't take care of that and the LAA. The only way to do that is be on the left side. They find that signals are often in the LoM. The Left Atrial Appendage (LAA) is always excised.

He believes this procedure will revolutionize the treatment of paroxysmal AF. It has a high cure rate. They try not to do large atriums or patients with 20 years of AF… and they do remove the LAA.

SHOULD SURGERY BE CONSIDERED FOR TREATMENT OF LONE ATRIAL FIBRILLATION?

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CONCESSIONS
-Progress in surgical ablation of AF has been impressive and should be encouraged.
-Surgical ablation during concomitant cardiac procedures can treat patients that are probably not well served by catheter ablation.
-Technology available for surgical ablation is more advanced than that for catheter ablation.

However,
-Catheter ablation for patients with early lone AF is safe and effective.
-Lone AF is an electrophysiologic disease and ablation should not be "one size fits all'.
-There are limited data regarding stand-alone surgical ablation (post MAZE III).

PROBLEMS WITH CATHETER ABLATION
-incidence of stroke – around 1% - need a procedure with no risk of stroke
-his own experience no strokes in last 320 cases with increased ACT
-pulmonary vein stenosis – about 1.6% -essentially eliminated with ICE guidance
-atrial-esophageal fistula – about 0.01% -
-EPs lack of uniform approach
- Inconsistent follow up and reporting of complications; no formal registry

PROBLEMS WITH SURGICAL ABLATION
(His comment: patients more ill and have worse AF. Difficult comparison)
-limited data regarding stand-alone AF ablation
-post-operative AF about 40% - expect lower with off pump, stand alone.
-atrial-esophageal fistula – around 1% (unipolar energy)

-surgical mortality/morbidity
-lack of uniform approach – technology fest
-inconsistent use of anti-arrhythmic agents
-complete avoidance of post-operative monitoring – (Dr. Wolf is starting intensive monitoring and he salutes him for this)
-no registry

WHERE DO WE GO FROM HERE? Adversarial relationships are unproductive; atrial fibrillation is a syndrome; surgical and catheter ablation will both have defined roles in patient treatment; nonpharmacologic therapy has been applied to <1% of the AF population – so there is plenty of work for everyone.. More data is necessary; need to set up registry; analogy to the STS registry surgeons have a registry for coronary disease.

His opinion: Surgical ablation is not appropriate for Lone Atrial Fibrillation. There is a lack of outcome data …there is a significant morbidity including pain in these patients. He says, "I was concerned about all those things going into holes in these patients."

SURGICAL TREATMENT OF ATRIAL FIBRILLATION WITH MITRAL VALVE DISEASE

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Mitral valve disease is common and progressively age-related. By ages 60 – 70, about 20-40% already have preexisting AF in addition to the mitral disease. Just because its there isn't a reason to treat but this is: "if mitral regurg is treated and stenosis is treated but the AF is not, then the patient is left with increased risk of stroke and death. The incidence of mitral valve disease with AF increases with age. By age 80, 40% of patients have mitral valve involvement.

Stats show MAZE people live longer than living with AF. With Maze, 99% of patients are free from stroke compared to about 70% with no maze. Most patients throughout the country are not treated for AF when they go in for mitral valve or coronary disease. They leave with untreated AF. We are a bit different here at the Clinic; we attempt to treat both in most patients as most have valve disease. Lone AF is not an indication for surgical treatment but newer treatments such as Dr. Wolf's may change that.

The Maze Procedure is extremely successful, but it is a big deal and patients often choose a less invasive approach. Takes time; lots of suture marks, but is successful and risk of stroke is reduced to about zero, in time. There is some morbidity as with all open-heart surgical procedures.

Summary: AF is a tenacious, erratic disease evolving over a lifetime, and brief post-interventional follows-ups over period of months should be interpreted cautiously. There are several dozen new technologies in development today which will probably available in 2006. We look to the future of tailoring surgical procedures for individual patients and hope to be able to assess the results and look patients in the eye some day and say…."you are cured of atrial fibrillation."

PATHOGENESIS AND GENETICS OF ATRIAL FIBRILLATION

David Van Wagoner, PhD. – Topic: INFLAMMATORY MECHANISMS OF ATRIAL FIBRILLATION

There are numerous associations between cardiovascular events and a systemic inflammatory state. In the examination of the inflammatory mechanism in AF, a common theme is emerging about the role of inflammation pathways, cellular and tissue response to inflammation and the result is adaptive changes in the heart. Risk factors associated with AF include, aging, hypertension, valvular disease (stretch) CAD, dyslipidemia, diabetes, autonomic imbalance, SVT (high rate electrical activation) and cardiac surgeries, along with elevated C-reactive protein levels indicative of inflammation, cell infiltration and tissue injury. Inflammatory changes in AF lower NO

and increase PAI-1 and promote thrombus formation in the LAA, stroke and death. CRP is a marker of inflammation and predicts the extent of scarring and also success of ablation.

The common mechanisms of AF are sympathetic stimulation related to rate and stretch; structural remodeling related to hypertrophy, apoptosis and fibrosis; electrical remodeling and vagal stimulation.

Mina K. Chung, MD, Electrophysiologist - Topic: GENETICS OF ATRIAL FIBRILLATION

Atrial fibrillation is an arrhythmia in which identification of underlying humoral or genetic factors might be beneficial. Genetic, biochemical or hormonal factors may contribute to the development or perpetuation of AF. Familial forms of AF have been reported. Parental atrial fibrillation increases the risk of AF in offspring. A gain-of-function mutation in the beta subunit of a potassium channel has also been associated with familial atrial fibrillation and a mutation in a sodium channel gene, has been associated with early dilated cardiomyopathy and atrial fibrillation. A study of familial Wolff-Parkinson-White Syndrome links metabolic instability with the electrical instability that promotes atrial fibrillation. Further study is needed to identify genetic factors that are more relevant to larger populations of atrial fibrillation and to better understand the pathogenesis

Bruce Stambler, MD – Topic: ATRIAL ANTIARRHYTHMIC EFFECTS OF SELECTIVE ALDOSTERONE BLOCKADE IN HEART FAILURE

Elevated Aldosterone (ALD) can have major deleterious effects on the heart since it leads to inflammation and myocardial fibrosis. Elevated ALD leads to cardiac fibrosis which leads to increased collagen synthesis and collagen deposition which leads to myocardial fibrosis which means LV stiffness and LVD and ultimately congestive heart failure.

The impact of elevated ALD includes: cardiovascular disorders and heart failure, myocardial fibrosis and remodeling, vascular injury and fibrosis, vascular compliance lowered, impaired baroreceptor function, catecholamine potentiation, prothrombic effects (incr. PAI-1), sodium reabsorption and water retention, K+ and Mg2 loss, progressive renal disease, heart rate variability. All these are contributory to cardiovascular disorders including pathways leading to AF, Atrial tachyarrhythmia and atrial flutter and hypertension, heart failure, stroke, ischemia, end stage renal failure.

Conclusions: the use of eplerenone as a selective aldosterone blockade in CHF, suppresses inducibility of sustained atrial tachyarrhythmias; prolongs atrial ERPs; attenuates diastolic dysfunction; is more effective than ACE inhibition with benzepril in suppressing atrial arrhythmias, prolonging ERP and attenuating diastolic dysfunction; has its effects on inducibility of atrial arrhythmias and prolongation of ERP reversed by isoproterenol.

DEBATE: MORE TECHNOLOGY OR MORE EXPERIENCE: WHAT DO WE NEED FOR PERCUTANEOUS ABLATION?

Pro:
Atul Verma, MD, FRCPC
Southlake Regional Health Center - Staff Electrophysiologist
University of Toronto, Newmarket, Toronto, Canada

THE ANSWER LIES IN TECHNOLOGY - MY ARGUMENT
We know a lot about the technique. There is a convergence in technique. Operator experience plateaus. We have enough “experience”. Major barriers or limitations to widespread use are practical ones and the answer to these limits lies in technology.

“Ever since the Bordeaux group perfected the technique, and despite all the arguing and debates out there, PV isolation has remained the cornerstone or bedrock procedure for ablation. PVI has remained a very consistent and enduring theme since 1998. As recently as last year, Karl Heinz Kuck, using the double lasso technique found if you can get true isolation in all pulmonary veins you can get incredibly high success rates (95%) in paroxysmal atrial fibrillation.

Fluoroscopy can be very challenging – it's two-dimensional and doesn't really give you a good feel for all variations of anatomy. With the development of real time imaging technology and procedure, the ICE monitor, we now have a better understanding of anatomy and keep the ablation pathway as well. Incidence of severe stenosis is dropping to almost zero and this topic went from hot to passé. Today's vexing issue is esophageal injury and we alter that in terms of time and power to minimize injury and with the latest technology.

Fluoroscopy time is a concern for both EP and patient. The day is right around the corner when not only will we see the left atrium but also the lasso within the left atrium and the ablation path in relationship to the lasso. We will see our catheters or lassos moving on real 3D CT or MRI images and we may never have to push on another fluoroscopy pedal again.

Con:
Gregory K. Feld, MD
Professor of Medicine - Director, Cardiac Electrophysiology Program
University of California - San Diego Medical Center -San Diego, CA

Drs. Feld and Verma discussed the debate beforehand and decided the number of cases you do is not that critical and rather than more experience, he feels a better description would be – "more knowledge" is needed for his position in this debate.

Certainly without technology, we wouldn't be anywhere. Technology has been rapidly advancing but we are ahead of ourselves. I'm not sure we have a good understanding of the potential mechanisms of AF and how they pertain to the patient. With all the different procedures there seems to be some convergence and consistency in approach but we still may not be appropriately targeting our individual patients with a specific procedure. And I propose that more experience and KNOWLEDGE will allow us to do that.

Regarding PV electrical activity triggering AF certainly it is one of the most important mechanisms specifically in paroxysmal AF patients. There may be non-electrical activity triggers as well as mechanical, but it's not entirely clear. Whether this is due to localized re-entry or other factors, research doesn't clearly tell us which mechanism may underlie the triggering in the PV. May be non PV electrical activity may be local reentry, local scarring or the old historical info on multiple wavelet bands maintaining afib leading to electrical remodeling or regional scarring. Certainly with the various types of technology available we can get a better handle on the types of mechanisms involved in various cases.

Multiple approaches and potentially multiple mechanisms, and at first blush, the success rates look very good, but there is even more data out there to show that we may be too optimistic about these success rates; we need more careful assessments with outcomes with event monitoring. In paroxysmal cases the success outcomes are higher, but certainly in persistent, these rates are lower. While the success rates are good, further improvement is still possible. And further efficacy will require greater experience and greater knowledge and not necessarily more technology.

Closing Remarks

Are We Curing Atrial Fibrillation?

Antonio Pacifico, MD
Founder and Chairman – Texas Arrhythmia Institute – Houston, TX

Dr. Pacifico presented the skeptic's view of the successful treatment of atrial fibrillation by all current methods. Tragically, not long after the Summit, he was killed in a plane crash and Dr. Steven Hao of Marin General offered this insight to his well-known role as skeptic.

"The passing of Antonio Pacifico is a true loss to the field of cardiology/electrophysiology and all those who knew him. His insights/discussions were always carefully crafted to provide perspective and inspire scientific thought, both necessary to rein in unbridled enthusiasm. He will be missed."

Following are my notes and I urge you to read his short published paper at the afibbers.com web site, especially if considering an ablation procedure
http://www.afibbers.com/forum/read.php?f=6&i=19014&t=19013#reply_19014

We have not long enough follow-ups to say 'cured'. Patients are just asymptomatic. He first challenged the Cox and modified procedures with these points:

- Stroke risk – incomplete evaluation
- Failure rate of sinus node function is high and this is not being assessed.
- No random trial for efficacy and safety of these procedures
- Post-procedure – pts wear a Holter for 7 days – this is not long enough to proclaim a cure or anything else.
- Method to detect arrhythmia recurrences not clearly described
- Not enough being assessed
- As stated in his published opinion, he repeated concern about silent atrial fibrillation with up to 50% asymptomatic afib recurrences.
- 70% of the reporting data comes from only three groups with a mean age of less than the majority of the patient population
- Important to look at left atrial function since, in time, the atrium is enlarged; stroke concerns.
- He expressed concern over long procedures over 90 minutes; the average time is 2-3 hours of fluoroscopy time

And his parting remarks left questions unanswered: …. "If we are ablating heart tissues for hours (and the area isn't that large to begin with), what amount of tissue is left unscarred? Are we endangering future lives?"

My Observations

Among the many videos I viewed last October, some images are still vividly present in my memory. Among my impressions are:

Many video examples of a fibrillating heart; small wonder we feel as badly as we do.

It was also obvious there is no one uniform technique; rather the judgment of either the cardiac surgeon or the EP is extremely important based on their experience with certain situations and history of the patient emphasizing the importance of going to a highly practiced and skilled professional.

Demonstration and discussion of placement of catheters, the proximity of the esophagus and the pulmonary vein burns to explain why esophageal fistulas are such a threat. No question; this procedure does not belong in the hands of the inexperienced. Amazing they are able to accomplish all they do - safely.

Saw a video of an excised LAA that was described as 'didn't know its job was done'...it lay there on a gauze pad still beating. A new (to me) area of potentials or drivers: The Ligament of Marshall, highly arrhythmogenic. The excision of this ligament in the Maze procedure eliminated AF. (As did the excision of the LAA.) The Ligament of Marshall is responsible for adrenergic stimulation of AF. Several presenters emphasized the importance of removing this ligament and showed many views of the size and shape both before and after excision.

Silent arrhythmia was mentioned by every speaker. It was very obviously of great concern. It even permeated the group discussion at my table at lunch.

When you see videos of the pulsing heart and the many catheters all pulsing inside in concert to each beat during a procedure, it reminded me of tiny dancing sea plants or little snakes curved at the tips and all affected

positionally by each contraction of the heart. To then, imagine that a burn is delivered accurately is certainly a test of skill.

One of the EPs said …this is not an art, but rather a science and we need to get back to delivering the science. IMHO I would tend to disagree and say it is definitely a combination of both. In the hands of the unskilled or inept, the science would mean nothing.

The lack of any reference to nutritional intervention was so powerful it was deafening; to my ears only, of course. I didn't expect otherwise. I was very much the lone ranger at that convention for the nutritional aspect.

My original impression was confirmed again as I completed this report. There is a wide collection of opinions amongst the experts as to which method of ablating heart tissue is most effective. There certainly was no one who proclaimed definitely a cure would be guaranteed with either a surgical or electrophysiological approach, although the surgeons were much more confident of 'cures.' However, that opinion was deflated a bit by some stats indicating some surgical patients are still on heart drugs. It was apparent to me that while ablation for AF has come a long way and many of us are enjoying the results of that success, Dr. Topol's comment on "Beating Afib is the New Frontier of Cardiology" was most appropriate.

In the meantime, as Hans has indicated in his surveys, the most success seems to be with the doctors and facilities doing the most number of cases. This may change significantly when the new technology arrives that provides more user-friendly equipment that relies less on operator skill and knowledge but for now, whether it's electrophysiology or surgical, if heading for an ablation, my advice is to choose the most knowledgeable and experienced in the field and do your due diligence. I don't think anyone should rush to have any ablation procedure unless all other options have failed. My forum posts give a wealth of references for research by the top cardiac AF specialists.

Subscribers can access Jackie's full conference notes at
http://www.afibbers.org/S/jackiesconferencenotes.pdf

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