THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

NUMBER 100 **JUNE 2010** **10th YEAR**

Welcome to our 100th issue. Our very first issue was published in January 2001 and among other tidbits contained the following paragraph:

"There is growing evidence that amalgam dental fillings and a magnesium deficiency in the heart tissue may be major problems for LAF sufferers and it now appears that the diet can have a profound influence on the stability of the autonomic nervous system and in consequence on the risk of an LAF episode."

Issue #5 published in May 2001 discussed the results of our very first LAF Survey and again focused on the importance of magnesium:

"The first supplement to consider, apart from a daily high-potency multivitamin pill, is magnesium. As discussed in earlier issues magnesium is extremely important in ensuring a steady heart beat and overall heart health. Magnesium and potassium calms the heart and oppose the action of sodium and calcium which excites it. About 99% of the body's magnesium is found in tissues and bones and the heart tissue is particularly rich in this vital mineral. Only 1% of the body's magnesium stores are found in the blood so a regular blood test is a very poor indicator of your magnesium status. Ideally you would measure the magnesium level in your heart tissue to see if you are deficient, but this is not terribly practical. Fortunately, researchers at the Cedar-Sinai Medical Center in Los Angeles have discovered that there is a direct correlation between heart tissue magnesium level and the concentration found in epithelial cells scraped from under the tongue or from between the gums and the upper and lower lips. Trace Elements Inc. (www.traceelements.com) can do the magnesium testing and can also recommend a physician in your area who can do the cell scraping. Thirteen per cent of the respondents have had their intracellular magnesium levels measured and 83% of them were deficient." NOTE: Intracellular magnesium testing is now done by Exatest (www.exatest.com).

We have come a long way since those early days, but ensuring adequate magnesium (and potassium) stores is still of utmost importance. Nevertheless, research proceeds apace and in this issue we report on some exciting new discoveries firmly linking lone atrial fibrillation to genetic mutations. Also, the association between alcohol consumption and afib is discussed as is the effect of catheter ablation on post-procedure left atrial function. The results of the latest worldwide survey of success rates for ablation are covered and the ins and outs of electrical cardioversion are discussed in detail.

Wishing you lots of NSR,

Hans

Highlights

Effect of ablation on left atrial function

WINSTON-SALEM, NORTH CAROLINA. A catheter ablation for the purpose of curing atrial fibrillation (AF) involves the creation of extensive scar tissue in the left atrium. An obvious question is, "Does the presence of this scar tissue impair the function of the left atrium?" A team of

electrophysiologists from Wake Forest University, the Cleveland Clinic (OH), the University of Rochester, and Duke University recently set out to answer this question.

Their meta-analysis included 17 studies involving 869 patients who had undergone a radio frequency-powered catheter ablation for paroxysmal, persistent or permanent AF. Left atrium diameter, volume and function (ejection and emptying fraction) were evaluated prior to the ablation and at least one month following the ablation. Ablation success rates ranged from 53% to 82% for paroxysmal AF, from 60% to 76% for persistent, and from 47% to 54% for permanent.

The researchers observed a significant decrease in left atrial diameter and volume in patients who did not experience AF recurrence following their procedure. No such decreases were observed for patients who did experience recurrence. In analyzing data for left atrial ejection fraction and left atrial active emptying fraction, the researchers noted that there was no change in these parameters in patients who did not experience recurrence, while a noticeable decline (detrimental) was noted in those who did experience recurrence.

They conclude that a successful radio frequency catheter ablation does not adversely affect the function of the left atrium, and leads to a desirable reduction in left atrial diameter and volume. They point out that it is difficult to say whether the decrease in left atrial function observed in patients with AF recurrence is related to the continued presence of AF, or to the presence of excessive scar tissue produced by the ablation procedure.

Jeevanantham, V, et al. Meta-analysis of the effect of radiofrequency catheter ablation on left atrial size, volumes and function in patients with atrial fibrillation. **American Journal of Cardiology**, *Vol. 105, 2010, pp. 1317-26*

Editor's comment: It is indeed comforting to know that a successful ablation does not impair the function of the left atrium, but rather results in a reduction of its diameter and volume which both, if elevated, are risk factors for heart failure.

Alcohol and arrhythmias

PHILADELPHIA, PENNSYLVANIA. Alcohol is probably the oldest mood-altering substance known to man. The earliest writings regarding alcohol use can be found in 6000-year-old Mesopotamian clay tablets. Warnings against alcohol abuse go back almost 4,000 years and can be found in ancient scriptures including the Koran and the Old and New Testaments. The observation that alcohol abuse can be detrimental to the heart was first reported in the medical literature in the 19th Century. More recently, medical literature has extolled the benefits of moderate alcohol consumption and linked it to reductions in heart attacks, strokes, and sudden cardiac death (SCD). It is believed that alcohol benefits the cardiovascular system by increasing high-density lipoprotein (HDL), increasing fibrinolysis, and enhancing endothelial function. It is also thought that alcohol reduces blood viscosity and decreases fibrinogen concentration and platelet aggregation and coagulation.

Unfortunately, alcohol can also precipitate arrhythmias as first discovered in 1959. In 1978 Dr. Philip Ettinger coined the term "holiday heart" defined as an acute cardiac arrhythmia, mostly atrial fibrillation (AF), associated with heavy drinking in a person without clinical evidence of heart disease. Dr. Ettinger observed a seasonal peak in the incidence of alcohol-induced arrhythmia at the end of the year and New Year's Day. Other researchers have reported that bouts of alcohol-related AF occur most frequently in the early hours of the morning or upon arising from an alcoholic binge.

Finnish researchers found that 15 to 30% of idiopathic AF may be alcohol-related, while researchers involved in the Framingham study concluded that consumption of more than 3 alcoholic drinks (36 grams/day) increased the risk of AF by 34% after adjusting for potential confounders. More recently, researchers at Brigham and Women's Hospital reported that women who consumed two or more alcoholic drinks a day had a 60% increased risk of AF.

Alcohol consumption has also been implicated in ventricular arrhythmias and SCD. However, the relationship is more complicated than that with AF. It now appears that individuals with a low alcohol intake (2 – 6 drinks a week) have a lower risk of ventricular tachycardia and SCD than do those who never or rarely consume alcohol or those with a high intake (3 – 5 drinks a day) and binge drinking.

A study involving one million individuals observed a J-shaped relationship between alcohol intake and total mortality. Ventricular arrhythmias and SCD are both associated with prolongation of the QT interval and alcohol has been found to prolong the QT interval.

Alcohol withdrawal is associated with a rebound beta-adrenergic hypersensitivity and elevated catecholamine levels both of which can precipitate arrhythmias if accompanied by low levels of magnesium and potassium. Acute alcohol intoxication and withdrawal are both associated with the development of magnesium and potassium deficiencies (hypomagnesemia and hypokalemia). It is also noted that magnesium deficiency is closely tied to potassium deficiency and can result in refractory hypokalemia.

The authors conclude that there is a strong correlation between alcohol abuse and AF, particularly among younger men. Alcohol consumption is also positively correlated with ventricular tachycardia and SCD in heavy drinkers. Nevertheless, moderate alcohol consumption produces desirable health benefits, which are lost as the amount consumed increases or a pattern of binge drinking develops.

George, A and Figueredo, M. Alcohol and arrhythmias: a comprehensive review. **Journal of Cardiovascular Medicine**, *Vol. 11, No. 4, 2010, pp. 221-28*

Editor's comment: Our early LAF surveys showed that alcohol consumption was the trigger for 6% of first ever AF episodes and triggered 22% of subsequent episodes.

Worldwide survey on ablation efficacy

MILAN, ITALY. A group of prominent electrophysiologists has updated their 2005 worldwide survey of the efficacy and safety of catheter ablation for atrial fibrillation (AF). The 2005 survey covered the years 1995 to 2002 and involved 8,745 patients treated in 90 centers. The new 2010 survey covers the years 2003 to 2006 and involves 16,309 patients treated in 90 centers. The final complete success rate (no AF, no antiarrhythmics) in the 2005 survey was 52% vs. 64.3% in the 2010 survey. The partial success rate (no AF, but only with the aid of previously unsuccessful antiarrhythmics) was 23.9% in the 2005 survey and 12.5% in the 2010 survey, so the combined final success rate (after an average of 1.3 procedures per patient) was 76% in the 2005 survey and 77% in the 2010 survey. After removing data from centers with the least and the most experience, complete success rate was 70% and partial success rate was 10%. Other highlights from the 2010 survey:

- Anatomically-guided circumferential ablation (CARTO) has replaced the Lasso-guided segmental procedure as the most popular. In the 2010 survey 48.2% were treated with the circumferential procedure vs. 27.4% for the segmental procedure. The success rates for the two procedures were similar; however, the incidence of atrial flutter resulting from the procedure (iatrogenic flutter) was 8 times higher in centers using exclusively CARTO-guided ablation than in centers using exclusively Lasso-guided ablation (14.3% vs. 1.8%).

- More than 98% of procedures used radio frequency energy in lesion creation and a cooled or irrigated catheter was used in 70% of cases.

- While all centers performed ablations for paroxysmal AF in both the 2005 and the 2010 surveys, the number of centers performing procedures for persistent and permanent AF increased from 53% to 86% and from 20% to 47% respectively.

- Most (95%) of centers required patients to have failed at least one antiarrhythmic drug before accepting them for ablation. However, more centers accepted patients with an enlarged left atrium, reduced left ventricular ejection fraction, and prior heart surgery in the 2010 survey.

- The odds of having a successful procedure were substantially less in patients with persistent or permanent AF.

- The odds of having a successful procedure (no AF, no antiarrhythmics) increased markedly with the number of procedures performed per center. The increase in success rate was found to be 4% for each additional 30 procedures performed.

- A major complication occurred in 741 patients (4.5%). There were 25 procedure-related deaths (0.15%), 152 strokes or transient ischemic attacks [TIAs] (0.94%), and 213 tamponades (1.31%). Six patients (0.04%) experienced an atrioesophageal fistula (71% fatal), while 48 patients (0.29%) experienced pulmonary vein stenosis serious enough to warrant surgical intervention.

The authors of the study conclude with the caveat, "*The variability in monitoring methods and their accuracy together with the intensity of monitoring inherently limit interpretation of data coming from a large survey. Based on this observation, it is possible that freedom of all AF episodes in the investigated population was 10% to 20% lower than that reported in this analysis*."

Cappato, R, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. **Circulation Arrhythmia and Electrophysiology**, *Vol. 3, February 2010, pp. 32-38*

Editor's comment: The results of our 2008 ablation/maze survey are in line with those reported in the latest Cappato survey. Average final complete success rate (no AF, no antiarrhythmics) was 47% for the period 1998 to 2004 (corresponding Cappato number for 1995 to 2002 was 52%) and 66% for the period 2007 to 2008 (Cappato number for 2003 to 2006 was 64.3%).

Left atrial size and ablation outcome

ROCHESTER, NEW YORK. There is evidence that a large left atrium (LA) is associated with poorer efficacy of antiarrhythmic drugs and poorer outcome of radio frequency catheter ablation for atrial fibrillation (AF). In routine practice the size of the LA is approximated by measuring the LA diameter (LAD) in the parasternal long-axis view using standard transthoracic echocardiography (TTE). A more accurate measurement can be obtained by the use of transesophageal echocardiography (TEE), but the most accurate method of measuring left atrial size (volume) involves the use of 64-slice contrast-enhanced computed tomography (CT).

Researchers at the University of Rochester Medical Center now report that left atrial volume (LAV) measured by CT can predict the risk of recurrence following ablation. Their study included 65 male afibbers and 23 females with an average age of 57 years (range of 30 to 78 years). Sixty percent of the patients had hypertension, and 22% had coronary artery disease or had undergone valve or coronary bypass surgery. At baseline 97% were taking an antiarrhythmic drug and 86% were on beta-blockers. Forty-five percent of study participants had paroxysmal AF, while the remaining 55% had the persistent variety.

All patients underwent an anatomically-guided, wide-area, circumferential pulmonary vein isolation procedure with additional linear lesions at the EP's discretion. Follow-up was at least one year. Success rate for the initial procedure was 55% for paroxysmal afibbers and 50% for persistent afibbers. After an average 1.5 procedures, success rate was 88% for paroxysmal afibbers and 52% for persistent afibbers. Thus, having persistent AF was a strong predictor of the likelihood of AF recurrence during follow-up.

However, the strongest predictor of failure turned out to be LAV as measured by CT prior to the ablation. Patients with a LAV above 130 cc had a 22 times greater risk of recurrence than did those with a smaller LAV. Thus the failure rate for patients with a LAV above 130 cc was more than 90%. LAD as measured by TTE correlated poorly with failure rate, while LAD measured using TEE correlated somewhat better, but not nearly to the extent of the correlation associated with CT. A pre-procedure LAD (measured by TEE) of greater than 4.9 cm and a LAV (measured by CT) greater than 117 cc were both associated with a greater than 30% failure rate.

The researchers conclude that a left atrial volume of 130 cc or larger is associated with a recurrence rate of more than 90%. They suggest that, in the case of such grossly enlarged left atria, the risk of undergoing catheter ablation far outweighs any clinical benefit.

Parikh, SS, et al. Predictive capability of left atrial size measured by CT, TEE, and TTE for recurrence of atrial fibrillation following radiofrequency catheter ablation. ***PACE****, Vol. 33, May 2010, pp. 532-40*

Russo, AM. Is atrial fibrillation ablation a futile effort in patients who have markedly enlarged left atria? ***PACE****, Vol. 33, May 2010, pp. 527-31*

Editor's comment: Although the patient group in the Rochester study included 22% with underlying

heart disease, it is likely that a grossly enlarged left atrium may also be associated with a poorer outcome of ablation in lone afibbers. Certainly it would seem prudent to get in line for a PVI once LAD, as measured by TEE, approaches 5.0 cm.

Genetic variations in lone atrial fibrillation

OTTAWA, CANADA. The observation that lone atrial fibrillation (LAF) may be inherited has spawned considerable research aimed at identifying the genes predisposing to LAF. Researchers at the Ottawa Heart Institute have determined six sub-classifications of LAF each associated with a specific mutation in a gene.

Genes 101

Genes are the "blueprint" that governs our initial "construction" and "repair and maintenance" for the rest of our lives. Humans have about 100,000 different genes made up by stringing together about 3 billion molecules of the four nucleic acids – adenine, thymine, cytosine, and guanine. The genes make up strands of DNA which in turn are bundled into chromosomes. The genes contain messages that tell each individual cell in our body what protein to produce and when to produce it. The DNA strands containing the genes duplicate themselves when our cells divide so that each cell contains a complete set of genes. Every time a DNA strand duplicates itself, there is a risk that an error (mutation) may occur, the sequence may be wrong, or there may be too many or too few nucleic acids in a gene sequence. The cells have special enzymes which repair errors in DNA duplication; however, even they sometimes fail and the error goes uncorrected. If the mutant DNA strand is able to replicate itself a number of times it can become established and one is left with a permanent faulty gene.

The six sub-classifications are:

1. Enhanced atrial action potential repolarization
2. Delayed atrial action potential repolarization
3. Conduction velocity heterogeneity
4. Cellular hyperexcitability
5. Hormonal modulation of atrial electrophysiology
6. Enhanced cholinergic (vagal) sensitivity

Heart Rhythm 101

The membrane (sarcolemma) of a resting heart cell (myocyte) is polarized – that is, the inside (intracellular space) of the cell (cytoplasm) is negatively charged in respect to the outside environment (extracellular space). Responding to an impulse from the sinoatrial (SA) node (the heart's natural pacemaker controlled by the autonomic nervous system) the myocytes depolarize resulting in contraction of the heart muscle. The ***depolarization*** is caused by a rapid influx of positive sodium (Na^+) ions followed by a slower influx of calcium ions (Ca^{++}). During depolarization the outward leakage of potassium ions (K^+) is restricted. Atrial depolarization shows up as a P wave on an electrocardiogram (ECG) while ventricular depolarization is identified as the QRS complex – that is, the time period on the ECG during which the ventricles depolarize (contract). The P wave is absent during atrial fibrillation. The time interval between the start of the P wave and the beginning of the QRS complex is a vulnerable period for afib initiation.

Depolarization is followed by ***repolarization*** (recovery). During this phase, an outflow of K^+ ions is followed by a period during which the intracellular concentrations of K^+ and Na^+ in the myocytes are restored to their resting potential through the action of Na^+/K^+ ATPase pumps "powered" by magnesium. Magnesium ions (Mg^{++}) also play an important role during this phase by slowing down the outward (from intracellular space to extracellular space) flow of potassium ions. At the risk of oversimplification, one could say that while Na^+ and Ca^{++} are "excitatory" ions K^+ and Mg^{++} ions are "calming". Thus it is not surprising that a deficiency of K^+ and Mg^{++} facilitate atrial fibrillation. Repolarization is identified on the ECG as the time period from the end of ventricular depolarization to the peak of the T wave (ST segment).

The period from the start of the QRS complex to the peak of the T wave is of particular interest when it comes to atrial fibrillation. During this period (the *effective refractory period or ERP*) myocyte depolarization cannot be triggered by stimulus originating from rogue atrial cells thus preventing afib from being initiated. However, atrial fibrillation can be triggered during the last half of the T wave (*relative refractory period or RRP*) making it highly desirable that the ERP is as long as possible and the RRP as short as possible. Several medications aim to exploit this fact by acting to extend the ERP so that the RRP (the vulnerable period) becomes as short as possible. This is particularly important in the case of the AV node as during the ERP the node cannot be stimulated and thus in essence filters out the erratic atrial impulses.

The speed with which an electrical impulse moves across the atrium (normally directly from the SA node to the AV node) is called the *conduction velocity* and is a measure of the effectiveness of cell-to-cell depolarization. It is measured in millimeter/millisecond (mm/ms) or in meter/second (m/s). Sympathetic (adrenergic) stimulation increases conduction velocity while parasympathetic (vagal) stimulation reduces it. Slow conduction is associated with the presence of *complex fractionated atrial electrograms* (CFAEs) defined as electrograms (direct measurements of electrical activity inside the atrium) with a cycle length less than or equal to 120 ms or shorter than in the coronary sinus or that are fractionated or display continuous electrical activity. CFAEs are believed to be associated with fibrosis and serve as targets in some ablation procedures for atrial fibrillation.

Enhanced atrial action potential repolarization

An enhanced repolarization results in a shortening of the overall action potential duration and a related reduction in the effective refractory period (ERP) thus favouring the initiation of atrial fibrillation. Four different gene mutations have now been identified (KCNQ1, KCNE2, KCNJ2 and KCNE5) all involved in the coding of the pores for various subtypes of potassium currents involved in repolarization.

Delayed atrial action potential repolarization

Somewhat paradoxically it is now also clear that delaying repolarization and thus extending the ERP can trigger atrial fibrillation. The presence of a mutated KCNA5 gene, which encodes the voltage-gated potassium channel responsible for the ultra-rapid component of the delayed rectifier potassium current, has been found to be associated with delayed atrial action potential repolarization as has the SCN5A gene encoding the voltage-gated sodium channel. It is estimated that mutations of the SCN5A gene can be found in as many as 20% of lone afibbers.

Conduction velocity heterogeneity

Although the initial genes implicated in familial AF encoded potassium channels, it is now clear that other gene mutations may be at play as well. Promising candidate genes include connexins, transmembrane spanning proteins that form gap junctions. Gap junctions serve as intercellular pores providing low-resistance pathways for the passage of current between adjacent cells. Research carried out at the Ottawa Heart Institute found mutations in the connexin 40 gene in 26% of paroxysmal afibbers. Mutant connexin 40 genes would cause exaggeration of regional differences in conduction velocity and thus predispose the atria to the initiation and maintenance of atrial fibrillation.

Cellular hyperexcitability

Rapid self-sustaining re-entry circuits have been identified as the culprit driving the ectopic foci in AF including those found in the pulmonary veins. Mutations in the SCN5A and K1493R genes have been associated with cellular hyperexcitability.

Hormonal modulation of atrial electrophysiology

Recent research has discovered that a mutation in the NPPA gene encoding for atrial natriuretic peptide (ANP) can shorten the ERP and thus make myocytes more vulnerable to initiation of an AF episode. The mutant gene contains 40 amino acid peptides as compared to only 28 in the normal gene and is far more prevalent than the normal gene in carriers of the mutation.

Enhanced cholinergic (vagal) sensitivity

The greatest density of vagal innervation within the left atrium occurs at the pulmonary veins which, perhaps not surprisingly, correspond to the location of rapidly firing ectopic foci capable of initiating and maintaining AF. Although no gene mutations associated with vagal dominance or indeed with autonomic nervous system balance have been found, it is very likely that such mutations exist and could be an important factor in elucidating the mechanism of vagally-mediated AF.

The Canadian researchers conclude that the heterogeneous nature of AF triggers and factors responsible for arrhythmia maintenance make it very difficult to find therapeutic approaches that will apply to all afibbers. However, if genetic testing could identify specific abnormalities in an individual, then it may be possible to eliminate, or at least ameliorate, that individual's AF burden by the use of a targeted pharmaceutical drug.

Roberts, JD and Gollob, MH. Impact of genetic discoveries on the classification of lone atrial fibrillation. **Journal of the American College of Cardiology**, *Vol. 55, No. 8, February 23, 2010, pp. 705-12*

Editor's comment: The finding that lone atrial fibrillation is associated with several seemingly common gene mutations is indeed very exciting and may herald a new era of targeted, highly effective pharmaceutical drugs.

RESEARCH REPORT

Electrical Cardioversion

Background

Cardioversion is used to convert a patient experiencing highly symptomatic or persistent atrial fibrillation (AF) to normal sinus rhythm (NSR). Conversion can sometimes be achieved by the infusion of drugs like ibutilide (Covert), dofetilide (Tikosyn) or flecainide (Tambocor) in a hospital setting (chemical conversion). Chemical conversion is most effective if started within a couple of hours of the onset of the episode and becomes less effective as time goes by. In cases where an episode has lasted longer than 7 days drug-induced conversion is not effective and electrical conversion (cardioversion) must be used to regain NSR, either alone or in combination with antiarrhythmic drugs. Cardioversion is also sometimes used instead of drugs in an attempt to convert an AF patient who has just arrived in hospital if the patient suffers severely (fainting, dizziness, breathlessness, etc).

Electrical cardioversion (also known as direct-current or DC cardioversion) is a procedure whereby a synchronized electrical current (shock) is delivered through the chest wall to the heart through special electrodes or paddles that are applied to the skin of the chest and back. The purpose of the cardioversion is to interrupt the abnormal electrical circuit(s) in the heart and to restore a normal heartbeat. The delivered shock causes all the heart cells to contract simultaneously, thereby interrupting and terminating the flutter or AF without damaging the heart. The heart's electrical system then restores a normal heartbeat controlled by the sinus node.

Research has shown that delivering the initial shock with an energy level of 200 to 360 joule is more effective than starting out at a lower level.[1] The procedure is preferably performed in the fasting state with the patient receiving short-acting anesthetic drugs or drugs that produce conscious sedation. Recovery is usually quick and overnight hospitalization is seldom required. Skin burns and ischemic stroke are the most common adverse effects accompanying the procedure. Patients with a low blood serum level of potassium or a toxic level of digoxin may experience life-threatening ventricular fibrillations when undergoing cardioversion. Thus potassium levels should always be checked prior to cardioversion and corrected if necessary.

Prevention of Cardioversion-Associated Stroke

The conversion of atrial fibrillation to NSR results in a transient mechanical dysfunction of the left atrium and the left atrial appendage (LAA) known as "stunning". During stunning, thrombi (blood clots) can form in the left atrium and the LAA. These thrombi are expelled once normal pumping action is restored and may result in an ischemic stroke or transient ischemic attack (TIA) usually within the first 10 days following cardioversion.

Depending on the time elapsed between the onset of an AF episode and the cardioversion procedure it is also possible that clots may form in the LAA and left atrium. These clots may be dislodged and cause a stroke or TIA once the stronger pumping action inherent in NSR is resumed. It is thus standard practice to postpone cardioversion for 3 to 4 weeks if an episode has lasted longer than 48 hours. During the waiting period, warfarin (Coumadin) adjusted to an INR between 2.0 and 3.0 is administered in order to prevent procedure-associated TIA or stroke. Warfarin is also prescribed for 4 weeks following the procedure.

In some cases it may be possible to safely perform electrical cardioversion without prior anticoagulation even if episode duration exceeds 48 hours. A team of American, Australian and German researchers has found that electrical cardioversion can be performed safely without the 3-week pretreatment with warfarin if a transesophageal echocardiogram (TEE) taken immediately prior to cardioversion shows no signs of thrombi in the left atrium.

The clinical trial involved 525 patients assigned to TEE prior to cardioversion and 509 patients assigned to the conventional 3-week course of warfarin. The average age of the patients was 65 years and most of them had one or more comorbid conditions such as hypertension, or congestive heart failure. All patients had been in AF

for at least 48 hours prior to enrolment and 82% were taking one or more antiarrhythmic drugs. The patients in the TEE group underwent TEE, anticoagulation with unfractionated heparin, and cardioversion within 3 days of enrolment, while patients in the conventional group underwent electrical cardioversion between 20 and 40 days after enrolment.

The immediate conversion rate (to normal sinus rhythm) was 82% in the TEE group and 78.4% in the conventional group. The TEE indicated the presence of thrombi in 62 patients and cardioversion was postponed for this group. After 6 months 62.5% of patients in the TEE group who had undergone cardioversion were still in sinus rhythm as compared to 53.9% in the conventional group. The incidence of ischemic (embolic) stroke and TIA (transient ischemic attack) was 1.9% in the TEE-guided group and 0.8% in the conventional group; however, this difference was not statistically significant. The rate of serious bleeding events was significantly higher in the conventional group (7.5%) than in the TEE-guided group (4.4%). Death from cardiovascular causes over the 6-month follow-up period was similar in the two groups at 2% and most were classified as sudden cardiac death not involving stroke or bleeding.

The researchers conclude that TEE-guided electrical cardioversion is a clinically effective alternative to the conventional anticoagulation strategy followed by cardioversion. They point out that the TEE-guided approach may be particularly useful in highly symptomatic, new onset AF and for patients at high risk for bleeding and stroke.[2]

Success Rate for Cardioversion

Although the immediate success rate of electrical cardioversion is quite high at 80 to 90%, the relapse rate is substantial. Researchers at the Mayo Clinic recently reported the results of a study aimed at determining the long-term effectiveness of cardioversion. The study included 351 patients with atrial fibrillation (179 with a first episode) and 126 patients with atrial flutter (78 with a first episode). The patients were all over the age of 60 years and most had hypertension (68%), while 49% had moderate to severe atrial enlargement. Most were on one or more medications including 29% on digoxin, 92% on warfarin, and 53% on ACE inhibitors or angiotensin-converting enzyme inhibitors.

The study participants underwent electrical cardioversion and were then followed-up for a year. At the one-year follow-up 63% of the patients who had been cardioverted after a first atrial flutter episode remained in NSR. However, only 33% of flutter patients with recurrent episodes remained in NSR.

The results for afibbers were even worse. Only 30% of patients in the new-onset afib group and 35% in the recurrent group were still in NSR after a year. It is interesting that not all atrial flutter patients relapsed into atrial flutter. In patients with recurrent atrial flutter, 39% relapsed into atrial fibrillation. AF patients, on the other hand, almost always (92-95% of cases) relapsed back into atrial fibrillation rather than into atrial flutter. Electrical cardioversion is clearly not very effective for the general afib population and there is no evidence that it is more effective for lone afibbers. However, there is some evidence that effectiveness increases if used together with antiarrhythmic drugs.[3]

A group of cardiologists at the James Cook University Hospital report that pre- and post-treatment with amiodarone greatly improves the chances of staying in NSR after cardioversion. Their clinical trial included 91 patients with persistent or permanent afib scheduled for cardioversion after 6 weeks of warfarin therapy. During the 6-week waiting period 20 patients were randomized to receive amiodarone (200 mg 3 times daily for the first week, 200 mg 2 times daily for the second week, and then 200 mg daily for the remainder of the trial period); 28 patients received sotalol (160 mg twice a day, or 80 mg twice a day if intolerant of the higher dose) and the remaining 29 patients received no antiarrhythmic drug. All patients were given beta-blockers (usually atenolol) or digoxin as required for rate control and all remained on the drug regimen in effect pre-cardioversion for the entire 6-month observation period. During the 6-week waiting period 7 patients in the amiodarone group and 7 in the sotalol group converted spontaneously to NSR and were not given cardioversion. None of the patients not receiving antiarrhythmics converted on their own.

The immediate success rate of cardioversion (patients in NSR at time of discharge from the hospital) was 92% for those in the sotalol group, 81% in the amiodarone group, and 74% in the no-antiarrhythmic group.

Unfortunately, the effects of the cardioversion did not last. Six weeks after DCC only 53% of those in the sotalol group, 67% in the amiodarone group, and 42% in the no-antiarrhythmic group were still in NSR. Corresponding numbers at the end of the trial were 39%, 63%, and 16%. The researchers conclude that amiodarone (200 mg a day) is more effective than sotalol (160 mg twice a day) in maintaining NSR after cardioversion. Adverse effects were observed in 4% of the patients assigned to amiodarone and in 11% assigned to sotalol. It is very clear from this clinical trial that electrical cardioversion on its own (without concomitant use of antiarrhythmics) is ineffective in maintaining NSR in persistent and permanent afibbers. Only 16% of converted patients in the no-antiarrhythmic group were still in NSR 6 months after cardioversion. Thus, the message to take away from this trial is that cardioversion without concomitant antiarrhythmic therapy is rarely worthwhile.[4]

Researchers at the Karolinska Institute have found that pretreatment with the beta-blocker metoprolol (time-release version, Toprol XL) significantly improves the success rate for cardioversion. Their study involved 168 persistent afibbers who were randomized to receive metoprolol or a placebo starting at least a week prior to cardioversion (NOTE: only about 15% of the study participants were lone afibbers). On average, the participants were on metoprolol or placebo for 28 days prior to cardioversion and they were also prescribed warfarin (INR 2.1 – 3.0) for at least 3 weeks before and 6 weeks after cardioversion. The starting dose of metoprolol was 50 mg/day with a 50 mg stepwise increase to a target dose of 200 mg once a day.

The participants were checked with an ECG two hours after cardioversion and then every week for 6 weeks, and then 3 and 6 months after cardioversion. During the first 6 weeks, 49% in the metoprolol group and 47% in the placebo group developed afib again and were given a second cardioversion. At the 6-month checkup, 46% of patients in the metoprolol group were still in NSR as compared to only 26% in the placebo group. It is also of interest to note that while 8% of placebo group members relapsed into afib within 2 hours of their first cardioversion, none of the patients in the metoprolol group did. Beta-blockers are contraindicated for vagal afibbers, so it is not at all certain that pretreatment with metoprolol would be beneficial in this case.[5]

Italian researchers have reported that flecainide and a combination of amiodarone and flecainide are safe and effective in maintaining NSR after cardioversion in patients with persistent afib and hypertension. Their trial showed that flecainide on its own maintained NSR in 88% of patients, while the combination maintained it in 80% at the 6-month check-up. In comparison, only 33% of patients on sotalol or amiodarone alone were still in NSR at the 6-month follow-up. The researchers also found that adding an angiotensin II receptor blocker (losartan, valsartan, irbesartan, candesartan) to the medication regimen was highly effective in maintaining NSR.[6]

It is also possible that an intravenous magnesium infusion may help improve cardioversion efficiency. Researchers at the University of Connecticut have reported that adding 4 grams of magnesium sulfate to a standard ibutilide (Corvert) infusion increases conversion efficiency by a factor of 3. The researchers speculate that the benefits of concomitant use of magnesium sulfate are related to magnesium's ability to increase intracellular potassium concentrations and regulate intracellular calcium concentrations.[7]

Although there were very few lone afibbers in the study group, there is no reason to believe that the addition of magnesium sulfate to the ibutilide protocol would not benefit them as well. Also, if the beneficial effect of magnesium is related to its ability to increase intracellular potassium concentrations and regulate calcium concentrations, then it would seem logical that adding magnesium to cardioversion protocols involving other antiarrhythmics, or even electrical cardioversion, would also be beneficial. Perhaps having a warm bath with plenty of Epsom salt when using the on-demand (pill-in-the-pocket) approach with flecainide or propafenone may improve the odds of a quick conversion.

British researchers report that pretreatment with angiotensin-converting enzyme inhibitors (ACE inhibitors) may help persistent afibbers stay in sinus rhythm after electrical cardioversion. Their study involved 47 patients with persistent atrial fibrillation (AF lasting longer than 48 hours, but less than 6 months) who were scheduled for cardioversion. Patients with left ventricular dysfunction (low left ventricular ejection fraction), valvular heart disease or permanent AF were excluded from the study.

Twenty-four of the patients had been taking ACE inhibitors [enalapril (11), lisinopril (8), and captopril (5)] for at least 6 months before inclusion and continued to do so for the 1-year follow-up. The researchers observed that

the patients taking ACE inhibitors required significantly less energy to effect electrical cardioversion (203 joules versus 271 joules on average) than did the controls. There was also a clear difference between ACE inhibitor-treated patients and controls in regard to P-wave duration 1 year after cardioversion (135 ms versus 150 ms). P-wave duration is prolonged in AF patients.

Finally, there was a trend for patients on ACE inhibitors to have fewer hospital admissions for repeat cardioversion during the follow-up period. The researchers noted that the use of beta-blockers was substantially higher in the control group than in the ACE inhibitor group (83% versus 4%). Both groups had similar left atrial size (48 mm and 49 mm). The researchers conclude that ACE inhibitor therapy may be useful in patients with persistent atrial fibrillation.[8]

Other researchers have observed substantial decreases in afib recurrence in patients with left ventricular dysfunction who were treated with enalapril (78% risk reduction) and trandolapril (47% risk reduction).[9]

The results of this study look intriguing, but certainly should be interpreted with caution. The majority of members of the control group (84%) were on beta-blockers, while only 1 patient (4%) in the ACE inhibitor group was taking beta-blockers. It is well established that beta-blockers can increase afib frequency in vagal afibbers. Presumably, there would have been some vagal afibbers in the control group and these would likely have experienced more episodes than those not on beta-blockers. Thus the lower incidence in hospital readmissions seen in the ACE inhibitor group could equally well stem from the absence of beta-blocker use as from the use of ACE inhibitors. Nevertheless, the findings of less cardioversion energy requirements and a shortening of P-wave duration in ACE inhibitor patients could well be important, but need confirmation in larger trials.

Timing of Cardioversion

Arrhythmia researchers at the University of Michigan have discovered that the timing of electrical cardioversion of afib episodes is all-important in determining the success of the procedure. Their study involved 315 afibbers who underwent cardioversion from 7 minutes to 8 years after the onset of their afib episode. Coronary artery disease was present in 24% of the patients, structural heart disease in 46%, valvular heart disease in 11%, and non-ischemic cardiomyopathy in 11%. Nine per cent were taking class I antiarrhythmics and 28% were being treated with class III drugs.

The researchers found that an immediate recurrence of AF (IRAF) within 1 minute was far more common if the cardioversion was attempted shortly after the episode began rather than after a wait of 24 hours or more. Overall, 20% of the patients experienced IRAF.

# of Patients	Episode Duration	Incidence of IRAF
48	less than 1 hour	56%
27	1-24 hours	37%
34	1-7 days	12%
45	1-4 weeks	12%
72	1-3 months	5%
36	3-6 months	10%
40	6-12 months	8%
13	1-8 years	12%

The researchers found that the risk of IRAF depended solely on the duration of the afib episode prior to the attempted cardioversion. Age, gender, structural heart disease, antiarrhythmic drug use, and energy level in cardioversion were not associated with IRAF incidence. They draw some very interesting conclusions from their observations:

- It is likely that the primary cause of IRAF is the continuing generation of ectopic beats in the pulmonary veins which would “reignite” AF as soon as the cardioversion “jolt” is over. The ectopic beat generation

from active foci would be most pronounced at the onset of the episode and would gradually decrease as the episode wears on. The following statement is of particular interest, "It is possible that arrhythmogenic pulmonary venous foci are activated by the rapid atrial activity that occurs during atrial fibrillation but that as the duration of atrial fibrillation lengthens, the cellular mechanisms responsible for this arrhythmogenic activity are progressively down-regulated or deactivated."

- It is very likely that the mechanism underlying IRAF (as above) is different from the mechanism involved in normal early recurrence of afib. Here progressive electrical and anatomic remodeling may play the greater role.

- The findings explain why IRAF is very common in connection with cardioversion performed during electrophysiology studies and ablation procedures.

- The findings also explain why internal cardioversion initiated by an ICD (implantable cardioverter-defibrillator) often results in IRAF if attempted shortly after the onset of the AF episode.

The researchers conclude that the ideal time for cardioversion may be approximately 24 hours after the onset when the risk of IRAF is low, electrical remodeling of the atrium is not pronounced, and when the need for anticoagulation prior to cardioversion has not yet arisen.[10]

It is quite clear from this article that one's chance of a successful cardioversion increases by waiting 24 to 36 hours before attempting it. This, of course, would also give one more time to see if the episode will terminate on its own. Blood clotting in the left atrial appendage and the accompanying risk of stroke is not considered a problem unless the episode has lasted longer than 48 hours. The conclusion that the early stages, at least of an afib episode, are likely fuelled by repeated ectopic activity in the pulmonary veins is also interesting. It underscores the importance of trying to reduce PACs (premature atrial complexes) and, at this point, magnesium supplementation is probably the best way of achieving this. Another intriguing possibility is that ICD wearers may be better off if their ICD is set to attempt to convert an episode after an hour or so rather than as soon as it is detected. Obviously, individual experimentation would be needed to establish this.

The timing of cardioversion is also of great importance when it comes to atrial flutter or fibrillation occurring after a pulmonary vein isolation procedure.

Drs. Fred Morady and Hakan Oral and colleagues at the University of Michigan have observed that the prompt use of electrical cardioversion in ablatees who develop persistent arrhythmia (AF or flutter lasting more than 24 hours) following an ablation may help reverse remodeling and materially reduce the need for a follow-up ablation. Their trial included 215 paroxysmal and 169 persistent afibbers who underwent a segmental PVI with additional lesions as required. Among these 384 patients 24% experienced a persistent arrhythmia (80% AF and 20% flutter) following their procedure. The arrhythmia occurred within 24 hours in 6%, within the first week in 37%, within the first month in 66%, and within the first 3 months in 88% of cases. All patients with persistent arrhythmias were treated with electrical cardioversion and in 52% of cases with antiarrhythmic drugs as well. Cardioversion was performed within 1 week in 34% of cases, within 1 month in 49%, and within 3 months in 75%. Sixteen months after the cardioversion 27% of the patients were in normal sinus rhythm without the use of antiarrhythmic drugs.

The University of Michigan researchers made the rather astounding discovery that patients who had been cardioverted within 30 days of their persistent arrhythmia occurring were 22 times more likely to be in sinus rhythm than were those who had been converted later. Put in another way, 50% of patients who had been cardioverted promptly, i.e. within 30 days were in sinus rhythm 16 months later as compared to only 4% in the group whose cardioversion was delayed by more than a month. This association held true for both patients with post-ablation persistent AF and post-ablation atrial flutter.

The researchers suggest that early restoration of sinus rhythm is likely to prevent progressive atrial electroanatomical remodeling and thus facilitate long-term maintenance of sinus rhythm.[11] This is clearly an enormously important finding and underscores the need to undergo cardioversion as early as possible if persistent AF or flutter develops after a PVI.

Inflammation and Cardioversion

Researchers at the Mayo Clinic have found 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.[12]

Several other studies have uncovered an association between elevated levels of the inflammation marker C-reactive protein (CRP) and atrial fibrillation (AF). Inflammatory markers, mainly CRP, have been related to the risk of developing AF, the persistence of AF (paroxysmal, persistent, permanent), recurrence after cardioversion, and left atrium enlargement.

A recently reported study carried out by a group of Greek researchers included 60 patients with persistent afib between the ages of 61 and 75 years, 60% of whom were men. The participants were free of valvular heart disease, congestive heart failure, prior heart attack, and thyroid dysfunction, so were a relatively healthy group although not classified as lone afibbers. A significant exclusion criteria was that the patients could not have been taking antioxidants or multivitamins. They had their CRP level measured prior to direct current cardioversion and were given amiodarone after the conversion (200 mg/day x 3 during first week, 200 mg/day x 2 during second week, and 200 mg/day thereafter). Patients who did not convert or who reverted back to AF within an hour were excluded from further follow-up.

The researchers found a clear correlation between CRP level and the percentage of patients who remained in sinus rhythm over the 3-year follow-up period. In the group of patients with a CRP level less than 0.43 mg/dL (4.3 mg/L), 45% were still in sinus rhythm at the end of 3 years. The corresponding figures for CRP levels between 0.43 and 0.8 mg/dL and CRP level greater than 0.8 mg/dL were 13% and 17% respectively. The researchers conclude that baseline CRP levels can be used to estimate the likelihood of persistent afibbers remaining in sinus rhythm after undergoing a successful electrical cardioversion.[13]

This study adds to the evidence of a close association between inflammation, as measured by CRP level, and the risk and persistence of AF. Although it is not entirely clear whether inflammation causes AF or AF causes inflammation, it would seem prudent for afibbers to maintain their CRP levels as low as possible. This can be achieved by regular supplementation with such natural anti-inflammatories as Zyflamend, beta-sitosterol, bromelain, curcumin, boswellia, Moducare, quercetin, and fish oil.

Italian researchers at the University of Brescia have confirmed that pre-cardioversion CRP level is indeed an important predictor of the likelihood of remaining afib-free after an electrical cardioversion. Their study involved 106 patients (74 men and 32 women) with new-onset, persistent lone AF who underwent cardioversion with a biphasic defibrillator using 150 to 200 J according to the weight of the patient. All study participants had an ECG one week following the procedure and a Holter monitor evaluation 1 and 6 months following cardioversion. All patients left the hospital in normal sinus rhythm. At the 1-week examination, 20% had reverted to AF and this percentage rose to 43% at the 6-month examination.

The researchers observed a strong correlation between elevated CRP (high sensitivity C-reactive protein) and the risk of afib recurrence. The average CRP level among afibbers experiencing recurrence was 5.8 mg/L (0.58 mg/dL), while it was only 0.9 mg/L (0.09 mg/dL) among the 60 patients who did not experience recurrence. NOTE: Ignoring CRP levels above 10 mg/L (an indicator of acute inflammation) did not change these numbers significantly. Among study participants who reverted to AF within the first week, 86% had an elevated CRP level; the corresponding number for patients reverting by 6 months was 92%. There were no statistically

significant differences between patients who remained in sinus rhythm and those who did not as far as the following variables are concerned:

Age	Left ventricular ejection fraction
Presence of diabetes	Fibrinogen level
Presence of hypertension	Left atrial diameter
Duration of AF	White blood cell count

The Italian researchers point out that ACE inhibitors and statin drugs have been found to have anti-inflammatory properties, that fish oils reduce risk of post-operative AF, and that methylprednisolone reduces the risk of post-cardioversion AF recurrence by decreasing CRP levels. They conclude that pre-cardioversion CRP levels predict the risk of relapse and that patients with high levels may benefit from therapy with antiarrhythmics prior to and after cardioversion.[14]

Other Factors Affecting Cardioversion Success

In the 2nd virtual LAF Conference in January 2003, the role of **aldosterone** in the initiation of AF episodes was discussed in considerable detail.[15,16] This was followed by an article in the March 2004 issue of *The AFIB Report* further elucidating the role of aldosterone in lone atrial fibrillation (LAF). Dr. Patrick Chambers also discussed the role of aldosterone in his article "P Cells and Potassium" published in the March 2005 issue of *The AFIB Report*. It is likely that aldosterone exerts its negative effects through one or more of the following mechanisms:

- Inflammation and fibrosis (tissue scarring and thickening);
- Increased tendency to blood clotting;
- Impaired fibrinolysis (impaired blood clot digestion and removal);
- Sodium retention;
- Potassium and magnesium loss;
- Disturbance of ANS balance;
- Increased activity of catecholamines (norepinephrine and epinephrine);
- Decreased heart rate variability;
- Increased production of reactive oxygen species (ROS), especially superoxide;
- Decreased production of nitric oxide (NO) and accompanying endothelial dysfunction.

A group of Polish researchers has just reported that a decrease in aldosterone level is associated with the maintenance of normal sinus rhythm (NSR) following a successful cardioversion. Their clinical trial involved 45 patients with persistent non-valvular AF and normal left ventricular ejection fraction and 20 matched control subjects with no evidence of AF. The average age of the patients was 59 years and 81% were men. Twenty percent of the group had LAF. The 45 patients were scheduled for electrical cardioversion (CV) after having been in persistent afib for an average of 12 weeks. Plasma aldosterone levels were measured 24 hours prior to CV and again 24 hours after. The baseline aldosterone level was 152 pg/mL in the afib group and 130 pg/mL in the control group (p=0.11).

Forty-three of the initial 45 patients left the hospital in NSR and were examined again 30 days later. At this examination 24 patients (56%) were still enjoying sinus rhythm, while the remaining 19 (44%) had reverted to persistent AF. The Polish researchers noted that while there was no significant difference in aldosterone levels 24 hours prior to CV and 24 hours after in the group that reverted to AF (126 pg/mL vs. 118 pg/mL), there was a sharp decrease from 176 pg/mL to 101 pg/mL in the group that maintained NSR 30 days after CV (p=0.003).

They conclude that a rapid drop of more than 13 pg/mL following CV predicts sinus rhythm maintenance with 87% sensitivity and 64% specificity. They speculate that a largely unchanged aldosterone level after cardioversion may reflect more advanced disease of the atria with enhanced expression of angiotensin converting enzyme (ACE) and local activation of aldosterone excretion. They found no correlation between baseline aldosterone levels and sinus rhythm maintenance 30 days following cardioversion.[17]

This study further emphasizes the crucial role of aldosterone in the genesis of atrial fibrillation and supports the evidence that ACE inhibitors, angiotensin receptor blockers (ARBs), or aldosterone antagonists may increase the chance of maintaining NSR following a cardioversion.

Brain natriuretic peptide (BNP), a cousin of atrial natriuretic peptide (ANP), is a hormone released from the walls of the ventricles when stretched such as during unusually strenuous activity. It is stored as a prohormone within secretory granules in the ventricles and is secreted as an N-terminal fragment, N-terminal pro-brain natriuretic peptide (nt-pro-BNP), and the smaller active hormone BNP. BNP has effects similar to those of ANP, that is, it decreases sodium reabsorption rate, renin release, and aldosterone release; it also increases vagal (parasympathetic) tone and decreases adrenergic (sympathetic) tone. Because nt-pro-BNP is easier to measure than BNP it is often used as a marker for BNP.

It is well established that BNP and nt-pro-BNP levels are elevated in heart failure and that the degree of elevation is directly proportional to the seriousness of the failure. However, researchers at the Massachusetts General Hospital have reported that lone afibbers also have elevated nt-pro-BNP values even when in sinus rhythm. Their study involved 150 participants with lone atrial fibrillation (LAF) and 75 afib-free controls matched according to age, gender, race, and ethnicity. The majority of participants (81%) were men, the average age at enrolment was 54 years, and the average age at first diagnosis was 45 years. The demographics of the study group thus closely mirrors that of the much larger groups involved in our own LAF surveys and, once again, puts "paid" to the still widely held notion that afib is solely a disease of old age, which it clearly is not. At the time of enrolment 130 afibbers had the paroxysmal variety, while 20 were in permanent AF.

Blood samples were obtained from all participants at enrolment. The researchers found that the median level of nt-pro-BNP was significantly higher among lone afibbers (even when in sinus rhythm) than among controls (166 versus 133 fmol/mL or 48 pg/mL versus 39 pg/mL); they also observed that nt-pro-BNP levels were higher in afibbers with permanent LAF than in those with paroxysmal LAF (55 pg/mL versus 45 pg/mL), and that afibbers with high nt-pro-BNP levels at study entry were more likely to progress to the permanent version than were those with lower levels (57 pg/mL versus 47 pg/mL). There were no significant differences in ANP levels between afibbers and healthy controls, but ANP levels in afibbers who later developed hypertension were significantly higher than in those who did not (1090 versus 470 pg/mL). The researchers speculate that BNP may be involved in sustaining fibrillatory rotors through its potentiating effect on vagal nerve impulses transmitted from the brain.[18]

Polish researchers investigated a group of afibbers with hypertension or coronary heart disease and found that BNP levels rise during an afib episode and tend to return to normal following a successful cardioversion. The decline in BNP level was quite significant with a drop from 95 to 28 pg/mL in paroxysmal afibbers and a drop from 75 to 41 pg/mL in persistent afibbers.[19]

In January 2010 Dr. Qi-xian Zeng and colleagues at the Shandong Communication Hospital in Jinan, China confirmed that patients with atrial fibrillation have elevated levels of both BNP and ANP when compared to healthy controls and that these levels decrease significantly after a successful cardioversion. The study included 100 consecutive patients with paroxysmal or persistent AF and 20 healthy controls. About half the patients had coronary heart disease or hypertension, but none had heart failure. Prior to their scheduled cardioversion (chemical using amiodarone or propranolol) all patients had their blood levels of BNP and ANP measured. The cardioversion was initially successful in 60 patients, but 18 experienced recurrence within 24 hours and were, together with the 40 patients not successfully cardioverted, classified as permanent afibbers.

Thus, 24 hours following the cardioversion 42 patients (42%) were in normal sinus rhythm (NSR), while 58 were still in afib. Both BNP and ANP levels decreased significantly immediately following the cardioversion with BNP levels dropping from an average of 162 pg/mL to 124 pg/mL and ANP levels declining from 200 pg/mL to 164 pg/mL. Both BNP and ANP levels were significantly higher in the 16 patients who relapsed into AF within 24 hours of being cardioverted than among those who remained in NSR (BNP of 180 versus 132 pg/mL and ANP of 188 versus 138 pg/mL).

The 42 patients still in NSR after 24 hours were followed for an additional 500 days. At the end of this period, 26 were still in NSR corresponding to an overall 500-day success rate of 26% for the 100 patients originally undergoing cardioversion. The average baseline BNP value for those who remained in NSR for 500 days was 122 pg/mL as compared to 147 pg/mL for the patients who relapsed during the 500 days. Corresponding numbers for ANP were 129 and 153 pg/mL. In comparison, BNP and ANP values for healthy controls were 81 and 100 pg/mL respectively.

The Chinese researchers conclude that baseline BNP and ANP levels can be used to predict the likely outcome of cardioversion and that afibbers with a BNP level of less than 138 pg/mL have a good chance of being successfully converted.[20]

In contrast to the findings of the Chinese researchers, Polish researchers recently reported that, while baseline ANP levels are substantially higher among persistent afibbers than among healthy controls, there was no correlation between the maintenance of sinus rhythm during 30 days after electrical cardioversion and baseline ANP level. They did confirm that ANP levels decreased significantly after a successful cardioversion.[21]

Thus, it would appear that, while a low baseline BNP is likely associated with better cardioversion outcome, a similar correlation with ANP is in doubt.

Conclusions

Electrical cardioversion is commonly used to convert atrial fibrillation and atrial flutter to normal sinus rhythm. Although the immediate efficacy of the procedure is acceptable, especially for recent onset atrial flutter, the long-term effectiveness of the procedure is poor. Cardioversion is usually not attempted without prior anticoagulation if an episode has lasted more than 48 hours, but there is emerging evidence that it can safely be performed beyond this time limit if a transesophageal echocardiogram (TEE) shows no evidence of clots in the left atrium or left atrial appendage. The most common side effects of cardioversion are skin burns (from the electrodes) and ischemic stroke or transient ischemic attack (TIA). Low serum potassium levels and toxic levels of digoxin prior to the procedure can result in life-threatening ventricular arrhythmias, so potassium levels should always be checked and, if necessary, adjusted prior to cardioversion.

The success rate of cardioversion can be improved by pre- and post-procedure administration of beta-blockers or antiarrhythmics, and it is possible that a magnesium infusion may be beneficial as well. There is evidence that the timing of cardioversion is important with the procedure being carried out 24 to 36 hours from the onset of an episode being optimal. The timing of cardioversion following a pulmonary vein isolation procedure is also critical with substantially better results being reported if the procedure is carried out within 30 days of relapsing into AF.

There is a close association between the presence of systemic inflammation and cardioversion success. Patients with high levels of C-reactive protein (CRP) prior to cardioversion are significantly less likely to remain in sinus rhythm than are those with lower levels. Similar associations have been found for high pre-procedure levels of aldosterone and brain natriuretic peptide.

It would appear that patients with AF or flutter can improve their chance of cardioversion success by ensuring adequate serum levels of magnesium and potassium and low levels of CRP prior to the procedure. There is also evidence that pre- and post-treatment with beta-blockers or antiarrhythmics may improve long-term outcomes.

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THE AFIB REPORT is published 10 times a year by:

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