Low incidence of Permanent Complications During Catheter Ablation for Atrial Fibrillation using open irrigated catheters: a multicenter registry

Low incidence of permanent complications during catheter ablation for atrial fibrillation using open-irrigated catheters: a multicentre registry

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ABSTRACT

Aims. Despite catheter ablation (CA) has become an accepted treatment option for symptomatic, drug-resistant atrial fibrillation (AF), safety of this procedure continues to be cause for concern. Aim of the present study was to assess the incidence of complications with permanent sequelae of CA for AF using open irrigated catheters in a contemporary, unselected population of consecutive patients.

Methods. From January 1, 2011 to December 31, 2011, data from 2,167 consecutive patients who underwent CA for AF using an open irrigated catheter in 29 Italian centers were collected. All complications occurring to the patient from admission to 30th post-procedural days were recorded.

Results. No procedure-related death was observed. Complications occurred in 81 patients (3.7%): 46 patients (2.1%) suffered vascular access complications; 13 patients (0.6%) cardiac tamponade, successfully drained in all cases; 6 patients (0.3%) arterial thromboembolism (4 transient ischemic attack and 2 ischemic strokes); 5 (0.2%) patients conservatively treated pericardial effusion; 3 patients (0.1%) phrenic nerve paralysis; 3 patients (0.1%) pericarditis; 3 patients (0.1%) hemothorax, and 2 patients (0.1%) other isolated adverse events. At multivariate analysis, only female sex (OR 2.5, CI 1.5-3.7, p<001) and operator experience (OR 0.5, CI 0.4-0.7, p<001) related to complications. Only 5 (0.2%) patients developed permanent sequelae from their complications.

Conclusion. CA for AF with the use of open irrigated-catheters is currently affected by a very low rate of complications leading to permanent sequelae.

KEY WORDS: atrial fibrillation; catheter ablation; permanent complications.

CONDENSED ABSTRACT

We assessed the incidence of complications with permanent sequelae in 2,167 consecutive patients who underwent catheter ablation for atrial fibrillation using open irrigated catheters. Complications occurred in 81 patients (3.7%). Female sex and operator experience were correlated with complications. Only 5 (0.2%) patients developed permanent sequelae from their complications.

What's New

1. This is the first multicenter study specifically aimed at collecting data regarding the incidence of complications with permanent sequalae in an unselected population of patients undergoing catheter ablation for atrial fibrillation by means of open irrigated catheters
2. No procedure-related death was reported. Out of a cumulative complication rate of 3.7%, only 0.2% of the patients developed permanent sequelae.
3. Complications were more frequent when catheter ablation was performed in females and by less experienced operators.

INTRODUCTION

Catheter ablation (CA) of atrial fibrillation (AF) is a well established treatment option for recurrent, symptomatic, drug-resistant atrial fibrillation (AF) (1,2). Despite the satisfactory results justifying (3-5) the recommendation for CA by international guidelines in selected patients, safety of this procedure remains cause for concern (1,2,6). Previous studies reported a rate of complications ranging from 3.5% to 6.3% (7-12). These reports, however, gathered events with extremely different outcomes: from groin hematomas requiring few days of rest to PV stenosis with pulmonary distress and thromboembolic events leading to permanent disability. Only one study specifically focused on complications and reported prevalence and causes of fatal outcome following CA of AF (13). Thus, the effect on prognosis of complications recorded during CA for AF is unknown. Open irrigated-catheters (OIC) are widely used for radiofrequency CA (14) in particular of AF (15-17). In fact, OIC overcome some limitations of 4-mm and 8-mm Radiofrequency catheter, such as coagulum formation and insufficient power delivery in areas of low blood flow. However, concern has been raised regarding the safety of OIC, especially when used with high power, due to an increased occurrence of cardiovascular and gastrointestinal complications (15).
Aim of the present study was to assess the incidence of complications with permanent sequelae of CA for AF using OIC in a contemporary population of consecutive patients.

METHODS

Study population. We prospectively collected clinical and procedural data concerning consecutive patients who underwent CA for AF in 29 Italian electrophysiology laboratories between January 1 and December 31, 2011 (18). In 2,167 of these patients

CA was performed using an OIC, and they represented our study population. This observational study was approved by the local institutional review committees, and written informed consent was obtained from each patient.

Anticoagulation. All patients were on oral anticoagulants (dicumarol or acenocumarol) with a therapeutic international normalized ratio (INR) higher than 2.0 for at least 4 weeks preceding the procedure, or performed transesophageal echocardiographic assessment to exclude the presence of left atrial thrombus. Oral anticoagulants were withdrawn 2 or 3 days before ablation, and substituted with low molecular weight heparin until 12 hours before the procedure. Unfractionated heparin infusion was started immediately after trans-septal catheterization, to maintain the mean Activated Clotting Time between 300 and 400 seconds. Low molecular weight heparin was restarted 4 to 6 hours after sheaths removal, and continued until oral anticoagulant therapy, started on the same day of the procedure, reached therapeutic target.

Ablation. All ablation strategies aiming at isolating or encircling the PVs were included in the Registry. Additional linear lesions in the right or left atrium were also allowed. For the purpose of this study we report data only on CA procedures performed by means of OIC [Navistar® ThermoCool® or ThermoCool SF® (Biosense Webster Inc., Diamond Bar, California) or Coolpath® or Cooflex® (St.Jude Medical inc. Endocardial Solutions St. Paul, MN, USA)]. Radiofrequency pulses were delivered with a temperature setting of 45° C and radiofrequency energy up to 50 W. In several centers, when ablation was performed in the posterior wall of the left atrium, radiofrequency power was usually reduced to 25 W to avoid the risk of injuring the adjacent structures. In the majority of centers ablation was guided by a 3D non-fluoroscopic mapping system [Carto™ system (Biosense Webster Inc.) or EnSite NavX™ (St.Jude Medical

inc. Endocardial Solutions S. Paul, MN, USA)] creating an electroanatomical map of left atrium and PVs with or without integration of left atrium computed tomography or magnetic resonance scans.

A circular mapping catheter was widely used to confirm PV's electrophysiological isolation, and intracardiac echo imaging was used to guide the PV antrum isolation in 2 laboratories.

Definitions. *Complications* were defined as all unexpected events which required intervention or prolonged hospital stay beyond the scheduled period. Early tachyarrhythmias (AF or atrial tachycardia/flutter) were not included even if requiring cardioversion.

Complications with permanent sequelae were defined as those leading to death or causing permanent harm not resolving within 30 days from CA.

Procedures were done by different operators. Personal background as first operator was considered to classify operator's experience: less than 100 procedures; between 101 and 500 procedures; and more than 500 procedures.

Data collection. The investigators were provided with the same data sheet for the collection of specific information on each ablation procedure. Data were collected retrospectively by each investigator, and sent via a computerized database in Excel format (Windows 7, XP, or Mac) to the coordinating center for analysis. Each author took responsibility for data integrity.

The Registry considered complications occurring from hospital admission of the patient to the 30^{th} post-procedural day. Complications occurring after the hospital stay and clinical status of patients developingcomplications were collected through out-patient visit or telephone interview.

Statistical analysis. Normally distributed continuous variables were expressed as means (SD) and compared by Student's T-Test. Normality was assessed using the Shapiro-Wilk test. Skewed variables were expressed as medians (quartiles) and compared by runk-sum test. Categorical variables were presented as counts and percentages, and compared by chi-square or Fisher's exact test, as appropriate. A logistic regression model was designed and stepwise backward selection was performed in order to identify significant and independent predictors of complications. Independent variables were chosen when a p value < 0.10 emerged at univariate analysis. The starting model included: gender; age; and operator's experience. A significant increase in risk was obtained if the 95% confidence interval exceeded 1 and the p value of the Wald test was <0.05.

Analysis was performed by means of SPSS (version 11.0, SPSS Inc., Chicago, Illinois, USA).

RESULTS

Clinical and procedural data. The final patient cohort included 2,167 consecutive patients. Baseline clinical characteristics of the study population are shown in Table 1, while procedural data are listed in Table 2.

Complications. No procedure-related death was observed. Complications occurred in 81 patients (3.7%): 46 patients (2.1%) suffered vascular access complications; 13 patients (0.6%) developed cardiac tamponade, successfully drained in all cases; 6 patients (0.3%) had arterial thromboembolism (4 transient ischemic attack and 2 ischemic strokes); 5 patients (0.2%) presented pericardial effusion not requiring specific intervention; 3 patients (0.1%) had phrenic nerve paralysis during right PV isolation; 3

patients (0.1%) had pericarditis; 3 patients (0.1%) had hemothorax requiring drainage in 2 cases. Other isolated but serious adverse events were documented in 2 patients (0.1%): hemorragic stroke in 1; transient ST elevation in 1.

In Table 3 clinical and procedural characteristic of patients with and without complications are shown. At univariate analysis, patients with complications were older and more frequently females, and ablation was less frequently performed by experienced operators. At multivariate analysis, female gender (OR 2.5, CI 1.5-3.7, p<001) predicted complications, while higher operator experience (OR 0.5, CI 0.4-0.7, p<001) inversely related to complications.

Complications with permanent sequelae. Out of all complications 5 (0.2%) did not result transient: 3 permanent neurological sequelae (2 ischemic and 1 hemorragic stroke), and 2 permanent symptomatic phrenic nerve palsy. Clinical and procedural characteristics of patients with permanent complications are presented in Table 4.

DISCUSSION

Main findings. This is the first multicenter study specifically aimed at collecting data regarding the incidence of complications with permanent sequalae in an unselected population of patients undergoing CA for AF by means of OIC. No procedure-related death was reported. Out of a cumulative complication rate of 3.7%, only 0.2% of patients developed permanent sequelae. Complications were more common when CA was performed in females and by less experienced operators.

Complications in CA for AF. The demonstration of superiority of CA over antiarrhythmic therapy in the management of several settings of AF patients (3-5) has greatly increased the procedure recommendation in the last decade (19,20). Despite

technological improvements, CA of AF is still affected by an high amount of complications mainly related to the extension of lesions in the left atrium, the need of a deep anticoagulation and the increasing number of centers starting to approach AF ablation (12,17,21). Thromboembolic complications seem to be affected by ablation technologies and by energy (22,23). In particular, OICs have been reported to reduce the risk of thrombus formation at the electrode-tissue interface, and the risk of steam pop (24). On the other hand, OICs deliver a large amount of saline solution during prolonged ablation procedures, and make deeper and larger lesions that might increase the risk of pericardial effusion or perforation.

Our study is the first to be designed to evaluate the complications during radiofrequency CA for AF by means of OICs, with an overall complication rate of 3.7%, slightly lower than that reported by recent multicenter studies using different technologies (12,18,21). Also the rate of thromboembolic complications (0.3%) and pericardial effusion or cardiac tamponade (0.8%) seems to confirm the safety of OICs, as recently reported (14,16,17).

We found an increase of complication rate when procedures were performed by less experienced operators. This finding is consistent with the observation that operators' experience and hospital volume related to better outcomes (12,21).

Complications with permanent sequelae. The more feared complications of CA are obviously those leading to death or to permanent sequelae (13). In the present study only a 0.2% of permanent sequelae was reported. Two of these were permanent symptomatic phrenic nerve palsy occurred during ablation of the right PVs. Impedance monitoring, avoiding high vein values, and strict monitoring of phrenic nerve function

by means of regular pacing of the nerve are crucial to avoid this complication, and should become mandatory during ablation especially of the right PVs.

Most of permanent complications were related to embolic events. This observation underlines once again the need of an aggressive procedural and periprocedural anticoagulation regimen. In particular, maintaining an ACT value ≥ 350 msec during ablation, and performing the procedure on warfarin have been effective in reducing such complications (25).

Previous registries (12,13,21) have reported a rate of death ranging from 0.1% to 0.46%. Although the low rate of death could require larger study populations to assess its true incidence, the lack of procedure-related death observed in our study further supports the safety of OICs.

Limitations. Unfortunately we did not have a control group of patients undergoing CA with different technologies, like cryoablation or multielectrode catheters associated with duty-cycled radiofrequency energy. For this reason any conclusion on the superiority of one tool over the others can be driven from the present study. However the safety profile of the OICs seems to be evident when comparing the present to previously published data.

By study design data collection focused on complications occurring within one month after ablation: some rare but feared complications like PV stenosis and late pericardial tamponade could be underrepresented.

Clinical implications. Complications with permanent sequelae in CA for AF with the use of OICs are very rare and mostly related to embolic events. Based on this evidence it becomes acceptable to pay a higher potential risk of hemorrhagic events to reduce dreadful cerebral embolic complications, particularly in female. Overall rate of

complications of CA for AF by mean of OICs is below 4% but the hazard is increased when CA is performed by less experienced operators arising once again the issue to recommend a volume threshold to enhance safety of the procedure.

DISCLOSURES

Claudio Tondo (Medtronic Inc.: Board member; Medtronic Inc. and St. Jude: payment for lectures)

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APPENDIX

The following centers and investigators participated in the study: Azienda Ospedaliera Careggi, Firenze: L Padeletti, P Pieragnoli; Azienda Ospedaliera San Camillo-Forlanini, Roma: A Avella, P De Girolamo, F Laurenzi, A Pappalardo; Casa di Cura Mediterranea, Napoli: A Iuliano, G Stabile, P Turco; Casa di Cura Montevergine, Mercogliano (AV): F Donnici, F Solimene; Casa di Cura San Michele Maddaloni (CE): A. De Simone, V. La Rocca, P Turco; Casa di Cura Villa Maria Cecilia, Cotignola (RA): A Pappone, C Pappone; Centro Cardiologico Monzino, Milano: G Fassini, S Riva, C Tondo; Fondazione Poliambulanza, Brescia: P Berra, F Morandi, D Pecora; Istituto Clinico Città Studi, Milano; G Augello, A Santagostino, SL D'Ascia; Istituto Clinico Humanitas Mater Domini, Castellanza (VA): A Sanzo, M Tritto; Istituto Clinico Sant'Ambrogio, Milano: V De Sanctis, M Mantica, S Panigada; Ospedale Ca' Foncello, Treviso: M Crosato, V Calzolari, R Mantovan; Ospedale Cisanello, Pisa: MG Bongiorni, E Soldati; Ospedale Civile, Arezzo: R Guida, A Fraticelli, P Notarstefano; Ospedale Civile, Conegliano (TV): L Corò, P Delise; Ospedale Civile, Mirano (VE): G Brandolino, F Zoppo; Ospedale Civile, Perugia: Zingarini; Ospedale Francesco Miulli, Acquaviva delle Fonti (BA): M Grimaldi, G Katsouras, F Quadrin; Ospedale Pietro Cosma, Camposampiero (PD): S Baccilieri, P Turrini, R Verlato; Ospedale Sandro Pertini, Roma: A Castro, ML Loricchio, F Turreni; Ospedale San Filippo Neri, Roma: C Pandozi; Ospedale Santa Chiara, Trento: M Del Greco, M Marini; Ospedale dell'Angelo, Mestre-Venezia: P China, A Rossillo, S Themistoclakis; Ospedale Santa Maria della Misericordia, Udine: D Murer, A Proclemer, L Rebellato; Ospedale Santa Maria Nuova, Reggio Emilia: N Bottoni, M Iori, F Quartieri; Policlinico Casilino, Roma: L Calò, L De Luca, E De Ruvo, L Sciarra; Policlinico Gemelli, Roma: ML

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Coordinators: E Bertaglia, G Stabile.

Table 1: Baseline clinical characteristics of the 2,167 enrolled patients

Male gender (%)		74.8
Age (years)		60 (52-67)
Duration of AF history (years)		3.0 (2-6)
Arrhythmic profile (%)		
	Paroxysmal AF	52.0
	Persistent AF	27.3
	Permanent AF	20.7
$CHADS_2$ score[†]		1 (0-1)
Mean left atrial diameter (mm)		42.0 (40-46)
Mean left ventricular ejection fraction (%)		57.4 (6.7)

Continuous variables are presented as mean (SD) or median (25%-75%iles).

AF=atrial fibrillation; REDO=patients who had already undergone PV catheter ablation.

Table 2: Procedural data of the 2,167 enrolled patients

Pre-ablation imaging (%)		
	MRI	13.0
	CT	22.0
	TEE	49.0
Mapping system (%)		
	None	7.0
	CARTO	56.9
	NAVx	36.0
	Other	0.1
Number of vascular accesses		3.0 (3-5)
Number of trans-septal punctures		1 (1-1)
Number of ablated PVs		4 (4-4)
CTI ablation (%)		19.2
Mitral to inferior left PV isthmus ablation (%)		40.3
Left atrial roof ablation (%)		43.1
Duration of fluoroscopy exposure (minutes)*		22 (13-43)
Duration of RF delivery (minutes)†		31 (24-39)
Ongoing warfarin (%)		6.0
Learning curve level (%)		
	$\leq$100 patients	6.0
	101-500 patients	22.0
	$\geq$501 patients	70.0

Continuous variables are presented as mean (SD) or median (25%-75%iles).

*: analysis based on 1920 subjects; †:analysis based on 1775 subjects.

MRI= magnetic resonance imaging; CT= computed tomography; CTI=cavo-tricuspidalic isthmus; LA=left atrium; PV=pulmonary vein; RF=radiofrequency; TEE=transoesophageal echocardiography.

Table 3. Univariate analysis for comparisons between patients with and without complications.

	No complications N=2084	Complications N=81	p
Age (years)	60 (53-66)	64 (60-68)	0.03
Male gender (%)	72.7	53.1	<0.001
$CHADS_2$ score	1 (0-1)	1 (0-1)	0.49
Arrhythmic profile (%)			
Paroxysmal	51.7	61.7	0.50
Persistent	27.6	21.0	
Permanent	20.7	17.3	
Duration of AF history (years)	4 (2-6)	3 (2-5)	0.12
Mean left atrial diameter (mm)	41 (40-45)	42 (40-45)	0.25
Left ventricular ejection fraction <55% (%)	18.0	14.8	0.27
Pre-ablation imaging (%)			
TEE	49.0	44.4	0.36
MRI	13.0	8.6	
CT	23.3	28.4	
ICE (%)	12.7	16.0	0.67
Mapping system (%)			
None	7.1	6.2	0.92
CARTO	56.9	55.5	
NAVx	35.9	38.3	
Other	0.1	0	
Number of vascular accesses	3 (3-5)	3 (3-4)	0.34
Number of transseptal punctures	1 (1-1)	1 (1-1)	0.38
Number of isolated PV	4 (4-4)	4 (4-4)	0.73
CTI ablation (%)	19.1	21.0	0.68
Mitral to inferior isthmus ablation (%)	40.6	33.3	0.19

Left atrial roof ablation (%)	43.4	34.6	0.11
Duration of fluroscopy exposure (minutes)	21 (13-41)	33 (14-49)	0.23
Duration of RF delivery (minutes)	30 (24-40)	33 (24-38)	0.11
Ongoing warfarin (%)	5.7	6.1	1.0
Learning curve level (%)			
< 100 patients	5.7	11.1	<0.001
101-500 patients	21.5	35.8	
> 501 patients	72.8	53.1	

Abbreviation as in Table 3.

Table IV: Clinical and procedural characteristics of the 5 patients with permanent complications.

	Complication	Gender	Age	$CHADS_2$	Type of AF	Hypertension	CHF	Diabetes	Previous Stroke/TIA
#1	PNP	Female	60	2	Paroxysmal	1	0	1	0
#2	PNP	Female	62	1	Paroxysmal	1	0	0	0
#3	Hemorragic stroke	Male	69	1	Persistent	0	0	0	0
#4	Ischemic stroke	Female	72	1	Persistent	1	0	0	0
#5	Ischemic stroke	Female	75	6	Persistent	1	0	1	1

PNP: phrenic nerve palsy; AF= atrial fibrillation; CHF= congestive heart failure; TIA= transient ischemic attack.