

# Atrial flutter / atrial fibrillation : long term follow-up of cryoablation with new pathophysiologic insights

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## Summary

Ablation of the cavotricuspid isthmus (CTI) is the treatment of choice in patients with common type atrial flutter (AFL). However, most data regarding long term outcome not only have a relatively short follow-up but are also restricted to radiofrequency ablation.

In **Chapter II** we present the long term follow-up of 180 patients with common type AFL submitted to CTI cryoablation. Our population had the following characteristics: mean age 58 y (from 18 to 86), 39 women (22%), no structural heart disease in 86 patients (48%), mean LA diameter  $44 \pm 7$  mm and mean LVEF  $57 \pm 7$  %. We achieved acute success in 171 (95%) of the patients. There were no complications.

Follow-up ranged from 12 to 60 months (mean of  $27 \pm 17$  months). The chronic success rate was 91%. A prior history of atrial fibrillation (AF) was present in 123 patients (68%). Of these, 85 patients (69%) remained having episodes of AF on long term follow-up. Sixty nine patients (81%) were treated with antiarrhythmic drugs, pulmonary vein isolation was performed in 14 patients (16%), and AV nodal ablation with pacemaker implantation in 2 patients (3%). Among the 57 patients without a history of AF prior to CTI ablation, new AF developed in 20 (35%) patients (all asymptomatic on AAD).

Our data show that cryoablation of the CTI in patients with common type AFL has a 91% chronic (range 12 to 60 months) success rate. Also we corroborated the frequent association of AF (69%) with AFL, the former being the main cause of burden in this group of patients.

In **Chapter III** we evaluated the long term data of patients with  $4\pm 1$  years of Paroxysmal AF submitted to segmental pulmonary vein (PV) cryoisolation. Patients with PAF were prospectively recruited from July 2001 to July 2005. Thirty days before ablation, a 12 lead ECG, Holter and daily transtelephonic telemetry (TTM) were obtained. The TTMs were continued for 180 days after the procedure. Thereafter, Holter monitoring was used at each outpatient clinic visit or if symptoms developed. A spiral CT scan to evaluate PVs morphology was performed in all patients before the procedure and in the majority of them during 3, 6 and 12 months of follow-up. If the triggers for AF were identified, PV cryoisolation of the arrhythmogenic vein(s) was performed. Otherwise, all PVs were isolated. Single cryotherapy applications (CryoCor™) were given lasting 3 minutes.

A total of 70 patients (54 men; age  $40 \pm 10$  years) were enrolled. The duration of PAF was  $4\pm 1$  years. Patients had failed 1 to 2 AAD before ablation and most of them had minimal or no heart disease. The LVEF and left atrial size were  $59\pm 8\%$  and  $41\pm 5$  mm, respectively. All targeted PVs were successfully isolated (mean of  $3\pm 1$  PVs per patient).

Arrhythmogenic veins were considered those that, during AF, had a tachycardia cycle length shorter than the one recorded in the coronary sinus catheter. Induction of AF was attempted first by manipulation of the LASSO™ catheter inside the vein (mechanical contact); if that did not result in arrhythmias, administrations of adenosine and isoproterenol infusion were used. An arrhythmogenic PV(s) was found in 10 patients (14%). Complications occurred in 3 (4%) patients (one stroke, one pulmonary embolus and one transient diaphragmatic paralysis). No PV stenosis or esophageal injury was detected during a mean follow up was  $33 \pm 15$  (15 to 60) months. Thirty four patients

(49%) had no recurrences and 23 patients (33%) improved > 50% (overall success rate of = 82%).

Patients in whom the arrhythmogenic PV(s) were identified and isolated had no recurrences. From this study we conclude that PV cryoisolation is effective in 82% of patients with PAF during a mean follow-up of  $33 \pm 15$  months (15 to 60). Most importantly, if the arrhythmogenic PV is identified and isolated, the long-term outcome is excellent indicating no need to isolate all PVs.

But what about the patients who have recurrences after PVI? Is immediate return of AF a bad prognostic sign showing that this patient has failed ablation? Those answers came from the study described in **Chapter IV**. No systematic study has been performed as to incidence and type of recurrences following percutaneous ablation of AF. Some types of early recurrences can lead to concern regarding the success of the procedure and may also result in unnecessary re-interventions. Recent literature suggests a poor correlation of patients' symptoms with their rhythm after AF ablation.

Our study prospectively evaluated 60 patients with paroxysmal AF submitted to PV cryoisolation (45 men; mean age 53 (21 to 68) years) using daily recordings with transtelephonic telemetry (from 30 days prior and up to 180 days after the procedure).

We were able to demonstrate three different types of behavior of AF recurrence after PVI: 1) Group A - 26 patients with no further episodes of AF immediately after the procedure, 2) Group B - 20 patients with a significant decrease of AF episodes after PVI (starting at 3 months and stabilizing at 9 months) or 3) Group C - 14 patients with immediate increase in the number of events (that declines throughout one year). A history

of prior atrial flutter ablation was found to be a sign of bad prognosis as to AF recurrences.

This finding led us to the following question: can common type AFL be a sign of an arrhythmogenic substrate in paroxysmal atrial fibrillation? In **Chapter V** we evaluated the clinical and ablative consequences in patients with coexistent AF/AFL.

Ninety eight patients with paroxysmal AF/AFL were prospectively recruited from July 2001 to July 2006 to undergo PV cryoisolation. Based on telemetry, 12 lead ECG and Holter, our cohort was assigned to two different ablation strategies: Group I included 36 patients who had cavotricuspid isthmus ablation (if at least one episode of sustained common type AFL was documented) followed by pulmonary vein isolation. The other 62 patients with PAF formed our Group II where only PVI was performed.

Our results show that in patients with paroxysmal AF and no documented common type AFL, PVI alone prevents the occurrence of AF in 82% and lowers the incidence of the sustained common type AFL. Furthermore, in patients with AFL/AF, CTI ablation and PVI cured AFL but did not prevent AF recurrences. The latter finding suggests that AFL may be a sign that non PV triggers (including in the right atrium) are the culprit of AF and/or enough electrical remodeling has occurred in both atria and an ablative strategy which includes substrate modification is already required.

The knowledge that pulmonary veins (PV) are the trigger in a large percentage of patients with paroxysmal atrial fibrillation (PAF) has contributed importantly to the development of percutaneous ablative techniques in the treatment of atrial fibrillation (AF). With the main emphasis on electrical potentials in the pulmonary veins of patients with AF, the approach was to isolate all veins with electrical activity. However, in the

majority of protocols used for the percutaneous treatment of AF, electrophysiological evaluation of PVs is not included.

Distinct electrophysiological properties of PVs such as shorter refractory periods and decremental properties were previously described in patients with AF. But these data were frequently affected by exposure to amiodarone (in one third of the patients). This drug has been shown to significantly alter the refractory periods of the PVs. In **Chapter VI** we therefore evaluated the electrophysiologic properties of different PVs and their adjacent tissue (in the same patient) in a population with PAF not exposed to amiodarone referred for PV cryoisolation.

A total of 10 patients with lone AF (8 men; mean age 54 y (42 to 60)) were enrolled. Mean left atrium (LA) diameter was 38 mm (33 to 44) with a mean LVEF of 64%. Of the 40 PVs studied, potentials with decremental properties were found in 38 PVs. No arrhythmias could be induced in 18 (47%) of those -> non-arrhythmogenic group (mean of 2 veins per patient).

Our findings suggest that in patients with paroxysmal AF not exposed to amiodarone, arrhythmogenic PVs have extremely low refractory periods with a significant refractory period gradient compared to the adjacent LA. Such a situation may promote reentry, especially since decremental properties are present in the pulmonary veins.

In accordance with that finding we show in **Chapter VII** an example of the importance of the pacing site in order to evaluate the arrhythmogenic location in patients with paroxysmal AF submitted to ablation.

Non fluoroscopic navigation systems play a beneficial role in AF ablation. But the most common system used (CARTO™) limits the operator to radiofrequency energy. In **Chapter VIII** we demonstrate the feasibility of another navigation system (NavX™) in AF ablation using cryotherapy.

The clinical implications of all our findings are given in the General Discussion session.