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Long term outcome of cavotricuspid isthmus cryoablation for the treatment of common atrial flutter in 180 patients: A single center experience

Wendel Moreira · Carl Timmermans · Hein J. J. Wellens · Yuka Mizusawa · David Perez · Suzanne Philippens · Luz-Maria Rodriguez

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Abstract
Objective Recent literature has shown that common type atrial flutter (AFL) can recur late after cavotricuspid isthmus (CTI) catheter ablation using radiofrequency energy (RF). We report the long term outcome of a large group of patients undergoing CTI ablation using cryothermy for AFL in a single center.
Methods Patients with AFL referred for CTI ablation were recruited prospectively from July 2001 to July 2006. Cryoablation was performed using a deflectable, 10.5 F, 6.5 mm tip catheter. CTI block was reassessed 30 min after the last application during isoproterenol infusion. Recurrences were evaluated by 12-lead ECG and 24 h Holter recording every clinic visit (1/3/6/9 and 12 months after the procedure and yearly thereafter) or if symptoms developed.
Results The 180 enrolled patients had the following characteristics: 39 women (22%), mean age 58 years, no structural heart disease in 86 patients (48%), mean left atrium diameter 44±7 mm and mean left ventricular ejection fraction 57±7%. The average number of applications per patient was 7 (3 to 20) with a mean temperature and duration of −88°C and 3 min, respectively. Acute success was achieved in 95% (171) of the patients. There were no complications. After a mean follow-up of 27±17 (from 12 to 60) months, the chronic success rate was 91%. The majority of the recurrences occurred within the first year post ablation. One hundred and twenty three patients had a history of atrial fibrillation (AF) prior to CTI ablation and 85 (69%) of those remained having AF after cryoablation. In 20 of 57 (35%) patients without a history of AF prior to CTI ablation, AF occurred during follow-up.
Conclusions This prospective study showed a 91% chronic success rate (range 12 to 60 months) for cryoablation of the CTI in patients with common type AFL and ratified the frequent association of AF with AFL.

Keywords Atrial flutter · Atrial fibrillation · Cryoablation · Long term follow-up · Cavotricuspid isthmus

1 Introduction

Ablation of the cavotricuspid isthmus (CTI) for the treatment of atrial flutter (AFL) has become standard practice. Most of the procedures are performed using radiofrequency energy (RF) [1–5]. High chronic success rates are described but the majority of the data comes from a relatively short term follow-up [1–13]. A recent study by Chinitz et al. [14] reported some interesting data regarding the long term follow-up of 80 patients with common type AFL who underwent CTI ablation using RF. They found a 12.5% (ten patients) recurrence rate at an average of 21 months after the procedure with most patients having a recurrence after the first year post ablation. Our prior experience using cryothermy in a limited number of patients

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W. Moreira · C. Timmermans · Y. Mizusawa · D. Perez · S. Philippens · L.-M. Rodriguez (✉)
Department of Cardiology, Academic Hospital Maastricht, P. Debyelaan 25, P.O. Box 5800, Maastricht, The Netherlands
e-mail: Lm.Rodriguez@cardio.unimaas.nl

H. J. J. Wellens
Cardiovascular Research Institute Maastricht (CARIM), Maastricht, The Netherlands

[15] also showed that AFL may recur 1 year after CTI cryoablation.

The purpose of this study was to evaluate the long term outcome of CTI cryoablation in a large patient population with common type AFL in a single center.

2 Methods

One hundred and eighty patients with sustained symptomatic common type AFL referred for CTI ablation were enrolled prospectively from July 2001 to July 2006 in our institution. Signed written consent, approved by the local ethics committee, was obtained from all participants.

Before CTI cryoablation, anticoagulation with warfarin aiming a therapeutic international normalized ratio of 2 to 3 was kept for at least 3 weeks. Antiarrhythmic drugs were not discontinued before ablation.

2.1 Electrophysiologic study and ablation

We focused our study on the clinical aspects and long term follow-up of patients with AFL who were submitted to CTI cryoablation.

Our CTI cryoablation protocol has been already reported [15]. Briefly, our methodology was as follows: under local anesthesia and via the femoral route, a decapolar catheter is positioned in the distal coronary sinus (for evaluation of left atrial activation), a duodecapolar catheter (2-mm interelectrode spacing, Halo catheter, Biosense Webster, Baldwin Park, CA) for mapping the right atrial lateral wall and a quadripolar catheter in the His bundle area. A deflectable, 10.5 F, 6.5 mm tip cryoablation catheter (CryoCor Inc., San Diego, CA) is inserted into the right atrium through a 12F, 65-cm-long sheath (DAIG, St. Jude Medical Inc., St. Paul, MN) [15–19].

Entrainment to confirm the isthmus dependence of the AFL circuit was performed in every patient in whom AFL was present or could be induced at the start of the procedure, according to previously published techniques [2, 10, 15, 16, 20, 21]. If AF, requiring cardioversion, was present or developed during stimulation or if we were unable, even under isoproterenol infusion, to induce AFL, CTI ablation was performed during sinus rhythm. Linear lesions were created by use of a point-by-point technique with gradual pullback of the cryocatheter in a ventricular atrial fashion. The first application was delivered at the ventricular insertion of the isthmus and applications were continued for an average of 3 min. In patients in whom ablation of the posterior isthmus proved insufficient, an attempt was made to ablate the septal isthmus (four patients). After documentation of bidirectional isthmus conduction block, the atrial pacing (from the proximal coronary sinus) protocol (up to three atrial extrastimuli at three pacing cycle lengths and incremental atrial pacing) was performed without and with isoproterenol infusion (1 to 3 μg/min). Acute success was defined as bidirectional isthmus conduction block, 30 min after the last application without and with isoproterenol infusion [22].

All patients were studied in the fasting state without sedation. Those presenting in AF while on the catheterization table were converted to sinus rhythm by internal or external cardioversion. During the procedure intravenous heparin was given as a 100-IU/kg bolus dose after the venous sheaths were inserted. The 12-lead ECG and intracardiac electrograms were recorded and stored by the BARD Labsystem PRO.

2.2 Post ablation management

All patients were monitored in hospital for 24 h and oral anticoagulation was started the day of ablation. Antiarrhythmic drugs (AAD) were stopped after the procedure in patients without a history of AF; in those with AF/AFL the same AAD were continued. All patients had anticoagulation for at least 1 month. Subsequently, the need for chronic anticoagulation was assessed by the amount of recurrences of AFL/AF and the presence of risk factors for thromboembolic events.

All patients had a 12-lead ECG and a 24 h Holter recording at discharge and during each clinic visit (1 month, 3, 6, 9, 12 months and yearly thereafter) or earlier if they had symptoms.

Due to the logistics of the Maastricht area—and also the presence of a dedicated research nurse (S. P.) who was available to address patients' concerns and questions at any time—we were able to follow every patient on an individual basis.

2.3 Statistical analysis

Continuous variables are presented as mean±SD, where appropriate. In cases of a non-Gaussian distribution, medians and quartiles are given. Categorical variables are expressed as numbers and percentages of patients.

Statistical analysis was performed using the Student *t* test for unpaired data. All values were considered significant at $P<0.05$.

The authors had full access to the data and take responsibility for its integrity.

3 Results

Of the 180 enrolled patients, 39 patients (22%) were women with a mean age of 58 (from 18 to 80) years. More

than half of the patients (92 patients, 52%) had structural heart disease: arterial hypertension: 57 patients, coronary artery disease: 22 patients, valvular heart disease: 13 patients, congenital heart disease: 11 patients, idiopathic cardiomyopathy: 18 patients. Counterclockwise AFL was documented in 91% (164) of the patients and clockwise AFL in 9% (16 patients).

The mean left atrial diameter and the mean left ventricular ejection fraction were 44±7 mm and 57±7%, respectively. A prior history of AF was present in 123 (69%) of the patients. The clinical characteristics of the patients, related to the presence or absence of AF before ablation, are described in Table 1. Note that AF during follow-up is significantly higher in the group with a prior history of this arrhythmia.

Total fluoroscopic—mean of 30±18 min (range, 12 to 152 min)—and procedure times—mean of 2.6±1.1 h (range, 1 to 6.5 h)—decreased throughout our study with a long duration of a procedure and fluoroscopy being attributed mainly to the learning curve of a new technology. An average of 7 (3 to 20) applications per patient were delivered with a mean temperature and duration of −88°C and 3 min, respectively.

The acute success rate for cryoablation of the CTI was 95% (171 patients). There were no complications. Of the nine patients in whom bidirectional CTI block was not achieved, three underwent a successful reablation. The other six patients had much improvement of their symptoms (despite an incomplete line) and preferred not to have another procedure.

After a mean follow-up of 27±17 (range from 12 to 60) months, recurrences of symptomatic AFL occurred in 15 patients (9%) resulting in a 91% chronic success rate. Those recurrences occurred in six patients within the first 3 months post ablation, in four patients from 3 to 6 months post ablation, in four patients from 6 to 9 months post ablation and in one patient at 14 months post ablation (Fig. 1). Ten of those 15 patients underwent a second successful cryoablation of the CTI. The other five had not only reablation of the isthmus but also pulmonary vein cryoisolation (PVI) for AF during the second procedure.

Despite the success as far as AFL was concerned, AF was still present in 85 patients (69%) with a prior history of this arrhythmia. Those patients were treated by AAD (69 patients, 81%), PVI (14 patients, 16%) or AV nodal ablation with pacemaker implantation (two patients, 3%). New episodes of AF developed in 20 (35%) of those 57 patients without documented AF prior to CTI cryoablation and were all controlled by AAD.

4 Discussion

4.1 Main findings

Our current study showed a 91% chronic success rate of CTI cryoablation in a large population (180 patients) with AFL followed for a long period of time (1 to 5 years, mean of 27 months).

According to the most recent ACC/AHA/ESC guidelines for the management of supraventricular arrhythmias CTI ablation is the only therapy with a class I indication for the long term management of AFL [2]. The majority of those ablations are done using RF energy. Concerning the follow-up length of those procedures, most of the literature available reports on a relatively short period, the majority of them being less than 2 years. However Chinitz et al. [14] published a study of 80 patients with AFL submitted to CTI ablation using RF that had up to 6 years follow-up. Interestingly, they found a 12.5% recurrence of AFL that occurred on an average of 21 months post ablation, ratifying the need of data with a longer follow-up. It is important to keep in mind though, that arrhythmias after ablation do not always correlate with symptoms [23, 24] and one could question if those patients with such a late recurrence had those episodes much earlier than what is reported. That might be one reason why our results, where most of our recurrences happened within 1 year, are

Table 1 Characteristics of the 180 patients with atrial flutter referred for CTI cryoablation related to the presence or absence of atrial fibrillation AF before ablation

	AF/AFL patients (123 patients), 69%	AFL only (57 patients), 31%	*p* value
Age (year)	57±13	58±13	ns
Women	19% (23 patients)	28% (16 patients)	ns
No SHD	55% (68 patients)	32% (18 patients)	< 0.05
LAd (cm)	4.4	4.5	ns
LVEF (%)	58	55	ns
Acute failures[a]	5% (6 patients)	5% (3 patients)	ns
AF in long term follow up	69% (85 patients)	35% (20 patients)	< 0.05

[a] Patients in whom CTI cryoablation did not result in bidirectional block (failed procedure).
AF Atrial fibrillation, *AFL* atrial flutter, *CTI* cavotricuspid isthmus, *Lad* left atrium diameter, *LVEF* left ventricular ejection fraction, *SHD* structural heart disease

discrepant with those from their study. The intrinsic characteristics of our hospital, our clinical follow-up and the population of Maastricht could be responsible for our ability to find those recurrences earlier.

Regarding cryothermy as energy source, a 9 months follow-up study in 39 patients undergoing CTI cryoablation with a different system was reported [25]. They achieved a chronic success rate of 100% in the cryoablated group, despite documenting reconduction through the isthmus in 31% of patients during a 3 month follow-up electrophysiologic study. The CRAAFT trial presented the results in 32 patients with AFL submitted to either cryo- or RF ablation of the CTI [26]. They report an 84% success rate after a follow-up of 14 months. Those two small studies, with a relatively short follow-up, reported similar success rates with RF and cryothermy for AFL ablation. The results from our study—which included a significant larger patient population (180) with a longer follow-up (1 to 5 years, mean of 27 months)—reinforces the effectiveness of cryothermy for the treatment of AFL, being the outcomes comparable to those reported in the literature using RF (where most outcome data also comes from non invasive follow-up) [1, 4–7, 11, 12, 27, 28]. Therefore, cryothermy can be considered as an efficient energy source for the treatment of common type AFL.

4.2 The relation of AF with AFL

The close relation between AF and AFL is well described [1, 5–14, 21, 29–39]. Our data showed a high prevalence of AF (123 out of 180 patients, 69%) in patients with predominant AFL referred for CTI ablation. A recent study

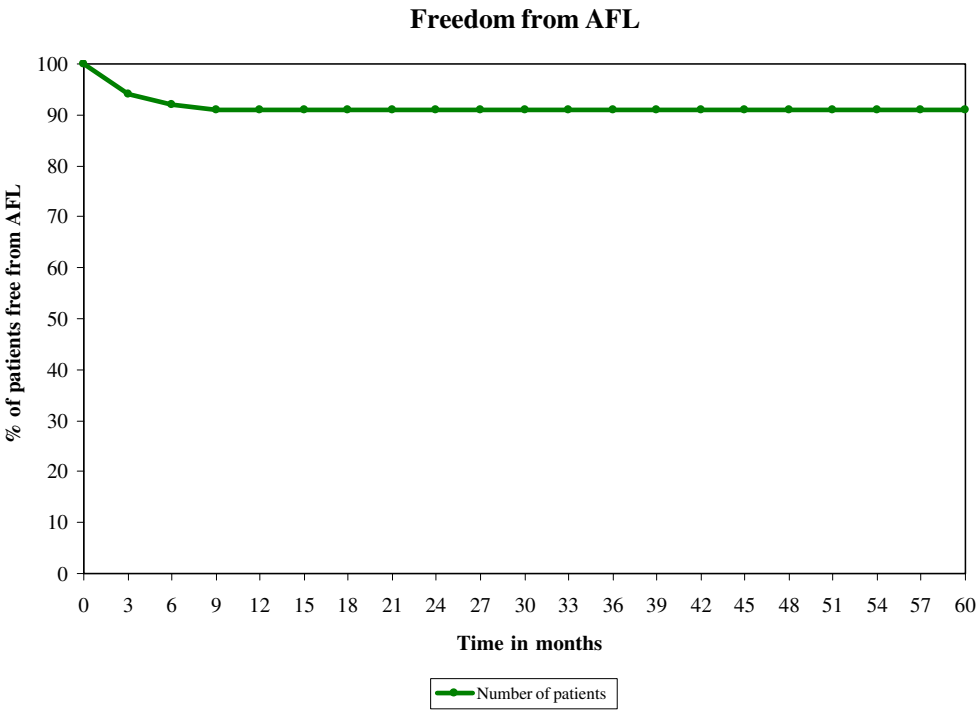

Fig. 1 Percentage of patients (171 successfully ablated) free of common type atrial flutter over time

Follow-up in months	0	3	6	9	12	18	24	30	36	42	48	54	60
Events	9	6	4	4	1	0	0	0	0	0	0	0	0
Number of patients at risk	180	171	165	161	157	156	134	112	92	72	57	42	28

Legend: After a mean follow-up of 27 ± 17 months, 91% (156 patients) did not have recurrences of atrial flutter.

by Ellis and colleagues [40] strengthened even more this association. They followed 363 patients with lone AFL who underwent CTI RF ablation—during a mean follow-up of 39 months—and reported an 82% incidence of drug refractory AF in their patient population.

The new development of AF in our patient population without a prior history of AF preceding AFL ablation may be a sign of an already present electrical and morphological change in the right and left atria. If in addition, a functional or anatomical line of block between the two venae cavae (or elsewhere) occurs, atypical AFL(s) may develop either in the right (because the CTI is already ablated) or in the left atrium [11, 14, 21, 31, 32, 37–39].

4.3 Study limitations

Our recurrence data rely mostly on the subjective assessment by the patient, like the great majority of RF data [1, 4, 6–8, 12]. Only an objective measurement (such as a repeat electrophysiological study with documented bidirectional block) will determine the long lasting effect of CTI ablation for the treatment of common type AFL.

5 Conclusions

In this prospectively studied large population of patients with common type AFL, cryoablation of the CTI has a 91% chronic success rate during long term follow-up (range 1 to 5 years, mean of 27 months). These results are similar to those obtained with RF, validating cryothermy as an efficient alternative energy source. We also were able to ratify the frequent association of AF with AFL.

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