Very long-term results of surgical and transcatheter ablation of long-standing persistent atrial fibrillation.

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Hybrid approach for AF ablation

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Abstract

Background

New hybrid approaches for atrial fibrillation (AF) ablation, combining surgical and percutaneous procedures, are emerging to enhance the long term success rate of these two procedures severally considered. Recent guidelines underline the need for long-term follow-up to really assess the efficacy of AF ablation.

Methods

From 2000 to 2002, 33 patients with long-standing persistent AF and valvular heart disease underwent valve surgery and cryoablation (pulmonary veins isolation and mitral isthmus and roof line lesions). The surgically created ablation scheme was validated with electroanatomic mapping and percutaneous radiofrequency ablation was performed in case of lesion incompleteness.

Results

In 19/33 patients (58%) the electroanatomic mapping showed a complete lesion scheme, which increased to 79% (26/33) with the addition of radiofrequency ablation.

At the mean follow-up of 10.7±3.1 years, 73% (24/33) of patients were in sinus rhythm (SR), whereas 27% had permanent AF. At the end of follow-up 81% of patients with a complete lesion scheme were in SR, while 43% with an incomplete one maintained SR (p=0.048).

Conclusions

In patients with long-standing persistent AF and valvular heart disease, the hybrid approach with surgical cryoablation consisting of pulmonary veins isolation and left atrial linear lesions combined with transcatheter radiofrequency ablation showed to be highly effective in maintaining SR in a very long-term follow-up. An electrophysiological evaluation, to validate the transmurality of the surgical lesions and to complete the lesion scheme applying radiofrequency energy, allowed to improve the long-term efficacy.

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Introduction

Atrial fibrillation (AF) ablation has become a major therapeutic technique over the past few years. In paroxysmal AF, triggers from the pulmonary veins (PVs) play an important role in the initiation of AF (1). On the other side, in non-paroxysmal AF, atrial substrate modification is thought to be more involved (2). This is especially true for patients with valvular heart disease, in which a dilated and remodeled atrium is present. In fact previous studies have shown that mechanisms as the elongation and stretch of the atrial fibers and the presence of atrial fibrosis are crucial in the initiation and maintenance of AF in such a patients (3). Therefore, procedures aiming to isolate the PVs and to modify the atrial substrate with the creation of linear lesions have been proposed (4-9).

Surgical AF ablation evolved from the original Cox-Maze (9) strategy toward a minimally invasive procedure with good results (10-11). Percutaneous transcatheter ablation, trying to mimic the surgical ablation scheme, have also proven to be effective in maintaining sinus rhythm (SR) (4-8,12-13). However, up to now most of the published studies on AF ablation have limited follow-up (14-21) and the need for long term follow-up to assess the real efficacy of AF ablation has been underlined in the recently published guidelines (22-23). In addition, long-term outcomes vary depending on the ablation strategy, since the use of different ablation schemes and different technology over the years have made the assessment of the AF ablation outcomes difficult to compare. New hybrid approaches, combining surgical and percutaneous ablation, are emerging to enhance the success rates of these two procedures severally considered (24-27). In fact, surgical ablation does not necessarily ensure the completeness and transmurality of the lesions created (28). The evaluation of the transmurality of the surgically created lesions with an electrophysiologic (EP) study and the detection of conduction gaps allow a correct and meaningful evaluation of AF recurrences during the follow-up. Moreover, the capability of adding an endocardial touch-up ablation to eliminate the conduction gaps should improve the long-term efficacy of the AF ablation procedure.

The aim of our study was to evaluate, in patients with long-standing persistent AF and valvular heart disease, the very long-term follow-up efficacy of an ablation strategy consisting of surgical PVs isolation and left atrial linear lesions (mitral isthmus and roof lines) validated by electroanatomic

mapping associated with endocardial radiofrequency (RF) ablation in case of incompleteness of the surgical lesions.

Methods

From 2000 to 2002, 33 patients with long-standing persistent AF suffering from mitral, aortic or tricuspid valve disease underwent valve surgery and concomitant cryoablation procedure consisting of PVs isolation and creation of left atrial linear lesions (mitral isthmus and roof lines). After the 3 month blanking period, the surgically created lesions were validated with a transcatheter EP evaluation using an electroanatomic mapping system (CARTO, Biosense Webster). In case of the incompleteness of the surgical lesions, an endocardial completion attempt with RF energy was performed. Success was considered if the patient maintained stable SR or only brief episodes of paroxysmal atrial tachyarrhythmias with spontaneous restoration of SR occurred during the follow-up. Even patients with paroxysmal episodes of atrial tachyarrhythmias requiring a direct current cardioversion to restore SR were considered successful unless frequent early recurrences of AF occurred after the cardioversion and the physician decided to stop any further attempt. In addition, in case of persistent or permanent AF during the follow-up the procedure was considered unsuccessful.

Surgical procedure details have been already described in a previous paper (28).

Every patient was discharged home on oral anticoagulation therapy and on antiarrhythmic drugs with oral amiodarone (maintenance dose after the oral loading dose) or propafenone if amiodarone contraindicated for dysthyroidism (either spontaneous or amiodarone induced).

EP evaluation

Three months after the surgical operation, every patient underwent an EP evaluation.

A nonfluoroscopic electroanatomic mapping (EAM) system was used to reconstruct the left atrium and to evaluate the PVs isolation, the lines of conduction block surgically created and the atrial activation sequence in case of organized atrial arrhythmias. In case of AF recurrence at the time of EP evaluation, direct current cardioversion was performed to restore SR. In case of organized atrial arrhythmias (left atrial flutter) the electroanatomic reconstruction was carried out during the arrhythmia. If conduction gaps were detected with the EAM, electrical isolation of the PVs or linear

lesions were completed, when possible, applying RF energy (NAVI-star Biosense Webster). Patients with AF recurrences before the EP study were treated with antiarrhythmic drugs (AAD) for at least 3 months after the EP evaluation and all the patients continued oral anticoagulation.

Follow-up with clinical examinations, ECG, Holter ECG monitoring and telephone interviews were performed at 3, 6, 12 months and every year afterwards. In case of symptom recurrences between follow-up visits, patients were examined with office visit and ECG.

For patients who died during the follow-up, SR or AF recurrences were considered until the time of death.

Results

Study population

Thirty-three patients underwent valve surgery and concomitant PVs isolation combined with left atrial linear lesion cryoablation for long-standing persistent AF.

At the time of surgery, the mean age of the population was 58 ± 13 years and the mean duration of AF was 29 ± 31 months (median 15 months, range 7-108 months). Baseline detailed clinical and echocardiographic characteristics are reported in Table 1.

At the time of the EP evaluation, 15 patients maintained stable SR after the surgical ablation, whereas in 18 patients an atrial arrhythmia recurred: AF in 13 patients and atypical atrial flutter in 5.

The EAM showed a complete lesion scheme in 58% of the patients (19/33). In the other 14 patients (42%) the surgically intended lesions were not achieved. Conduction gaps were found in the mitral isthmus in 11 patients (79%), in the roof line in 3 patients (21%), while in 3 patients at least 1 PV ostia was not isolated (21%). Conduction gaps were eliminated by successful RF energy application in 7 out of 14 patients (50%). In the remaining 50% mitral isthmus block was not obtained. Therefore, after the EP study, a complete lesion scheme was present in 79% of patients (26/33).

Follow-up

The mean follow-up time was 10.7 ± 3.1 years. During the follow-up 7 patients died: 4 patients for cancer about 8 years after the index procedure, 2 for an ischemic stroke (1 pt in SR, the other one in

permanent AF, both on therapeutic oral anticoagulant) and 1 for mesenteric ischemic necrosis occurred in the post operative period of a subsequent CABG operation.

At the end of follow-up or at the time of death, 73% (24/33) patients were in SR, whereas 27% (9/33) were in permanent AF. The freedom from AF survival curve is shown in Figure 1.

The 9 patients with permanent AF at the end of follow-up suffered from early and frequent AF relapses despite AAD; after a median elapsed time of 2 years the AF became permanent and rate control strategy was chosen.

Considering patients in SR, 42% (10/24) no longer suffered from atrial arrhythmias after the EP study (9/10 off AAD, 1/10 on amiodarone), whereas 58% (14/24) experienced paroxysmal atrial arrhythmia recurrences (12 AF and 2 atypical atrial flutter): in 7 of them SR restored spontaneously, while in the other 7 at least one direct current cardioversion was required. In particular 5 patients had 1 cardioversion, in 1 case 2 cardioversions were necessary, while 3 cardioversions were performed in a patients who underwent a second surgical operation. Seven out of 14 recurrences occurred in patients off AAD. In the remaining 7 patients, amiodarone was used in 4 patients, propafenone in 2 of them and sotalol in 1 case.

Four patients belonging to the SR group underwent a second ablation procedure in the left atrium, 2 of them for recurrent paroxysmal AF episodes and the other 2 for atypical atrial flutter. In both patients with atypical atrial flutter the EAM revealed a perimitral reentry due to conduction gaps along the mitral isthmus. Application of RF energy in that area eliminated the tachycardia. Both patients remained in stable SR without AAD during the follow-up. The other 2 patients suffered from AF recurrences. In one case the EP evaluation revealed several conduction gaps in the lines surgically created and a complete lesion scheme was obtained applying RF to eliminate the gaps. The latter patient underwent a second operation for a severe mitral valve re-stenosis. During the surgical procedure, a box shape lesion surrounding the left PVs and a line along the mitral isthmus was created. Despite this procedure, the patient still experienced paroxysmal AF on AAD.

One patient belonging to the permanent AF group underwent a second transcatheter ablation procedure during the follow-up for frequent AF recurrences but even the second procedure was ineffective to maintain SR.

Considering the patients who completed the follow-up, 2 suffered from an ischemic stroke. Both patients had AF and were on therapeutic oral anticoagulation. Two patients had a major bleeding while on oral anticoagulation (1 intracranial and 1 gastrointestinal hemorrhage); three patients underwent a second valve surgery; five patients underwent pace-maker implantation.

Correlation with EAM

At the end of the EP evaluation, 79% (26/33) of patients showed a complete lesion scheme obtained with surgical cryoablation alone or with transcatheter RF energy completion.

Among these patients, 81% (21/26) were in SR at the end of follow-up, 76% (16/21) off AAD and 24% (5/21) on AAD, whereas 19% (5/26) were in permanent AF.

Among the 10 patients who never experienced an arrhythmia recurrence, 9 patients showed a complete lesion scheme; in the latter patient a conduction gap still remained after the percutaneous RF ablation. He remained in SR with AAD during the follow-up.

On the other side, in patients in which a complete linear lesion scheme was not obtained, 43% (3/7) were in SR during follow-up, all of them on AAD; 57% (4/7) of patients were in permanent AF despite previous rhythm control attempt with AAD.

A statistically significant difference in the freedom from AF survival curves was noted between patients in which a complete linear lesion scheme was obtained and patients in which conduction gaps still remained after the EP evaluation and RF ablation ($p = 0,048$) (Figure 2).

Discussion

Major findings of the present study are as follows:

- The hybrid approach combining surgical ablation procedure, consisting of PVs isolation and the creation of left atrial linear lesions (mitral isthmus and roof lines), associated with endocardial RF transcatheter ablation when necessary, allowed to obtain a significant clinical improvement in a large percentage of patients with long-standing persistent AF and valvular heart disease during a long-term follow-up (> 10 years).
- With the hybrid approach, PVs isolation and transmural left atrial linear lesions were obtained in a high percentage of patients. When achieved and electrophysiologically demonstrated, the

complete ablation scheme was effective in more than 80% of patients in maintaining SR in a very long-term follow-up.

For two decades, the cut-and-sew Cox-Maze III procedure has been the gold standard for the surgical treatment of atrial fibrillation and proved to be effective at eliminating this arrhythmia (9). In recent years the development of ablation technologies has dramatically changed the field of AF surgical ablation. For example, the introduction of new energy sources (29), allowing the replacement of the surgical incisions with the linear ablation lines, has transformed a technically complex procedure into one accessible to the majority of surgeons. The principal shortcoming of the use of these different energy sources is that they do not always create transmural lesions. In this context, electrophysiological validation may permit a correct and meaningful evaluation of the real effects of the surgical ablation procedure and allows to perform, at the same time, a transcatheter ablation completion when necessary (28).

In patients with long-standing persistent AF and valvular disease, characterized by dilated and remodeled atria, ablation results have been at least disappointing compared to transcatheter ablation results in paroxysmal AF where the maintaining of SR seemed more favorable. Moreover, the lack of long-term follow-up data makes difficult to assess the real AF ablation effectiveness (14-21, 30-31). Based on the above considerations, we considered a more than 10 year evaluation of a group of patients with long-standing persistent AF and valvular heart disease who underwent surgical PVs isolation together with left atrial linear lesions ablation and subsequent validation with an EAM study. In case of the detection of incomplete surgical lesions at the EP study, endocardial RF ablation was performed to eliminate the conduction gaps. To our knowledge, this represents the longest follow-up reported in the literature of AF ablation.

At the end of the EP evaluation 79% of patients showed a complete lesion scheme. In a small percentage of patients the transmurality of the lesions was not achieved, mostly for the presence of conduction gaps along the mitral isthmus. This fact can be explained by the following reasons: first, transmurality is technically difficult to achieve in the left mitral isthmus since it is a thick area (32-33); secondly, cryoenergy was utilized for surgical ablation. The cryoablation system used nitrous oxide as refrigerant gas which can reach a temperature of -60°C, creating a lesion depth of no more than 4-5

mm (34). To achieve a higher percentage of complete and transmural lesions a different energy source (RF, microwave, laser) or even cryoenergy with argon-based cooling system, capable to reach temperatures down to -160°C (35), could hypothetically decrease the percentage of conduction gaps. In addition, in our study, both surgical and transcatheter ablation used an endocardial approach, making more difficult to obtain the transmurality.

However, when the EP evaluation demonstrated the completeness of the lesions created (with surgical cryoablation alone or with transcatheter RF energy touch-up), the success rate was 81%. This result suggests that probably in the 20% of cases different left atrial or even right atrial areas not included in our ablation scheme are important in the initiation and maintenance of AF (36-37). In the protocol of our study right atrial isthmus lesions were not considered during surgery because they could have been easily done percutaneously in case of the occurrence of right sided atrial flutter. Fortuitously, all the arrhythmia recurrences other than AF during the follow-up were atypical left atrial flutter.

Comparing the clinical results of patients in which a complete linear lesion scheme was obtained to patients in which the conduction gaps still persisted, a statistically significant difference in the freedom from permanent AF survival curves was noted: a complete linear lesion scheme, either surgically created or completed by RF energy, correlates positively with the procedural success at 10-year follow-up.

Among patients in which a complete linear lesion scheme was not achieved, 43% were in SR with AAD at the end of follow-up. It appears that also the combination of AAD and incomplete ablation can be quite effective in maintaining SR.

Another important issue regards the thromboembolic complications of AF. Literature reports a stroke annual incidence rate in surgically treated valvular patients varying from 0.8% to 3% (38). This thromboembolic risk is higher if AF is present (39). In our population 4 patients experienced a stroke during the follow-up, giving an annual incidence rate of 1.1%. The thromboembolic events occurred despite therapeutic oral anticoagulation and 2 of them were fatal. At the time of the cerebral ischemic event 3 patients were in AF and only 1 in SR. The maintenance of SR seems to be a protective factor against stroke, even in a population with surgical valvular heart disease in which the risk for thromboembolic events is inherently increased.

Study limitations

The favorable outcome of the hybrid approach for long-standing persistent AF in patients with valvular heart disease in our population should be viewed also in light of the limitations of the study.

In fact the study assessed retrospectively a small size population. For this reason, no clinical predictors of success other than the completeness of the lesion set after the EP study were found.

In addition our patients were heterogeneous regarding the valvular disease (i.e. mitral, aortic and tricuspid heart disease) and the use of AAD during the follow-up was not standardized.

Conclusions

In patients with long-standing persistent AF and valvular heart disease, the hybrid approach with surgical cryoablation consisting of PVs isolation and left atrial linear lesions combined with transcatheter RF ablation, when necessary, showed to be highly effective in maintaining SR or significantly reducing the AF burden in a very long-term follow-up. An electrophysiological evaluation, to validate the transmurality of the surgically created lesions and to complete the lesion scheme applying RF energy improved the long-term efficacy of the ablation procedure.

Disclosures: none

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Table 1

Patients characteristics

Sex male/female	15 / 18
Mean age at the time of surgery (years)	58 ± 13
Mean AF duration (months)	29 ± 31
Mean left atrium antero-posterior diameter (mm)	51 ± 6
Mean left atrium major axis (mm)	66 ± 7
Mean left atrium minor axis (mm)	56 ± 7
Mean left ventricular ejection fraction (%)	53 ± 11
Mitral stenosis	14
Mitral regurgitation	23
Aortic stenosis	3
Aortic regurgitation	3
Tricupid regurgitation	3
Mitral valve repair	14
Mitral valve mechanical prosthesis	15
Mitral valve biological prosthesis	1
Aortic valve mechanical prosthesis	5
Tricuspid valve repair	3
CABG	2

Figure Legends

Figure 1

Kaplan Meier freedom from permanent AF survival curve at 10-year follow-up.

Figure 2

Comparison of freedom from permanent AF between patients with a complete and an incomplete ablation lesion scheme after the EP study. Kaplan Meier freedom from permanent AF survival curves at 10-year follow-up (p=0.048).

List of abbreviations

AF: atrial fibrillation

PVs: pulmonary veins

SR: sinus rhythm

EP: electrophysiological

RF: radiofrequency

EAM: electroanatomic mapping system

AAD: antiarrhythmic drugs

CABG: coronary artery bypass graft