Europace (2010) **12**, 337–341
doi:10.1093/europace/eup422

Pericardial effusion in atrial fibrillation ablation: a comparison between cryoballoon and radiofrequency pulmonary vein isolation

Gian Battista Chierchia[1]*†, Lucio Capulzini[1]†, Steven Droogmans[1], Antonio Sorgente[1], Andrea Sarkozy[1], Andreas Müller-Burri[1], Gaetano Paparella[1], de Asmundis Carlo[1], Yoshinao Yazaki[1], Dirk Kerkhove[2], Guy Van Camp[2], and Pedro Brugada[1]

[1]Heart Rhythm Management Centre, UZ Brussel-VUB, Laarbeeklaan 101, 1090 Brussels, Belgium; and [2]Cardiology Department, Non-Invasive Imaging Unit, UZ Brussel-VUB, Brussels, Belgium

Received 19 October 2009; accepted after revision 7 December 2009; online publish-ahead-of-print 6 January 2010

Aims Atrial fibrillation (AF) ablation is increasingly being performed in electrophysiology laboratories. Pericardial effusion (PE) is certainly one of the most frequently observed complications during AF ablation. The aim of our study was to investigate the incidence and outcome of PE following cryothermal energy balloon ablation (CBA) in comparison with conventional circumferential pulmonary vein isolation with a focal radiofrequency (RF) catheter.

Methods and results A total of 133 consecutive patients (105 males) with paroxysmal AF were included in this study. Forty-six patients (36 males) underwent CBA (Arctic Front, Medtronic, USA) and 87 (69 males) point-by-point RF ablation guided by electroanatomical mapping (Carto, Biosense Webster, Diamond Bar, CA, USA). Ablation was performed under general anaesthesia with both techniques. All patients underwent a 2D transthoracic echocardiogram within 24 h before and after the procedure as routinely performed in our centre. Pericardial effusion was detected in 19 (14.2%) of 133 patients. Sixteen patients presented mild effusion, one moderate effusion, and two pericardial tamponades. There was no significant difference in the incidence of PE between the cryoballoon and the RF group (11 vs. 16%). A longer procedural time, coronary artery disease, and arterial hypertension were found to be independent predictors of PE during AF ablation.

Conclusion Pericardial effusion occurred in a similar proportion following CBA and RF ablation for AF. Pericardial effusion was mostly mild and asymptomatic, with benign clinical outcome not requiring additional hospitalization days.

Keywords Cryoballoon • Atrial fibrillation ablation • Pericardial effusion

Introduction

Atrial fibrillation (AF) is certainly the most frequent arrhythmia reaching epidemic proportions in occidental society. Today, catheter ablation has become a popular procedure in the treatment of drug resistant AF. Since the demonstration that pulmonary vein (PV) ectopic activity is the main trigger of paroxysmal AF,[1,2] isolation of the PVs has become the cornerstone of AF ablation.[3] Most commonly, PV isolation is achieved with a 'point by point' ablation technique using radiofrequency (RF) energy. However, other technological approaches have been designed. Among them, the cryothermal energy balloon ablation (CBA) (Arctic Front, Medtronic, USA), which uses cryothermal energy, allows successful isolation of the PVs in ~90–100% of cases.[4] Unfortunately, ablation of AF can be accompanied by minor and major complications. According to a recent worldwide survey, adverse events occur in up to 6% of the patients.[5] Among the complications related to this procedure, pericardial effusion (PE) is

* Corresponding author. Tel: +32 2 476 3038; fax: +32 2 477 6840. *E-mail address*: gbchier@yahoo.it; jeanbaptiste.chierchia@uzbrussel.be

†The first two authors contributed equally to the study.

certainly one of the most frequently observed. Pericardial effusion can manifest itself from acute pericardial tamponade to asymptomatic effusion. Although asymptomatic PE can be detected by a simple echocardiographical examination, limited data are available on its incidence following AF ablation.[6] To the best of our knowledge, no systematic study has been done comparing the incidence of PE following RF and cryoablation of the PVs. Because of the increasing number of procedures in the electrophysiology laboratories, safety issues are of primary concern. Therefore, in a series of consecutive patients undergoing PV isolation for paroxysmal AF, we aimed to study the incidence and clinical significance of PE within 24 h after CBA compared with circumferential PV isolation using RF energy.

Methods

Patients who underwent AF ablation in our centre for highly symptomatic paroxysmal AF from December 2007 to February 2009 were consecutively included in our study. All patients signed an informed consent prior to the procedure. A total of 133 individuals (105 males) were included. Forty-six patients (36 males) underwent CBA (Arctic Front, Cryocath, Medtronic) and 87 (69 males) point-by-point RF ablation guided by electroanatomical mapping (Carto, Biosense Webster, Diamond Bar, CA, USA). Inclusion criteria were based on the frequent occurrence of recurrent episodes of AF, self-terminating within 7 days, and developing in spite of treatment with at least two antiarrhythmic drugs. Oral anticoagulation was stopped 5 days prior to ablation and replaced with low-molecular-weight heparin according to patients' weight. To exclude the presence of thrombi in the left atrial appendage, all patients underwent 2D transoesophageal echocardiography (TEE) the day before the procedure, along with a transthoracic examination (TTE) enabling the assessment of the left atrium (LA) dimensions, left ventricular and valvular functions, and the presence or absence of pre-procedural PE. All patients underwent a 2D TTE within 24 h after the procedure as routinely performed in our centre.

Cryothermal energy balloon ablation was performed under general anaesthesia. In all patients, a 6 F pigtail catheter was positioned in the aortic root via a left femoral approach, to monitor arterial pressure and to assess the position of the aorta. A 6 F quadripolar catheter was inserted in the right jugular vein and advanced into the coronary sinus. A single transseptal puncture was then performed under TEE and fluoroscopic guidance, using the right femoral venous approach. After gaining left atrial access, a 70 UI/kg heparin iv bolus was given. A 0.32 F Emerald exchange wire (Cordis, Johnson & Johnson, Diamond Bar, CA, USA) was advanced in the left superior PV, and a steerable 15 F over-the-wire sheath (FlexCath, Cryocath) was positioned in the LA. A circular mapping catheter (Lasso, Biosense Webster, Inc., Diamond Bar, CA, USA) was then advanced in each PV ostium to obtain baseline electrical information of the PVs. After withdrawing the mapping catheter, a 28 mm double-walled cryoballoon (Arctic Front, Cryocath, Medtronic) was advanced over the wire up to the LA, inflated, and positioned in the PV ostium of each vein. Optimal vessel occlusion was considered to have been achieved when selective contrast injection showed total contrast retention with no flow into the atrium. For each vein, CBA consisted of a minimum of two applications lasting for 5 min each. Whenever possible, we tried to engage two different branches of the same vein and to orient the balloon differently, in the attempt of covering a wider ostial surface. However, if successful occlusion could only be obtained in one branch, both applications were delivered by leaving the guide-wire in the same branch. Usually, the left superior pulmonary vein was treated first, followed by the left inferior, right superior (RSPV), and right inferior. In order to avoid phrenic nerve palsy, a complication observed during RSPV ablation with the cryoballoon, a quadripolar catheter was inserted in the superior vena cava, and diaphragmatic stimulation was achieved by pacing the ipsilateral phrenic nerve with a 1000 ms cycle and a 12 mA output. The reason of pacing at such a slow rate was to prevent catheter displacement, due to diaphragmatic contraction, in the early phases of application. During the whole procedure, activated clotting time (ACT) was maintained strictly between 250 and 300 s by supplementing heparin infusion, as required.

Radiofrequency ablation was performed also under general anaesthesia. A double-transseptal puncture was performed under TEE and fluoroscopic guidance using anatomical landmarks as described earlier. After having achieved an electroanatomical map of the LA with the Carto system (Biosense Webster, Inc.) in all patients, RF ablation was performed with an open irrigated cool tip 3.5 mm catheter (Navistar, Biosense Webster, Inc.). Circumferential lines around each PV were created at a distance >5 mm from the venous ostium as described previously.[7] Ablation was delivered during the monitoring of electrical activity in the PV ostium by means of a circular mapping catheter (Lasso, Biosense Webster, Inc.). Radiofrequency pulses were applied for a maximum of 60 s outside the ostium with a power limit of 35 W. Power was decreased to 25 W when ablating on the posterior wall in order to avoid oesophageal injury. Ablation was continued at each point until the amplitude of the bipolar electrogram was reduced by 80% or decreased below 0.2 mV. No additional ablation lines were performed. The procedure was stopped when circumferential lines were completed, and PV isolation could be demonstrated within each vein. During the whole procedure, ACT was strictly maintained between 250 and 300 s by supplementing heparin infusion, as required. Post-ablation anticoagulation management was identical regardless of the technique utilized. Low-molecular-weight heparin was started from the evening following the procedure. Oral anticoagulation was started within 1 week from the ablation. When the INR values reached the therapeutic interval, low-molecular-weight heparin was stopped, and only oral anticoagulation was continued.

All examinations were analysed by two experienced operators. As mentioned previously, a 2D TTE was performed in all patients the day before and within 24 h after ablation. Pericardial effusion was measured in the parasternal long-axis and the apical four-chamber views. We defined PE following the current guidelines[8] as mild <10 mm, moderate >10 mm posteriorly, large >20 mm all in diastole and pericardial tamponade >20 mm with haemodynamic compromise.

Data are expressed as mean and standard deviations. Comparisons between groups were performed by using the Mann–Whitney *U* test (if one group had <30 patients) and Student's *t*-test for the continuous variables and the Fisher's exact test for the categorical variables. Multivariate analysis was performed with logistic regression. All *P*-values were two-tailed. A value of $P < 0.05$ was considered significant. Statistical analysis was done using SPSS (version 17.01, SPSS Inc., Chicago, IL, USA).

Results

Baseline population characteristics are shown in *Table 1*. No significant differences were observed in baseline parameters between the two groups. No patient exhibited PE at the pre-procedural 2D TTE. Mean RF energy application time in patients undergoing circumferential RF PV isolation was 33 ± 4 min

Table 1 Baseline characteristics of the cryothermal energy balloon ablation and the radiofrequency ablation groups

	Cryoballoon group (46 patients)	RF ablation group (87 patients)	*P*-value
Age (years)	56 ± 11	56 ± 9	0.924
Female (%)	22	21	1
EF (%)	64 ± 6	64 ± 6	0.988
La D (mm)	41 ± 5	42 ± 5	0.544
Arterial hypertension (%)	24	23	1
CAD (%)	8.6	4.5	0.447
AF (years)	3.3 ± 1.9	3.2 ± 1.7	0.673
Procedural time (min)	168 ± 30	188 ± 28	<0.001

All values are expressed as mean ± SD or percentage. AF, atrial fibrillation; CAD, coronary artery disease; EF, left ventricular ejection fraction; La D, left atrial antero-posterior diameter.

Table 2 Post-procedural pericardial effusion in the cryothermal energy balloon ablation and in the radiofrequency ablation groups

	CBA (46 patients)	RF ablation (87 patients)	*P*-value
PE (%)	5 (11%)	14 (16%)	0.623
Mild	4	12	
Moderate	0	1	
Large	0	0	
Tamponade	1	1	

All values are expressed as numbers and/or percentage. CBA, cryothermal energy balloon ablation; PE, pericardial effusion; RF, radiofrequency.

($P > 0.05$). Mean freezing time in the group of patients undergone CBA was 40 ± 7 min ($P > 0.05$). Note that the mean procedural time proved to be significantly shorter if ablation was performed with CBA ($P < 0.001$).

Pericardial effusion was detected in 19 (14.2%) of 133 patients. Sixteen patients presented mild effusion, one moderate effusion, and two pericardial tamponades. Mild PE was detected in the posterior region most of the time (80%); the only moderate PE was documented in the antero-apical region. Importantly, there was no significant difference in the incidence of PE between the CBA and the RF groups (*Table 2*). No patients had a prolonged hospitalization stay because of mild PE. Additionally, patients with mild PE received no invasive treatment and did not develop any symptom related to PE at any time. Pericardial effusion completely disappeared at a control 2D TTE at an average 3 ± 1 months. The patient exhibiting moderate effusion (RF group) in the antero-apical region (12 mm) was discharged after 2 additional observational hospitalization days without complications. Echocardiographic follow-up showed complete disappearance of PE after 6 months in this patient. Haemodynamic compromise during the two pericardial tamponades was readily reversed by subxifoidal puncture. Tamponades, one patient in each group, were related to transseptal puncture. Both patients required 4 adjunctive hospitalization days.

When comparing patients presenting PE with patients not exhibiting this finding in our population, at both the univariate and multivariate analyses, procedural time ($P = 0.044$), arterial hypertension ($P = 0.002$), and coronary artery disease (CAD)($P = 0.066$) were significant predictors of PE. Left ventricular ejection fraction (EF) was found to be significantly lower in patients presenting PE at the univariate analysis alone (*Table 3*).

Table 4 shows possible predictors of PE in the CBA group. At the univariate analysis, age was the only parameter found to be significantly higher in patients with PE ($P = 0.02$). Additionally, arterial hypertension and CAD were more frequent in patients with PE, but the differences were not significant ($P = 0.085$ and $P = 0.057$, respectively). Freezing times in the PE group was longer but not statistically significant ($P = 0.360$). Finally, multivariate analysis showed no variables significantly associated with PE in patients treated with CBA.

Univariate analysis of the baseline characteristics of the patients who underwent ablation with RF is shown in *Table 5*. Procedural time ($P = 0.008$), arterial hypertension ($P = 0.016$), and CAD ($P = 0.013$) were significantly correlated with PE in this group. Surprisingly, RF application times were not correlated with post-procedural PE ($P = 0.250$). However, with multivariate analysis, only arterial hypertension ($P = 0.019$) and CAD ($P = 0.023$) were found to be independent predictors of PE in this group.

Three patients experienced phrenic nerve palsy during CBA energy delivery in the RSPV with total recovery of diaphragmatic contraction before the end of the procedure (recovery time 20 ± 9 min). No cerebrovascular accident occurred during or after any procedure. An arterovenous fistula which required vascular intervention and a 2-day prolongation of hospitalization stay occurred in one patient of the RF group.

Discussion

In our population, PE was found in ~14% of patients after AF ablation. This finding is comparable with a previously published report in the literature.[6] However, these reports concerned procedures all performed with RF. The present study is the first to describe the incidence and outcome of PE following CBA in comparison with conventional circumferential PV isolation with a focal RF catheter. Although the incidence of PE reported in both our observation and in the article by Schaer *et al.*[6] might appear higher than in other reports, we believe that this might, in part, be due to the fact that the echocardiographists were not blinded to the aim of the study.

In our study, the incidence of PE after AF ablation with either technique was comparable. Various factors might explain this finding. First, extensive lesions in the LA during AF ablation may play a central role in creating PE. In our study, all cryoballoon procedures were performed with the larger diameter (28 mm)

Table 3 Clinical and procedural predictors of post-procedural pericardial effusion

	PE (19 patients)	No PE (114 patients)	*P*-value	Multivariate *P*-value
Age (years)	59 ± 10	55 ± 9	0.181	0.750
Female (%)	32	19	0.240	0.390
Procedural time (min)	197 ± 31	179 ± 29	0.006	0.044
La D (mm)	41 ± 5	42 ± 5	0.473	0.436
EF (%)	60 ± 7	64 ± 6	0.016	0.057
Arterial hypertension (%)	53	19	0.003	0.002
CAD (%)	26	3	0.002	0.006

All values are expressed as mean ± SD or percentage. CAD, coronary artery disease; EF, ejection fraction; La D, left atrial dimension; PE, pericardial effusion.

Table 4 Baseline characteristics of patients undergone cryothermal energy balloon ablation according to the presence or absence of post-procedural pericardial effusion

	CBA (PE) (5 patients)	CBA (no PE) (41 patients)	*P*-value	Multivariate *P*-value
Age (years)	67 ± 10	55 ± 10	0.02	0.189
Female (%)	20	22	1	0.655
Procedural time (min)	174 ± 41	167 ± 29	0.515	0.316
La D (mm)	43 ± 6	41 ± 5	0.515	0.643
EF (%)	60 ± 5	64 ± 7	0.073	0.238
Arterial hypertension (%)	60	20	0.085	0.130
CAD (%)	40	5	0.057	0.379
Freezing time (min)	42 ± 4	37 ± 13	0.360	0.878

All values are expressed as mean ± SD or percentage. CAD, coronary artery disease; EF, ejection fraction; La D, left atrial dimension; PE, pericardial effusion.

Table 5 Baseline characteristics of patients undergone radiofrequency ablation according to the presence or absence of post-procedural pericardial effusion

	RF ablation (PE) 14 patients	RF ablation (no PE) 73 patients	*P*-value	Multivariate *P*-value
Age (years)	56 ± 9	56 ± 9	0.842	0.296
Female (%)	36	18	0.158	0.199
Procedural time (min)	206 ± 23	185 ± 28	0.008	0.421
La D (mm)	41 ± 4	42 ± 5	0.166	0.602
EF (%)	60 ± 8	64 ± 5	0.095	0.120
Arterial hypertension (%)	50	18	0.016	0.019
CAD (%)	21	1	0.013	0.023
RF time (min)	34 ± 5	32 ± 5	0.250	0.403

All values are expressed as mean ± SD or percentage. CAD, coronary artery disease; EF, ejection fraction; La D, left atrial dimension; PE, pericardial effusion; RF, radiofrequency.

balloon. Recent data report that this larger balloon targets a greater portion of the atrium, thus creating extensive lesions similar to wide RF circumferential PV isolation.[9,10] Additionally, PE might be an expression of lesion depth. Although demonstrated with RF, various experimental studies have shown that transmurality during cryoablation is rather difficult to achieve.[11–13] However, these observations were conducted on focal tip cryocatheters. Recent data report an incidence of 17% of oesophageal ulcerations in a series of patients undergoing AF ablation with CBA.[14] Although no fistula was observed and all ulcerations healed at control examinations, this might be a proof that the cryoballoon can achieve deep lesions. If this is the case, PE may also be a marker of transmurality of the lesion. Finally, although microperforations of the LA wall are probably more related to RF than cryoablative energy, irritative or traumatic phenomena during catheter manipulation with a great calibre sheath (15 F) in the LA might also be held into consideration as a possible cause of PE when performing AF ablation with CBA.

Among the variables analysed in the entire study population, arterial hypertension, CAD, and procedural time predicted the occurrence of PE on multivariate analysis. Coronary artery disease has already been shown to be a significant predictor of PE in a multicentre study conducted on a large cohort of patients following AF ablation.[15] Interestingly, in the subgroup analysis, neither total RF energy application time nor total freezing time was a predictor of PE. Larger studies are needed to confirm the association of arterial hypertension and longer procedural time with effusion.

The major clinical implication of our study is that, regardless of the technique used, PE following AF ablation is mainly mild and has mostly benign clinical outcome. Furthermore, in our study, when PE was diagnosed in the complete absence of symptoms, the post-procedural anticoagulation protocol was not modified. This might raise the question on the real utility of a systematic post-ablation echocardiographical examination, especially in asymptomatic patients.

Limitations

This is a single-centre non-randomized study, hence results may not be generalized. Subgroup analysis has to be interpreted with caution due to the relatively small number of patients. Furthermore, due to the fact that both echocardiographists were not blinded to the aim of the study, the percentage of PE reported in our study might very probably have been overestimated.

Conclusions

Pericardial effusion following AF ablation is relatively common and occurs in similar proportion after RF and CBA. Pericardial effusion is benign and usually asymptomatic, not requiring additional hospitalization days. Thus, TTE after AF ablation might not be mandatory in asymptomatic patients, especially in shorter lasting procedures and in patients not affected by CAD or arterial hypertension.

Conflict of interest: none declared.

References

1. Haisseguerre M, Jais P, Shah D, Takahashi A, Hocini M, Quiniou G *et al.* Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998;**339**:659–66.
2. Chen YJ, Chen SA. Electrophysiology of the pulmonary veins. *J Cardiovasc Electrophysiol* 2006;**17**:1080–5.
3. Jais P, Sanders P, Hsu LF, Hocini M, Haissaguerre M. Catheter ablation for atrial fibrillation. *Heart* 2005;**91**:51–7.
4. Klein G, Oswald H, Gardiwal A, Lüsebrink U, Lissel C, Yu H *et al.* Efficacy of pulmonary vein isolation by cryoballoon ablation in patients with paroxysmal atrial fibrillation. *Heart Rhythm* 2008;**5**:802–6. Published online ahead of print 16 February 2008.
5. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J *et al.* Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation* 2005;**111**:1100–5. Published online ahead of print 21 February 2005.
6. Schaer BA, Maurer A, Sticherling C, Buser PT, Osswald S. Routine echocardiography after radiofrequency ablation: to flog a dead horse? *Europace* 2009;**11**:155–7.
7. Pappone C, Rosanio S, Oreto G, Tocchi M, Gugliotta F, Vicedomini G *et al.* Circumferential radiofrequency ablation of pulmonary vein ostia: a new anatomic approach for curing atrial fibrillation. *Circulation* 2000;**102**:2619–28.
8. Blomstrom-Lundqvist C, Scheinman MM, Aliot E, Alpert JS, Calkins H, Camm AJ *et al.* ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for practice guidelines (writing committee to develop guidelines for the management of patients with supraventricular arrhythmias) developed in collaboration with NASPE-Heart Rhythm Society. *J Am Coll Cardiol* 2003;**42**:1493–531.
9. Van Belle Y, Knops P, Janse P, Rivero-Ayerza M, Jessurun E, Szili-Torok T *et al.* Electro-anatomical mapping of the left atrium before and after cryothermal balloon isolation of the pulmonary veins. *J Interv Card Electrophysiol* 2009;**25**:59–65. Published online ahead of print 16 January 2009.
10. Klein G, Gardiwal A, Oswald H. Catheter based cryoablation of atrial fibrillation: state of the art. (Review). *Minerva Cardioangiol* 2008;**56**:623–33.
11. Lustgarten DL, Bell S, Hardin N, Calame J, Spector PS. Safety and efficacy of epicardial cryoablation in a canine model. *Heart Rhythm* 2005;**2**:91–2.
12. Reek S, Geller JC, Schildhaus HU, Ripley KL, Klein HU. Feasibility of catheter cryoablation in normal ventricular myocardium and healed myocardial infarction. *Pacing Clin Electrophysiol* 2004;**27**:1530–9.
13. Kettering K, Al-Ghobainy R, Wehrmann M, Vonthein R, Mewis C. Atrial linear lesions: feasibility using cryoablation. *Pacing Clin Electrophysiol* 2006;**29**:283–9.
14. Ahmed H, Neuzil P, d'Avila A, Cha YM, Laragy M, Mares K *et al.* The esophageal effects of cryoenergy during cryoablation for atrial fibrillation. *Heart Rhythm* 2009;**6**:962–9.
15. Bertaglia E, Zoppo F, Tondo C, Colella A, Mantovan R, Senatore G *et al.* Early complications of pulmonary vein catheter ablation for atrial fibrillation: a multicenter prospective registry on procedural safety. *Hearth Rhythm* 2007;**4**:1265–71.