“Εμμένουσα Κολπική Μαρμαρυγή. Ο ρόλος της Κρυοκατάλυσης”

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Ιατρικό Κέντρο Αθηνών
Illustration of Possible Mechanisms

LA
Wood (substrate)

PV
Lighter (trigger)
AF is a progressive disease$^{1–5}$


- Stroke and mortality rate
- Comorbidity prevalence
  - Degree of atrial structural remodelling
- Left atrium size

**Risk of progression to persistent/permanent AF increases in presence of specific risk factors**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Score rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>+1</td>
</tr>
<tr>
<td>Age (≥ 75 years)</td>
<td>+1</td>
</tr>
<tr>
<td>TIA or stroke</td>
<td>+2</td>
</tr>
<tr>
<td>COPD</td>
<td>+1</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+2</td>
</tr>
<tr>
<td><strong>Maximum score</strong></td>
<td><strong>7</strong></td>
</tr>
</tbody>
</table>

Time

First diagnosis → Paroxysmal → Persistent → LS Persistent → Permanent

HATCH rule:
- Hypertension: +1
- Age (≥ 75 years): +1
- TIA or stroke: +2
- COPD: +1
- Heart failure: +2

Maximum score: 7
Relative contribution of different ablation targets in the AF disease continuum

<table>
<thead>
<tr>
<th></th>
<th>Paroxysmal</th>
<th>Persistent</th>
<th>Long-standing persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV Triggers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-PV Triggers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substrate?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-PV Triggers</td>
<td></td>
<td></td>
<td></td>
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<td>Non-PV Triggers</td>
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<td></td>
</tr>
<tr>
<td>Substrate?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PV Triggers</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Realistic goal

Treatment of AF as an arrhythmia?
Treatment of AF as a disease?
Therapy of the arrhythmia, not the disease
B. Indications for catheter atrial fibrillation ablation in populations of patients not well represented in clinical trials

Congestive heart failure
It is reasonable to use similar indications for AF ablation in selected patients with heart failure as in patients without heart failure. Ila B-R

Older patients (> 75 years of age)
It is reasonable to use similar indications for AF ablation in selected older patients with AF as in younger patients. Ila B-NR

Hypertrophic cardiomyopathy
It is reasonable to use similar indications for AF ablation in selected patients with HCM as in patients without HCM. Ila B-NR

Young patients (< 45 years of age)
It is reasonable to use similar indications for AF ablation in young patients with AF (< 45 years of age) as in older patients. Ila B-NR

Tachy-brady syndrome
It is reasonable to offer AF ablation as an alternative to pacemaker implantation in patients with tachy-brady syndrome. Ila B-NR

Athletes with AF
It is reasonable to offer high-level athletes AF as first-line therapy due to the negative effects of medications on athletic performance. Ila C-LD

Asymptomatic AF**
Paroxysmal: Catheter ablation may be considered in select patients. IIb C-EO
Persistent: Catheter ablation may be considered in select patients. IIb C-EO
CASTLE-AF first trial to report positive impact of CA on hard endpoints in patients with HF

- HF patients are considered separately in guidelines because it is recognised that CA can be demanding in these patients.\(^1\)
- The evidence from CASTLE-AF should be interpreted with caution because there are some limitations in the study, including open-label design, number of patients screened for eligibility and number lost to follow-up.

CASTLE-AF study characteristics\(^2\)

<table>
<thead>
<tr>
<th>Design:</th>
<th>Randomised, multicentre, open-label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients:</td>
<td>N=363</td>
</tr>
<tr>
<td>AF type:</td>
<td>Symptomatic paroxysmal or persistent AF with unacceptable side effects or unwillingness to take ADT, NYHA class II, III, or IV HF and a LVEF of 35% or less</td>
</tr>
<tr>
<td>Interventions:</td>
<td>CA (PVI) vs medical therapy (rate or rhythm control)</td>
</tr>
<tr>
<td>Median follow-up:</td>
<td>37.8 months</td>
</tr>
<tr>
<td>Primary endpoint:</td>
<td>Composite of death from any cause or worsening of HF that led to unplanned overnight hospitalisation</td>
</tr>
</tbody>
</table>

Proportion of patients experiencing an event in the ablation vs medical treatment group (N=363)\(^2\)

<table>
<thead>
<tr>
<th></th>
<th>Proportion of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite endpoint</td>
<td>n=51 28.5</td>
</tr>
<tr>
<td>Death any cause</td>
<td>n=46 13.4</td>
</tr>
</tbody>
</table>

HR: 0.62; 95% CI: 0.43, 0.87; P=0.007
HR: 0.53, 95% CI: 0.32, 0.86; P=0.004

Therapy of the consequences of the disease

Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

![Graph showing the probability of survival with ablation and medical therapy over months of follow-up. The graph indicates a significant reduction in death from any cause with ablation treatment. The hazard ratio for ablation is 0.53 (95% CI, 0.32–0.86) with P=0.01 by Cox regression and P=0.009 by log-rank test.

- Ablation, not the successful one
- Therapy of the consequences of the disease
Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest (Per Protocol))

Ablation vs. Drug
Hazard ratio: 0.73 (95% CI, 0.54–0.99)
P=0.046

-27%

-40% mortality

Ablation, not the successful one

Therapy of the consequences of the disease
Which benefits more from AF ablation?

**More benefit**
- Increased burden of AF
- Cardiac function deteriorated by AF
- Increased risk of stroke

**Higher success rate**
- Lone AF
- Paroxysmal AF
- Younger age
- Controlled risk factors
- Favorable cardiac structure
ABSTRACT: Our understanding of the risk factors and complications of atrial fibrillation (AF) is based mostly on studies that have evaluated AF in a binary fashion (present or absent) and have not investigated AF burden. This scientific statement discusses the published literature and knowledge gaps related to methods of defining and measuring AF burden, the relationship of AF burden to cardiovascular and neurological outcomes, and the effect of lifestyle and risk factor modification on AF burden. Many studies examine outcomes by AF burden classified by AF type (paroxysmal versus nonparoxysmal); however, quantitatively, AF burden can be defined by longest duration, number of AF episodes during a monitoring period, and the proportion of time an individual is in AF during a monitoring period (expressed as a percentage). Current guidelines make identical recommendations for anticoagulation regardless of AF pattern or burden; however, a review of recent evidence suggests that higher AF burden is associated with higher risk of stroke. It is unclear whether the risk increases continuously or whether a threshold exists; if a threshold exists, it has not been defined. Higher burden of AF is also associated with higher prevalence and incidence of heart failure and higher risk of mortality, but not necessarily lower quality of life. A structured and comprehensive risk factor management program targeting risk factors, weight loss, and maintenance of a healthy weight appears to be effective in reducing AF burden. Despite this growing understanding of AF burden, research is needed into validation of definitions and measures of AF burden, determination of the threshold of AF burden that results in an increased risk of stroke that warrants anticoagulation, and discovery of the mechanisms underlying the weak temporal correlations of AF and stroke. Moreover, developments in monitoring technologies will likely change the landscape of long-term AF monitoring and could allow better definition of the significance of changes in AF burden over time.
Ablation in persistent atrial fibrillation

1. When to do it
2. How to do it
3. What do the studies tell us
4. What is the role of cryoablation
Ablation is more effective earlier

- Delays in catheter ablation procedure are associated with increased rates of adverse outcomes.
- Adverse long-term outcomes correlate with increasing time between 1st diagnosis and ablation.
- In a separate retrospective study, multiple drug failures were associated with higher recurrence rates, suggesting that earlier intervention may be more effective.
- Delays in treatment with catheter ablation negatively impact on success rates and patient outcomes.

Conclusions—In patients with PersAF undergoing ablation, the time interval between the first diagnosis of PersAF and the catheter ablation procedure had a strong association with the ablation outcomes, such as shorter diagnosis-to-ablation times were associated with better outcomes and in direct association with markers of atrial remodeling. *(Circ Arrhythm Electrophysiol. 2016;9:e003669. DOI: 10.1161/CIRCEP.115.003669.)*
Ablation in persistent atrial fibrillation

1. When to do it
2. How to do it
3. What do the studies tell us
4. What is the role of cryoablation
PV Antrum isolation is necessary for persistent AF ablation, but is it sufficient? Should we do more?

Lines?

Scars?

Rotors?

CAFE?

Autonomic Ganglia?

LA Appendage?

Non PV Triggers?
Persistent AF Ablation: My Personal Thoughts

- Complex fractionated electrograms
- Rotor
- Linear ablations

Superficial EP phenomenon

Empirical

Am J Cardiology 1996; 77:10A-23A;
Targeting substrate
Targeting substrate
Ablation in persistent atrial fibrillation

1. When to do it
2. How to do it
3. What do the studies tell us
4. What is the role of cryoablation
Randomized Ablation Strategies for the Treatment of Persistent Atrial Fibrillation

RASTA Study

Sanjay Dixit, MD; Francis E. Marchlinski, MD; David Lin, MD; David J. Callans, MD; Rupa Bala, MD; Michael P. Riley, MD, PhD; Fermin C. Garcia, MD; Mathew D. Hutchinson, MD; Sarah J. Ratcliffe, PhD; Joshua M. Cooper, MD; Ralph J. Verdiino, MD; Vickas V. Patel, MD, PhD; Erica S. Zado, PA; Nancy R. Cash, PA; Tony Killian, RN, CCRC; Todd T. Tomson, MD; Edward P. Gerstenfeld, MD

Background—The single-procedure efficacy of pulmonary vein isolation (PVI) is less than optimal in patients with persistent atrial fibrillation (AF). Adjunctive techniques have been developed to enhance single-procedure efficacy in these patients. We conducted a study to compare 3 ablation strategies in patients with persistent AF.

Methods and Results—Subjects were randomized as follows: arm 1, PVI + ablation of non-PV triggers identified using a stimulation protocol (standard approach); arm 2, standard approach + empirical ablation at common non-PV AF trigger sites (mitral annulus, fossa ovalis, eustachian ridge, crista terminalis, and superior vena cava); or arm 3, standard approach + ablation of left atrial complex fractionated electrogram sites. Patients were seen at 6 weeks, 6 months, and 1 year; transtelephonic monitoring was performed at each visit. Antiarrhythmic drugs were discontinued at 3 to 6 months. The primary study end point was freedom from atrial arrhythmias off antiarrhythmic drugs at 1 year after a single-ablation procedure. A total of 156 patients (aged 59±9 years; 136 males; AF duration, 47±50 months) participated (arm 1, 55 patients; arm 2, 50 patients; arm 3, 51 patients). Procedural outcomes (procedure, fluoroscopy, and PVI times) were comparable between the 3 arms. More lesions were required to target non-PV trigger sites than a complex fractionated electrogram (33±9 versus 22±9; P<0.001). The primary end point was achieved in 71 patients and was worse in arm 3 (29%) compared with arm 1 (49%; P=0.04) and arm 2 (58%; P=0.004).

Conclusions—These data suggest that additional substrate modification beyond PVI does not improve single-procedure efficacy in patients with persistent AF.
Biatrial linear ablation in sustained nonpermanent AF: Results of the substrate modification with ablation and antiarrhythmic drugs in nonpermanent atrial fibrillation (SMAN-PAF) trial

Gareth J. Wynn, MB ChB, MRCP, MD(Res),*,†† Sandeep Panikker, MBBS, MRCP,*,†† Maureen Morgan, RN,*,† Mark Hall, MD, FRCP,*,† Johan Waktare, MD, FRCP,*,† Vias Markides, MD, FRCP,*,†† Wajid Hussain, MB ChB, MRCP,*,†† Tushar Salukhe, MD(Res), MRCP,*,†† Simon Modi, MBBS, MRCP,*,† Julian Jarman, MA, MBBS, MRCP, MD(Res),*,†† David G. Jones, MBBS, MD,*,†† Richard Snowdon, MD, MRCP,*,† Derick Todd, MD, FRCP,*,†† Tom Wong, MD, FRCP,*,†† Dhiraj Gupta, MD, FRCP*††

BACKGROUND More advanced atrial fibrillation (AF) is associated with lower success rates after pulmonary vein isolation (PVI), and the optimal ablation strategy is uncertain.

OBJECTIVES To assess the impact of additional linear ablation (lines) compared to PVI alone.

METHODS In this multicenter randomized controlled trial, 122 patients (mean age 61.9 ± 10.5 years; left atrial diameter 43 ± 6 mm) with persistent AF (PeAF) or sustained (> 12 hours) paroxysmal AF (SusPAF) with risk factors for atrial substrate were included and followed up for 12 months. Patients were randomized to PVI-only or PVI + lines (left atrial roof line, mitral isthmus line, and tricuspid isthmus line) group. Holter monitoring was performed at 3, 6, and 12 months and according to symptoms. The primary outcome was atrial tachyarrhythmia recurrence lasting ≥ 30 seconds.

RESULTS Baseline characteristics were comparable between groups; 61% had PeAF and 39% SusPAF. Successful PVI was achieved for 98% of pulmonary veins, and bidirectional block was obtained in 90% of lines. The primary end point occurred in 38% of the PVI + lines group and 32% of the PVI-only group (P = .50), which was consistent in both PeAF (36% vs 28%; P = .45) and SusPAF (42% vs 39%; P = .86). Compared with the PVI-only group, the PVI + lines group had higher procedure duration (209 ± 52 minutes vs 172 ± 44 minutes; P < .001), ablation time (4352 ± 1084 seconds vs 2503 ± 1061 seconds; P < .001), and radiation exposure (Dose-area product 3992 ± 6496 Gy · cm² vs 2106 ± 1679 Gy · cm²; P = .03). Quality of life (disease-specific Atrial Fibrillation Effect on Quality of Life questionnaire and mental component scale of the Short Form 36 Health Survey) improved significantly during the study but did not differ between groups.

CONCLUSION Adding lines to wide antral PVI in substrate-based AF requires significantly more ablation, increases procedure duration and radiation dose, but provides no additional clinical benefit.

KEYWORDS Atrial Fibrillation; Ablation; Clinical trial; Persistent atrial fibrillation; Atrial substrate; Outcomes; Quality of life

ABBREVIATIONS AAD = antiarrhythmic drug; AF = atrial fibrillation; AFEQT = Atrial Fibrillation Effect on Quality of Life; AT = atrial tachycardia; CI = confidence interval; CTI = cavotricuspid isthmus; ITT = intention-to-treat; OR = odds ratio; PAF = paroxysmal atrial fibrillation; PeAF = persistent atrial fibrillation; PV = pulmonary vein; PVI = pulmonary vein isolation; RCT = randomized controlled trial; SusPAF = sustained paroxysmal atrial fibrillation; WACA = wide area circumferential ablation

(Heart Rhythm 2016;13:399–406) © 2016 Heart Rhythm Society. All rights reserved.
Beyond PVI: no value of extra lesions

**STAR AF 2 trial: Persist AF pts**
- PVI
- PVI + linear
- PVI + CFE

- Most AF recurrences after PVI associated with PV reconnection

Verma A, NEJM 2015
Surgical Ablation of Atrial Fibrillation during Mitral-Valve Surgery

Figure 1. Freedom from Atrial Fibrillation.
Freedom from atrial fibrillation was defined as the absence of the condition at both 6 months and 12 months, as assessed by means of 3-day Holter monitoring. MVS denotes mitral-valve surgery, and PVI pulmonary-vein isolation.
Left Atrial Appendage Isolation in Patients With Longstanding Persistent AF
BELIEF Trial – Randomized Study

Lesion Set

Freedom from Recurrence

LAA ablation better (*p* = 0.001)

PVI only strategy has not been evaluated!

### 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on AF ablation

#### Survey of the writing group members

**Query:** Do you routinely use adjunctive strategies in addition to PVI during persistent AF ablation?

<table>
<thead>
<tr>
<th>Technique</th>
<th>Initial Ablation</th>
<th>Redo Ablation</th>
<th>Class</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear lesions</td>
<td>25%</td>
<td>45%</td>
<td>IIb</td>
<td>B-NR</td>
</tr>
<tr>
<td>CFAE</td>
<td>10%</td>
<td>26%</td>
<td>IIb</td>
<td>B-R</td>
</tr>
<tr>
<td>Non-PV triggers</td>
<td>35%</td>
<td>46%</td>
<td>IIby</td>
<td>C-LD</td>
</tr>
<tr>
<td>LAA ablation</td>
<td>9%</td>
<td>11%</td>
<td>IIb</td>
<td>B-R</td>
</tr>
<tr>
<td>Posterior wall ablation</td>
<td>22%</td>
<td>38%</td>
<td>IIb</td>
<td>B-R</td>
</tr>
<tr>
<td>Rotational activity</td>
<td>7%</td>
<td>9%</td>
<td>IIb</td>
<td>B-NR</td>
</tr>
<tr>
<td>Autonomic ganglia</td>
<td>7%</td>
<td>7%</td>
<td>IIb</td>
<td>B-NR</td>
</tr>
<tr>
<td>Dominant frequency</td>
<td>2%</td>
<td>2%</td>
<td>IIb</td>
<td>C-LD</td>
</tr>
<tr>
<td>Scar ablation (MRI;EAM)</td>
<td>15%</td>
<td>22%</td>
<td>IIb</td>
<td>B-R</td>
</tr>
</tbody>
</table>

*Heart Rhythm, Vol 14, No 10, October 2017*
Ablation in persistent atrial fibrillation

1. When to do it
2. How to do it
3. What do the studies tell us
4. What is the role of cryoablation
The 28mm Cryoballoon Creates Wide Circumferential Antrally Located Lesions

*Post Procedure Voltage Maps*

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>4</td>
<td>43</td>
</tr>
<tr>
<td>Balloon and Application Time</td>
<td>CB1 28 mm, 5 min</td>
<td>CB2 28 mm, 3 min</td>
</tr>
<tr>
<td>Extent of posterior wall ablation</td>
<td>40%</td>
<td>73%</td>
</tr>
<tr>
<td>6 month Freedom from AF</td>
<td>75%</td>
<td>95%</td>
</tr>
</tbody>
</table>

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31
Arctic Front Advance is Significantly More Effective vs Arctic Front in PAF Patients at 12 month FU

Single Procedure Freedom From AF

Arctic Front Cryoballoon
Arctic Front Advance Cryoballoon
Good Efficacy of PVI Alone for Persistent AF: Systematic Review and Meta-Analysis

Single-procedure 12-month arrhythmia-free survival

Fourteen studies of 956 patients

Contemporary technologies

RF with 3-D mapping or Cryoballoon (2nd generation)

RF 45% of patients
Cryo 55% of patients

Reasonable outcomes!

Overall Success 66.7%

Voskoboinik et al Heart Rhythm 2017;14:661–667
Single-Procedure Outcomes and Quality-of-Life Improvement 12 Months Post-Cryoballoon Ablation in Persistent Atrial Fibrillation

Results From the Multicenter CRYO4PERSISTENT AF Trial

Serge Boveda, MD, Andreas Metzner, MD, Dinh Q. Nguyen, MD, K.R. Julian Chun, MD, Konrad Goehl, MD, George Noellker, MD, Jean-Claude Deharo, MD, George Andrikopoulos, MD, Tillman Dahme, MD, Nicolas Lellouche, MD, Pascal Defaye, MD

(JACC Electrophysiology in press 2018)

**Conclusions** Cryoballoon ablation for treatment of PerAF demonstrated 61% single-procedure success at 12 months post-ablation in addition to significant reduction in arrhythmia-related symptoms and improved quality of life. (Cryoballoon Ablation for Early Persistent Atrial Fibrillation [Cryo4 Persistent AF]; NCT02213731) (J Am Coll Cardiol EP 2018;■ ■ ■ ■) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Single PVI-only Procedure Freedom from Persistent AF with Cryoballoon *Single Center Studies at 12 month FU*

Single procedure freedom from persistent AF at 12 month FU

- Lemes et al. (n=49) - 69%
- Ciconte et al. (n=50) - 60%
- Dorwarth et al. (n=243) - 68%
- Koektuerk et al. (n=113) - 62%
- Perrotta et al. (n=21) - 71%

Cryoballoon Advance is significantly faster than Contact Force RF with equivalent outcomes in Persistent AF!

100 consecutive patients with drug-refractory persistent AF (CB-Adv: 50; Contact Force RF: 50).

CB-Adv: PVI only with AFA 28mm with 240sec cryo applications.

Contact Force RF:

- PVI with Thermocool® SmartTouchTM, BSW & Tacticath® Endosense, SJM.
- Contact Force RF target: 10g (max. 50g) with perpendicular vector to the tissue.

<table>
<thead>
<tr>
<th>Procedure duration, minutes</th>
<th>CB-Adv (n = 50)</th>
<th>RFCA (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>90.5 ± 41.7</td>
<td>140.2 ± 46.9</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fluoroscopy duration, minutes</th>
<th>CB-Adv (n = 50)</th>
<th>RFCA (n = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.5 ± 6.6</td>
<td>19.8 ± 6.8</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

Cryoballoon ablation changes the natural history of persistent atrial fibrillation. Pointing sinus rhythm burden as an end-point of success.

**Study population**

64 patients
60.2±9 years
75% males
52% hypertensives
17.2% diabetics)
✓ with symptomatic persistent AF (despite ≥1 antiarrhythmic drug(s) in 91%)
Study protocol

• Wide antral PVI using 28mm second-generation cryoballoon (Arctic Front Advance, Medtronic, Inc, Minneapolis, MN).
• In case of late (>60sec) isolation a second cryoapplication was performed in each pulmonary vein.
• Antiarrhythmics were administered in the first 3 months after ablation and its use extended to 6 months in case of recurrence during the 3-month blanking period.
End-points

Recurrence was defined as a symptomatic or documented arrhythmia episode of >30 seconds excluding a 3-month blanking period.

In patients with AF recurrence, downgrade from persistent to a paroxysmal type of AF was defined in cases with recurrence only of paroxysmal AF episodes not requiring hospitalization or electrical cardioversion.
Mean duration of AF since the first episode was **3.8 years**.
Mean duration of the longest persistent episode was **8 months**.
Mean ejection fraction was **53%** (10 patients with tachycardiomyopathy, 6 after failed cardioversion)
Mean left atrium diameter was **44 mm (38-55)**.
Cavotricuspid isthmus ablation was performed in 6 patients.
Asymptomatic persistent phrenic nerve palsy occurred in 2 of 64 patients while no pericardial effusion was observed.
Study follow-up

- After a mean follow up period of 23.1 months, 45 patients (70.3%) remained free from AF.
- Among the 19 patients with AF recurrence, a downgrade from persistent to a paroxysmal type of AF was present in 10 (15.6%).
- In total, persistent AF recurred only in 9 out of 64 patients (14.1%).

**Conclusion:** Our findings indicated that PVI using the second-generation cryoballoon is associated with a change of the natural history of AF after a follow up period of 2 years.
Future perspective – One-stage Approach for Hybrid Atrial Fibrillation Treatment

**Advantages**

Value-based atrial fibrillation treatment

- Single hospital stay

Communication between EP and surgeon:
  - Confirm endocardially performed conduction block of epicardial ablation lines
  - Guide endocardially/epicardially ablation resting epicardial/endocardially substrates
  - Discuss best isolation of potentially remaining substrates of activity

- Limited tamponade risk
- Reduced phrenic nerve damage

**Disadvantages**

- Restraints on logistic organisation (timing, space)

- Peri-myocyte oedema following epicardial ablation and potentially more difficult assessment for the electrophysiologist
Maze IV Lesion Set

- Left Atrial Appendage
- Coronary Sinus
- Mitral Annulus
- Circumflex Coronary Artery
- SVC
- Right Atrial Appendage
- Right Coronary Artery
- IVC
- Tricuspid Annulus

Legend:
- Bipolar RF Clamp
- Surgical Incision
- Cryo - Endocardial
- Cryo - Epicardial
1. Cryoballoon is **as efficient and safe** as RF for PVI

2. Cryoballoon has a **shorter learning curve** and is **more reproducible** than RF for PVI

3. Cryoballoon is nowadays one of the references, and **sufficient for PVI**

4. But, **persistent AF** ablation remains challenging, with lower success rate... This is not limited to Cryo, but also true for the other techniques (RF, Surgery...)

5. Improvements are expected and necessary in order to better select and **phenotype** the patients (PV or non-PV dependent...)

6. ... And to better identify **non-PV targets** (triggers / substrate...)

7. Meanwhile, for better results, **select the patients**, and... try to ablate **before AF becomes persistent**...