

Cryoballoon ablation for paroxysmal atrial fibrillation: mid-term outcome evaluated by ECG monitoring with an implantable loop recorder

Riccardo Maj MD¹, Sergio De Ceglia MD¹, Elena Piazzì MD¹, Mattia Pozzi MD¹, Elisabetta Montemerlo MD¹, Mirko Casiraghi MD¹, Marianna Fienga¹, Sara Gressoni¹, Giovanni Rovaris MD¹.

1. Cardiovascular Department, San Gerardo Hospital, ASST-Monza, Monza, Italy.

Address for correspondence: Riccardo Maj MD, maj.riccardo@gmail.com, +39/3200879472.

Funding: none.

Disclosures: Dr. Giovanni Rovaris has received compensation for teaching and proctoring purposes from Medtronic and Biotronik. None from the other authors.

BACKGROUND

The success rate after cryoballoon ablation (CB-A) performed for paroxysmal atrial fibrillation

(PAF) might be underestimated by traditional noninvasive monitoring techniques. The purpose of this study was to evaluate the mid-term outcome of CB-A in patients with PAF implanted with an implantable loop recorder (ILR) after the procedure.

METHODS

Between January 2017 and March 2019, all patients who underwent CB-A for PAF and who were subsequently implanted with an ILR were retrospectively included. All devices were equipped with remote monitoring. All ILR-documented atrial tachycardia (AT) or AF episodes ≥ 6 minutes were considered as recurrence; both true and false episodes were collected. A 3-month post-procedural blanking period (BP) was applied.

RESULTS

A total of 102 patients (77 male, mean age 60.6 ± 9.6 years) who underwent pulmonary vein isolation (PVI) by CB-A were included; mean time from first diagnosis of AF to PVI was 51.5 ± 46.9 months. Mean follow-up was 29.3 ± 8.1 months; at 12-month follow-up, the success rate was 64.7%, while at 2-year follow-up, freedom from AT/AF recurrences was achieved in 44.1% of the patients. In the follow-up, a total of 4987 ECG strips were analyzed; true-positive episodes were confirmed in 2026 cases (40.6%), while 2961 episodes (59.4%) were considered false-positive.

CONCLUSION

In patients with PAF implanted with an ILR, CB-A results in freedom from any AT/AF recurrence in 64.7% of patients at 12-month follow-up and in 44.1% of patients when evaluated at 2-year. Careful adjudication of all ILR-documented AF episodes is required to avoid misdiagnosis.

Cryoballoon • Paroxysmal atrial fibrillation • Ablation • Outcome • Implantable Loop Recorder

1) INTRODUCTION

Cryoballoon ablation (CB-A) is an established treatment option for patients with drug-resistant

symptomatic paroxysmal atrial fibrillation (PAF)¹⁻³. In PAF, pulmonary vein isolation (PVI) with cryoballoon results in a 72.83% single-procedure 1-year freedom from recurrent AF⁴. In the STOP-AF trial⁵, after a 3-month blanking period (BP), 69.9% of the cryoballoon patients were free of recurrent AF at 1 year (versus 7.3% in the anti-arrhythmic drug group). Still, in these studies, both symptomatic and asymptomatic recurrences were detected by serial ambulatory electrocardiogram, Holter monitoring and event recorders. On the other hand, implantable loop recorders (ILRs) are known to be valuable tools to improve the detection of AF occurrence after AF ablation⁶. In the recent CIRCA-DOSE study⁷, different catheter ablation technologies (i.e. contact force-guided radiofrequency ablation and second-generation CB-A) were compared in terms of effectiveness of PVI: 346 patients (95% with PAF) were randomized to radiofrequency ablation guided by tissue contact force (CFRF), short 2-minute CB-A duration and standard 4-minute CB-A; after the ablation, arrhythmia recurrences were assessed for 12 months by continuous rhythm monitoring using an ILR. In this study, we determined the mid-term impact of CB-A on AF recurrences in PAF patients by using an ILR.

2) METHODS

2.1 Patient selection

Consecutive patients who underwent CB-A for symptomatic paroxysmal AF in our center from January 2017 to March 2019 who were later implanted with an ILR were retrospectively included in our study. The indication for ILR implantation was to evaluate the effectiveness of the procedure and to quantify accurately the real number of AF episodes after CB-A. Exclusion criteria were persistent AF, prior AF ablation and left ventricle ejection fraction <35%. The study was approved by our local ethics committee and was carried out in accordance with the ethical principles for medical research involving human subjects established by the Declaration of Helsinki.

2.2 CB-A procedure

All procedures were carried out under conscious sedation and with intravenous analgesia. Initially, a 4F radial artery sheath was placed for continuous blood pressure monitoring. Double venous femoral access was achieved and a decapolar catheter was inserted into the coronary sinus (CS), used as a landmark to guide the transeptal puncture (TSP). Then, left atrial (LA) access was achieved by TSP performed under fluoroscopic guidance; before the puncture, the transeptal needle was connected to a pressure transducer, in order to allow the visualization of low pressure (LA waveform) prior to advancing the sheath⁸. After obtaining LA access through a single TSP, a steerable 15 Fr sheath (FlexCath Advance, Medtronic, Minneapolis, USA) was placed in the LA, and selective PVs angiography was performed. Before introducing the CB in the sheath, the inner

lumen mapping catheter (ILMC) was inserted in its lumen. A 28-mm CB (Arctic Front Advance or Artic Front Advance PRO cryoballoon, Medtronic, Minneapolis, USA) was then advanced, inflated and positioned in each PV ostium. Optimal vessel occlusion was considered when selective contrast injection showed total contrast retention; once occlusion was documented, cryoenergy applications were started. Initially, if PVI was obtained within the first-freeze application and time to isolation (TTI) was <40 seconds, then a “short-freeze” protocol was performed (i.e. total ablation time of 180 seconds); if TTI occurred between 40 and 120 seconds, then a 240 seconds application was delivered. In case of TTI achieved > 120 seconds, a bonus-freeze protocol was selected⁹. During ablation, if pulmonary vein potentials (PVP) were visible, time to isolation (TTI) was recorded when PVP completely disappeared or were dissociated from LA activity. Applications order was as follow in all the described procedures: left superior (LSPV), left inferior (LIPV), right inferior (RIPV), and right superior (RSPV) pulmonary veins. To avoid phrenic nerve injury (PNI), standard diaphragmatic stimulation was achieved by high output phrenic nerve pacing (20 mA, 1200 ms) during right PVs ablation. In case of diminished/loss of pacing capture, cryoapplication was immediately stopped¹⁰. During the whole procedure, activated clotting time was maintained over 250 seconds by supplementing with heparin infusion as required.

2.3 ILR for continuous arrhythmia monitoring

Within 3 months from the CB-A, all the patients have been implanted with an ILR over the fourth intercostal space. All devices were equipped with remote monitoring. Patients were asked to send transmissions fortnightly or following any symptom. Every episode of AF or atrial tachycardia (AT) and its corresponding ECG (when available) was collected and analyzed by a single investigator (R.M.), in order to exclude false-positive episodes. For data analysis, both true and false episodes were exported and collected. Because some ILR algorithm has a standard confirmation time for AF episode of 6 minutes, only episodes with a duration of at least 6 minutes were included in our analysis¹¹. A standard 90-day BP for early AF recurrences was used¹². Clinical visits and follow-up were performed regularly according to our center strategy.

2.4 Statistical analysis

Categorical variables are expressed as absolute and relative frequencies. Continuous variables are expressed as mean \pm standard deviation or median and range as appropriate. Event-free survival rates were estimated by the method of Kaplan–Meier. Data analysis was performed by means of SPSS 20.0 (IBM Corp, Armonk, NY).

3) RESULTS

3.1 Clinical characteristics

The study included 102 patients (77 male, mean age 60.6 ± 9.6 years) with a diagnosis of PAF. Sixty-nine patients (67.6%) were affected by arterial hypertension, CHADS-VASc score was 1.5 ± 1.0 ; mean LA diameter was 39.8 ± 5.2 mm, mean LA area was 21.0 ± 6.0 cm². All patients included in the present study had failed at least one anti-arrhythmic drug (AAD) before undergoing AF ablation. Baseline characteristics of the study population are presented in Table 1.

3.2 Procedural characteristics of CB-A

A total of 102 CB-A procedures were analyzed. All patients underwent CB-A performed with either the second-generation AFA 28 mm CB either the recent AFAPRO 28 mm CB. Mean procedure (i.e. from the first groin puncture to complete sheath extraction) and fluoroscopy times were 79.9 ± 20.3 and 17.1 ± 6.6 minutes, respectively. All PVs were successfully isolated with CB-A without the need for additional focal-tip ablation. The mean nadir temperatures achieved were: $-48.2 \pm 5.0^{\circ}\text{C}$ in the LSPV, $-44.3 \pm 4.5^{\circ}\text{C}$ in the LIPV, $-47.3 \pm 6.2^{\circ}\text{C}$ in the RIPV and $-50.9 \pm 5.6^{\circ}\text{C}$ in the RSPV. In case of the documentation of left or right common ostium, the PVs were normally treated separately¹³. Procedural details are shown in Table 2.

3.3 Safety

There was no major complications in any patient of our population, while impending or transient PNI occurred in 6 patients (5.9%).

3.4 Outcome and repeat procedure

Mean follow-up was 29.3 ± 8.1 months. If considering a BP of 3 months, the freedom from AT/AF at 12-month follow-up as showed in the Kaplan-Meier survival analysis was 64.7% (Figure 1); when evaluated at 2-year follow-up, freedom from AT/AF recurrences was achieved in 44.1% of the patients. A new ablation procedure was suggested for those patients who recurred after the 3-months BP; in the end, 10 patients who experienced new arrhythmic episodes after the BP underwent redo AF procedure.

3.5 ILR-detected AF episodes

All patients were implanted with an ILR after the CB-A; 57 patients (55.9%) were implanted with the Reveal XT (Medtronic, Minneapolis, USA), 14 patients (13.7%) received the Biomonitor 2-AF (Biotronik, Berlin, Germany) while in 31 patients (30.4%) the Reveal LINQ (Medtronic, Minneapolis, USA) was positioned. Overall, 39 patients (38.2%) did not reveal any AT/AF episode during the whole follow-up. Among the other 63 patients, a total of 6525 episodes of AT/AF ≥ 6

minutes were recorded; a total of 4987 ECG strips were collected and analyzed. True-positive episodes were confirmed in 2026 cases (40.6%), while the remaining 2961 episodes (59.4%) were diagnosed as false-positive; false arrhythmia detection was due to T-wave oversensing (0.8%), undersensing (1.4%), frequent ventricular premature complexes (VPCs) (0.4%), frequent atrial premature complexes (APCs) (4.6%), artifacts (86.1%), atrial couplets (1.2%) and sinus arrhythmia (5.5%) (Figure 2). Of note, artifacts episodes were observed in only 9 patients (8.8%).

4) DISCUSSION

To the best of our knowledge, this is the first study evaluating the mid-term clinical outcomes of patients undergoing CB-A for PAF by means of ILR recordings. The main finding of our study is that, after a single CB-A procedure, considering a 3-month BP, 64.7% of patients were free from any AT/AF at 12-month follow-up; when evaluated at 2-year follow-up, freedom from AT/AF recurrences was achieved in 44.1% of the patients in our population.

Previous study in the last years have focused on the outcomes after CB-A in patients with PAF, both at 12-month¹⁴ and at a longer follow-up¹⁵⁻¹⁶. Still, the rate of AF recurrences after the procedure was evaluated and measured using noninvasive intermittent monitoring techniques (i.e. Holter-ECG recordings, scheduled follow-up visits, etc) and according to the clinical status of the patient. Since silent AF episodes may eventually increase after AF ablation¹⁷, and given that symptomatic and asymptomatic episodes may coexist in the same patient¹⁸⁻¹⁹, this approach would necessarily lead to some grade of overestimation of the efficacy of the procedure.

In the recent C2C study²⁰, a total of 105 patients with PAF were implanted with an ILR before the procedure and underwent AF ablation according to the CLOSE protocol²¹; after 1.13 ± 0.39 procedures per patient throughout 2-year follow-up, a significant decrease in AF/AT burden was observed both during the first year (from 2.68% at baseline to 0%, $p < 0.001$) and the second year (from 2.68% at baseline to 0%, $p < 0.001$). Moreover, single-procedure freedom from any AT/AF declined from 87% after 1 year to 78% after 2 years ($p = 0.343$). Except for the different technology used (i.e. CFRF vs cryoenergy), the difference in the clinical outcomes might be at least partially explained by the relatively short mean time from the first AF episode to PVI in the C2C study (15 months), when compared to our study population (51.5 ± 46.9 months). Recent evidence²²⁻²⁵, in fact, suggests that an increased time between first diagnosis of AF and catheter ablation might adversely affect long-term outcomes, increasing the risk of AF recurrence in the follow-up.

In the multicenter, prospective, randomized CIRCA-DOSE study, Andrade et al⁷ assigned 346 patients with PAF to CFRF and 2 different regimens of CB-A and analyzed the outcome in terms of time to first recurrence of symptomatic or asymptomatic atrial tachyarrhythmia documented by any form of monitoring, including ILR; all documented AT/AF episodes of > 30 seconds after the index

procedure were considered as a recurrence. After a single ablation procedure, there was no significant difference in terms of 1-year freedom from AT/AF among the 3 groups (53.9% for the CFRF group, 52.2% for the 4-minute CB-A group, and 51.7% for the 2-minute CB-A group). Although the primary end-point of the CIRCA-DOSE study was – like in our study – the time to first recurrence of any atrial tachyarrhythmia (showing a ~53% success rate), still the authors underlined that importance of reduction in AF burden (~99% compared with the burden before ablation) as the possible optimal end-point when evaluating the impact of AF catheter ablation. Indeed, although duration threshold was different in our study (i.e. 6 minutes vs 30 seconds), still it remains unclear whether the small differences in AF duration threshold would result in significantly different clinical meanings²⁶.

Interestingly, in our study 59.4% of the ILR recordings after CB-A were finally labeled as false-positive episodes. Although ILR implant might be beneficial for patients after catheter ablation in order to precisely assess the AF recurrence rate after the procedure²⁷, still a careful and detailed review by an expert healthcare provider might be warranted. In a recent work from Afzal et al²⁸, the incidence of false-positive transmissions was 46% (201/440) in patients whose indication for ILR implant was AF surveillance. Of note, at least for false-positive episodes due to artifacts in our population, we observed a tendency to form clusters in few patients, that may be reported and in whom the programming of the ILR should be adequately tailored.

5) LIMITATIONS

Our study has some important limitations. First, a major limitation of our study is its nature (i.e. non-randomized, single-center, retrospective). Second, AT/AF detection depends on the specific accuracy of the ILRs, therefore false-negative or short-lasting AT/AF episodes might have occurred unnoticed in the follow-up; moreover, all the devices were programmed according to nominal programming, and no adjustments were made in the follow-up. Third, no analysis or differentiation of symptomatic episodes from the asymptomatic ones was performed. Fourth, since all ILRs were implanted after CB-A, reduction in AT/AF burden after the procedure could not be measured. Fifth, the use of different ILRs and therefore different AF detection algorithms may have at least partially influenced the results of our study. Future multicenter studies conducted with longer follow-up are warranted to confirm our findings.

6) CONCLUSIONS

We observed that CB-A performed in 102 patients with PAF subsequently implanted with an ILR results in freedom from AT/AF recurrences in 64.7% of patients at 12-month follow-up and in 44.1% of patients when evaluated at 2-year follow-up. Careful adjudication of all ILR-documented

AF episodes is required to avoid misdiagnosis and potential errors in clinical management. Future prospective studies are needed to confirm the results of our study.

7. REFERENCES

- 1) Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Nielsen JC, Curtis AB, Wyn Davies D, Day JD, d'Avila A, de Groot NMSN, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, Haines DE, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ, Yamane T. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: executive summary. *J Interv Card Electrophysiol*. 2017 Oct;50(1):1-55.
- 2) Kuck KH, Brugada J, F rnkranz A, Metzner A, Ouyang F, Chun KR, Elvan A, Arentz T, Bestehorn K, Pocock SJ, Albenque JP, Tondo C; FIRE AND ICE Investigators. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. *N Engl J Med*. 2016 Jun 9;374(23):2235-45.
- 3) Chierchia GB, Di Giovanni G, Ciconte G, de Asmundis C, Conte G, Sieira-Moret J, Rodriguez-Ma ero M, Casado R, Baltogiannis G, Namdar M, Saitoh Y, Paparella G, Mugnai G, Brugada P. Second-generation cryoballoon ablation for paroxysmal atrial fibrillation: 1-year follow-up. *Europace*. 2014 May;16(5):639-44.
- 4) Andrade JG, Khairy P, Guerra PG, Deyell MW, Rivard L, Macle L, Thibault B, Talajic M, Roy D, Dubuc M. Efficacy and safety of cryoballoon ablation for atrial fibrillation: a systematic review of published studies. *Heart Rhythm*. 2011 Sep;8(9):1444-51.
- 5) Packer DL, Kowal RC, Wheelan KR, Irwin JM, Champagne J, Guerra PG, Dubuc M, Reddy V, Nelson L, Holcomb RG, Lehmann JW, Ruskin JN; STOP AF Cryoablation Investigators. Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. *J Am Coll Cardiol*. 2013 Apr 23;61(16):1713-23.
- 6) Kusiak A, Jastrz bski M, Bednarski A, Ku akowski P, Piotrowski R, Ko luk E, Baszko A, Czarnecka D. Diagnostic value of implantable loop recorder in patients undergoing cryoballoon ablation of atrial fibrillation. *Ann Noninvasive Electrocardiol*. 2020 Jul;25(4):e12733.
- 7) Andrade JG, Champagne J, Dubuc M, Deyell MW, Verma A, Macle L, Leong-Sit P, Novak P, Badra-Verdu M, Sapp J, Mangat I, Khoo C, Steinberg C, Bennett MT, Tang ASL, Khairy P; CIRCA-DOSE Study Investigators. Cryoballoon or Radiofrequency Ablation for Atrial Fibrillation

Assessed by Continuous Monitoring: A Randomized Clinical Trial. *Circulation*. 2019 Nov 26;140(22):1779-1788.

8) Ross J Jr, Braunwald E, Morrow AG. Transseptal left atrial puncture; new technique for the measurement of left atrial pressure in man. *Am J Cardiol*. 1959 May;3(5):653-5.

9) Moltrasio M, Sicuso R, Fassini GM, Riva SI, Tundo F, Dello Russo A, Casella M, Majocchi B, Zucchetti M, Cellucci S, Tondo C. Acute outcome after a single cryoballoon ablation: Comparison between Arctic Front Advance and Arctic Front Advance PRO. *Pacing Clin Electrophysiol*. 2019 Jul;42(7):890-896.

10) Ghosh J, Sepahpour A, Chan KH, Singarayar S, McGuire MA. Immediate balloon deflation for prevention of persistent phrenic nerve palsy during pulmonary vein isolation by balloon cryoablation. *Heart Rhythm*. 2013 May;10(5):646-52.

11) Healey JS, Connolly SJ, Gold MR, Israel CW, Van Gelder IC, Capucci A, Lau CP, Fain E, Yang S, Bailleul C, Morillo CA, Carlson M, Themeles E, Kaufman ES, Hohnloser SH; ASSERT Investigators. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med*. 2012 Jan 12;366(2):120-9.

12) Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Nielsen JC, Curtis AB, Davies DW, Day JD, d'Avila A, de Groot NMSN, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, Haines DE, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ, Yamane T. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm*. 2017 Oct;14(10):e275-e444.

13) Heeger CH, Tscholl V, Wissner E, Fink T, Rottner L, Wohlmuth P, Bellmann B, Roser M, Mathew S, Sohns C, Reißmann B, Lemeš C, Maurer T, Santoro F, Riedl J, Goldmann B, Landmesser U, Ouyang F, Kuck KH, Rillig A, Metzner A. Acute efficacy, safety, and long-term clinical outcomes using the second-generation cryoballoon for pulmonary vein isolation in patients with a left common pulmonary vein: A multicenter study. *Heart Rhythm*. 2017 Aug;14(8):1111-1118.

14) De Regibus V, Mugnai G, Moran D, Hünük B, Ströker E, Hacıoglu E, Ruggiero D, Coutiño-Moreno HE, Takarada K, Brugada P, DE Asmundis C, Chierchia GB. Second-Generation Cryoballoon Ablation in the Setting of Lone Paroxysmal Atrial Fibrillation: Single Procedural Outcome at 12 Months. *J Cardiovasc Electrophysiol*. 2016 Jun;27(6):677-82.

- 15) Takarada K, Overeinder I, de Asmundis C, Stroker E, Mugnai G, de Regibus V, Moran D, Coutino-Moreno H, Abugattas JP, Choudhury R, Ruggiero D, Paparella G, Iacopino S, Brugada P, Chierchia GB. Long-term outcome after second-generation cryoballoon ablation for paroxysmal atrial fibrillation - a 3-years follow-up. *J Interv Card Electrophysiol*. 2017 Jun;49(1):93-100.
- 16) Knight BP, Novak PG, Sangrigoli R, Champagne J, Dubuc M, Adler SW, Svinarich JT, Essebag V, Hokanson R, Kueffer F, Jain SK, John RM, Mansour M; STOP AF PAS Investigators. Long-Term Outcomes After Ablation for Paroxysmal Atrial Fibrillation Using the Second-Generation Cryoballoon: Final Results From STOP AF Post-Approval Study. *JACC Clin Electrophysiol*. 2019 Mar;5(3):306-314.
- 17) Hindricks G, Piorkowski C, Tanner H, Kobza R, Gerds-Li JH, Carbucicchio C, Kottkamp H. Perception of atrial fibrillation before and after radiofrequency catheter ablation: relevance of asymptomatic arrhythmia recurrence. *Circulation*. 2005 Jul 19;112(3):307-13.
- 18) Page RL, Tilsch TW, Connolly SJ, Schnell DJ, Marcello SR, Wilkinson WE, Pritchett EL; Azimilide Supraventricular Arrhythmia Program (ASAP) Investigators. Asymptomatic or "silent" atrial fibrillation: frequency in untreated patients and patients receiving azimilide. *Circulation*. 2003 Mar 4;107(8):1141-5.
- 19) Ziegler PD, Koehler JL, Mehra R. Comparison of continuous versus intermittent monitoring of atrial arrhythmias. *Heart Rhythm*. 2006 Dec;3(12):1445-52.
- 20) Duytschaever M, De Pooter J, Demolder A, El Haddad M, Philips T, Strisciuglio T, Debonnaire P, Wolf M, Vandekerckhove Y, Knecht S, Tavernier R. Long-term impact of catheter ablation on arrhythmia burden in low-risk patients with paroxysmal atrial fibrillation: The CLOSE to CURE study. *Heart Rhythm*. 2020 Apr;17(4):535-543.
- 21) Taghji P, El Haddad M, Philips T, Wolf M, Knecht S, Vandekerckhove Y, Tavernier R, Nakagawa H, Duytschaever M. Evaluation of a Strategy Aiming to Enclose the Pulmonary Veins With Contiguous and Optimized Radiofrequency Lesions in Paroxysmal Atrial Fibrillation: A Pilot Study. *JACC Clin Electrophysiol*. 2018 Jan;4(1):99-108.
- 22) Bunch TJ, May HT, Bair TL, Johnson DL, Weiss JP, Crandall BG, Osborn JS, Anderson JL, Muhlestein JB, Lappe DL, Day JD. Increasing time between first diagnosis of atrial fibrillation and catheter ablation adversely affects long-term outcomes. *Heart Rhythm*. 2013 Sep;10(9):1257-62.
- 23) Bisbal F, Alarcón F, Ferrero-De-Loma-Orsorio A, González-Ferrer JJ, Alonso-Martín C, Pachón M, Vallés E, Cabanas-Grandío P, Sanchez M, Benito E, Sarrias A, Ruiz-Granell R, Pérez-Villacastín J, Viñolas X, Arias MA, Martí-Almor J, García-Campo E, Fernández-Lozano I, Villuendas R, Mont L. Diagnosis-to-ablation time in atrial fibrillation: A modifiable factor relevant to clinical outcome. *J Cardiovasc Electrophysiol*. 2019 Sep;30(9):1483-1490.
- 24) Pranata R, Chintya V, Raharjo SB, Yamin M, Yuniadi Y. Longer diagnosis-to-ablation time is

associated with recurrence of atrial fibrillation after catheter ablation-Systematic review and meta-analysis. *J Arrhythm*. 2019 Dec 27;36(2):289-294.

25) Chew DS, Black-Maier E, Loring Z, Noseworthy PA, Packer DL, Exner DV, Mark DB, Piccini JP. Diagnosis-to-Ablation Time and Recurrence of Atrial Fibrillation Following Catheter Ablation: A Systematic Review and Meta-Analysis of Observational Studies. *Circ Arrhythm Electrophysiol*. 2020 Apr;13(4):e008128.

26) Steinberg JS, O'Connell H, Li S, Ziegler PD. Thirty-Second Gold Standard Definition of Atrial Fibrillation and Its Relationship With Subsequent Arrhythmia Patterns: Analysis of a Large Prospective Device Database. *Circ Arrhythm Electrophysiol*. 2018 Jul;11(7):e006274.

27) Kusiak A, Jastrzębski M, Bednarski A, Kułakowski P, Piotrowski R, Koźluk E, Baszko A, Czarnecka D. Diagnostic value of implantable loop recorder in patients undergoing cryoballoon ablation of atrial fibrillation. *Ann Noninvasive Electrocardiol*. 2020 Jul;25(4):e12733.

28) Afzal MR, Mease J, Koppert T, Okabe T, Tyler J, Houmsse M, Augustini RS, Weiss R, Hummel JD, Kalbfleisch SJ, Daoud EG. Incidence of false-positive transmissions during remote rhythm monitoring with implantable loop recorders. *Heart Rhythm*. 2020 Jan;17(1):75-80.

ORCID

Riccardo Maj <https://orcid.org/0000-0002-7794-6414>

Figure 1. Kaplan-Meier curve depicting the time to the first recurrence of any implantable loop recorder (ILR)-detected atrial tachycardia (AT)/atrial fibrillation (AF) episode on during the first 2 years after cryoballoon pulmonary vein isolation. A 3-month blanking period was considered (red line).

Figure 2. Examples of rhythm strips from episodes automatically identified by implantable loop recorder (ILR) as atrial fibrillation (AF) due to A) T-wave oversensing, B) undersensing, C) frequent PVCs, D) frequent PACs, E) artifacts, F) atrial couplets and G) sinus arrhythmia. Of note, artifacts may also occur during real AF episodes (H).