Hybrid therapy of atrial fibrillation

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Antiarrhythmic drugs have shown a poor long-term efficacy in the management of atrial fibrillation. It has been suggested that the association of antiarrhythmic drugs and non-pharmacological treatments may be superior to the prescription of a single treatment only.

Electrical cardioversion of atrial fibrillation can be ineffective in several cases (long-lasting atrial fibrillation, large atria, advanced age, underlying diseases, high transthoracic impedance): the prescription of antiarrhythmic drugs prior to electrical shock has been demonstrated to be able to increase the success rate and to reduce the energy requirement. Ibutilide, amiodarone and sotalol are the most effective, while the efficacy of class IC drugs is controversial.

The use of conventional atrial stimulation in case of the brady-tachy syndrome is related to the need of sustaining the atrial rhythm during bradycardia which can be exacerbated by the use of antiarrhythmic drugs. New overdrive algorithms, such as consistent atrial pacing and atrial rate stabilization, can increase the efficacy of physiological pacing. Painless electrical therapies, such as ramp and burst, have been implemented in specific devices, in order to combine the prevention and treatment of atrial arrhythmias. Multisite atrial stimulation has been introduced to improve the activation sequence and to reduce atrial asynchrony in case of slow conduction in the right atrium and of retrograde activation of the left atrium. Two methods are available for multisite atrial pacing: 1) simultaneous biatrial stimulation with the leads placed in the right appendage and in the left atrium through the coronary sinus; 2) dual site right atrial pacing with the leads positioned in the roof of the right atrium and proximal to the ostium of the coronary sinus. Single site non-conventional atrial pacing with the lead placed at the level of the interatrial septum, in the triangle of Koch, has been proposed in order to modulate the anisotropic conduction of this zone, responsible for the onset of atrial fibrillation. Non-conventional stimulation in association with drug therapy has been demonstrated to be more effective than conventional pacing in reducing the incidence of paroxysmal atrial fibrillation. The use of a dual-chamber defibrillator equipped with painless antitachy pacing therapies and atrial cardioversion can be considered the next step in the evolution of implantable devices.

Atrioventricular nodal ablation and pacemaker implantation (ablate and pace) has been the first radiofrequency ablation procedure used to control the atrial fibrillation rate. Recently, it has been demonstrated that the survival rate in these patients was similar to that observed in subjects who received antiarrhythmic therapy. In patients in whom the administration of antiarrhythmic drugs (mainly class IC or amiodarone) modified atrial fibrillation in atrial flutter, linear lesions on the isthmus have been demonstrated to be effective in inhibiting the recurrence of arrhythmia. The first approach attempted in order to directly treat atrial fibrillation was the creation of linear lesions in the right atrium by means of radiofrequency current in patients refractory to drug therapy. This procedure was found to be feasible and safe, while lesions on the left atrium were associated with a high rate of side effects. The aim of the lesions was to create block lines in intra-atrial conduction, in order to electrically compartmentalize the atria and to avoid the propagation of reentry waves. More recently the ablation of the automatic activity originating from the posterior wall of the left atrium or within the pulmonary veins, which can trigger the onset of atrial fibrillation, has been performed.

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Introduction

Atrial fibrillation is the most common sustained arrhythmia encountered in clinical practice. Its prevalence is expected to increase with the aging of the general population and it is associated with significant morbidity and mortality. Therapeutic objectives include rate control, cardioversion, the maintenance of sinus rhythm and stroke prevention. Pharmacological treatment strategies directed to heart rate control or to the prevention of the recurrence of atrial fibrillation are frequently ineffective or should be withdrawn because of adverse effects including ventricular proarrhythmia. In particular, pharmacological approaches, when used alone, have a poor long-term efficacy with 50 to 70% of patients eventually progressing to chronic atrial fibrillation[1]. Consequently, newer non-pharmacological therapeutic approaches have been developed. The use of antitachycardia devices such as atrial defibrillators and antitachycardia pacemakers has been implemented in clinical trials[2-4]; at the present time, the anatomically guided ablation of the venous orifices in the left atrium, or the creation of

linear lesions in the right atrium has been attempted[5,6]. Nevertheless, in the general population, the clinical efficacy of both approaches in the restoration of sinus rhythm in the short term has been modest with little evidence of long-term freedom from symptomatic atrial fibrillation or of a reduction in asymptomatic atrial fibrillation. There is some preliminary evidence that the combination of antiarrhythmic drugs and non-pharmacological treatment strategies or the combination of different interventional methods, may be superior to a single treatment alone. A hybrid approach for the treatment of atrial fibrillation may provide the following effects: an increased treatment efficacy due to a synergistic effect and the reduction of side effects.

Antiarrhythmic drugs prior to electrical cardioversion

Antiarrhythmic therapy has been demonstrated to be effective in improving the efficacy of electrical cardioversion, in view of the decrease in the number of unsuccessful procedures and in the threshold of atrial defibrillation. Class IA, IC, and III antiarrhytmic agents are used for the facilitation of electrical cardioversion. Several factors may predict failure with electrical cardioversion alone (the duration of atrial fibrillation, atrial size, age, underlying disease, and factors that influence the transthoracic impedance), calling for empiric pharmacotherapy to facilitate cardioversion. With regard to this aspect, class IA agents hold some promise, evidence for class IC agents is conflicting, and class III agents are the most effective. Adverse effects are rare given the short course before cardioversion, but ibutilide, the most efficacious in this regard, may be proarrhythmic after just a single dose.

The mechanism by means of which ibutilide enhances the efficacy of the electrical conversion of atrial fibrillation has been evaluated in the canine model[7]. The authors concluded that ibutilide prolongs the cycle length of vagally-mediated acute atrial fibrillation and, furthermore, it facilitates the electrical conversion of atrial fibrillation by lowering the energy requirement. Oral et al.[8] evaluated the effect of 1 mg of ibutilide on the energy requirement for atrial transthoracic defibrillation. One hundred patients with persistent atrial fibrillation were randomly assigned before cardioversion to pre-treatment or no pre-treatment with ibutilide. Successful cardioversion was achieved in all the patients treated with ibutilide and, with regard to the 14 patients in whom electrical treatment alone failed, sinus rhythm was restored when cardioversion was attempted again after the administration of ibutilide. A significant reduction in the mean energy required for defibrillation was associated with prior drug administration. Li et al.[9] reported similar results. The authors repeated direct-current cardioversion of atrial fibrillation after ibutilide injection in patients in whom conventional cardioversion alone had failed. In 11 of 12 patients (92%) cardioversion was successful and internal cardioversion was not required. Amiodarone infusion has been demonstrated to be effective in facilitating electrical cardioversion. Capucci et al.[10], in a controlled randomized study on a population of 92 patients with persistent atrial fibrillation, demonstrated that electrical cardioversion was more successful after pre-treatment with amiodarone (88 vs 56%), but no influence on the electrical threshold was observed. The effects of sotalol infusion on the transthoracic electrical cardioversion of atrial fibrillation have been investigated by Lai et al.[11]. Eighteen patients with persistent atrial fibrillation were submitted to transthoracic cardioversion before and after sotalol i.v. infusion (1.5 mg/kg). In the 14 patients in whom atrial fibrillation was terminated by cardioversion before sotalol infusion, the atrial defibrillation energy required was significantly reduced after sotalol infusion; furthermore, in 2 of the 4 patients in whom baseline electrical treatment was ineffective, sinus rhythm was restored by cardioversion after sotalol infusion.

The effects of class IC drugs on electrical cardioversion are conflicting. Bianconi et al.[12] evaluated the benefits and risks of administering propafenone before electrical defibrillation for chronic atrial fibrillation. One hundred patients with chronic atrial fibrillation were randomly assigned to oral treatment with either placebo or 750 mg/day of propafenone for 48 hours before the delivery of the direct current shock. After successful cardioversion, all patients received propafenone therapy and were followed up for 48 hours. The authors observed that the mean defibrillation threshold and the rate of sinus rhythm restoration were not significantly influenced by pre-treatment with propafenone; nevertheless, this approach decreased the recurrence of atrial fibrillation early after shock, allowing a rapid discharge from the hospital. Boriani et al.[13] evaluated the effects of intravenous flecainide on the defibrillation energy requirements in patients treated with low-energy internal atrial cardioversion. They observed a favorable effect of flecainide both in persistent and in paroxysmal atrial fibrillation, with a significant decline in energy requirements for effective defibrillation, and with an important reduction in the scores of shock-induced discomfort.

Antiarrhythmic drugs and implantable device therapy

Single site permanent atrial pacing. Different electrophysiological mechanisms are involved in the antiarrhythmic effect of atrial pacing:
- the prevention of bradycardia-related atrial fibrillation;
- a reduction in the number of premature atrial contractions triggered by atrial fibrillation;

- the suppression of "long-short" and of "short-long-short" atrial cycles;
- a reduction in the dispersion of conduction and in atrial refractoriness.

In sick sinus disease including a brady-tachy syndrome, the use of atrial stimulation has been related to the need of sustaining the atrial rhythm during bradycardia. The latter may be exacerbated with the use of antiarrhythmic drugs which, on the other hand, are effective on tachyarrhythmic runs. Recently, atrial pacing has been suggested to be effective *per se* on tachyarrhythmic episodes[14]. The increase in the percentage of atrial pacing and contemporarily the rhythm stabilization, by means of the rate-responsiveness function[15] or by pacing algorithms, can contribute to the prevention of recurrences of atrial fibrillation. The algorithms more frequently employed have been the "consistent atrial pacing" (CAP) and the "atrial rate stabilization" (ARS). CAP[15-18] allows the beat-to-beat monitoring of spontaneous atrial activity, continuously revising the atrial pacing interval so as to achieve the maximum possible percentage of atrial pacing. ARS stimulates the atrium after a premature atrial beat with a cycle equal to a programmable percentage of the previous one, in order to achieve stabilization of the atrial rhythm and to avoid the "short-long-short" cycle phenomenon[19].

A prospective, randomized cross-over study[20] evaluated the impact of CAP on the number of premature atrial contractions and on the recurrences of paroxysmal atrial fibrillation in 61 patients with brady-tachy syndrome and treated with antiarrhythmic drugs. During the DDDR + CAP stimulation mode, a high percentage of atrial pacing (> 95%) was observed; moreover, in patients with a pacing percentage < 90% during the DDDR mode, a significant reduction (79%) in the number of premature atrial contractions and a decrease in the incidence of paroxysmal atrial fibrillation was observed.

Finally, new devices (AT500, Medtronic Inc., Minneapolis, MN, USA) equipped with prevention algorithms (ARS and CAP) and allowing the detection and treatment of supraventricular tachyarrhythmias with electrical therapies have become recently available. The therapeutic power and the diagnostic contribute of these devices have been evaluated in a recent work by Israel et al.[21]. In 40 patients with documented atrial tachyarrhythmias treated using the AT500 pacemaker, the arrhythmia episodes were classified into three groups according to the degree of organization of the arrhythmia as detected at the atrial electrograms. The authors observed that the majority of patients with a history of atrial fibrillation also presented with highly organized episodes of atrial tachyarrhythmias. When treated with antitachycardia pacing, the success rate was proportional to the degree of organization of the arrhythmia. These findings were successively confirmed in a larger study[22]. In 325 patients in whom the AT500 pacemaker was employed, the detection of atrial tachyarrhythmias was confirmed in 97% of cases and 53% of episodes were successfully terminated by antitachycardia pacing.

Multisite and single site non-conventional permanent atrial pacing. Slow conduction in the right atrium and retrograde activation of the left atrium cause an inhomogeneous dispersion of electrical activity with intra and interatrial asynchrony[23.] Slow conduction has been recognized as being a determinant of the onset of paroxysmal atrial fibrillation[24,25]. In these patients multisite or single site non-conventional permanent atrial pacing has been proposed in order to improve the activation sequence, to reduce the asynchrony in atrial activation, to preexcite some areas potentially involved in the reentry circuits and, finally, to reduce the dispersion of the refractory periods.

Two methods are now available for multisite atrial stimulation: the first proposed by Daubert et al.[26-29], consisting in simultaneous biatrial stimulation with leads placed, through the medium or distal coronary sinus, in the right appendage and in the left atrium. In a prospective study[28] 64% (55/86) of patients wearing a biatrial pacemaker were still in sinus rhythm after a mean follow-up of 33 months. The second method, proposed by the group of Saksena[30,31], is based on the simultaneous stimulation of the roof of the right atrium and of the ostium of the coronary sinus. The lower rate was programmed at 80-90 ppm, in order to achieve a consistent atrial capture; contemporarily, an optimal drug regimen was maintained. After 1 year, 78% and after 3 years 56% of patients were still in sinus rhythm.

Single site non-conventional permanent atrial stimulation has been recognized as being effective in preventing atrial fibrillation. Papageorgiou et al.[32] demonstrated that the area of the triangle of Koch is characterized by anisotropic conduction responsible for the onset of atrial fibrillation after atrial premature beats and that pacing at the ostium of the coronary sinus can reduce the induction of atrial fibrillation. Padeletti et al.[33] randomized 46 patients with recurrent atrial fibrillation resistant to drug therapy, to receive an atrial lead positioned in the atrial appendage (24 patients; 6.0 ± 10.1 monthly episodes of atrial fibrillation within 3 months before the study) or fixed to the interatrial septum proximal to the coronary sinus ostium (22 patients; 5.4 ± 7.1 atrial fibrillation episodes). The authors observed a significant decrease in the number of episodes of atrial fibrillation with the association of conventional pacing (with and without the CAP algorithm) and drugs which were ineffective when used alone (CAP-off 2.1 ± 4.2, $p < 0.05$; CAP-on 1.9 ± 3.8, $p < 0.05$); this benefit was more relevant in patients paced at the triangle of Koch (CAP-off 0.2 ± 0.5, $p < 0.05$; CAP-on 0.2 ± 0.5, $p < 0.05$); the atrial fibrillation burden was significantly lower in patients paced in the interatrial septum when compared with those paced in the right appendage, both in CAP-off (47 ± 84 vs 140 ± 217

min/die, $p < 0.05$) as well as in CAP-on (41 ± 72 vs 193 ± 266 min/die, $p < 0.05$). Other authors proposed stimulation of the high interatrial septum proximal to the Bachmann bundle[34] in order to obtain a symmetric activation of the two atria and thus maintain the normal activation sequence. The authors demonstrated a significant decreased conduction delay in patients with paroxysmal atrial fibrillation; nevertheless, at the moment, conclusive data on the prevention of atrial fibrillation are not available. In a recent study, Bailin et al.[35] observed an improvement in the duration of the P wave with Bachmann bundle pacing; moreover, the progression of atrial fibrillation was significantly slowed (at 1 year 75% of patients with Bachmann bundle stimulation were atrial fibrillation free, compared with only 47% of those paced in the appendage).

For optimal results, however, patients usually require a combination of pharmacological therapy and pacing. In all the trials illustrated above, antiarrhythmic medications were allowed during the study period and most of the included patients were on either class I or class III antiarrhythmic drugs. In addition, in some cases, a response to antiarrhythmic drugs, previously ineffective, was observed after atrial pacing, suggesting synergistic effects of this hybrid approach. Vice versa, antiarrhythmic drugs can enhance the effects of devices by modifying the rate and organization of tachyarrhythmias (in order to improve the effectiveness of atrial pacing therapies) or by increasing the efficacy of painless pacing therapies.

Atrial implanted defibrillator. Long-lasting atrial fibrillation may beget atrial fibrillation[36]. The atrial defibrillator was introduced in clinical practice with the purpose of quickly restoring sinus rhythm and thus avoid electrical remodeling.

After an experience with the atrial defibrillator Metrix[37-41], an implantable atrial defibrillator used in patients with symptomatic, recurrent and drug refractory atrial fibrillation, the possibility of coexisting atrial and ventricular arrhythmias suggested the use of a device for both atrial and ventricular defibrillation (dual defibrillator), mainly for patients with structural heart disease. The main feature of these devices is that they allow for the detection and treatment of ventricular and supraventricular arrhythmias. Available options include preventing stimulation algorithms (ARS, switchback delay, CAP), antitachycardia pacing (burst or ramp), high frequency pacing (burst 50 Hz) and shock. By using preventive stimulation, atrial antitachy pacing therapies and internal cardioversion according to the different phases of the disease, patients with the brady-tachy syndrome can derive benefit from these devices[42] (Fig. 1). Antiarrhythmic drugs may be used in patients wearing a dual defibrillator as well as in those with permanent atrial pacing; however, the main indication may be the need of limiting the number of low-energy shocks and the incidence of early recurrences of atrial fibrillation after successful cardioversion. In a recent experience, for the Medtronic 7250 Italian Registry, Ricci et al.[43] implanted a dual defibrillator (Jewel AF 7250, Medtronic Inc.) in 105 patients with paroxysmal atrial fibrillation and submitted to an optimal antiarrhythmic drug treatment regimen. During a follow-up of 6 ± 5 months, 863 atrial episodes were evaluated; on the basis of the f-f cycle length, 54.8% were classified as atrial fibrillation and 45.2% as atrial tachycardia. The efficacy of the atrial antitachycardia pacing therapy was: 48% globally, 70.9% for atrial tachycardia, and 24.3% for atrial fibrillation; the success rates of atrial shock were 100% for atrial tachycardia and 80% for atrial fibrillation. In particular, the atrial burst+ and ramp effica-

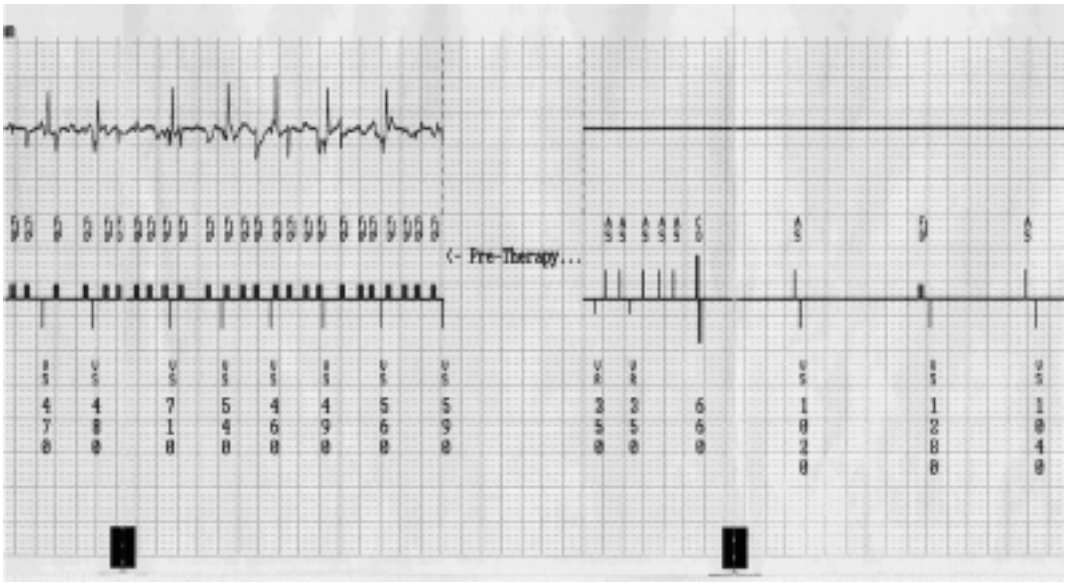

Figure 1. *Atrial shock delivered on atrial fibrillation and restoration of sinus rhythm.*

cy showed a high correlation with the f-f cycle length. If we consider that class IC drug treatment was associated with longer mean atrial cycles when compared either with no therapy or with class III drugs, it is possible to speculate that antiarrhythmic drugs may slow down and regularize the atrial fibrillation cycle, thus improving the efficacy of atrial pacing therapies.

Radiofrequency ablation and pacing or drugs

Atrioventricular nodal ablation and pacemaker implantation. The first routinely used mode of catheter ablation for the treatment of symptomatic atrial fibrillation resistant to antiarrhythmic therapy was the combination of atrioventricular nodal ablation and pacemaker implantation (ablate and pace). In patients affected by persistent or permanent atrial fibrillation with a rapid ventricular response, in whom a rate modulation with antiarrhythmic drugs is not obtainable, the persistent high rate may produce a tachycardiomyopathy that is usually reversible when sinus rhythm is restored or the ventricular rate controlled[44]. This treatment reduces symptoms and improves exercise tolerance, left ventricular function and quality of life, without eliminating atrial fibrillation or the necessity of anticoagulant therapy[45-47]. A single-chamber VVI pacemaker is sufficient in patients with permanent atrial fibrillation, while in those with paroxysmal or persistent atrial fibrillation a DDDR system with mode switching is necessary. Although several authors reported that the "ablate and pace" strategy is associated with a significantly improved quality of life and left ventricular function, the long-term follow-up of these patients continues to constitute a controversial issue. In a recent study, Ozcan et al.[48] observed, during a mean follow-up of 36 ± 26 months, the survival rate in 350 patients with atrial fibrillation and submitted to the "ablate and pace" strategy. The survival rate (78 deaths) was significantly lower than that observed in the general Minnesota population ($p < 0.001$), while it was similar to that of the control group with atrial fibrillation who received drug therapy ($p = 0.44$). On the other hand, in the absence of heart disease (121 patients), the mortality rate in the ablation group was similar to that of the general population ($p = 0.43$).

Isthmus ablation and antiarrhythmic drug therapy. Antiarrhythmic drugs have been recognized as being able to transform atrial fibrillation into atrial flutter[49]. Although the mechanism responsible for the switching of atrial fibrillation into atrial flutter is not yet clear, a growing body of evidence indicates that catheter ablation of drug-induced atrial flutter (lesions on the isthmus between the tricuspid annulus and the inferior caval vein) may provide an effective means of treatment for paroxysmal atrial fibrillation. A change of atrial fibrillation to atrial flutter has been most commonly observed in about 10% or more of patients with class IC drugs such as flecainide and propafenone and the class III drug amiodarone[50,51]. In a recent experience, Reithmann et al.[52] treated 10 patients who developed atrial flutter after amiodarone therapy for atrial fibrillation with catheter ablation of the isthmus. In comparison with two control groups respectively with isolated atrial flutter (28 patients) and with both atrial flutter and atrial fibrillation (54 patients) treated in the same way (i.e. with isthmus ablation), in a follow-up period of 8 ± 3 months, the authors observed that the recurrence of paroxysmal atrial fibrillation was similar in patients with drug-induced atrial flutter (2 patients, 20%) and in those with isolated atrial flutter (7 patients, 25%), while atrial fibrillation arose more frequently in patients presenting with both arrhythmias before isthmus ablation (41 patients, 76%). Later, Stabile et al.[53] confirmed the data previously described. Seventy-one patients with paroxysmal or chronic atrial fibrillation, in whom flecainide infusion transformed atrial fibrillation into atrial flutter, were randomly divided into three groups, according to the following treatments: oral flecainide, catheter ablation of the inferior vena cava-tricuspid annulus isthmus or isolated catheter ablation of the isthmus. During a mean follow-up of 24 ± 7.2 months, the recurrence rates of atrial flutter and atrial fibrillation were significantly lower in the group submitted to the hybrid treatment. We can conclude that, in patients in whom antiarrhythmic drugs organize the activation of atrial fibrillation into atrial flutter, isthmus ablation and consistent antiarrhythmic drug treatment can successfully prevent the recurrence of atrial fibrillation.

Linear lesions in the atrium and antiarrhythmic drug therapy. The experience with the surgical procedure called "Maze"[54] allowed an evolution towards transcatheter ablation of atrial fibrillation. The first approach consisted in linear lesions in the right and/or in the left atrium, in order to electrically compartmentalize these chambers. The aim of the lesions was to create block lines of intra-atrial conduction, in order to avoid the propagation of reentry waves. This, on the basis of the Moe hypothesis which suggests that a few reentry waves are responsible for the persistence of atrial fibrillation[55]. In all experiences, a variable number of patients remained free from atrial fibrillation; nevertheless the association with antiarrhythmic drug therapy significantly increased the success rate. Linear lesions in the right atrium represent the first approach attempted and have been demonstrated to be feasible and safe. On the contrary, lesions in the left atrium showed a high rate of side effects such as pericardial effusion, myocardial infarction and stroke.

Gaita et al.[56] submitted 16 patients with idiopathic atrial fibrillation and characterized by vagal atrial fibrillation to treatment consisting of three linear lesions of the right atrium. During a follow-up of 9 ± 6 months 4 patients remained in sinus rhythm without therapy

and other 5 patients with antiarrhythmic drugs, previously ineffective. Garg et al.[57], in a population of 12 patients with paroxysmal, persistent and permanent atrial fibrillation, electrically divided the right atrium with four linear lesions. The technique was successful in 8 patients (7 with concomitant antiarrhythmic therapy), while in 4 patients atrial fibrillation recurred. In a recent study Natale et al.[58] observed that among 18 patients with paroxysmal atrial fibrillation treated with two-four linear lesions in the right atrium, 5 remained free of atrial fibrillation without antiarrhythmic therapy, while in 4 pharmacological treatment was necessary. Recently, Calò et al.[59] reported the efficacy and the impact of a new ablative approach in the right atrium on the quality of life. Thirty-two symptomatic patients with paroxysmal (n = 17) or permanent (n = 15) refractory atrial fibrillation underwent radiofrequency ablation. A non-fluoroscopic electroanatomical mapping system was used to perform four linear lesions as follows: from the superior vena cava to the inferior vena cava, in the posterior and septal wall, a transverse lesion connecting the previous two lines, and across the tricuspid-inferior vena cava isthmus (Fig. 2). There were no complications. Post-ablation remapping showed the absence of discrete electrical activity inside and just around the ablation lines. During follow-up (14 ± 5 months) sinus rhythm was maintained in 29 patients (91%): 22 (69%) were totally asymptomatic and 7 (22%) referred a relevant reduction in symptoms. The majority of these patients continued the previously ineffective antiarrhythmic drug treatment. After ablation, the quality of life was significantly improved, reaching the levels of the general Italian population.

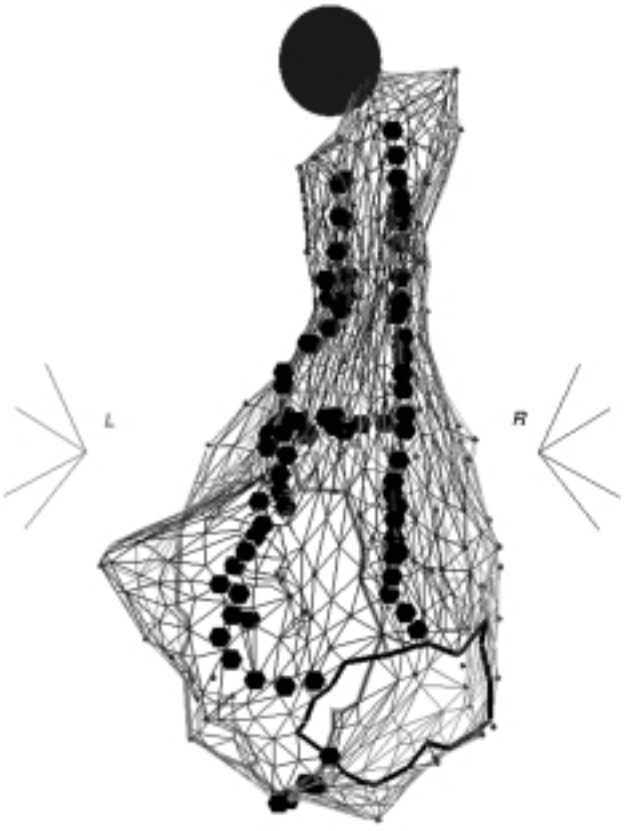

Figure 2. *Anatomical reconstruction of the right atrium (postero-anterior view), with the ablation lines superimposed. Black spheres represent the radiofrequency lesions.*

In a first experience on the ablation of atrial fibrillation by linear lesions in the left atrium[60], a very high incidence of side effects was observed. Later, Jais et al.[61], by means of a square ablation in the left atrium of 44 patients with atrial fibrillation, reported that the procedure was successful in 37 cases; 25 of them without antiarrhythmic therapy, while 12 needed drug therapy to consistently maintain sinus rhythm. Among these patients, the authors reported pericardial effusion in 5 cases and pulmonary embolism, myocardial infarction and stroke in one case each.

Ablation of the pulmonary vein ostia and antiarrhythmic drug therapy. The onset of atrial fibrillation may be due to trigger activity originating from the posterior wall of the left atrium or inside the pulmonary veins. Haissaguerre et al.[5] demonstrated that the ablation of these foci resulted in a significant decrease in the recurrence rate. In such highly selected populations, ablative treatment may be successful without the association of antiarrhythmic drugs[62]. Nevertheless, in another experience[63], the assumption of drugs after ablation was associated with a significant increase in the success rate. Using the Carto system, the circumference of the pulmonary vein ostium was ablated in 26 patients with paroxysmal or persistent atrial fibrillation. These patients were followed for 9 ± 3 months. Eighty-five percent of patients remained free from atrial fibrillation; among these, 62% did not require antiarrhythmic therapy. In a recent study, Pappone et al.[64], in a large cohort of patients with paroxysmal or permanent atrial fibrillation, observed that 85% of subjects remained free from atrial fibrillation during a follow-up period of 10.4 ± 4.5 months after treatment with circumferential pulmonary vein radiofrequency ablation. Seventy-eight percent of patients with paroxysmal atrial fibrillation were discharged without antiarrhythmic drugs whereas the others were prescribed pharmacological therapy; on the other hand, patients with permanent atrial fibrillation were all treated with drug therapy in order to improve the likelihood of modifying the atrial electrical remodeling and of maintaining sinus rhythm.

Conclusions

The first step in the treatment of atrial fibrillation consists of the termination of the arrhythmia and of the maintenance of sinus rhythm; nevertheless, within 1 year of cardioversion, about 50% of patients experience a new episode of atrial fibrillation. With regard to patients with paroxysmal or persistent atrial fibrillation,

in the majority of cases pharmacological treatment alone does not prevent the recurrence of episodes of atrial fibrillation. For this reason, the combination of non-pharmacological treatment and medical therapy may be necessary in order to implement a hybrid therapeutic strategy. At present, no data from large scale, prospective, randomized studies on the efficacy of therapeutic hybrid approaches are available. Ongoing prospective studies and observational registries have been started in order to highlight this new approach. At the moment case reports and small scale studies suggest that a hybrid approach may be an effective strategy for the treatment of atrial fibrillation.

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