Current perspectives

Non-pharmacological treatment of atrial fibrillation

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In the last decade various non-pharmacological treatments for the cure of atrial fibrillation (AF) have been proposed. These may be divided into only palliative (i.e. pacing therapy or atrioventricular node ablation) – since it does not influence the factors favoring AF persistence – or radical with the aim to eliminate the factors causing AF with the goal of preventing its recurrences. This can be achieved either by eliminating the trigger responsible for the initiation or by modifying the substrate that permits the maintenance of the arrhythmia or both.

Surgical results clearly show how, in a higher percentage of cases, it is possible to cure AF by modifying the substrate. Nowadays, this should be performed in almost every patient with permanent or paroxysmal AF who is submitted to heart surgery, while it is not yet time to extend this technique to patients with idiopathic AF.

Percutaneous catheter ablation has not yet reached optimal results. The elimination of triggers seems to be the first step in patients with idiopathic lone AF; this may be accomplished by electrically isolating the pulmonary veins and when possible by directly eliminating extrapulmonary foci if present. The results of this technique were relatively good but still need to be improved. In case of permanent AF or in the presence of atrial enlargement, the removal of the triggers alone is not enough to eliminate the arrhythmia since the substrate anomalies seem to play a more important role in its maintenance than the trigger itself.

Ablative therapy of AF is a technique that still needs further improvement before it may be considered a definite approach and it is still to be proposed only to selected patients with drug-resistant and poorly tolerated AF.

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Atrial fibrillation (AF) is the most common supraventricular arrhythmia and a large part of the population is affected by this arrhythmia either in a paroxysmal or permanent form. The incidence of AF increases with age and as the average age of the general population increases, the prevalence of this arrhythmia is also increasing[1-3]. Therefore, also considering the related symptoms and the possible frequent hospitalizations, the medical impact that this arrhythmia may have is quite clear. Despite its large prevalence both in patients with and without associated cardiac disease, therapy is still unsatisfactory; no new drugs, except for dofetilide, have been developed in recent years and all have been used for the last 20-30 years. They are not specific for atrial electrical activity and can have profound effects on ventricular electrophysiology. The promising results have not been confirmed in the long-term follow-up neither in terms of efficacy nor safety; in fact, the use of antiarrhythmic drugs may be associated with side effects that may sometimes be life-threatening such as the pro-arrhythmic effects and hepatic or pulmonary toxicity or lead to drug discontinuation.

AF has been considered a benign arrhythmia for many years; however, studies showing an increased risk for cardiovascular morbidity and mortality have been recently published[2-5]. Therefore attempts aiming to maintain sinus rhythm have been performed in recent years.

Electrophysiology

Since the beginning of the 20th century different mechanisms for the development of AF appearance have been proposed and the "focal" or single reentry circuit theories were the first to be hypothesized. In the '60s, it was postulated that AF was based on multiple reentrant wavelets occurring in a random fashion[6]. Human and animal studies subsequently supported this hypothesis and the concept of the "wavelength of reentry"

was proposed[7,8]. The wavelength is the distance traveled by the electrical impulse in one refractory period and is the product of the refractory period and the conduction velocity. Thus, the wavelength is the shortest path-length that can sustain reentry. Either the decrease in the refractory periods or the slowing down of the conduction velocity or both can reduce the wavelength thus facilitating the onset of AF. As a consequence, the number of reentrant circuits simultaneously activating the atria depends on the wavelength and on the atrial size. Subsequent mapping studies of the atria showed how the greater was the number of the reentrant wavelets the higher was the probability of autosustained AF[7].

The electrophysiological heterogeneity of the atria that is necessary to permit the appearance of the multireentrant wavelets is well demonstrated by the simultaneous coexistence of more or less organized regions during AF. A paper in 2001[9] showed how, during AF, certain regions were more often characterized by the presence of a very fast and completely disorganized atrial activity while other regions were more prone to be activated in a relatively regular fashion. Furthermore, it was clearly demonstrated how paroxysmal and permanent AF had a different pattern of atrial activation, the latter being characterized by more regions with a disorganized pattern.

Observations made over the past 5 years have challenged this predominant model of multiple circuit reentry. On one hand, optical mapping studies of AF in sheep hearts point to a primary local generator, consisting of either a single small reentry circuit or an ectopic focus[10,11]; on the other hand, AF is often initiated by very rapid ectopic foci and the elimination of these foci, localized in most cases inside or at the ostium of the pulmonary veins, prevented the reappearance of AF[12].

It is nowadays clear that both theories are still valid; it is known that the term AF does not identify only one arrhythmia but includes different kinds of arrhythmias. In fact, AF may be present in very different clinical situations so that its electrophysiological substrate and clinical meaning are different too. The ectopic foci are important as triggers for the initiation of AF while the modification of the atrial refractoriness and conduction velocities are important as a substrate for the perpetuation of the arrhythmia. Probably, the former are more important in case of paroxysmal lone AF, while the latter may play a predominant role in patients with atrial disease secondary to associated heart pathologies or with permanent AF.

The non-pharmacological therapy of AF may be divided into two groups. The first one (i.e. pacing therapy or atrioventricular-AV node ablation) is only palliative since its aim is not to eliminate the factors favoring the persistence of AF, but either just to modify them hence reducing the probability of arrhythmic recurrences or to attenuate the symptoms related to fast ventricular rates by simply blocking AV conduction without affecting the electrophysiological mechanisms responsible for AF. The second one, on the contrary, is a radical therapy aimed at the elimination of the factors causing AF with the goal of preventing its recurrences. This can be achieved either by eliminating the trigger responsible for its initiation or by modifying the substrate that permits the maintenance of the arrhythmia or both.

Palliative therapy

Pacing therapy. The role of pacing therapy in the management of AF has often been discussed; the prevention of AF was previously attempted with single site atrial pacing[13-17], originally from the high right atrium, more recently from other sites such as the interatrial septum or coronary sinus[18-20]. In the last few years multisite atrial pacing has been proposed.

Single site pacing. Bradycardia with short-long atrial sequences elicited by atrial premature beats has been considered as promoting the dispersion of refractoriness and the vulnerability to reentrant activation. It seems that atrial pacing may be useful to prevent AF that manifests after sinus pauses; however, this type of fibrillation is uncommon.

Taking a wider view of the antiarrhythmic effects of atrial pacing in the paced population as a whole, the benefits have not been at all established and most of the studies were retrospective[13,14]. In recent years the results of three randomized, prospective trials[15-17] have shown that atrial pacing (either AAI or DDD) had a slight but statistically non-significant advantage over ventricular pacing. At the end of the '90s it was reported that pacing from the atrial septum was associated with a decrease in AF recurrences[20].

These studies clearly demonstrate that patients with sick sinus syndrome benefit from atrial pacing. However, in other groups of patients atrial pacing offers no clear improvement in terms of the incidence of AF, stroke and cardiovascular mortality.

Multisite pacing. The rationale for biatrial pacing and for dual site right atrial pacing is based on the fundamental premise that intra-atrial and interatrial delays are essential to the initiation of the intra-atrial reentrant mechanisms that are responsible for the maintenance of AF. The validity of this hypothesis has been tested in acute studies with acute inducible arrhythmias[18,21], but primary verification by means of long-term prospective studies has not yet provided conclusive results except for bradycardic patients[22-24].

Similar results have been reported in studies evaluating the effectiveness of special pacing algorithms in the prevention of AF. Overdrive atrial pacing decreased the symptomatic AF burden to a greater extent than conventional atrial (or dual chamber) pacing alone in patients with sick sinus syndrome and AF. However, just as the other pacing therapy proposed, no conclusive

data have been demonstrated for other groups of patients with AF[25-27].

Therefore, it may be concluded that pacing therapy for AF prevention is nowadays indicated only in those patients who have a concomitant sick sinus syndrome.

Atrioventricular node ablation/modulation. This was the first non-pharmacological approach proposed for patients with AF in the early '80s using DC shock; the aim was to create a complete AV block and a pacemaker implant was necessary. In the subsequent decade the use of radiofrequency energy substituted the direct current used in the first cases. This different source of energy reduced the risk of procedure-related complications, and in particular the risk of sudden death reported in case of DC shock ablation was significantly decreased.

However independently of the energy used, ablation of the AV node cannot be considered a cure of AF since the arrhythmia is not eliminated. The only goal is to avoid a high ventricular rate; anticoagulation to prevent thromboembolism has to be continued and patients often become pacemaker-dependent. To avoid the latter it was proposed that smaller lesions be made on the AV node with the aim of resolving the rapid ventricular rate whilst maintaining a physiologic conduction at a slower velocity. This technique that is called AV node modulation is indeed associated both with a high incidence of recurrences and undesired complete AV block. Furthermore, the persistence of an irregular ventricular rhythm, although at lower rates, often does not eliminate the symptoms.

The reduction in the ventricular rate leads to an improvement in symptoms such as palpitations and dyspnea and it slows the progression of the disease towards frank cardiomyopathy. Some studies have reported a globally improved functional capacity and ventricular ejection fraction[28-32].

This technique is indicated for the small group of patients, generally elderly, with permanent AF and a high ventricular rate not amenable to drug therapy and generally associated with a cardiomyopathy.

Radical therapy

The aim of radical therapy is to prevent AF recurrences. This may be achieved either by surgical or catheter ablation.

Surgical ablation. The first attempts at a radical cure of AF were surgical; in all cases the aim was to modify the substrate so as to resolve the persistence of the multiple wavelets. The first procedure which proved to be effective was the Maze procedure proposed in the early '90s[33].

This technique, and the subsequent modifications, consisted in an extensive surgical dissection of both the right and left atria creating a sort of maze through which the electrical activation is forced. The aim is to prevent the formation and perpetuation of the multiple wavelets that are responsible for the maintenance of AF. This is a relatively complex technique requiring not only open-chest surgery but also a long operative time with a consequent significant lengthening of both the aortic cross-clamping and extracorporeal circulation times. The success rate was high but complications and a perioperative mortality varying from 1.3 to 2.1%[34,35] were reported. For this reason, this procedure never gained widespread acceptance.

Recently, more limited and simpler procedures were proposed. Surgical dissection has been substituted by lesions created by different sources of energy such as radiofrequency[36-41] or cryothermy[42,43] with the aim of reducing the risk of bleeding and the procedural time; most techniques are purely endocardial[36,40-43], others include a combined endocardial and epicardial approach[38,39]; in some cases a biatrial procedure[40,41] is still performed, in others it is limited to the left atrium[36-38,42,43]. All these techniques, however, have in common that the posterior part of the left atrium and the pulmonary veins are involved in the ablation.

In most surgical techniques the main objective is to create limited linear lesions in the left atrium[36,42,43] although in some cases, isolation of the pulmonary veins is the principal aim[37-40,44]. These approaches have been attempted mostly in patients with valvular heart disease and permanent or paroxysmal AF. The success rate varies from 60 to 90% depending on the type of the lesion scheme utilized and the population studied. It is noteworthy that the posterior part of the left atrium and the ostia of the pulmonary veins are involved in all cases regardless of the energy sources used (radiofrequency or cryoenergy) and the different design of the intended lesion (Fig. 1)[33,36-38,41-43,45]. These results imply that the posterior part of the left atrium is crucial in the genesis and maintenance of AF. Atrial activation during AF is not spatially homogeneous and regions with more or less disorganized activation usually coexist in the same patient[9]. The posterior left atrium represents a region with a high degree of disorganized atrial activity and seems to be critical in the maintenance of the reentrant fibrillating wavelets. Reviewing the data from the clinical studies published it is still unclear which is the predominant effect of ablation. Is the clinical success due to the modification of the substrate by linear lesions, or to the abolition of the atrial foci inside the pulmonary veins, or both?

Different techniques, more or less extensive, have been proposed. However, it is still debated which is the best one and how extensive the lesions must be[46]. A post-procedure extensive electrophysiological evaluation that would be useful to evaluate the real electrophysiological effects of the surgical lesion has never been extensively performed. Occasionally the intended surgical goal is not reached; in fact, the lesions may be

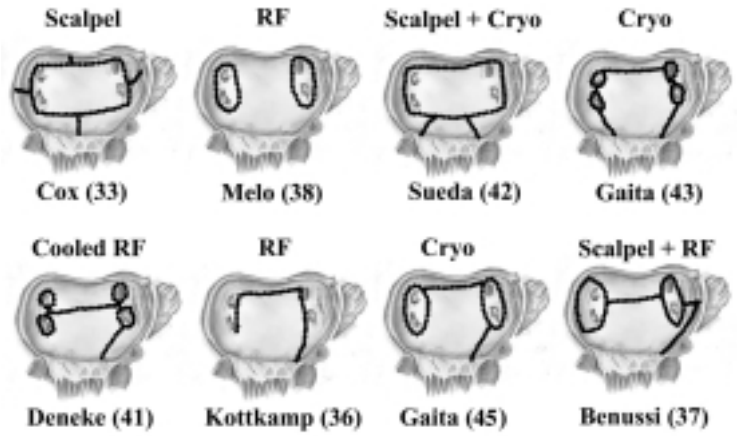

Figure 1. *Different schemes of surgical ablation proposed all involving the pulmonary veins and the posterior part of the left atrium.*

non-transmural or incomplete and consequently gaps may persist. Confirming the completeness of the lines of conduction block and/or the actual isolation of the pulmonary veins and their correlation with the clinical results may help in understanding the clinical outcome during follow-up. Similarly it might solve the issue regarding which among the proposed lesion schemes may be the most effective to eliminate AF using the simplest, fastest and least disruptive kind of lesion. We performed an extensive electrophysiological study using non-fluoroscopic electroanatomic mapping of the left atrium in patients with a history of permanent AF prior to cryoablation performed during heart surgery for valvular disease. The intended lesion was achieved by the surgeon under direct vision only in about 50% of cases, while in the other cases incomplete lesions were obtained and the presence of gaps were often responsible for left atrial flutter. However, it is noteworthy that in case of complete linear lesions including the four pulmonary veins and the mitral annulus, sinus rhythm was restored and maintained during the long-term follow-up without any antiarrhythmic drugs in more than 90% of cases[45,47].

Various reports have shown that in most cases AF is triggered by rapidly firing atrial foci mostly localized within the pulmonary veins. Catheter ablation of these foci is able to prevent AF recurrences in a percentage varying from 60 to 80% regardless of the use or otherwise of antiarrhythmic drugs. On the basis of the above, some authors resorted to ablation procedures consisting mainly in the electrical isolation of the pulmonary veins[39,40]. However, the importance of modifying the substrate is highlighted by the evaluation of the different ablative approaches. Pure electrical isolation of the pulmonary veins aimed at eliminating the triggers was compared with a linear lesion connecting the four pulmonary veins and the left inferior one to the mitral annulus ("7" lesion). Both these procedures were performed with the goal of modifying the substrate and thus prevent the maintenance of the circulating wavelets. Electrophysiological study showed that when the intended lesion was adequately achieved by the surgeon sinus rhythm, without any antiarrhythmic drugs, was restored in 92% of the patients who underwent the linear lesion in the posterior left atrium, while this was achieved only in 30% of those with total electrical isolation of the pulmonary veins[45,47]. This can be explained considering that patients in whom surgical ablation is performed generally present with permanent AF associated with other cardiac disease. In such patients, the substrate anomalies may prevail on the trigger for the onset of AF.

Surgical ablation is therefore indicated in almost all patients with paroxysmal or persistent AF who have to be submitted to heart surgery for other reasons. The patients who benefit most from this operation are those with mitral valvulopathy in whom a valvuloplasty is performed or a biologic prosthesis is implanted; in fact, in these patients, if AF is eliminated the restoration of a normal mechanical contraction of the atria in addition to the improvement in the hemodynamic performance may render chronic anticoagulant therapy unnecessary. However, even if a mechanical prosthesis is implanted the said hemodynamic effect is beneficial for the quality of life and survival independently of the need of anticoagulant therapy[48]. In case of non-valvular heart surgery considering the absent or very low additional risk, surgical ablation should be performed whenever the patient's clinical history includes AF episodes; in these cases an epicardial approach is to be preferred.

Percutaneous catheter ablation. *Linear ablation (substrate modification).* The good results obtained by the surgeons, in particular with the Maze operation, led the electrophysiologists to develop percutaneous catheter ablation mimicking the surgical atrial compartmentalization. Unfortunately, the first experiences with linear ablation in the left atrium were non-satisfactory at all; in fact, the relatively good results in terms of sinus rhythm maintenance (about 79%) reported at the NASPE congress of 1996, were counterbalanced by a rate of severe complications reaching 15%, too high to propose this technique even in experimental studies.

Similar studies performed in small groups of patients by other authors showed a lower success rate varying from 0 to 58%[49-51] although they were also associated with a lower incidence of complications.

In the meantime, animal studies showed that in some cases a more limited ablation scheme, sometimes limited only to the left or the right atrium, with the objective of eliminating the substrate critical for the maintenance of the arrhythmia may also be effective, thus avoiding the complexity of a thorough compartmentalization[52-54].

On the basis of this study, different groups performed an ablation limited to the right atrium in selected patients (Fig. 2)[49,51,55-58]. In 1995 the first attempt to correlate the effectiveness of the ablation with the electrophysiological pattern of endocardial activation during AF was performed[55]. Two or three lines of ablation were made in the right atrium in patients with lone "vagal" paroxysmal or persistent AF. At 1 year of follow-up 56% of the patients were in sinus rhythm, although only 25% did not require antiarrhythmic drugs. However, the success rate decreased to 40 and 11% respectively when the persistence of sinus rhythm was evaluated at 3 years of follow-up.

Two interesting findings were observed in this study. First 79% of the patients who underwent AF ablation also showed several atrial extrasystoles with the "P on T" phenomenon at the onset of the AF episodes, a pattern later described as typical for AF originating in the pulmonary veins.

The second observation derived from the analysis of atrial mapping during AF. The probability of success of the ablation was higher when it was performed in regions with disorganized atrial activity than when radiofrequency energy was delivered in areas of organized atrial activation or in case of a completely and uniformly disorganized AF in most of the atria[55]. Similar observations were then reported by others[56]. These findings supported the hypothesis that although the atria as a whole participate in the process of AF, not all the parts of the atria contribute equally to the perpetuation of the fibrillatory process. This suggests that selective ablation of the areas characterized by abnormal conduction patterns and which are critical for the perpetuation of AF, may be effective.

However, in most cases the substrate underlying AF perpetuation is not confined to the right atrium. Rather, the left atrium is mainly involved. The main finding that emerged from these studies[49,51,55-57] was the fact that linear ablation in the right atrium is effective only in a small percentage of patients with lone AF and furthermore most of them still need antiarrhythmic drugs.

In all the studies a fundamental issue was the difficulty encountered in creating continuous transmural lesions. Different parameters have been used to assess these results. These include the reduction in the amplitude of the atrial electrogram by at least 75% compared with that prior to ablation and the appearance of double potentials. Other groups used electroanatomical mapping with non-fluoroscopic techniques.

Focal ablation (trigger elimination). Considering the difficulty in creating linear lesions with the technology available in the '90s and the unsatisfactory results in terms of efficacy and safety, different techniques have been studied. An important breakthrough was the observation made in 1998[12] that in most cases of paroxysmal AF, the arrhythmia is triggered by atrial foci firing very rapidly with a consequent disorganization of the activity in the atria; a second observation was that these arrhythmogenic foci were mostly localized in the pulmonary veins[12]. The arrhythmogenic nature of these fo-

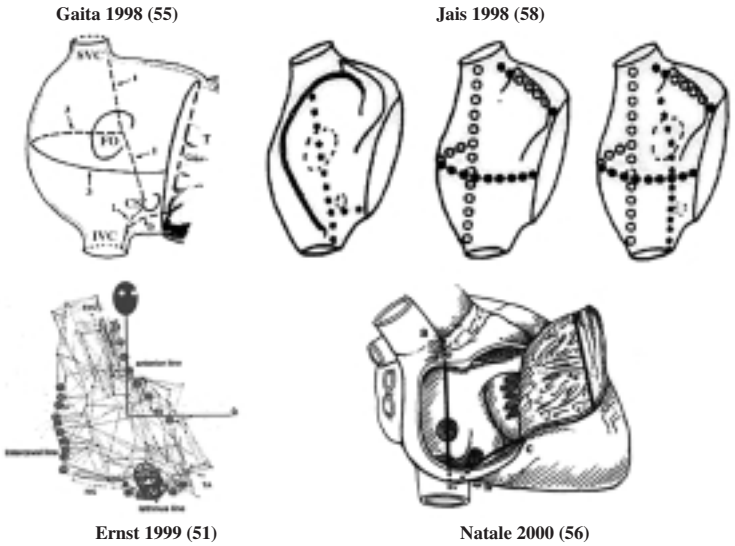

Figure 2. *Different schemes of linear lesions in the right atrium. CS = coronary sinus; FO = fossa ovalis; IVC = inferior vena cava; SVC = superior vena cava; T = tricuspid valve.*

ci may be explained by the presence of sleeves of myocardial tissue present in the first centimeters of the pulmonary veins and by the common embryogenetic origin of this tissue with the conduction system[59]. Haissaguerre et al.[12] were the first to suggest mapping of the inside of the pulmonary veins in order to search for these foci and ablate them. In their experience they observed that these ectopic foci were characterized on the electrocardiogram by early atrial extrasystoles inscribing on or before the apex of the T wave; this phenomenon was therefore called "P on T" extrasystoles. Ectopic foci triggering the onset of AF were localized between 2 to 4 cm inside the pulmonary veins in 94% of cases. Ablation of these foci was effective in preventing AF recurrence in 64% of patients at a follow-up of 9 months; however, numerous procedures were generally necessary. Subsequently, similar results were reported by other authors[60,61].

Several limitations of this technique were evident since the first studies, particularly the complications, the necessity of repeat procedures and the unpredictability of the ectopic foci. The technique consisted in mapping of the ectopic foci inducing AF. Therefore, these must be activated during the electrophysiological study either spontaneously or with pharmacological maneuvers. We have found that in about 40% of cases the ectopic foci were not activated during the electrophysiological procedure; thus, they could not be identified and eliminated[60]. Furthermore, the ablation of one focus does not exclude the possible presence of other foci which also could be responsible for the initiation of AF in other sites. This explains the high incidence of AF recurrences.

With regard to complications, cerebrovascular (< 2%) events and pericardial effusion or cardiac tamponade (< 2%) were reported together with pulmonary stenosis[12,61].

In view of these limitations a different interventional philosophy was proposed. Total electrical isolation of all the four pulmonary veins was proposed independently of the activation or otherwise of the ectopic foci; in order to avoid or at least reduce the risk of stenosis, the energy was delivered at the ostia of the veins and not inside them.

Different techniques, all with the same aim, were proposed. The first[62] was based on the anatomic knowledge that the myocardial sleeves going inside the veins do not necessarily extend throughout the ostial circumference but may be present only in a few segments of it thus allowing electrical conduction between the atria and the pulmonary veins in sinus rhythm and vice versa during activation of the ectopic foci within the vein[63]. The isolation is achieved by ablating only in the sites where the myocardial fibers are present thus reducing the amount of radiofrequency delivery and consequently the risk of complications.

Starting from this experience a second purely anatomical technique was proposed. This consisted in circumferential ablation just inside or around the ostia, without any attempt to localize the sectors in which a connection between the atrium and the vein is present. The procedure is performed using either ultrasound[64] or non-fluoroscopic electroanatomical mapping[65]. Despite the different techniques used and the increase in experience the success rate is still not completely satisfactory. The high incidence of AF recurrences, requiring numerous ablation procedures, may depend on several factors such as the possible reappearance of pulmonary vein potentials or the presence of foci localized outside the pulmonary veins, generally in the posterior left atrium or inside other venous structures such as the coronary sinus or superior vena cava.

Furthermore, different results in terms of the success rate for paroxysmal and permanent AF have been reported; a randomized study[66] showed a success rate for patients with persistent AF of only 22% compared to 70% for paroxysmal AF at 5 months of follow-up.

The lower efficacy of this ablation procedure in patients with persistent or permanent AF further strengthens the hypothesis of a different electrophysiological substrate present in the various forms of AF. Certainly, the presence of a trigger is the main factor leading to the appearance of AF in patients with paroxysmal AF. Thus, a technique able to eliminate them may be effective to cure these patients. On the contrary, we can speculate that the persistence of AF over long periods may lead to modifications of the atrial myocardium and consequently of the substrate. It is conceivable that in these latter cases substrate modifications play the major role in the maintenance of AF. Therefore, the elimination of the pulmonary vein foci is not effective in preventing AF recurrences that may be due to other non-early atrial extrasystoles.

Our ablative strategies are performed in a stepwise fashion. First of all the patient is submitted to cardiac magnetic resonance (Fig. 3) in order to obtain informa-

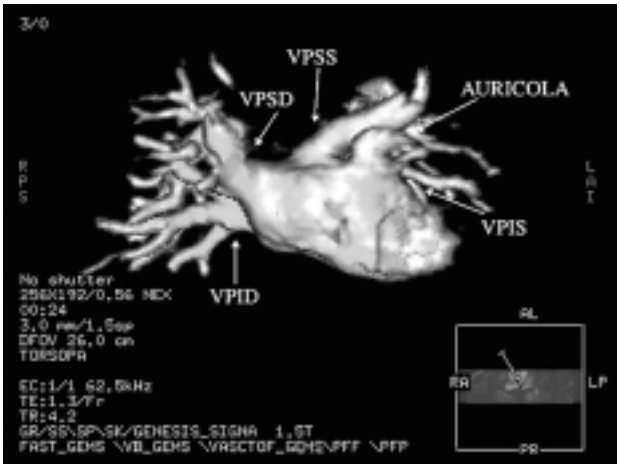

Figure 3. *Three-dimensional reconstruction of the left atrium and pulmonary veins. VPID = right inferior pulmonary vein; VPIS = left inferior pulmonary vein; VPSD = right superior pulmonary vein; VPSS = left superior pulmonary vein.*

tion on the anatomy of the atria and of the pulmonary veins, in particular on the dimensions of the ostia and the presence or otherwise of additional veins. Then the first ablative procedure consists in the electrical isolation of the four pulmonary veins using a combined approach (electrogram guided with a multipolar catheter and electroanatomical with the Carto system). The Carto system allows a good anatomical reconstruction of the pulmonary vein ostia and the identification of possible accessory veins. Besides, it facilitates repositioning of the catheter in different sites. The multipolar catheter positioned at the ostia permits the localization of the myocardial sleeves connecting the left atrium with the vein. Then the ablation was performed selectively in the critical site, when possible, guided by the vein potentials (Fig. 4).

In case of AF recurrences a second procedure is performed with two objectives; first, to eliminate the non-pulmonary vein foci (if they appear during the procedure) or the pulmonary vein potentials if these recurred; second, to perform linear lesions in the left atrium in order to modify the substrate. These are generally designed in order to anatomically close defined isthmuses such as the ones between the left inferior pulmonary vein and the mitral annulus[1,2,9,10] (Fig. 5) or between the left superior pulmonary vein and the left appendage. The lesion scheme that we generally perform is based on our surgical experience; the "7" lesion which consists in an ablation line connecting the right with the left pulmonary vein and the left inferior pulmonary vein with the mitral annulus together with pulmonary vein isolation is the scheme that we generally perform considering the good results in AF prevention in patients submitted to surgical ablation. The aims of this procedure include both the elimination of the triggers and the modification of the substrate. Nowadays, the different technology and, in particular, the irrigated (or

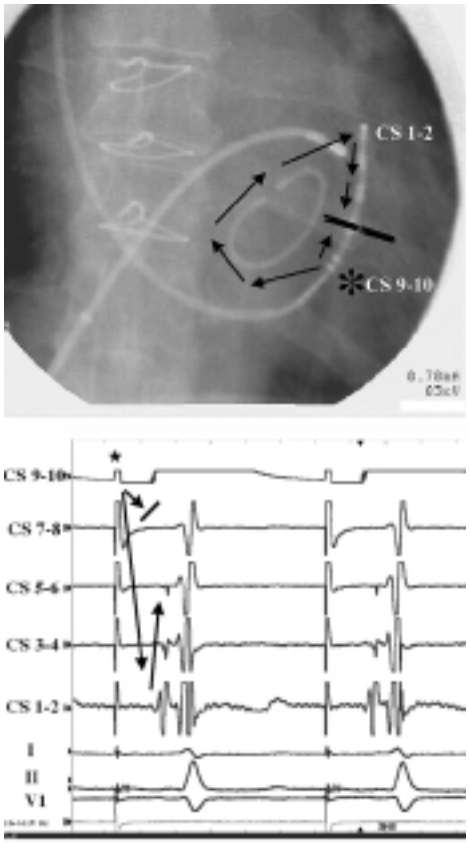

Figure 5. *Conduction block through the mitral annulus and the left inferior pulmonary vein isthmus after surgical ablation.* Upper panel: *fluoroscopic view in the left anterior oblique projection. A decapolar catheter is positioned in the coronary sinus from the right jugular vein. A second catheter is positioned in the left atrium through a transseptal approach. The* arrows *indicate the direction of electrical activation around the mitral annulus. The* black lines *represent the site of conduction block.* Lower panel: *endocardial recordings during pacing from the proximal electrode bipole of the coronary sinus catheter. The* arrows *show that the activation in the distal bipole of the coronary sinus catheter occurs earlier than the more proximal bipoles which are anatomically closer to the pacing site (*). CS 1-2, CS 9-10 = recordings from the proximal (9-10) to the distal (1-2) coronary sinus catheter. I, II, V_1 = ECG leads.*

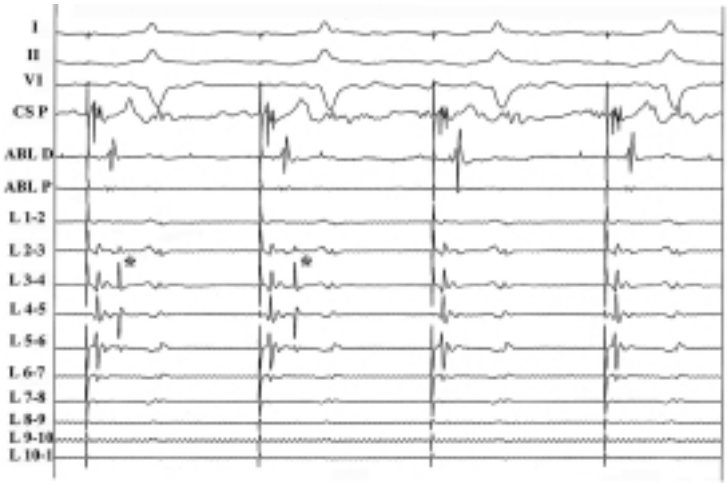

Figure 4. *Left inferior pulmonary vein ablation. Radiofrequency is applied at the ostium of the left inferior pulmonary vein during pacing from the coronary sinus. The pulmonary vein potential (*) disappears suddenly (third beat) during radiofrequency delivery. ABL = recordings from the distal (D) and proximal (P) ablation catheters; CSP = proximal coronary sinus. I, II, V_1 = ECG leads; L 1 → L 10 = recordings from the Lasso catheter positioned at the left inferior pulmonary vein ostium level.*

cooled) tip catheter has facilitated the achievement of linear lesions. However, it should be borne in mind that in some regions it is still not easy to obtain continuous linear lesions. This is due to the thickness of the tissue and the presence of conduction gaps which are often responsible for atypical left atrial flutter.

Since the modification of the technique, pulmonary vein stenosis no longer seems to be a threatening complication; on the contrary, the risk of thromboembolism or, on the other hand, of bleeding (particularly hemopericardium) due to anticoagulant therapy, has not yet been eliminated. The persistence of these risks and the difficulty in performing continuous linear lesions prevent percutaneous catheter ablation of AF from being considered as first-line therapy as it is for other arrhythmias. Catheter ablation can be proposed for those patients with poorly tolerated AF, especially if young, if the persistence of AF determines the so-called tachycardia-induced cardiomyopathy or if complications related to the arrhythmia, such as thromboembolism, have occurred. However, at present, in all cases drug therapy should always be tested before ablation and the procedure should be limited to those who do not respond to antiarrhythmic agents, even if recent non-prospective studies have suggested percutaneous catheter ablation as an alternative choice to drug therapy.

Conclusions

AF therapy is still a challenge for cardiologists; it is a benign arrhythmia especially when present in a "normal" heart, but on the other hand, it may significantly worsen the quality of life of the patients affected and it may, although rarely, cause severe complications (such as thromboembolism or hemodynamic impairment) and side effects due to drugs. This is the reason why in the last decade various ablative therapies have been developed. In contrast to what has happened for most of the other arrhythmias, to date, none has been proven to be effective and safe enough as to be proposed as first-line therapy.

The results of surgery clearly show that it is possible to cure AF in a high percentage of cases by modifying the substrate. In view of the good results, nowadays surgical ablation should certainly be performed as a routine procedure in almost all cases in which a patient with permanent or paroxysmal AF is submitted to heart surgery. On the other hand, it is not yet time to extend this technique to patients with idiopathic AF.

The available technologies do not permit one to reproduce the surgical scheme at percutaneous catheter ablation. However, the demonstration of the role played by triggers together with the substrate in the initiation and perpetuation of AF and their preponderance inside the pulmonary veins allowed the development of different strategies to cure AF.

The elimination of triggers seems to be the first step in patients with idiopathic lone AF; this may be accomplished by means of electrical isolation of the pulmonary veins and, when possible, by direct elimination of extrapulmonary foci if present. The results of this technique are relatively good but they still need to be improved in terms of safety, feasibility and efficacy. In case of permanent AF or in the presence of atrial enlargement, the elimination of the triggers alone is not enough to resolve AF since the substrate anomalies seem to play a more important role in the maintenance of the arrhythmia than the trigger itself. In these patients it is necessary to create more complex lesions in the atria; however as demonstrated by the unsatisfactory results, the difficulty in creating continuous transmural lesions in the left atrium presently constitutes a significant limitation.

Therefore, in contrast to other arrhythmias, percutaneous catheter ablation of AF is still a newborn technique that needs further improvement before it may be considered as a definite therapy. To date it is still to be proposed only to selected patients with drug-resistant and poorly tolerated AF.

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