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Atrial Fibrillation in Athletes - The story behind the running hearts

-Shaolong Li, MD, Zhihui Zhang, MD, Benjamin J. Scherlag, PhD, Sunny S. Po, MD, PhD.

Current perspectives: Rheumatic atrial fibrillation

Determining esophageal anatomy with a new electroanatomical mapping system

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Case description

A 53-year-old woman with symptomatic paroxysmal atrial fibrillation was referred for pulmonary vein isolation (PVI). After obtaining access to left atrium (LA) and placement of catheters by standard technique, a high-resolution electroanatomical map of the LA and the pulmonary veins (PVs) was constructed using a map catheter (EZ Steer® Bi-directional catheter, Biosense Webster, Inc. Diamond Bar, USA) and the Carto® 3 System (Biosense-Webster Inc. Diamond Bar, USA) in the Fast Anatomical Mapping (FAM) mode.

Before ablation was begun, the patient swallowed 20 mL of barium sulphate cream (E-Z-Paste, E-ZEM Canada Inc., Westbury, New York). While the cream defined the anatomical location of the esophagus during anteroposterior fluoroscopy [Figure 1A], a series of points were added to the electroanatomical map, corresponding to the esophageal margins. This technique allowed us to define the position of the esophagus relatively to the posterior LA and PVs. Pulmonary vein isolation was then performed with application of radiofrequency energy (RF) around the PV ostia [Figure 1B]. In the posterior aspect of the LA, RF energy application was not delivered in areas where esophageal margins were previously defined [Figure 1C]. All the four pulmonary veins were successfully isolated and patient did not experience any short or long term complications during follow up.

Discussion

Atrial-esophageal fistula is a rare (0.03% to 0.5%), but serious complication of pulmonary vein isolation and it carries a very high mortality rate.¹ It is thought to occur due to conductive heat transfer to the esophagus that causes transmural tissue necrosis, mediastinitis and fistulous connection between the esophageal lumen and the left atrium. This can lead to sepsis and stroke.²

Strategies to limit or avoid RF energy application closer to the esophagus require an accurate location of this structure relative to the LA. Over the past decades several techniques have been developed in order to better understand the anatomic relationship between the posterior LA and the esophagus. Methods to localize the esophagus during RF energy delivery (real-time imaging techniques) are the preferred method, since some studies have shown the esophageal position is dynamic during ablation procedures. Contrast-enhanced computed tomography and magnetic resonance imaging have been used.³ ⁴ However, these procedures are expensive, time consuming and do not allow real-time image acquisition during RF ablation. The use of intracardiac ultrasound or the insertion of a multipolar catheter in the esophagus are good options. However, these techniques are expensive and sometimes necessi-
Figure 1: (A) Fluoroscopic image in of the esophagus (*) in anteroposterior projection after barium swallowing. (B) Electroanatomical map in anteroposterior view showing the right (orange) and left (blue) pulmonary veins; the gray area represents the left atrial chamber; the red dots mark areas where radiofrequency ablation was applied. (C) Electroanatomical map in posteranterior view showing the esophagus projection as determined by fluoroscopy and its relation with the posterior left atrial wall. The other colors represent the same as in B.
tate the use of general anesthesia. Contrary to the other techniques, barium swallow is inexpensive and practical. Dynamic changes in the esophageal position during ablation can be easily verified and integrated into the electroanatomical map because most patients have residual barium staining in the esophagus. Otherwise, additional swallows of barium cream during the procedure can be performed, since patient is under conscious sedation. The main concern of barium swallow is its aspiration to respiratory tract leading to pneumonitis. However, this risk is very small and can be readily identified by fluoroscopy.

The present case demonstrates the integration of barium swallowing with the Carto 3 electroanatomical map as a promising technique to minimize esophageal damage during atrial fibrillation catheter ablation.

References

Effect of Statins in Preventing Postoperative Atrial Fibrillation Following Cardiac Surgery

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Abstract

Background: Postoperative occurrence of AF has been associated with less favorable outcomes in patients undergoing cardiac surgery and may result in increased postoperative morbidity and mortality.

Objectives: A focused clinical question was designed and a Meta-analysis of published studies was performed to identify the effect of preoperative use of statins on the occurrence of AF after cardiac surgery.

Methods: Using the Medline database, the Cochrane clinical trials database and online clinical trial databases, we reviewed all RCTs and observational studies examining the effect of statins on AF occurrence following cardiac surgery. We searched for literature published before April 2009 and earlier.

Results: This analysis identified 6 studies (observational studies) which examined the effect of preoperative use of statins on AF occurrence following cardiac surgery, involving 10165 patients. Contradictory to most of previous studies, the overall outcomes suggested that the statins group did not have a significant decrease in AF occurrence following cardiac surgery comparing to control group (P = 0.19).

Conclusions: The preoperative medication of statins showed no significant decrease in AF occurrence following cardiac surgery in this Meta-analysis result. More prospective studies and researches are needed to explore and demonstrate the accurate mechanism and effect of statins on postoperative AF.

Key Words: Statins; Atrial Fibrillation; Cardiac Surgery; Postoperative; Meta-analysis

Introduction

AF is one of the most common complications following cardiac surgery, which has important clinical and economic implications. Patients undergoing cardiac operations are more likely to develop AF during their postoperative period with the incidence ranging from 25% to 50%.

Moreover, recent studies have shown that postoperative AF is associated with increased morbidity and prolonged hospitalization, which requires additional medical and nursing time, even intensive care unit stay.

The preoperative medication of amiodarone and β-Blocker are thought to be useful to prevent postoperative AF, though recently in an increasing number of studies, they showed no effect on AF occurrence following cardiac comparatively.

Although the exact cause and mechanism of AF
following cardiac surgery have not been testified, inflammatory component of this postoperative arrhythmia has been verified by several articles. Statin drugs, which have both antioxidant and antiinflammatory properties, have showed efficacy in attenuating postoperative AF and may constitute a potential preventive approach for postoperative arrhythmia. But there are several studies which showed different outcomes in the prophylactic use of statins. Whether statins would maintain efficacy in preventing AF following cardiac surgery has not been verified.

Therefore, we conducted a Meta-analysis over the evidence obtained from observational studies to evaluate the effect of statins on AF occurrence following cardiac surgery, which we think can provide useful clinical evidence for the prophylactic medication of cardiac surgery to decrease the complications.

1. Methods

We performed this analysis according to the guidelines of the MOOSE.

Inclusion criteria

Studies were considered eligible for this review if they met the following criteria: (1) the study must have observational study design. Patients included were assigned into statins group and control group, (2) the study should describe the basic characteristics of patients involved in the study, and (3) evaluate the postoperative effect of statins on AF occurrence.

Search strategies

Published and unpublished studies from 1990-2009 without language restriction were included. The databases of MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched. The following keywords: “atrial fibrillation” “statins” “cardiac surgery” “effect” “outcome” were used to help find the articles. Titles and abstracts as well as the reference lists of all of the identified reports were also independently examined. The whole searching process was examined by two reviewers independently (YW and WW). Discussion was launched or consensus with the third reviewer (XY) was taken when disagreement occurs.

Quality assessment

According to the checklist of the Dutch Cochrane Centre which was proposed by MOOSE, we assessed several key points of study quality of the included studies. The factors involved in assessment include: (1) whether there is clear definition of outcomes, (2) whether independent assessment of outcome is performed, (3) whether the author carries out a follow-up in a certain period of time, (4) whether there is elective loss during follow-up, and (5) whether important prognostic factors are identified for each study. The result is showed in Table 1.

Table 1  Quality assessment of included studies

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<td>Important prognostic factors identified?</td>
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+: eligible; .: not eligible.

The quality assessment showed that all the included articles had clear definition of study population, definition of outcomes, and assessment of outcome and identified prognostic factors. But 4 of them were lack of follow-up and none of them mentioned the selective loss during follow-up.
neity was tested a random-effects model was used, otherwise, with a fixed-effects model.\textsuperscript{16-21} All the statistical strategies were performed by the professional statistical reviewer independently (LY). Disagreements were resolved by consensus with a second reviewer (XY).

2. Results

2.1 Articles

Fourteen records were identified by the primary literature search. However, finally 6 studies were included in this analysis, the other 8 studies were excluded because they were either laboratory studies, review articles, or irrelevant to the current analysis. There were altogether 10165 patients included, with the publication year ranging from 2006 to 2009. The characteristics of each study are depicted in Table 2.

In the 6 included articles, 4 of which favored that preoperative statins use may be protective against AF after cardiac surgery, especially in CABG. Marín\textsuperscript{13} demonstrated that this protective effect was possibly due to alterations in the extracellular matrix and remodeling by statins. Also, in another report,\textsuperscript{22} preoperative statins use was associated with a 42% reduction in risk of AF development after CABG surgery, and patients undergoing elective revascularization may benefit from a preventative statins approach. In favor of this result, Kourliouros’s research\textsuperscript{45} suggested that higher-dose statins had the greater preventative effect, whereas low-dose statins did not influence postoperative AF. Lertsburapa and his colleagues\textsuperscript{14} also got the same result that higher-dose statins seemed to more protective than the low-dose statins. But the other two articles refused to support this idea. In a total of 2096 patients study, Virani\textsuperscript{12} found that preoperative statins therapy was not associated with decreased incidence of postoperative AF in patients undergoing cardiac surgery (OR = 1.13). Furthermore, in the study reported by Miceli\textsuperscript{36} they even demonstrated that based on the similar baseline characteristics preoperative statins was associated with a significantly higher incidence of postoperative atrial fibrillation compared with no statins treatment in patients undergoing CABG.

2.2 Effect of statins on the AF occurrence following cardiac surgery

Of all the 6 studies, there were totally 10165 patients included, with 5483 patients in the statins group and 4682 for the control. Using the software of Review Manager Version 4.2 it was found that there was significant heterogeneity within the 6 articles ($P = 0.0002$), so random-effects model was used. Compared with the control group, the result showed that the statins group did not have a significant decrease in the AF occurrence following cardiac surgery. The overall statistical result is that the OR was 0.85 units (95% confidence interval 0.66 to 1.09), and the z-score for overall effect was 1.30 ($P = 0.19$) [Figure1].

3. Discussion

Postoperative AF following cardiac surgery remains a problem, especially in CABG which is associated with an increasing hospital stay. Furthermore, it may result in hypotension, congestive...
heart failure and stroke, the risk of thromboembolic complications also increases in patients with AF after cardiac surgery.1,13,32 But the mechanisms underlying remains unknown and are thought to be multifactorial. Recently there are reports which demonstrate the role of inflammation in the initiation of AF, especially in postoperative AF following cardiac surgery.7,23-25 The association between CRP and AF in non-postoperative patients has been reported by many studies, which aroused new exploration into the mechanism of AF. These reports suggested that levels of CRP are higher in patients with AF and are significantly associated with unsuccessful cardioversion to sinus rhythm.26-27 In a recent study, Manuel L and his colleagues demonstrate that a rise in the WBC count immediately after surgery has been recognized and attributed to inflammatory reaction in postoperative AF patients and they also suggested that preoperative leukocytosis was a significant predictor of AF independent of CRP.27

Though preoperative medication of β-blocker and amiodarone are thought to be effective to prevent postoperative AF, recent studies challenged this idea.28-29 Statins, a type of lipid-lowering agents, which is also known for its effect of attenuation of inflammation, shows great effect in prevention AF following cardiac surgery by some previous reports. It used to be considered as lipid-lowering agents but more studies demonstrate a pleiotropic effect rather than lipid-lowering[30]. The anti-inflammatory property of statins has been suggested as one of the mechanisms by which they exhibit their protective role in parthenogenesis and possibly in the development of AF.30 And the anti-inflammatory role of statins as a regulatory mechanism for AF has been used preoperatively to reduce the occurrence of AF following cardiac surgery, which showed great efficacy.31-33 This beneficial effect of statins on AF has been described in different reports. Two recent studies observed a significant reduction in AF risk following cardiac surgery on patients with preoperative statins use. In a study published by Patti and his colleagues, a randomized 200 patients with preoperative atorvastatin use starting 7 days before operation showed a significant decrease in postoperative AF than placebo.34 But there are studies by other researchers which argued that preoperative statins therapy is not associated with a decrease in the incidence of postoperative AF in patients.12,35,36 So the exact efficacy of statins in preventing AF occurrence following cardiac surgery needs more studies to be verified. And we searched related articles to give a Meta-analysis and to provide clinical evidence for the prophylaxis of AF in cardiac surgery.

Our study is a Meta-analysis, we searched published studies related to the effect of statins on the occurrence of AF following cardiac surgery to conduct this analysis. In the 14 studies, 6 met our criteria and are included in this analysis. Finally we include a total of 10165 patients, 5483 of which had

Figure 1: Meta-analysis result of the included 6 articles on AF occurrence following cardiac surgery. Compared with the control group, the statins group did not have a significant decrease in AF occurrence. The overall odds ratio (OR) was 0.85 units (95% confidence interval 0.66 to 1.09), and the z-score for overall effect was 1.30(P = 0.19).
used statins preoperatively and showed no significant decrease in the occurrence of AF compared to the control group, which is contradictory to most previous studies’ demonstration that statins could decrease the postoperative AF occurrence greatly. In a recent Metaanalysis conducted by Saso and his team, they reviewed the same purpose with mixed RCTs and retrospective reports, by which they got the result that statins administration results in a reduction in the incidence of AF in patients who undergo cardiac surgery. Since there are a number of factors causing AF in patients undergoing cardiac surgery, including the age, weight, history of hypertension, obesity, use of β-Blocker and ACEI, diabetes, coronary diseases and others, which may have important impact on the AF occurrence after surgery. In our study, the two groups were reasonably balanced in the preoperative baseline characters, but their effect was thought to be inevitable. More prospective studies and researches are needed to explore and demonstrate the exact effect of statins on postoperative AF occurrence.

In a recent study, Dimitrios and his colleagues found that therapy with statins in patients with coronary artery disease and AF was associated with an increase in collagen degradation and cholesterol lowering. And previous studies have also shown that atrial fibrosis with collagen deposition is the underlying substrate in AF, Kumagai also reported that a decreased fibrosis was found in all atrial regions in the atorvastatin group compared with the control group in a prospective study. This evidence may imply that the anti-remodeling effect of statins may play an important role in preventing the occurrence of AF following cardiac surgery in some cases. In some cases whose AF occurrence did not decreased more than the control group, a decreased fibrosis was also found. In other reports the most researches found the decreased AF occurrence after electrical cardioversion by the use of statins, and most studies are observational designed. Until now the indication and mechanism are still not well known exactly, so further research is need to be done. The contradictory result of our analysis is absolutely a support for the further research.

4. Study limitations

Our study adds to the prevention effect of statins on AF occurrence following cardiac surgery. However, some potential limitations may be apparent. Firstly, because of the lack of prospective published studies, the analysis based on 6 observational articles, which definitely would affect the final outcomes. Secondly, our included studies are not enough and it requires more related studies, which may be subjected to the potential biases of such studies. Thirdly, in converting non-normally distributed statistics to normally distributed statistics, there may be a cause of bias in this analysis. But in conclusion, our studies may be useful for clinical evidence.

References

Journal of Atrial Fibrillation


Original Research

2010 | Vol 2 | Issue 5

www.jafib.com

11                           Mar-May, 2010 | Vol 2 | Issue 5
An Update on the Energy Sources and Catheter Technology for the Ablation of Atrial Fibrillation

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Abstract

The ablation of atrial fibrillation (AF) is an area of intense research in cardiac electrophysiology. In this review, we discuss the development of catheter-based interventions for AF ablation. We outline the pathophysiologic and anatomic bases for ablative lesion sets and the evolution of various catheter designs for the delivery of radiofrequency (RF), cryothermal, and other ablative energy sources. The strengths and weaknesses of various specialized RF catheters and alternative energy systems are delineated, with respect to efficacy and patient safety.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, with a prevalence that increases with age to 30 per 1000 between 55 and 60, and 80-100 by age 80.1-6 Patients with AF have a five-fold increased risk of stroke when compared with normal individuals.7 Pharmacologic rhythm control has shown limited efficacy, only slightly better than 50%. In addition, the use of antiarrhythmic agents can be pro-arrhythmic and carry significant side effects.8, 9, 10, 11, 12 Currently, the MAZE III operation is the most effective rhythm treatment of AF, with a long-term success rate of over 90%.13,14,15,16,17 The success of the Maze procedure demonstrates that in order to cure AF, it is important to reduce the surface area of the atria into partitions that do not allow the formation of reentrant circuits.18

With a variety of intracardiac catheters and energy sources, growing research suggests that a minimally invasive approach can be applied to treat AF successfully. Among these energy sources are radiofrequency, cryoenergy, laser, microwave and ultrasound. At the present time, radiofrequency energy is the most widely used energy source, and various specialized centers have achieved high success rates in treating arrhythmias with catheter ablation techniques using conventional radiofrequency energy. However, catheter ablation procedures remain technically challenging and operator-dependent, and centers that have less experience have lower success and higher complication rates. Therefore, further developments of catheter ablation technology are still required to improve procedural success and long-term outcomes and to reduce complication rates.

The desirable characteristics of an efficient energy source for catheter ablation should include: (a) ability to form uniform linear lesions; (b) adequate depth for transmural ablation, (c) freedom from contact dependence, (d) short procedure time, (e) lower risk of endocardial disruption/perforation and thrombosis formation, and (f) no injury to extracardiac structures. In this review article...
we focus on the potential role of energy sources and catheter design for catheter-based treatment of AF.

The evidence for PV isolation

It is now well established that in a subset of patients with paroxysmal AF, one or several foci, which initiate premature atrial contractions (PACs) or recurrent runs of atrial tachycardia (AT), result in the initiation of paroxysmal AF. The most intriguing aspect of this arrhythmia is that the foci are often identified to be within the pulmonary veins (PVs). It is hypothesized that bursts of AT, or even PACs, may lead to atrial electrical remodeling, which in turn leads to persistent and, eventually, chronic AF.19 The current clinical experience with the ablation of paroxysmal AF points to a single or multiple triggering foci that initiate rapid runs of atrial tachycardia that may lead to AF. Additional support to the hypothesis that focal activity may be the cause of chronic AF is provided by another publication of the ablation of chronic AF in humans.20 In this report, linear lesions in the left atrium (LA) were directed at the regions of maximally fractionated electrical activity, resulting in termination of the AF and unmasking of focal AT originating from PV ostia, trabeculated portions of the atrium, and the LA appendage. However, it is also possible that the AT is an iatrogenic result of noncontiguous and/or non-transmural linear lesions.

The unique structural anatomy of the PV insertion into the LA strongly supports the argument that the LA tissues spiraling deep into the PVs, especially the superior PVs, may provide the substrate for atrial reentry arrhythmia.21,22 Muscle fibers form spirals around the PVs, and pacemaker-type cells can be found within these structures, supporting the hypothesis of both ectopic activity and one or multiple reentrant circuits leading to the formation of AT. If this AT is persistent, it will cause atrial electrical remodeling and the initiation of AF.23

Catheters used for Pulmonary Vein Isolation

RF Technology:

The introduction of RF current for catheter ablation of cardiac arrhythmias represented a significant stride and an important tool for catheter ablation procedures compared to DC energy and chemical energy. Over years of clinical and research applications, the RF technique has emerged as the most successful and effective energy source for catheter arrhythmias. The radiofrequency band of 30 KHz to 30,000KHz is used for ablating cardiac tissue, with most RF ablation generators operating at 550KHz.24 RF energy is applied as a sinusoidal current through a small endocardial electrode to provide effective tissue heating. The primary mechanism of tissue injury by radiofrequency ablation is thermal. The mode of heating by RF is resistive heating, meaning that only a thin rim of tissue in immediate contact with RF electrode is directly heated. Deeper tissues are not heated as a direct result of dissipation of electrical energy, because tissue heating decreases as a function of 1/r4. Therefore, the deep tissues are heated via conductive heating from the tissue near the electrode-tissue interface.25, 26

Presently, the predominant RF ablation catheters in use employ single or bidirectional deflection with several deflection lengths. However, it is common that ablation procedures are significantly prolonged, at times failing as the result of an inability to deliver effective RF energy to the appropriate arrhythmogenic tissues. Although magnetically guided technology may resolve the ability of the catheter tip to reach the targeted tissues, it is markedly more expensive than designing simple catheters that properly fit the intended anatomy.

Myocardial tissue is irreversibly damaged at temperatures over 50°C. Deeper lesions are produced as the catheter tip–tissue interface temperature increases, until it reaches 100°C, at which point plasma boils, resulting in coagulum formation at the catheter tip. This can result in clot embolization, a sudden increase in impedance, loss of thermal conductivity, and/or ineffective tissue heating. In certain situations, excessive heating of the deep tissue layers can result in the production of steam within the tissue, ultimately leading to a “steam pop,” tissue disruption, and possible cardiac perforation. To prevent such events and to monitor lesion efficacy, RF ablation is generally performed in the temperature-control mode.

One critical element involved in maintaining ef-
fective levels of RF power is to provide electrode cooling, especially in areas of lower blood flow. Two strategies have been devised to accomplish this process. The first approach is to increase the electrode surface area exposed to the blood; thus, the development of 8-to-10-mm tip catheters. This greater surface area increases convective cooling. The second approach is to cool the electrode tip with infusion of saline. Saline infusion allows greater power delivery to the tissue and shifts the point of maximal heating to the tissue itself. Ultimately, this results in deeper conductive heating and the production of deeper lesions.27,28

In general, there are two types of irrigated catheters [figure 1]. The first type is the closed-loop irrigation catheter, which has an internal thermocouple and continuously circulates saline within the electrode tip. The second type is the open irrigation catheter, which has an internal thermocouple and multiple irrigation holes located around the electrode through which saline is continuously flushed, providing both internal and external cooling. In a direct comparison between open-irrigated and closed-irrigated RF ablation catheters, Yokoyama et al. found that open irrigated systems resulted in greater interface cooling, with lower interface temperatures and lower incidences of both thrombus formation and steam pops than seen with closed-loop irrigated catheters.29

**J Catheter**

An additional approach to define the ostial region of the PV as well as maintain tissue contact with the ablation catheter tip can be achieved with a simple modification of the current deflectable ablation catheters. The creation of a tight deflection of the distal shaft of the ablation catheter permits insertion of the shaft into a PV with the ablation tip protruding from the vein and deflected 90 degrees to create contact with the LA tissue. The shaft characteristics allow transmission of catheter-handle rotation to the ablation tip via long 11F pre-shaped sheaths designed to engage the PVs. By rotating the catheter handle, torque is transmitted to the ablating tip, which rotates around the orifice. The ablation tip is 8 mm, followed by a 2 mm ring electrode and an additional pair placed 5 mm from the distal electrodes for recording the electrical activity within the PV ostium. Using a long sheath, the catheter is delivered into the PVs across the atrial septum. The position of the ablation catheter tip is ascertained using contrast injection [figure 2].

The J catheter was tested in animals were local electrogram amplitude recordings and pacing thresholds were recorded before and after each RF application (55 °C for 1 min) from the distal ablating and ring electrodes. After each circumfer-

![Figure 1: Schematic representation of the irrigated electrode catheters. A, Closed loop irrigation catheter has 7F, 4-mm tip electrode with an internal thermocouple. A 5% dextrose solution at room temperature was circulated continuously through the tip electrode at a flow rate of 36 mL/min, cooling the ablation electrode internally. B, Open irrigation catheter has 7.5F, 3.5-mm tip electrode with an internal thermocouple and 6 irrigation holes (0.4-mm diameter) located around the electrode, 1.0 mm from the tip. Heparinized (1 U/min) normal saline at room temperature was irrigated through the electrode and 6 irrigation holes at a flow rate of 17 mL/min during each RF application, providing internal and external electrode cooling.29](image1)

![Figure 2: Plates B,C. The J Catheter in the left upper PV](image2)
ential ablation, the intra-PV electrical activity was measured by rotating the catheter within the vein using the proximal recording electrodes on the catheter. PV isolation required 8-11 lesions. Pacing thresholds increased from 3.9±2.1 to 6.1±4.0 mA (84% increase, p<0.0001). P-wave amplitudes decreased from 2.0±1.5 to 1.1±1.2 mV (45% decrease, p<0.001). At the completion of the isolation, no PV potentials were recorded. Post-ablation burst pacing could not induce AF or atrial tachycardia. No PV stenosis was found with any of the lesions likely related to application of the RF lesion in the left atrial tissues.30

This simple modification of the current ablation catheters can easily create circumferential lesions around the PVs and is effective and easy to use. It defines its anatomical position around the PVs and has the potential to reduce both ablation time and radiation exposure without decreasing efficacy of AF ablation and without increasing the current catheter cost.

Spiral Catheter

An additional example of a catheter that is designed to specifically isolate the PV ostia cork-screw shape is shown in Figure 3. This catheter is equipped with 4 12 mm coil electrodes, with two thermistors placed at the edges of each coil to regulate the RF power, adjusting to the maximal sensed temperature from each thermistor.31

The ablation catheter is introduced into the PVs via a 9 F sheath. Once the tip of the catheter is in the PV, the sheath is withdrawn while maintaining the catheter position in the PV. As shown below, the spiral catheter expands within the vein and the coil electrodes are embedded within and under the orifice of the PV [figure 4].

The spiral catheter was tested in animals to assess the safety and efficacy of placing circumferential lesions around the PVs. Lesion efficacy was assessed with pre- and post-ablation changes in pacing threshold, intra-PV electrogram amplitude measurements, PV angiography and intra-PV ultrasound. All of these measurements were taken pre/post ablation and during the final study following 2.5 months of recovery. RF energy was delivered in the temperature control mode and power was delivered to one electrode at the time. Pre-ablation pacing threshold and P-wave amplitude were measured on each electrode [Figure 5]. Intracardiac Echocardiography (ICE) was used to measure PV diameter before and immediately after ablation. Pulmonary angiography was performed in two perpendicular projections (LAO and RAO) before and after ablation, and during the final study. Transthoracic echocardiography (ECHO) and pulsed Doppler evaluation of left atrial (LA) size and mitral flow was performed before and one month after ablation. Detailed histological evaluation was then performed using H&E and trichrome staining. The average temperature reached was 72 ± 3.6°C. The average power to reach the desired temperature was 23.6 ± 5 Watts applied for 118 ± 8 sec. No perforations, pericardial or plural effusion, or hemorrhage occurred with the use of this technique. LA size, transmitral flow, and PV

Figure 3: PV ostia spiral catheter.31
Doppler flow patterns did not change one month post-ablation. In 11/13 PVs the amplitude of the local electrograms was reduced by 40% (p<0.01), and the pacing threshold increased from 6.9 ± 3.1 mA to more than 10 mA (p<0.04). No visible PV narrowing was seen during final PV angiography. PV circumferential lesions were documented in PVs and no PV stenosis was documented post mortem. However, to create a circular PV isolation lesion the catheter has to be rotated to a different position to create a circumferential lesion.

The Lasso Ablation Catheter

The PVAC (Ablation Frontiers, Inc., Carlsbad, CA, USA) is a 9F, over-the-wire, circumlinear (diameter 25mm), decapolar mapping and ablation catheter [figure 6]. The 3 mm long platinum electrodes have an outer diameter of approximately 1.5 mm and are spaced 3 mm apart. Each electrode contains a thermocouple positioned on the surface contact side of the electrode. The catheter has 2 control handles. One allows bidirectional deflection of the shaft and
the other is used to move the distal tip forward along the 0.032 mm guidewire, allowing a change of the catheter from its circular shape to a spiral configuration and finally a longitudinal shape. The catheter is advanced through the sheath in its longitudinal shape and then deployed in the atria with a guidewire positioned in the vein.

The GENius RF generator (Ablation Frontiers, Inc., Carlsbad, CA, USA) is a multichannel, duty cycled RF generator capable of independently delivering energy simultaneously to a maximum of 12 electrodes. RF energy can be delivered in unipolar (between ablation electrode and reference patch) and bipolar (between 2 adjacent ablation electrodes) configurations. Pairs of electrodes can be selected independently. During RF application, energy delivery is controlled by a software algorithm that modulates power to reach the user-defined target temperature (60˚C), but always limits power to a maximum of 10W per electrode. In this way the ablation is “temperature controlled”. Although with this 10W power limit the peak power delivered to each electrode is lower than with a non-irrigated 4 mm tip catheter, the current density applied at the tissue surface is approximately the same due to the smaller surface area of the electrodes. To achieve PV isolation it is necessary to rotate the catheter and apply overlapping circumferential lesions.

Boersma et al studied 98 patients with paroxysmal or persistent AF to evaluate the feasibility and safety of this multielectrode catheter. All target PVs were isolated using this catheter, and follow-up after 6 months without antiarrhythmic drugs showed freedom from AF in 83% of patients. This study also demonstrated that fluoroscopy and procedural time appear to be shorter than those associated with current AF ablation techniques, without the need for sophisticated mapping and/or steering modalities.

### Loop Catheter

The loop catheter design for the creation of linear lesions in an effort to ablate AF was introduced in 1997. There are two main loop catheter systems mostly used for experimental studies: 24 4-mm ring and 14 12-mm coil electrodes (Boston Scientific, EP Technologies, Sunnyvale, CA, USA) [34]. Both catheter designs are shown in figure 7. The first catheter system has 24 4mm ring electrodes that can create loops in the atria. Although AF could not be induced after the completion of the lesion set using ring electrodes, sustained atrial tachycardia (AT) could be induced in 25% of the hearts. In an effort to increase the efficiency of the ablation system, the second loop catheter was designed with 14 12-mm long coil electrodes 2 mm apart, equipped with two thermistors that were positioned at the two edges of each coil. The power is regulated to the maximal temperature measured.
sured between the two thermistors. Depending on the magnitude of the guidewire retraction and the size of the catheter portion extending from the sheath, the electrode portion of the catheter can form loops of various sizes. The body of the catheter applies pressure on the thin atrial walls and forces them to stretch around the catheter, maintaining consistent electrode–tissue contact along the entire length of the ablation portion of the catheter. Because the forces that are applied to the atrial walls are distributed along the catheter shaft around the loop, it is presumed that no single point is exposed to excessive forces. A locking mechanism holds the catheter and guidewire firmly in position.

The loop catheter was tested in the animal model, linear lesions were placed in five anatomic targets. These sites were chosen based on the Maze procedure, the need to create atrial linear lesions, and the mechanical characteristics of the loop catheters that cause them to adapt to the maximal circumference within a globular chamber. By positioning the sheath at different levels, a variety of positions can be achieved in the RA and LA [figure 9,10]. Each repositioning of the catheter was counted as an additional linear lesion. The linear lesions were created in a variety of sequences at five targeted locations (figure 8). The electrodes can be used to record electrical activity and deliver RF power for ablation.

Figure 8: Loop catheter positions. RA Loop (upper left panel) circular lesion from the anterior septal tricuspid valve (TV) to the right atrial appendage, to the superior vena cava (SVC) and back to the inferior vena cava (IVC); RAV (upper right panel) vertical loop connecting the SVC, IVC, and RA lateral wall; LAH (left lower panel) circular horizontal lesion placed under the pulmonary veins (PVs) in the mid-LA, above the mitral valve (MV), as indicated by a coronary sinus catheter and the atrial and ventricular electrograms recorded from each of the 24 electrodes on the catheter; LAV (middle lower panel) a vertical lesions extending from the MV annulus medial of the PVs; LAV (right lower panel) a vertical lesion extending from the MV to the LA appendage, lateral of the PVs.

Figure 9: The Loop catheter is deployed in the left atrium of a human heart during an endocardial, catheter-based Maze procedure. The view is left anterior oblique. The catheter emerges from the transeptal sheath and a loop is created after the tip of the catheter is pulled to the end of the sheath with a pull-wire as the body of the catheter is advanced into the atrium. There are 14 individual ablation coils on the catheter. Coils number 1, 4, 7, 8, 11, and 14 are more radiopaque to improve identification. An intracardiac echo probe can be seen in the body of the right atrium.
Lesion Formation with the Loop Catheter

The most important determinant in the effective creation of a RF lesion is the electrode–tissue contact. Using the variable loop concept, the globular shaped atrial chambers will adapt around the catheter providing continuous contact. When using temperature control with this technology, over 90% of the lesions created in both atria were both contiguous and transmural; the incidence of impedance rises was minimized. The catheter can be used to create linear lesions 6 mm wide and up to 16 cm long with minimal manipulation. Linear lesions were made by ablating at individual electrodes. The time required to create an entire linear lesion could be greatly reduced by using a closed-loop system to simultaneously deliver RF power to multiple electrodes to maintain a set temperature. Having multiple ablation electrodes on a single shaft allows for minimal catheter manipulation in creating long linear lesions and, therefore, reduces both thromboembolic risk and radiation exposure. Once the catheter is in place, it remains in position for the duration of the power application to all of the electrodes. Initial efforts to assess the efficacy of this technology for the ablation of AF in humans has not resulted in a great success most likely related to the lack of PV isolation.

The Development of Balloon and Balloon-like Catheters for the Isolation of the PV

MESH Catheter

Despite the promising results from the use of different energy sources for circumferential ablation of PVs, their limited clinical efficacy may arise from variable PV ostial sizes, orientations, and bifurcations. To simplify the PV-antrum isolation procedure, it would be desirable to use a single device capable of both high-resolution recording and RF current delivery. Recently, an expandable, variably shaped catheter (MESH, Bard Electrophysiology) has been developed that may overcome these limitations. The HD Mesh Ablation System (Bard Electrophysiology, Lowell MA, USA) comprises a 36-pole, high-density mapping and ablation catheter which has a braided, expandable mesh electrode configuration mounted onto a non-steerable 8F shaft. The mesh electrode is constructed of 36 wires that can be used to record 36 bipolar electrograms (EGM) [Figure 11]. The geometry of the electrodes is two opposing 18-electrode interwoven helices with thermocouples placed at the edge of each of four quadrants of the circumference to provide temperature sensing during ablation. Figure 12 shows a schematic representation of the HD Mesh Ablator catheter construction, showing the relative position of the four temperature sensors (TC). The HD Mesh Ablator catheter delivers pulsed RF energy via Pulsed RF Controller, a device that accepts the output of a compatible RF generator and distributes the RF energy to

Figure 11: HD Mesh Ablator Catheter schematic showing interwoven double helix construction

the electrodes of the BARD HD Mesh Ablator in a pulsed-energy manner. Pulsed RF is delivered to the HD Mesh catheter electrodes to create the desired lesion geometry. The RF Controller uses temperature information sensed by the thermocouples on the HD Mesh Ablator to titrate the pulsed RF energy delivery to the catheter.\textsuperscript{37,38}

Balloon Technologies for PV Isolation

RF Hot Balloon

The RF hot balloon technology is another technique for isolating the PV ostia. Tissue heating with the balloon is enhanced by the temporary obstruction of blood flow. The balloon is filled with saline and contrast medium, which allows the balloon size and location to be visualized on fluoroscopy. The saline is heated internally by RF power applied to two ring electrodes located on the catheter shaft within the balloon. This technology, although simple, is perhaps adequate for small vessels, where the size of the heating chamber is only 0.5 to 1 cm in diameter (figure 13). It is likely that the size of the human PV is too large for this technology to create adequate heating at the PV atrial junction.\textsuperscript{39}

Cryo Technology

Cryothermal energy produces lesions through hypothermic exposure, with a very different mechanism of tissue injury from RF. Cryotechnology has been used for cardiac ablation for three decades, but catheter-based ablation has been a more recent development. Cryolesions are generated by applications of a cryoprobe cooled with liquid nitrous oxide for 2-5 minutes.\textsuperscript{40} Progressive cooling of the cardiac tissue slows down conduction and eventually blocks electrical activity when the temperature is reduced to 0 to -20 °C. Permanent lesions are created when temperatures are reduced to -60 to -80 °C.\textsuperscript{41} Applying the cryoprobe to the tissue surface causes the formation of a hemisphere of frozen tissue, or iceball. The size of the cryolesion is determined by a variety of factors including temperature, the size of probe used, and the duration of freeze cycles to which the tissue is subjected. The potential advantages of cryoablation over RF for ablation include a low risk of endocardial disruption causing cardiac perforation, reduced incidence of thrombus formation, and stable adhesion of the catheter tip to the endocardium during freezing.\textsuperscript{42}

Cryoablation of Cardiac Arrhythmias

The use of low temperature as a therapeutic agent in the treatment of cardiac disease can be traced to a report by Harrison et al.\textsuperscript{43} in 1977 which described a new method of producing AV block. Since that early report, the use of cryotherapy in
the treatment of tachyarrhythmias has expanded as new techniques have evolved. In 1980, Klein et al. cryoablated the AV node to treat a recurrent supraventricular tachycardia followed by implantation of a cardiac pacemaker. In subsequent years, tachyarrhythmias related to accessory pathways and AV nodal reentry were successfully managed by cryoablation. Atrial fibrillation, often treated by Maze procedures, can be managed without surgical excision through cryoablative procedures. Cox have used surgical incision combined with cryoablation of the coronary sinus to ensure interruption of conduction across the posterior-inferior portion of the left atrium. Gaita and associates have successfully treated atrial fibrillation by linear cryoablation of the tissue between the four pulmonary veins and the mitral annulus. Recently, arrhythmias have been treated by two-step cryotherapeutic techniques involving reversible electrophysiological mapping followed by targeted ablation. Skanes, et al. have used cryo mapping to demonstrate the functionality of potential ablation sites without provoking permanent injury. The two-step procedure is designed to identify and ablate arrhythmogenic areas within the myocardium. Identification of the focus of aberrant excitation (ectopic foci) is critical to the success of this procedure. Recent clinical studies have demonstrated that transvenous cryoablation is a safe and feasible method for PV isolation for treatment of AF. Skanes et al. reported the initial results of a novel circular cryoablation catheter with a 64-mm freezing segment for PV isolation (Arctic Circler, CryoCath Technologies). This study has shown a 91% acute success rate for PV isolation and improved arrhythmic control in 78% patients after one or two procedures.

Cryoballoon

Avitall et al demonstrated that new cryo balloon technology can safely and effectively electrically isolate the PVs in dogs. The cryo balloon catheter (Boston Scientific Corporation, Natick, MA, USA), shown in figure 14, creates cryo lesions by delivering liquid N2O into the semi compliant balloon (15-22 mm diameter). After multiple consecutive cryo lesions no PV stenosis was noted 3 months after ablation. After cryo ablation, PV electrograms was eliminated and tissue recovery exhibits no cartilage formation. Acute tissue hemorrhage and hemoptysis are short-term complications of cryo ablation. Further development of catheter designs, such as use of a larger turnip shaped balloon will allow for improved adaptation of the balloon to the human PVs.

Microwave

Microwave energy represents a portion of electromagnetic spectrum occupying roughly the frequency range between 500MHz-100MHz. In contrast with radiofrequency, heating with microwave does not result from current flow through the tissue. The mechanism of heating from high-frequency microwave energy is dielectric.
Microwave heating occurs when the propagating electromagnetic radiation interacts with biological tissue, causing the dipoles (particularly water molecules) to oscillate and rotate under the influence of the alternating electromagnetic field. This results in conversion of electromagnetic energy to kinetic energy (or heat). Tissues with higher water content, such as cardiac muscle, will allow better energy transfer during propagation of the microwave. This mode of heating, gives microwave ablation the potential for a greater depth of heating, possibly resulting in a larger lesion size. Also, the delivery of heat directly to the deeper tissues reduces surface heating, with less endocardial disruption or coagulation formation. Recent studies have shown that the acute histological lesions of microwave were similar to RF, but the chronic lesions using microwave energy were deeper and wider than with RF.

Whayne et al conducted a study to determine the effect of various microwave antenna designs, frequencies, and ablation times on the radial tissue temperature gradients and lesion size. These were compared to RF lesions of similar durations. The major findings of the study were that 915- and 2450-MHz microwave antennas had similar tissue temperature profiles and produced lesion sizes that were not significantly different [figure 15]. The time course of lesion formation with microwave ablation was significantly longer than that seen with radiofrequency ablation, but the microwave lesion continues to increase in size over a 600 sec of energy delivery while the RF lesion reaches steady state by 60 sec. Another study demonstrated that ablation depth can be predictably controlled by microwave energy power and ablation time, and that the temperature at the tissue surface remains below 100˚C over the time required to produce a 6 mm deep lesion, thus preventing endocardial charring, carbonization, cavitation, and disruption. Microwave ablation has been shown to be safe and efficient method and have potential advantages over radiofrequency ablation as shown in following table.

### Ultrasound Balloon and HIFU Balloon

Another ablation strategy is the use of ultrasound technology to focus the heat dissipation caused by sound waves into atrial tissues. Sound is a propagation of oscillatory displacements of atoms/molecules around their average position in the direction of propagation. When the cyclical events occur at frequencies of >20,000 Hz, the sound is defined as ultrasound. The energy transported by an ultrasound beam is attenuated as it propagates through viscous media such as human soft tissues. The attenuation partly represents a conversion of ultrasound energy into heat. Pressure waves (sound
waves) propagating in gas-containing tissues cyclically expand (explode) and shrink (implode) microbubbles in the tissue, a process known as cavitation. This represents a major mechanism of damage to tissues exposed to high-intensity ultrasound (2–20 MHz). Ultrasound beams can be treated in a manner analogous to light beams, including focusing (ultrasonic lens) and minimization of convergence and divergence (collimation).61 These manipulations allow for ultrasound to be directed toward confined distant (deep) tissues, a pivotal capability of therapeutic ultrasound.62

The amount of ultrasound energy transferred to the tissue is proportional to the intensity of the wave and absorption coefficient of the tissue. Due to this property, ultrasound ablation does not require direct contact with the myocardium, as compared to RF ablation. Ultrasound energy falls off proportionally with the distance (1/r) whereas RF ablation current density falls off 1/r⁴. This feature allows ultrasound energy to create deeper, transmural lesions. The ability of ultrasound to be collimated through a fluid medium makes it ideal for a balloon delivery system. In this method, an ultrasound transducer is mounted on a catheter shaft within an expandable balloon. As a result, a balloon ultrasound ablation catheter system (Atrionix, Inc., Sunnyvale, CA, USA) delivered with an over-the-wire technique has been developed for AF ablation.63 The system is advanced over a guidewire into the target pulmonary vein. Ablation system

<table>
<thead>
<tr>
<th>Features</th>
<th>Radiofrequency</th>
<th>Microwave</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical experience</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Potential for endocardial Disruption</td>
<td>High</td>
<td>Low/ Medium</td>
</tr>
<tr>
<td>Thrombogenicity</td>
<td>High</td>
<td>Medium</td>
</tr>
<tr>
<td>Mapping capability</td>
<td>Limited</td>
<td>NO</td>
</tr>
<tr>
<td>Ability to create transmural lesion</td>
<td>Require optimal Contact</td>
<td>Optimal contact/ antenna orientation required</td>
</tr>
<tr>
<td>Lesion size</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Linear lesion</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td>Perforation rate</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Procedure time</td>
<td>Shorter</td>
<td>Longer</td>
</tr>
<tr>
<td>Injury to adjacent structures:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phrenic nerve</td>
<td>+++</td>
<td>Unknown</td>
</tr>
<tr>
<td>Esophagus</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Coronary artery</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>PV stenosis</td>
<td>+++</td>
<td>no</td>
</tr>
</tbody>
</table>

Table 1 | Comparison of Cryoablation versus Radiofrequency Ablation

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Marked differences lesion morphology (minimal collagen formation).</td>
<td>1. Pressurized gas system.</td>
</tr>
<tr>
<td>2. Preserved atrial contraction and size.</td>
<td>2. Complexity of control and delivery</td>
</tr>
<tr>
<td></td>
<td>5. Intramural hemorrhage and risk of hemoptysis.</td>
</tr>
<tr>
<td></td>
<td>6. Requires tissue contact</td>
</tr>
</tbody>
</table>

Table 2 | Comparison of Radiofrequency with Microwave

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performance and tissue heating were monitored and confirmed by thermocouples on the balloon and the ultrasound transducer. A cylindrical ultrasound transducer is mounted axially near the distal end of the catheter, with a saline-filled compliant balloon that is inflated over the region of the transducer. An occlusive pulmonary venogram is taken to confirm the transducer position.

Surprisingly, several applications were required to achieve isolation of the pulmonary veins (PVs). Overall, acute procedural success was achieved in only 73% with ultrasound balloon systems, and long-term cure was observed in about 30% of patients. During PV ablation, only 40% of the ostial lesions reached a temperature of >60°C in patients with recurrence of AF, compared with 64% of those who were free of recurrence. The variability of the PV anatomy was thought to be the main reason for system failure [figure 16]. In addition, the system delivered a narrow band of ultrasound energy radially from a centrally located transducer. This limitation in lesion positioning prevented the operators from including the antrum of the PVs in the lesion boundaries.

The HIFU (High Intensity Focused Ultrasound) technology was introduced in an effort to overcome some of the limitations presented with the initial design of the ultrasound ablation balloon. HIFU energy travels up to a distance of 10 mm through all layers of the left atrial wall. It is delivered in three sequential phases from endocardium to epicardium. During the first phase the energy ablates the subendocardial tissue. The second phase ablates myocardial tissue, and epicardium is ablated during the final phase.

High-intensity focused ultrasound was delivered by the Epicor Cardiac Ablation System (St Jude Medical, St. Paul, MN, USA) [figure 17]. The system consists of four main components: (1) the Ablation Control System (ACS), which provides fully automated ultrasound energy to the transducers and continuously monitors frequency, temperature and energy levels; (2) the Positioning and Sizing System (PAS), which is placed around the pulmonary veins and measures the appropriate size for the UltraCinch band; (3) the UltraCinch ablation device, which creates a continuous transmural lesion around the orifices of pulmonary veins; and (4) the UltraWand, which provides additional linear ablation lesions. Focused ultrasound ablation was performed using an investigational catheter designed to deliver forward directed,
focused ultrasound energy (Transurgical Inc., Se-tauket, NY). The system is composed of a multi-lumen 8 Fr main shaft, with a central lumen for passage of a 0.035-in wire, and separate lumen for access to both an inner and outer balloon. The liquid/gas interface between the two balloons creates an impedance mismatch, allowing reflection and focusing of the ultrasound energy. The focus zone is ring shaped and designed to have its peak intensity 2 mm off the surface of the distal portion of the balloon, schematically represented. The straightening and collapsing mechanism is also located centrally within the inner balloon on the distal catheter shaft [figure 18].

A 103-patient trial, conducted at 5 centers in 4 European countries, was the first clinical feasibility study of AF ablation with HIFU applied epicardially on the beating heart. The authors reported that the majority of the surgical procedures were conducted through a median sternotomy; however, 8 of the ablative procedures were performed through a minimally invasive approach. There were no attempts to exclude the left atrial appendage. During the ablation procedure, the Epicor system was placed so that lesions were formed encircling all 4 pulmonary veins. In addition, in 34% of the patients, the handheld Ultra Wand was used to create a single, epicardial mitral ablation line (also created epicardially) extending from the pulmonary vein lesion down to the mitral valve annu-
lus. The duration of the entire ablation procedure averaged about 12 minutes (mean time of actual ablation was 9.7 minutes), all of which was off-pump. During all but 2 minutes of this time, the surgeons were free to prepare for the subsequent heart surgery. Therefore, the researchers concluded that the “AF ablation portion of the procedure added an average of only 2.2 off-pump minutes to the overall combined operative procedure.” They also noted that “no extra time was required for epicardial fat dissection or removal.”

Freedom from AF or atrial flutter at 6-month follow-up was evaluated in 94 patients. There was an 85% success rate in the entire group at 6 months, with 88% success in the patients who received the additional mitral ablation line. In the subset of patients with continuous AF, freedom from AF at 6 months was 80%. Among patients with paroxysmal AF, 100% were AF-free at 6 months. The investigators found that duration and type of AF were 2 factors that independently increased the risk of AF recurrence after surgical intervention (P = .03 and P = .01, respectively). There were no early or late complications or deaths related to either the HIFU device or the ablation procedure, and there were no instances of left atrial reentrant tachycardia or left-sided flutter. A total of 8 pacemakers were implanted during follow-up, including 4 for complete heart block and 4 for sinus node dysfunction. In comparison to these results, the gold-standard surgical Cox Maze procedure has demonstrated 80% to 95% AF cure rates over the long term. However, the study authors point out that HIFU ablation offers several advantages over both traditional surgery and other ablation energy sources, which still require significant additional pump and aortic crossclamp times. The Epicor HIFU ablation procedure can be performed completely off-pump via a minimally invasive approach, and it preserves the endocardial layer, thus avoiding problems associated with gradient-driven ablation technologies. Moreover, there is no need to remove or dissect epicardial fat prior to the ablation, and the system can create a transmural lesion (and a mitral line) throughout the entire range of thicknesses of the atrial wall.67,68

**Laser AF Ablation**

Light amplification by stimulated emission of radiation (laser) produces a monochromatic, phase coherent beam at a specific wavelength. This beam can be directed for a specific duration and inten-
sity and as it penetrates into the tissue, after which it is absorbed and scattered. The photo-thermal effect occurs with the absorption of photon energy, producing a vibrational excited state in surrounding molecules. By absorbing this energy, the tissue is heated and a lesion is created. Laser energy can create deeper lesions with less reliance on thermal diffusion, and can reduce tissue vaporization and coagulum formation. Prior experimental studies have shown a significant linear correlation between the total delivered laser energy and the lesion dimension.

With the use of low-power energy settings, no crater formation was noted, and lesion depth was more related to duration of application rather than the power of the application. Histologically, laser lesions were homogeneous and sharply demarcated, without epicardial crater or endocardial thrombus formation. This indicates that the focused nature of the energy below the tissue-device interface minimizes the collateral atrial tissue damage that can compromise contractility and become arrhythmogenic substrate [figure 19].

The efficacy of the laser balloon depends on good contact around the balloon circumference. In view of this, fiber optic technology is being developed to facilitate the establishment of contact once the balloon is deployed and to improve the performance of such systems. Nd-YAG laser and Diode laser have been used in clinical applications. Previous canine experiments have shown that Nd-YAG laser could create deep, continuous, linear lesions over the myocardium both in vitro and in vivo without any evidence of tissue charring or vaporization.

Diode laser, a continuous low-energy laser with a wavelength of 980 nm, can minimize endocardial disruption, charring, and clot formation, allowing for more precise lesion creation.

A laser balloon has been developed to allow the delivery of circular beams of photonic energy to perform PV isolation without PV stenosis and with minimal endothelial disruption. Photonic energy is delivered through a fiberoptic balloon catheter with a 12 Fr collapsed profile [Figure 20]. The light is transferred from the fiberoptic core using a modified glass fiber tip, through an optically transparent shaft into the balloon, and projected as a ring onto the distal balloon surface. The balloons used were 21 mm or 26 mm in diameter, and the projected ring had a maximum diameter of 17 mm and 22 mm, respectively. The balloon is filled with a 3ml mixture of contrast and D2O (Deuterium Dioxide). D2O is used to eliminate self-heating of the balloon by shifting the absorption to wavelengths longer than the 980 nm utilized. D2O has been used in humans and animals for measuring water spaces, and if inadvertent rupture of the balloon occurred, the small amount of D2O would not be expected to have any deleterious effects. The intensity of the emitted light around the ring delivered to the tissue varies by less than 15% and is continuous with no gaps.

A linear laser delivery may offer a number of potential advantages over conventional radiofrequency catheter ablation: (1) the laser diffuser is a single flexible and compliant...
fiber that can create thin lesions; (2) continuous intimate contact between the catheter and the endocardium may not be essential for delivery of laser energy; (3) the laser diffuser is Teflon coated and is not directly heated during energy delivery, and thus is not prone to char formation on the catheter; and (4) laser energy delivery is not subject to disruption by rises in impedance.

Summary

Catheter Approach to the Creation of Linear Lesions for the Ablation of Atrial Fibrillation:

Initial experience has shown that AF ablation in the RA is possible but with very low (13-42%) success rate. Greater success can be achieved with linear lesions in both atria in patients with paroxysmal AF, with reported success rates of over 62%.

No long-term success data is available for chronic AF. Most of the procedures have been done with the use of the catheter drag technique and its considerable complication rates. We have also learned that the current ablation technology is not suitable for the creation of transmural contiguous linear lesions, thus subjecting the patient to the prolonged procedures with considerable complication risk. The use of the loop catheter design and perhaps other designs of ablation technology specifically targeted for the creation of linear lesions should be developed if the catheter approach for the ablation of AF is to succeed.

Conclusions

The goal of catheter-based ablation of AF should be safe, minimal tissue destruction allowing the restoration of NSR. Additionally, it should be combined with preservation of atrial mechanical transport to prevent the development of thromboembolic events and allow for full hemodynamic benefits to the patient. To justify exposing the patient to this procedure, a high safety margin is imperative. Theoretically, ablating the majority of the atrial tissues can terminate AF; however, if mechanical function is not restored, the risk of thromboembolic stroke will remain, requiring continuous anticoagulation. Furthermore, other than rate control, no mechanical benefit will be provided to the patient. If this is the outcome of a catheter-based AF intervention, AV node modification followed by permanent pacer insertion and continued anticoagulation may be a more appropriate therapy for those highly symptomatic patients whose medical therapy has failed. Such an approach presents with minimal acute risk and often is rewarding.

In this paper we have summarized the effort made to date in the development and testing of catheter-based systems and the development of methodologies for the effective ablation of AF in experimental models. However, the ablation of AF has been associated with mixed results and numerous complications. It is thought that patients with paroxysmal AF require PV isolation and those with persistent AF need more extensive ablation involving linear lesions. The concept of ablating the tissues exhibiting maximal fractionated activity and or those with the maximum dominant frequency has yet to yield consistent results. It remains to be seen if catheter-based AF ablation in the human atria provides long-term protection from AF. More importantly, incomplete lesions may introduce new substrate for reentrant arrhythmia by leaving gaps in ablation lines creating atrial tachycardia. The medical management of such arrhythmia may be significantly more difficult requiring additional ablation procedures. Thus, at this time the guiding light for the effective ablation of AF remains the Cox MAZE template. We believe that with an appropriate catheter ablation strategy targeting the complex LA anatomy, such as balloon ablation devices for PV isolation and expandable loop catheters to create linear connecting lesions, it may be possible to reproduce the MAZE-type atrial lesions.

References

5. Furberg CD, Psaty BM, Manolio TA, Gardin JM, Smith VE, Rautaharju PM. Prevalence of atrial fibrillation in el-
37. Arruda M, He DS, Freidman P, Nakagawa H, Bruce C, Aze-


64. Lustgarten DL, Keane D, Ruskin J; Cryothermal ablation: Mechanism of tissue injury and current experience in the treatment of tachyarrhythmias; Progress in Cardiovascular Diseases (1999) 41, 6, 481-498.


76. de Gouveia RH, Melo J, Santiago T, Martins AP; Comparison of the healing mechanisms of myocardial lesions induced by dry radiofrequency and microwave epicardial ablation. Pacing Clin Electrophysiology 2006;29:278-282.


Featured Review

Journal of Atrial Fibrillation


Introduction

Atrial fibrillation (AF) is the most commonly encountered arrhythmia in clinical practice but the mechanisms underlying the initiation and maintenance of AF are yet to be clarified. It is well known that regular exercise is beneficial to health and reduces the risks of cardiovascular diseases. However, recent studies suggest that long-term endurance exercise, including running, swimming, rowing and cycling, or vigorous competitive sports may increase the incidence of AF in these athletes. Since different studies used different criteria to define the intensity of exercise, the association between exercise and AF in people who exercise simply for fitness is not well established. For instance, in the Cardiovascular Health Study, the incidence of AF in elderly people was lower with moderate-intensity but not high-intensity exercise. However, people who practice competitive sports or endurance sports have a higher incidence of developing AF in the absence of structural heart diseases (lone AF). Elosua et al. discovered that if the cumulative hours of life-time sports activities are longer than 1500 hours, there is an increased incidence of lone AF in these subjects. Another study by Mont et al. showed an increase in AF incidence if the subjects practiced more than 3 hours of endurance sports weekly for more than two years. A study on the incidence of lone AF in marathon runners, in comparison to sedentary men, demonstrated a higher incidence of AF in runners (annual incidence: 0.43/100 for runners, 0.11/100 for sedentary men). Karjalainen et al. followed a group of elite male orienteers (N=300, 35-59 of age) and 495 age and gender matched control for 10 years. They found that although the mortality of the orienteers was much lower than controls (1.7% vs. 8.5%), the incidence of AF was much higher (5.3% vs. 0.9%). All these aforementioned studies suggest that the incidence of AF in male athletes is 1.8-8.8 folds higher than sedentary men.

Exercise and AF

It is widely accepted that regular aerobic exercise reduces cardiovascular risks. For instance, moderate physical activities can reduce the incidence of AF in elderly people. However, people who practice competitive sports or endurance sports have a higher incidence of developing AF in the absence of structural heart diseases (lone AF). Elosua et al. discovered that if the cumulative hours of life-time sports activities are longer than 1500 hours, there is an increased incidence of lone AF in these subjects. Another study by Mont et al. showed an increase in AF incidence if the subjects practiced more than 3 hours of endurance sports weekly for more than two years. A study on the incidence of lone AF in marathon runners, in comparison to sedentary men, demonstrated a higher incidence of AF in runners (annual incidence: 0.43/100 for runners, 0.11/100 for sedentary men). Karjalainen et al. followed a group of elite male orienteers (N=300, 35-59 of age) and 495 age and gender matched control for 10 years. They found that although the mortality of the orienteers was much lower than controls (1.7% vs. 8.5%), the incidence of AF was much higher (5.3% vs. 0.9%). All these aforementioned studies suggest that the incidence of AF in male athletes is 1.8-8.8 folds higher than sedentary men.
Characteristics of AF in Athletes

AF in endurance athletes appears to have the following characteristics. First, they are typically young or middle-aged adults and have practiced endurance sports for several years. Several studies indicate that young or middle-aged athletes who had undergone longterm high intensity training have the highest incidence of AF. Second, it is more prevalent in male than female athletes. Furlanello et al. followed 146 young elite athletes who had arrhythmia problems (male: 122, female: 24) for a mean of 62 months. In the 13 athletes who developed AF, all of them were male. Third, AF often occurs at night or after meal and less frequently during exercise, which implies that AF in endurance athletes may be related to increased vagal tone. However, AF does occur in endurance athletes during exercise, suggesting that the role of the sympathetic tone cannot be ignored. Fourth, lone, paroxysmal AF in endurance athletes can progress to persistent AF, in contrast to what was originally described. Hoogasteen et al. found that 17% exercise-related paroxysmal AF progressed to persistent AF. This finding was later verified by the GIRAFA study showing that 43% patients with exercise-related AF were in persistent AF.

The Mechanisms Underlying Exerciserelated AF

1. Exercise and the autonomic nervous system

Although high vagal tone manifesting as sinus bradycardia and asymptomatic AV conduction delay in well-trained athletes has been known for decades, clues suggesting the relationship between the autonomic nervous system (ANS) and AF in athletes originally came from the striking resemblance of the typical symptoms of this type of AF and the “vagal AF” originally described by Coumel. The classical symptoms of “vagal AF” described by Coumel include: (1) predominantly male between 30 and 50 of age, (2) usually occurs at night and rarely occurs between breakfast and lunch when the sympathetic tone is high, (3) rarely occurs during exercise or emotional stress, (4) relaxation following stress frequently triggers AF and (5) AF is often preceded by bradycardia lasting from seconds to hours. Since vagal stimulation had been used to induce AF for nearly a century, a logic explanation for AF in athletes is that chronic exercise “tunes” the ANS to be vagally predominant, which in turn triggers paroxysmal AF. However, this hypothesis has not been proven and “vagal AF” continues to be viewed as a rare form of AF that only occurs in a very small population of AF patients, such as endurance athletes.

The heart is richly innervated by the autonomic nervous system (ANS). The cardiac ANS can be divided into the extrinsic and intrinsic components. The former consists of the soma in brain nuclei and chains of ganglia along the spinal cord and the axons that course en route to the heart. The latter is composed of a neural network formed by axons and autonomic ganglia concentrated at the ganglionated plexi (GP) embedded within epicardial fat pads on the heart itself. The intrinsic cardiac ANS functions as the “little brain” on the heart as proposed by Armour et al.

In the past decade, the role of the cardiac ANS in the initiation and maintenance of AF has been actively investigated. Several basic and clinical studies have indicated that the initiation of paroxysmal AF requires the activation of both the sympathetic and parasympathetic components of the cardiac ANS, indicating that perhaps some degree of sympathetic influence may play a cooperative role in the initiation of “vagal AF.” Autonomic denervation has been shown in multiple clinical and experimental studies to suppress AF. Unfortunately, there is no animal model that reproduces the type of cardiac remodeling that is present in endurance athletes. Whether AF in endurance athletes is associated with a hyperactive autonomic state will require further basic and clinical studies.

2. Exercise and Atrial Enlargement (LAE)

Exercise increases the level of circulating catecholamine and leads to a hyperdynamic state of the circulation. In athletes undergoing long-term training, their hearts often develop adaptive changes such as LAE, left ventricular hypertrophy and enlargement. Increased left atrial pressure leads to stretch of the left atrial wall, resulting in shortening of the effective refractory period (ERP) and increasing ERP dispersion, which in turn facilitates the initiation and maintenance of AF. Using echocardiography, Pelliccia et al studied 1777 athletes...
with structurally normal hearts who participated in 38 types of sport activities. The left atrial dimension was larger than 40 mm in 347 subjects (20%) and larger than 45 mm in 38 subjects (2%). None of the athletes had LV wall motion abnormality or reduced LV ejection fraction. Among the 38 sports, the incidence of LAE was significantly increased in 28 sports, particularly rowing (18%), cycling (10%), ice hockey (10%), rugby (7%) and soccer (7%). Interestingly, athletes with LAE are more likely to win an international competition (40%) than those without LAE (20%). In athletes with LAE, 86% of them had an increased LV end diastolic diameter (>55 mm), in contrast to 34% in athletes without LAE. Although the incidence of AF in athletes was not different from non-athletes, the authors concluded that LAE might be a physiological adaptation to exercise. In contrast, another study by Mont et al² found the LA dimension in former athletes, several years off vigorous training, remained larger than control subjects (38.4±6 mm vs. 34.5±3 mm). Even years after vigorous training had been discontinued, the incidence of AF in these former athletes remained higher than control subjects. Whether LAE is an epiphenomenon of vigorous exercise or is truly a risk factor for AF remains to be investigated.

3. Exercise and Inflammation.

Studies have shown that excessive exercise induced inflammatory responses in the body. For instance, excessive training may lead to tissue injury and subsequently activates circulating monocytes, which in turn produces large quantities of IL-1β, and/or IL-6, and/or TNF-α and systemic inflammation.²⁷ In patients with lone AF, histological examination of the atrium revealed inflammatory responses compatible with the diagnosis of myocarditis in 66% of the patients.²⁸ Chung et al²⁹ discovered that patients with AF ≤24 hours had higher C-reactive protein (CRP) levels than those in sinus rhythm. Persistent AF patients had a higher CRP level than paroxysmal AF patients and both groups had higher CRP levels than controls. That study is the first to document elevated CRP in non-postoperative arrhythmia patients. These findings were reinforced by a stepwise CRP elevation with higher AF burden. Despite the correlation between inflammation and AF, it remains unclear if inflammation helps initiate or maintain AF or is only a by-product of AF. Moreover, the relationship between exercise, inflammation and AF are yet to be better understood.

4. The Relationship between the Cardiac ANS and AF in Athletes.

The heart is richly innervated by the autonomic nervous system (ANS). The cardiac ANS can be divided into the extrinsic and intrinsic components. The former consists of the soma in brain nuclei and chains of ganglia along the spinal cord and the axons that course en route to the heart. The latter is composed of a neural network formed by axons and autonomic ganglia concentrated at the ganglionated plexi (GP) embedded within epicardial fat pads on the heart itself. The intrinsic cardiac ANS functions as the “little brain” on the heart as proposed by Armour et al.²⁹ As discussed before, endurance athletes have the propensity for an elevated vagal tone, a higher level of biomarkers for inflammation and dilated atria. The one-million dollar question is: “What is the common trigger and substrate which help initiate and maintain AF in endurance athletes?” Atrial stretch in a dilated atrium is capable of abbreviating the atrial action potential and effective refractory period (ERP) as well as an increasing the ERP dispersion, providing an ideal reentry substrate for AF. However, a timely spontaneous premature beat (trigger) from the PV or non-PV site is still required to initiate AF in atria that have been preconditioned as a reentry substrate. An attractive candidate that provides both the trigger and substrate is a hyperactive state of the cardiac autonomic nervous system.²¹ Activation of the parasympathetic elements shortens the action potential and effective refractory period of the atrium and PV whereas activation of the sympathetic elements provides a larger Ca++ transient.²⁰ A synergistic action of the sympathetic and parasympathetic elements can lead to early after depolarizations and subsequently spontaneous premature depolarizations (triggers). Meanwhile, a hyperactive state of the cardiac ANS may have already prepared a substrate for reentry which is caused by an increased dispersion of the refractoriness as a result of the heterogeneous innervation of the heart by the cardiac ANS.²⁰⁻²² Moreover, cardiac ANS also activates bradykinins and interleukins that can lead to inflammation.³⁰ In other word, the cardiac ANS
may serve as the common facilitator for the dynamics of AF initiation and maintenance in athletes. Future studies will be needed to examine the role of the cardiac ANS in AF among athletes to develop a selective therapy to treat them.

5. Treatment for AF in athletes

The first step to treat AF in athletes is to exclude other medical conditions that may predispose endurance athletes to AF, such as hyperthyroidism and pericarditis. Substances such as cocaine, caffeine, anabolic steroids and sympathomimetics in cold medicines should be discontinued. In addition, structural heart diseases or other cardiac arrhythmias (e.g. Wolff-Parkinson-White syndrome, hypertrophic cardiomyopathy, long QT syndrome) should be excluded. As the mechanisms underlying AF in endurance athletes are not well understood, management of this type of AF is mainly based on limited evidence-based studies and therefore remains controversial. The following recommendations are proposed by the Study Group on Sports Cardiology of the European Association for Cardiovascular Prevention and Rehabilitation.

After all the contributing factors have been eliminated, it is recommended that athletes in early stage of paroxysmal AF temporarily discontinue training for two months to stabilize sinus rhythm. The degree of improvement during this resting period determines if athletes can resume their training. In athletes without other cardiac disorders, the recommendation for sports participation also largely depends on the ventricular rate during AF. If history reveals a high ventricular rate or hemodynamic instability during AF, the athletes should be instructed to stop exercising on the emergence of palpitation or related symptoms. Such patients may need medications that slow the ventricular rate, ideally at doses that do not cause sinus bradycardia at rest or chronotropic incompetence during exercise.

Of note, the Task Force 7 of the 36th Bethesda Conference recommended that athletes with asymptomatic AF in the absence of structural heart disease who maintain a ventricular rate that increases and slows appropriately and is comparable to that of a normal sinus response in relation to the level of activity, while receiving no therapy or therapy with AV nodal-blocking drugs, can participate in all competitive sports. It remains to be determined if athletes with symptomatic AF should discontinue training for two months to stabilize sinus rhythm as recommended by the European task force.

There is a theoretical risk of using β-block to treat this type of AF as it may further slow the sinus rate and produces an unopposed hyper-cholinergic state, which may indeed facilitate the formation of AF. The use of class Ia or Ic agents to treat AF in athletes remains to be clarified. Of note, AV nodal conduction can be enhanced during atrial tachyarrhythmia. Using class Ia or Ic agents may convert AF to atrial flutter, resulting in 1:1 conduction to the ventricle. Therefore, AV nodal blocking agents such as a β-blocker or Ca++ channel blocker should always be used in conjunction with class Ia or Ic agents.

Since the landmark report by Haissaguerre et al indicating that focal AF is often induced by rapid focal discharges originating from the pulmonary veins and/or adjacent atrial tissue, catheter ablation for AF has evolved to be the treatment of choice for drug-refractory AF, particularly for paroxysmal AF. Furlanello et al performed catheter ablation (PV isolation ± atrial flutter ablation) on 20 male competitive athletes who had very symptomatic lone AF. Except for one patient whose right inferior pulmonary vein could not be isolated, all other patients had successful PV isolation in the first ablation procedure. Interestingly, when all the patients were restudied, 62 (81%) of the previously isolated PVs have resumed conduction. Most importantly, the incidence of conduction recurrence did not correlate with the recurrence of AF, suggesting that the triggers and/or substrate for AF in these patients are not limited to PVs and adjacent atrial tissue. After 2.3 ± 0.4 ablation procedures, only two athletes continued to have short episodes of AF during 36.1 ± 12.7 months of follow-up. The maximal exercise capacity also significantly improved after ablation. Whether AF in endurance athletes responds differently to ablation than non-athletes remains to be clarified. In addition, AF in athletes may be related to a hyperactive state of the ANS. Ablation targeting the ganglionated plexi along with PV isolation theoretically may yield better results but it remains to be proven.
Conclusions

The association between moderate-intensity exercise and AF varies controversial. But in athletes undergoing high-intensity and long-term exercise, this association appears to be much stronger. A hyperactive state of the cardiac autonomic nervous system may play an important role in the initiation and maintenance of AF in endurance athletes.

References

Introduction

AF is a common arrhythmia associated with large burden of morbidity and mortality.\(^1\) In areas with a high prevalence of rheumatic heart disease, valve disease is the most common substrate for the occurrence of AF and this problem assumes greater importance because the resulting escalation in morbidity and mortality involves relatively younger population. As is true of the general population, the prevalence of AF in patients with rheumatic mitral valve disease (RMVD) increases with advancing age. When compared to patients with mitral valve disease without AF, those with AF are at a higher NYHA class, have more severe left ventricular dysfunction and show greater left atrial enlargement. Mitral valve is the most commonly involved valve among patients with AF with valvular heart disease. Mitral stenosis, Mitral regurgitation and Tricuspid regurgitation comprise 70% of valvular heart disease related to AF. Diker et al in an Echo Doppler study had found AF in 29% of patients with isolated mitral stenosis, in 16% with isolated mitral regurgitation, in 52% in combined mitral stenosis and regurgitation but in only 1% of patients with aortic valvular disease.\(^2\)

Pathophysiology And Electrophysiology

While the mechanisms of non-valvular AF have been extensively studied, the literature is sparse concerning pathophysiological mechanisms leading to AF in patients with underlying valvular diseases. There are apparent differences in the pathologic findings in these two subsets of patients. Occurrence of AF is known to correlate with LA size; the incidence of AF rises from 3% when the left atrial diameter is < 40mm to 54% if the left atrial diameter is > 40 mm.\(^3\) Mitral valve disease is associated with large left atria, and the elevated left atrial pressure causes myocardial stretch, which in turn results in slow conduction velocities, increased dispersion of refractoriness and increased automaticity, all of which create the milieu for initiating and perpetuating sustained AF.

A large postmortem study on patients with AF and associated organic heart disease showed a spectrum of histologic abnormalities that diffusely involved both the right and left atria. It was postulated that fibrosis and degeneration of the atrial myocardium in valvular heart disease, especially those of rheumatic etiology, disturb impulse propagation in the atria and lead to AF.\(^4\) Atrial fibrosis probably contributes to persistent AF after balloon valvuloplasty or surgical valve replacement and repair. AF also occurs more frequently when mitral valve is calcified or is prolapsing.\(^5\)

An insight into the role of substrate in perpetuation of AF in patients with mitral stenosis was provided in an elegant study by Fan et al.\(^6\) The regional ERP's in the atria increased after mitral valvuloplasty in patients with sinus rhythm and in AF; but in those with AF the increase was heterogeneous, while in those with sinus rhythm it was homogenous. A study of a small group of patients with rheumatic AF, who had undergone balloon...
mitral valvuloplasty, had revealed that there was an organized atrial activity most often at the Os of the Coronary Venous Sinus preceding initiation of AF, with no evidence of focal firing from the pulmonary veins.\textsuperscript{7}

Intuitively, left atrial mapping in these patients should throw light on the substrate perpetuating the fibrillation. However, literature is sparse in this regard. In our small series, the electroanatomic maps showed extensive left atrial scarring of diverse patterns [Fig 1]. The significance of this finding remains speculative at this point and merits further investigation.

While the exact mechanism of development AF is yet to be fully elucidated the impact of it on the patient, especially patients with mitral stenosis has been studied. The impact almost entirely depends on the ventricular rate. As the ventricular rate increases the diastole decreases, therefore mitral flow increases. In MS increased mitral flow causes increased left atrial and pulmonary venous pressure. The loss of atrial contraction per se has minimal impact on the patient with significant MS. Unlike the situation in normal patients, atrial contraction does not cause an increase in flow across an obstructed mitral valve. This reflected as a loss of the A wave in the M-mode in echocardiogram of MS patients who are in sinus rhythm.\textsuperscript{8}

**Thrombo- Embolism and Anticoagulation**

AF is a major cause of systemic thrombo-embolism and in patients over the age of 65 years, it is responsible for more than one-third of all strokes.\textsuperscript{9} Advancing age, history of previous thromboembolic event, presence of mitral valve disease, congestive heart failure, enlarged left atrium, previous MI, hypertension and left atrial thrombus on transesophageal echocardiography predict occurrence of embolic strokes in patients with AF.\textsuperscript{10} The presence of AF multiplies the risk of stroke 5 times in a patient with structurally normal heart, and increases by a factor of 17 in those with mitral valvular disease. The lifetime recurrence rates for strokes in these patients may be as high as 30\%–75\%.\textsuperscript{11} The risk of recurrent strokes appears to be similar with chronic and paroxysmal AF. Transesophageal echocardiographic studies have shown that the presence of significant mitral regurgitation is associated with a lower incidence of spontaneous echo contrast in the left atrium and thus with a lower

Figure 1: Schematic diagram showing the varied scar pattern in the 5 rheumatic AF patients who underwent ablation. The overlap in numbers is due to patients having scar in more than one area. scars are coloured in red.
risk of thrombi and embolization as compared to Rheumatic mitral stenosis. A particular study has demonstrated that 20% of patients with mitral stenosis and none with mitral regurgitation show left atrial thrombi. More importantly, 28 of the 30 patients (93%) with atrial thrombi showed AF, demonstrating the role of rhythm disturbance in the generation of left atrial thrombus. In patients with mitral valve disease, thrombi are found not only in the left atrial appendage but also in the body of the left atrium. This is in contrast to nonvalvular AF in which thrombi form pre dominantly (90%) in the left atrial appendage.

In a surgical clinicopathologic study in patients with AF, the prevalence of left atrial clot with predominant mitral regurgitation was 8.3% in comparison with 54% in patients with predominant mitral stenosis (p < 0.0001. In sinus rhythm, the prevalence of left atrial clot was 0% in predominant mitral regurgitation and 14.3% in patients with mitral stenosis (p < 0.001). None of the patients with AF and severe mitral regurgitation had left atrial clot.

All patients with Rheumatic AF need to be anticoagulated in the absence of contraindications. The use and timing of anticoagulation for patients in sinus rhythm with mitral stenosis is still a moot point as the risk of thromboembolism is unrelated to the severity of the disease. However, successful balloon valvuloplasty results in resolution of echo contrast and decrease in thromboembolic risk. Correction of the valvular lesion thus should be undertaken whenever feasible. There are no dosing trials to guide anticoagulant therapy in patients with AF in valvular heart disease. Based on single-center studies in patients with valvular disease and on the results of large multicenter studies involving patients with AF of nonvalvular etiology, however, similar recommendations can be made.

Management

The natural history of non-valvular AF is extremely variable. A good number of patients with non-valvular AF have paroxysmal episodes for long periods that become chronic or persistent in only a few. On the other hand, the initial attacks of AF in valvular heart disease are paroxysmal, but almost invariably progress to chronic AF. The symptoms are related to the irregular and rapid ventricular rate, development of heart failure and thromboembolic complications. These complications are related to the duration of AF and occur more often in AF associated with valvular heart disease. While the treatment of the underlying valvular disease is of primary importance, the management of the arrhythmia is aimed at either control of ventricular rate without attempting to restore sinus rhythm, or to restoration of sinus rhythm with followup aggressive therapy to maintain it. As embolic complications are the major cause of morbidity, chronic anticoagulant therapy is important in all patients with AF and valvular heart disease.

Correction of underlying disorder

Treatment of the underlying valvular abnormality should be considered, e.g. surgical repair or replacement of mitral or tricuspid valve in severe regurgitant lesions, or valvuloplasty in mitral stenosis. However, in patients with enlarged and dysfunctional atria, despite correction of the underlying valvular lesion, AF often persists. As a general rule in all these patients correction of reversible factors like thyrotoxicosis and alcohol intake must be addressed.

Delayed correction of underlying disorder would bring down the chance of maintaining these patients in sinus rhythm. This is partly reflected in the American Heart Association practice guidelines. It recommends mitral valve surgery in asymptomatic patients with severe MS as a Class IIb indication, if there is new onset AF. In patients with severe MR it is a Class IIa indication. However, this is based on consensus opinion and not on substantial data.

Control of ventricular rate

The control of ventricular rate is one of the main goals of the treatment of patients with all forms of AF when sinus rhythm cannot be restored immediately. This strategy remains the mainstay in patients with valvular heart disease as most of them have chronic AF not readily amenable to rhythm conversion. Of the several drugs used Digitalis, which was most often used earlier, is very often
ineffective during exercise because its electrophysiologic action is mediated largely through augmentation of vagal tone on the AV node. Beta-blockers such as propranolol, metoprolol and atenolol, as well as negative chronotropic calcium-channel blockers such as verapamil and diltiazem, are effective agents for control of ventricular rate with a low incidence of adverse effects. Studies have shown that combining digoxin and a beta-blocker that has intrinsic sympathomimetic activity keeps ventricular rates at peak exercise low while minimizing the effects of these drugs when heart rates are slowest, as is usually seen during the night. Catheter ablation of the AV junction and implantation of a rate-responsive ventricular permanent pacemaker should be considered in drug-refractory patients or patients who cannot take beta-blockers and calcium-channel blockers.

Rhythm Control

The clinical advantage of maintaining patients in sinus rhythm following corrective procedures for mitral valvular disease has been demonstrated in a few studies. Vaturi et al showed worse functional class and increased transmural gradients in patients with atrial fibrillation compared to those in sinus rhythm following Mitral Replacement Surgery.

In a study by Leon et al, patients with AF, BMV resulted in inferior immediate and long-term outcomes, as reflected in a smaller post-BMV mitral valve area (1.7 6 0.7 vs. 2.6 0.7 cm2; p, 0.0001) and a lower event free survival (freedom of death, redo-PMV and mitral valve surgery) at a mean follow-up time of 60 months (32% vs. 61%; p, 0.0001). AF by itself does not unfavorably influence the outcome, but is a marker for clinical and morphologic features associated with inferior results after PMV.

Maatouk et al compared outcomes at ten years in a fairly large group of patients with and without AF who underwent balloon mitral commissurotomy. They reported a lower ten year survival and a lower ten year event free survival in the AF group. The AF group also had higher rate of restenosis. However the cause of death were not reported and the events described were reinterventions and mitral valve replacements.

Rheumatic AF has also been shown to increase the incidence of prosthetic valve thrombosis in a study that was primarily looking at the results of thrombolytic therapy in patients with prosthetic valve thrombosis.

In patients with valvular AF, conversion and maintenance of sinus rhythm is difficult due to valvular abnormalities, large left atria and the presence of unhealthy substrate. Cardioversion to sinus rhythm may be achieved by chemical means or by electrical cardioversion. Chemical agents are less effective as in most cases the AF is of long duration. Antiarrhythmic agents of Vaughan Williams classes IA, IC or III are effective. Success rates in the range of 60% have been reported with flecainide, propafenone and amiodarone. Newer class III agents such as intravenous ibutilide and intravenous or oral dofetilide are most effective in atrial flutter and fibrillation of recent onset. Short-term amiodarone with or without electrical cardioversion has been shown to be effective in the restoration of sinus rhythm in chronic AF after mitral valve surgery. Prophylactic use of oral amiodarone and sotalol has been shown to prevent AF immediately following cardiac surgery.

The debate on preference of rate over rhythm control that was addressed by the AFFIRM, RACE, STAF trials predominantly involved non-valvular AF patients. These trials failed to demonstrate superiority of rhythm control strategy. However further analysis of the AFFIRM data showed that the presence of AF was associated with a 47% increased mortality compared with sinus rhythm and the use of an antiarrhythmic medication was associated with a 49% increased mortality, suggesting that any mortality benefit from the maintenance of sinus rhythm was offset by increased mortality from currently available antiarrhythmics. The more recently published randomized trial by Roy et al showed no benefit of rhythm control over rate control in patients with LV dysfunction. Non pharmacological methods, that have evolved from the surgical to radiofrequency catheter based pulmonary vein isolation with and without linear lesions have shown reasonable success in maintenance of sinus rhythm. Trials comparing these modalities against rate control need to be conducted for determining the guidelines for the best modality of management.
Suggested Management Algorithm

**RHEUMATIC AF**

**SIGNIFICANT VALVULAR HEART DISEASE**

See next page

**MILD & MOD VALVULAR DISEASE**

**AF BURDEN**

**Recurrent AF**

**SYMPTOMS/VENTRICULAR RATE DURING RECURRENCES**

Fast ventricular rate Symptomatic

Controlled ventricular rate No disabling symptoms

**Infrequent AF**

**RATE CONTROL**

RF ABLATION

**SIGNIFICANT VALVULAR HEART DISEASE**

**CATHETER INTERVENTION (PBMV)**

DCCV

Successful

No recurrences

Frequent recurrences

**SURGICAL INTERVENTION**

**INTRA OPERATIVE RFA**

**AF BURDEN, LA SIZE**

Persistent AF LA diameter > 50 mm

Rate control

Intermittent AF LA diameter ≤ 50 mm

RF ABLATION
Both pharmacological and non-pharmacological methods of conversion and maintenance of sinus rhythm which have been studied in non-valvular AF have also been studied in valvular/rheumatic AF albeit in smaller and less well-conducted studies. Similar to non-valvular AF there is no conclusive data to determine the best modality of management in rheumatic AF.

CRAAFT trial was a prospective study of 144 rheumatic valvular patients comparing rate control (using Diltiazem) and rhythm control (Amiodarone versus placebo). Besides demonstrating a mortality benefit with rhythm control, the study showed a improvement in NYHA class, quality of life and exercise capacity on achievement of sinus rhythm. There was no difference in rates of hospitalization or thromboembolism or bleeds between the two groups. In contrast to the trials involving non-valvular AF, this study had individuals of young age (mean age 39 yrs), and only those who sustained sinus rhythm at one year (69%) were compared with the rate control group. The mortality observed in the rate control arm was due to prosthetic valve thrombosis. The other major limitation of the study was its small sample size, a dropout of 13% and a relatively short follow-up.

Maze surgery and its modifications have been successfully attempted by many investigators to restore sinus rhythm in RVHD and atrial fibrillation patients. Patients undergoing mechanical valve replacement and concomitant AF surgery, the incidence of stroke 5 years after surgery is lower than in those who undergo mitral valve replacement alone. Although initial studies had shown insufficient rates of sinus rhythm restoration (59%) for the Maze procedure in AF associated with rheumatic valve disease, subsequent studies by other investigators have shown comparable conversion rates with acceptable operative risk to that of non-valvular AF. Patwardhan et al pioneered the technique of radiofrequency bipolar maze for atrial fibrillation during valve surgery. There was 80% freedom from atrial fibrillation at five months along with restoration of atrial transport function. Guang et al have also had similar experience with radiofrequency maze during mitral valve surgery, with a longer follow-up of 3 years wherein 77% of patients remained in sinus rhythm. The outcome of surgical maze for atrial fibrillation is similar in rheumatic and non-rheumatic atrial fibrillation in terms of sinus rhythm achievement and restoration of left-atrial function. Lee et al showed that the maze procedure is equally effective in AF of rheumatic and non-rheumatic etiology in terms of sinus conversion rate. Patwardhan’s group recently evaluated the efficacy of three different methods of ablative procedures - biatrial lesions, left atrial lesions and pulmonary vein isolation - and found them all comparable in a group of rheumatic patients.

It may be recommended that all patients with a history of AF undergo concomitant AF surgery/ablation at the time of their valve procedure, if it can be performed without adding significant morbidity to the procedure.

Multiple approaches for catheter ablation of AF are under clinical investigation, and although preliminary results are encouraging, indications, safety and long-term success are still not well defined; it is particularly less well studied in rheumatic AF.

A small study among patients with AF and rheumatic heart disease has shown that in a good number the arrhythmia is a relatively organized rhythm with earliest atrial activity near the os of the coronary sinus. Catheter ablation in this area was successful in restoring sinus rhythm in most of these patients. All these patients were on amiodarone but details of long-term follow-up of these patients are not available.

Furthermore, a recent study showed efficacy of Hybrid Therapy of Radiofrequency Catheter Ablation and BMV in Patients with Atrial Fibrillation and Mitral Stenosis. Twenty consecutive patients with drug-resistant AF and rheumatic MS underwent RFA combined with a BMV or transthoracic direct cardioversion (DC) following a BMV. During a mean follow-up period of 4.0 +/- 2.7 years, 8 patients (80%) in the RFA group were maintained in SR, as compared to 1 (10%) in the DC group. However if this efficacy translated into better clin-
Conclusions

In geographical regions where rheumatic heart disease is prevalent AF is an important health care issue affecting younger population. It significantly contributes to mortality and morbidity and constitutes a burden on healthcare resources of the society.

The benefit of long term anticoagulation is well established. Whether the rate control or rhythm control constitutes a better strategy is not clearly determined in non-valvular AF. Compared to patients with non-valvular AF maintenance of sinus rhythm in rheumatic AF patients appears to be more beneficial, particularly among those undergoing mitral valve surgery.

However, the benefit of restoring sinus rhythm are not clear in rheumatic heart disease patients who are haemodynamically stable and do not require valvular surgery. Although small studies have shown benefit in terms of functional class it remains to be seen if it will significantly alter important clinical endpoints.

Pharmacological methods of rhythm control have drawbacks and it appears prudent to compare nonpharmacological methods of rhythm control against rate control, considering the advancements of these modalities and their success rates in maintenance of sinus rhythm.

Despite lack of large supportive evidence it seems reasonable to attempt conversion to sinus rhythm in rheumatic heart disease in patients undergoing corrective valve surgery. However the best strategy of achieving it is not well established.

References


