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The Need of a Hybrid Approach for the Treatment of Atrial Fibrillation

Gianluigi Bisleri, MD,[1] Antonio Curnis, MD,[2] Tomaso Bottio, MD, PhD,[1] Giosuè Mascioli, MD,[2] Claudio Muneretto, MD[1]

[1]Division of Cardiac Surgery; [2]Section of Electrophysiology, Division of Cardiology, University of Brescia Medical School, Brescia, Italy

ABSTRACT

Atrial fibrillation represents nowadays one of the most important burdens in the field of arrhythmia. Albeit often inadequate, medical treatment is still considered the "first-step" approach. Non-pharmacological strategies, either surgical or interventional, recently gained an increasing interest among both cardiac surgeons and electrophysiologists. From the surgical standpoint, the introduction of different energy sources and the development of minimally invasive techniques as an alternative to the original "cut-and-sew" technique allowed a new dawn in the surgical treatment of atrial fibrillation. In the meanwhile, electrophysiologists developed more complex ablation systems that allowed the creation of linear lesions, similar to the surgical ones, while mapping the atria with three-dimensional (3D) navigation systems.

Nevertheless, the success rate in terms of sinus rhythm restoration was around 80%-85% in both fields. We foresee that the combination of the two approaches (i.e., surgical and percutaneous approach), in common hybrid approach, will allow a substantial reform for the definitive cure of atrial fibrillation, either paroxysmal or permanent, providing the highest success rates along with the best care for patients' health.

BACKGROUND

Atrial fibrillation represents the most common supraventricular tachyarrhythmia occurring in the general population: its prevalence ranges between .5% and 2% and increases in the elderly population, peaking up to 8%-10% in the patients over 70 years of age [Benjamin 1998, Feinberg 1995].

Besides well-recognized aetiologies for atrial fibrillation (as hyperthyroidism, mitral valve disease and systemic hypertension), a considerable number of patients are affected by idiopathic, lone-standing atrial fibrillation [Cain 2002].

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Address correspondence and reprint requests to: Gianluigi Bisleri, MD, UDA Cardiochirurgia – Spedali Civili, P.le Spedali Civili, 1, 25123 Brescia, Italy; 39-030-3996401; fax: 39-030-3996096 (e-mail: gianluigi_bisleri@katamail.com).

Despite being often considered as a "benign" arrhythmia, several studies recently demonstrated that patients affected by atrial fibrillation have an increased risk of cardiovascular morbidity and mortality mainly as a consequence of thromboembolism [Benjamin 1998, NHLBI Working Group 1993].

PATHOPHYSIOLOGY OF ATRIAL FIBRILLATION

The electro-anatomical mechanisms underlying the occurrence of atrial fibrillation can be summarized as:

1 *Focal triggers*. Recently, Hassaiguerre and colleagues demonstrated that rapidly firing ectopic foci located within or near the pulmonary veins are responsible for induction of paroxysmal atrial fibrillation in over 95% of patients [Haissaguerre 1998]. Nevertheless, this mechanism is likely to be exclusive of the paroxysmal subset and not enough to explain the pathophysiology of "chronic" atrial fibrillation (either persistent and permanent), when more complex macro-reentrant circuits are involved in the perpetuation of atrial fibrillation.

2 *Multiple reentrant wavelets*. In most cases of atrial fibrillation, multiple, small reentrant circuits are constantly arising in the atria. Wavelets can vary from larger to smaller loops, depending on the wavelength of the circuit, which in turn is related to the conduction velocity and the refractory period. Several factors (as fibrosis, inflammation, thyrotoxicosis, ischemia and autonomic tone) can influence either the conduction velocity or the refractory period. Additionally, a critical mass of atrial tissue is required to sustain the minimal number of simultaneous circuits necessary for the perpetuation of the arrhythmia; therefore, atrial enlargement as occurs in mitral valve disease has a key-role in the maintenance of atrial fibrillation.

The electrophysiological consequence of sustained episodes of atrial fibrillation is a marked shortening of the atrial refractory period, a phenomenon referred to as electrical remodelling. However, this process may be reversible with the maintenance of sinus rhythm. An elegant example of the concept of atrial remodelling following continuous atrial fibrillation has been provided by Alessie, stating that "atrial fibrillation begets atrial fibrillation" [Allessie 1999].

Finally, sustained episodes of atrial fibrillation frequently cause mechanical dysfunction of the atrium. Restoration of sinus rhythm is generally associated with the normalization of function over a period of 2 to 4 weeks.

PHARMACOLOGICAL THERAPY

Albeit often inadequate, it is still considered the "first-step" approach. Nevertheless, medical treatment has several limitations related to the toxicity of long-standing antiarrhythmics intake, sudden death risks and maintenance of an adequate range of anticoagulation.

Recently, a multicenter prospective randomized study comparing rate-control versus rhythm-control pharmacological therapy in patients with atrial fibrillation evidenced no advantages in terms of survival and stroke rates following sinus rhythm restoration when compared to ventricular rate control alone. Additionally, patients receiving antiarrhythmics were at a higher risk of adverse drug effects [AFFIRM study 2002].

Despite the results of AFFIRM study seem to lead to a radical reform in the management of atrial fibrillation, it is more likely that this important study may affect the therapeutical strategy only in a specific subset of patients, like the ones enrolled in the study. In fact, the studied population was mainly made of elderly patients, with no significant symptoms (as palpitations) and with permanent atrial fibrillation: a population of younger, symptomatic patients with paroxysmal atrial fibrillation may have shown different results, especially in terms of quality of life.

Additionally, despite rate control was possible in the majority of patients with atrial fibrillation, this goal was achieved only by means of frequent medication changes and drug combinations [Olshansky 2004].

ELECTRICAL CARDIOVERSION

Sinus rhythm can be restored in a significant proportion of patients by direct current cardioversion, but relapse is high unless antiarrhythmic therapy is administered concomitantly. Despite immediate success, the recurrence rate of atrial fibrillation may peak up to 75% during the first year following electrical cardioversion [Lundstrom 1988]; however, prophylactic medical treatment, in particular with amiodarone, has been demonstrated to maintain sinus rhythm in approximately 60%-80 % of patients undergoing electrical cardioversion [Marcus 2001].

Additionally, thromboembolic events have been reported in patients without an adequate anticoagulation protocol before cardioversion [Arnold 1992].

NON-PHARMACOLOGICAL THERAPEUTICAL OPTIONS

Surgical Approach

Since the introduction in 1989 by Cox and colleagues [Cox 1989] of the Maze procedure and the initial excitement for the impressive results in terms of sinus rhythm restoration (up to 96%), its use has been mainly hampered by the technical complexity, the use of cardiopulmonary bypass, the risk of bleeding and the high rate of pacemaker dependence (up to 15%). The development of modified ablative strategies (either endocardial or epicardial) and lesion sets [Knaut 2000, Maessen 2002, Melo 2000] and several innovative energy sources [Williams 2002] led to a new dawn in the surgical treatment of atrial fibrillation with an average efficacy rate of 80%. In particular, the most importance advance was represented by the possibility to treat effectively patients not necessarily requiring mitral valve surgery while sparing the opening of the left atrium. Such a significant progress widely extended the concomitant treatment of atrial fibrillation in cardiac surgery also to patients not affected by mitral valve disease (as coronary or aortic valve diseased patients). Additionally, the epicardial approach overcame the most devastating risk related to endocardial ablation, i.e. esophageal perforation [Doll 2003].

Further technical development and surgical refinement recently allowed the application of a minimally invasive closed-chest approach in patients suffering from lone atrial fibrillation [Argenziano 2003, Bisleri 2005, Saltman 2003].

Among the most important advantages of surgical treatment of atrial fibrillation, it is noteworthy the possibility to ablate wide areas of either the left or the right atrium, in a considerably short time, ranging from 1-10 minutes for concomitant ablations to 1.5 hours for the totally endoscopic epicardial pulmonary veins isolation as a stand-alone procedure.

Percutaneous Approach

The percutaneous ablation in the treatment of atrial fibrillation initially gained wide popularity in those patients affected by paroxysmal atrial fibrillation where a focal ablation was able to terminate the arrhythmia in the majority of cases [Haissaguerre 1998].

Nevertheless, several procedural drawbacks of the procedure were evident, such as a high percentage of recurrences, pulmonary veins stenosis and the risk of heart perforation and stroke with a success rate ranging between 50% and 75% [Chen 1999, Gaita 2003, Haissaguerre 2000].

Afterwards, a novel "anatomic" approach was introduced in order to overcome the limited success rates of focal ablations: a restoration in 85% of patients was demonstrated [Pappone 2000]. Such encouraging results led to a wider use of circumferential "anatomical" ablation lines to be adopted by many electrophysiologists, albeit this technique is technically challenging, time-consuming (up to 6-8 hours per procedure) and may cause excessive patient exposure to radiations.

Still the percutaneous approach holds an extremely important advantage when compared to surgical ablation, i.e. the real-time mapping of the atria. Recently, the innovative 3D non-contact mapping systems allow precise definition of chamber geometry, identification of crucial sites for maintenance of re-entry circuits, and navigation of the ablation catheter to critical sites [Hindricks 2001].

HOW TO DEVELOP A HYBRID APPROACH?

Despite the hybrid approach may be used in patients undergoing also other surgical procedures than treatment of atrial fibrillation (as coronary or valve surgery), it can be foreseen that the hybrid treatment of *lone atrial fibrillation* will represent the most important subset of patients.

In order to develop an effective surgical (minimally invasive, either thoracoscopic or robotic-enchanced)/percutaneous approach several factors must be taken into account, which are discussed below.

Simplification of the Lesion Set

Lammers and colleagues experimentally analyzed the refractory period differentials in the left and right atrium suggesting that the right atrial lesions of the Maze procedure might be replaced by a simpler approach. In fact, while the refractory periods are shorter in the left atrium (therefore sustaining the smaller macro-reentrant circuits typical of atrial fibrillation), the refractory periods in the right atrium are relatively longer: as a consequence, the right atrium "per se" is more likely to be unable of sustaining atrial fibrillation unless a considerable enlargement occurs [Lammers 1990].

This observation is extremely important for the implications in the treatment of atrial fibrillation, since it may be primarily focused on the left atrium while the right atrium could be treated mainly with respect to atrial flutter alone, by placing a lesion in the isthmus between the coronary sinus and the tricuspid valve.

Different surgical experiences are suggesting that a left-sided alone strategy (mainly focused on the isolation of the pulmonary veins), either surgical [Kalil 2002] or ablative [Knaut 2004, Maessen 2002, Todd 2003] are effective in restoring sinus rhythm in the majority of patients. A similar success rate has been reported by several electrophysiological experiences [Kottkamp 2004, Pappone 2000] targeting on the pulmonary veins isolation plus few additional lines (as the connection between the right and left pulmonary veins and lesion to the mitral annulus).

The Posterior Aspect of the Left Atrium

While a lot of attention has been given to the arrhythmogenic "firing" foci located in the ostia of the pulmonary veins, the posterior aspect has been relatively neglected lately.

However, this region of the left atrium may hold a consistent importance not primarily in the induction of atrial fibrillation while in its maintenance.

Embryogenetic studies demonstrated the proliferation pulmonary veins from the dorsal mesocardium and its incorporation into the left atrium [Blom 2001] and those areas derived from the developing cardiac conduction system may contribute to the arrhythmogenic substrate in adult hearts [Jongbloed 2004]. In particular, these areas are limited not only to the pulmonary veins but are present also in the posterior aspect of the left atrium.

Management of the Left Atrial Appendage (LAA)

Removal of the LAA is commonly advocated in the original Cox-Maze procedure and accounts for the extremely low incidence of cerebrovascular accidents (0%-1%) [Cox 1999]. Some authors even reported a minimally invasive procedure for LAA exclusion [Odell 1996] which may have important implications for the minimally invasive thoracoscopic approach.

However, removal of the LAA may result in undesirable physiological sequelae (reduced atrial compliance and capacity for ANF secretion in response to pressure and volume overload) [Al-Saady 1999, Stollberger 2003]. Moreover, several concerns have been raised with respect to the efficacy of the internal obliteration (during mitral valve surgery) [Pennec 2003] and about the potential bleeding risks during thoracoscopic LAA stapling [Lindsday 1996].

Finally, a growing evidence from electrophysiological clinical experiences is progressively demonstrating that the incidence of thromboembolic events is low despite the LAA being not excluded [Pappone 2003, Wong 2004].

As a consequence, it may be foreseen that exclusion of the LAA should be performed in selected cases at higher risk, as in the presence of previous history of cerebrovascular accidents, left atrial enlargement, left ventricular dysfunction, coagulative disorders and high levels of hematocrit.

Recently, a novel therapeutical option has been introduced by interventional cardiologists, i.e. the percutaneous left atrial appendage transcatheter occlusion [Sievert 2002], albeit this relevant innovation raises concerns in terms of procedural risks (as hemopericardium, estimated around 6%-7 %) and completeness of LAA occlusion. Nevertheless, percutaneous LAA occlusion represents an important additional tool for the non-pharmacological treatment of atrial fibrillation, especially for the hybrid electrophysiological–surgical approach.

HYBRID PROCEDURAL TIMING

As in the issue of hybrid revascularization procedures, the correct timing (either surgical or percutaneous ablation first) has to be defined.

When surgical ablation is performed first, the percutaneous procedure can be performed if the patients show clinical (palpitations) or electrocardiographic signs of atrial fibrillation recurrences: we believe that this procedure should be performed at least 3 months following the surgical ablation in order to have a stabilization of the lesion. Earlier recurrences of atrial fibrillation are common even after percutaneous ablation and do not predict the rate of sinus rhythm restoration.

During the electrophysiological procedures any kind of possible gap in the surgical ablation may be identified and treated or new ablation lines created (e.g., lesion to the mitral annulus).

Conversely, if the percutaneous ablations are performed first, the intra-procedural mapping can allow a clear definition of the mechanism underlying the arrhythmic disease. However, the disadvantage of this timing is related to the fact that patients usually undergo a long procedure (for isolation of the pulmonary veins) that may fail and require anyway the surgical intervention.

ARRHYTHMIA SURGERY PROGRAM: THE BRESCIA EXPERIENCE

Recently, at the University of Brescia Medical School we started a program of total endoscopic surgical treatment of atrial fibrillation [Bisleri 2005].

To date, we have performed this procedure on 13 patients refractory to medical treatment/electrophysiological procedures. AF was paroxysmal in 76.9% and permanent in 23.1% of patients. The surgical procedure was performed in 12 patients: thoracoscopic (in 9 patients) and via ministernotomy

The microwave ablation probe is positioned around the four pulmonary veins in order to create a "box" lesion set.

in 3 patients due to presence of pericardial/pleural adhesions. In an effort to further reduce the invasiveness of closed-chest atrial fibrillation surgery, we recently developed a novel monolateral approach that was successfully used in the last 6 patients of this series. The microwave ablation probe once positioned around the pulmonary veins is depicted in the Figure. Mean ablation time was 15±2 minutes, mean overall procedural time was 1.5±.7 hours; the procedure was withdrawn during the initial manoeuvres in 1 patient with previous history of myocardial infarction due to hemodynamic instability. At the end of the procedure, all patients were extubated in the operating room and went back to the ward, without any post-operative stay in the intensive care unit. The post-operative course was uneventful in all cases. At a mean follow-up of 275 days (range: 5-420), 83.4% of patients were in stable sinus rhythm, 1 patient (8.3%) experienced recurrent bouts of atrial fibrillation while another patient (8.3%) is in AF. We already performed in 1 patient a post-operative 3D mapping of the left atrium in a patient with recurrent AF episodes demonstrating a full transmurality of the surgical epicardial ablation ("box" lesion set) and the need for a focal ablation at the mitral isthmus level: following the electrophysiological procedure, the patient did not experience any AF recurrences.

THE NEXT STEP

To date, treatment of atrial fibrillation has been mainly based on pharmacological strategies along with electrical cardioversions, despite often being ineffective.

The recent advances both from the surgical (with the development of closed-chest techniques for epicardial isolation of the pulmonary veins) and the electrophysiological standpoint (with the development of new catheters for pulmonary veins isolation, tools for ablation at the mitral annulus and 3D mapping systems) will allow a substantial reform in the near future for the definitive cure of atrial fibrillation, either paroxysmal or permanent, providing the highest success rates along with the best care for patients' health.

REFERENCES

Allessie MA. 1999. Atrial fibrillation-induced electrical remodeling in humans: what is the next step? Cardiovasc Res 44(1):10-2.

Al-Saady NM, Obel OA, Camm AJ. 1999. Left atrial appendage: structure, function, and role in thromboembolism. Heart 82:547-55.

Argenziano M, Williams MR. 2003. Robotic atrial septal defect repair and endoscopic treatment of atrial fibrillation. Semin Thorac Cardiovasc Surg 15(2):130-40.

Arnold AZ, Mick MJ, Mazurek RP, Loop FD, Trohman RG. 1992. Role of prophylactic anticoagulation for direct current cardioversion in patients with atrial fibrillation or atrial flutter. J Am Coll Cardiol 19:851-5.

Benjamin EJ, Wolf PA, D'Agostino RB. 1998. Impact of atrial fibrillation on the risk of death – the Framingham Heart Study. Circulation 98:946-52.

Bisleri G, Manzato A, Argenziano M, Vigilance DW, Muneretto C. 2005. Thoracoscopic epicardial pulmonary vein ablation for lone paroxysmal atrial fibrillation. Europace 7:145-8.

Blom NA, Gittenberger-de Groot AC, Jongeneel TH, DeRuiter MC, Poelmann RE, Ottenkamp J. 2001. Normal development of the pulmonary veins in human embryos and formulation of a morphogenetic concept for sinus venosus defects. Am J Cardiol 87:305-9.

Cain ME. 2002. Atrial fibrillation — rhythm or rate control. N Engl J Med 347:1822-3.

Chen SA, Hsieh MH, Tai CT, et al. 1999. Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins: electrophysiological characteristics, pharmacological responses, and effects of radiofrequency ablation. Circulation 100:1879-86.

Cox JL, Schuessler RB, Cain ME, et al. 1989. Surgery for atrial fibrillation. Semin Thorac Cardiovasc Surg 1:67-73.

Cox JL, Ad N, Palazzo T. 1999. Impact of the Maze procedure on the stroke rate in patients with atrial fibrillation. J Thorac Cardiovasc Surg 118:838-40.

Doll N, Borger MA, Fabricius A, et al. 2003. Esophageal perforation during left atrial radiofrequency ablation: Is the risk too high? J Thorac Cardiovasc Surg 125:836-42.

Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. 1995. Prevalence, age distribution, and gender of patients with atrial fibrillation: analysis and implications. Arch Intern Med 155:469-73.

Gaita F, Riccardi R. 2003. Non-pharmacological treatment of atrial fibrillation. Ital Heart J 4:745-54.

Haissaguerre M, Jais P, Shah DC, et al. 1998. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 339:659-66.

Haissaguerre M, Shah DC, Jais P. 2000. Mapping-guided ablation of pulmonary veins to cure atrial fibrillation. Am J Cardiol 86(9 Suppl 1): K9-K19.

Hindricks G, Kottkamp H. 2001. Simultaneous noncontact mapping of left atrium in patients with paroxysmal atrial fibrillation. Circulation 104(3):297-303.

Jongbloed MR, Schalij MJ, Poelmann RE, 2004. 2004. Embryonic conduction tissue: a spatial correlation with adult arrhythmogenic areas. J Cardiovasc Electrophysiol 15(3):349-55.

Kalil RA, Lima GG, Leiria TL, et al. 2002. Simple surgical isolation of pulmonary veins for treating secondary atrial fibrillation in mitral valve disease. Ann Thorac Surg 73:1169-73.

Knaut M, Tugtekin SM, Spitzer S, Gulielmos V. 2000. Combined atrial fibrillation and mitral valve surgery using microwave technology. Semin Thorac Cardiovasc Surg 14:226-31.

Knaut M, Tugtekin SM, Matschke K. 2004. Pulmonary vein isolation by microwave energy ablation in patients with permanent atrial fibrillation. J Card Surg 19:211-5.

Kottkamp H, Tanner H, Kobza R, et al. 2004. Time courses and quantitative analysis of atrial fibrillation episode number and duration after circular plus linear left atrial lesions. J Am Coll Cardiol 44:869-77.

Lammers WJ, Schalij MJ, Kirchhof CJ, Allessie MA. 1990. Quantification of spatial inhomogeneity in conduction and initiation of reentrant atrial arrhythmias. Am J Physiol 259(4 Pt 2):H1254-63.

Lindsay BD. 1996. Obliteration of the left atrial appendage: A concept worth testing. Ann Thorac Surg 61:515.

Lundstrom T, Ryden L. 1998. Chronic atrial fibrillation. Long-term results of direct current conversion. Acta Med Scand 223:53-9.

Maessen JG, Nijs JF, Smeets JL, Vainer J, Mochtar B. 2002. Beating-heart surgical treatment of atrial fibrillation with microwave ablation. Ann Thorac Surg 74:S1307-11.

Marcus GM, Sung RJ. 2001. Antiarrhythmic agents in facilitating electrical cardioversion of atrial fibrillation and promoting maintenance of sinus rhythm. Cardiology 95:1-8.

Melo J, Adragao P, Neves J, et al. 2000. Endocardial and epicardial radiofrequency ablation in the treatment of atrial fibrillation with a new intra-operative device. Eur J Cardiothorac Surg 18:182-6.

Odell JA, Blackshear JL, Davies E, et al. 1996. Thoracoscopic obliteration of the left atrial appendage: Potential for stroke reduction? Ann Thorac Surg 61:565-9.

Olshansky B, Rosenfeld LE, Warner AL, et al. 2004. The atrial fibrillation follow-up investigation of rhythm management (AFFIRM) study: approaches to control rate in atrial fibrillation. J Am Coll Cardiol 43:1201-8.

Pappone C, Rosanio S, Oreto G, et al. 2000. Circumferential radiofrequency ablation of pulmonary vein ostia: A new anatomic approach for curing atrial fibrillation. Circulation 102(21):2619-28.

Pappone C, Rosanio S, Augello G, et al. 2003. Mortality, morbidity, and quality of life after circumferential pulmonary vein ablation for atrial fibrillation. J Am Coll Cardiol 42:185-97.

Pennec PY, Jobic Y, Blanc JJ, Bezon E, Barra JA. 2003. Assessment of different procedures for surgical left atrial appendage exclusion. Ann Thorac Surg 76:2168-9.

Saltman AE, Rosenthal LS, Francalancia NA, Lahey SJ. 2003. A completely endoscopic approach to microwave ablation for atrial fibrillation. Heart Surg Forum 6(3):38-41.

Sievert H, Lesh MD, Trepels T, et al. 2002. Percutaneous left atrial appendage transcatheter occlusion to prevent stroke in high-risk patients with atrial fibrillation: early clinical experience. Circulation 105:1887-9.

Stollberger C, Schneider B, Finsterer J. 2003. Elimination of the left atrial appendage to prevent stroke or embolism? Chest 124:2356–62.

The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. 2002. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med 347:1825-33.

The National Heart, Lung, and Blood Institute Working Group on Atrial Fibrillation. 1993. Atrial fibrillation: current understandings and research imperatives. J Am Coll Cardiol 22:1830-4.

Todd DM, Skanes AC, Guiraudon G, et al. 2003. Role of the posterior left atrium and pulmonary veins in human lone atrial fibrillation. Circulation 108:3108-14.

Williams MR. 2002. A review of the methods of atrial tissue ablation. Heart Surg Forum : HSF Reviews 1:7-8.

Wong T, Markides V, Peters NS, Davies DW. 2004. Percutaneous pulmonary vein cryoablation to treat atrial fibrillation. J Interv Card Electrophysiol 11:117-26.