

# ATRIAL FIBRILLATION 2018: AN UPDATE ON RECENT DEVELOPMENTS IN DIAGNOSIS AND MANAGEMENT

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**A**t the annual conference of the European Society of Cardiology (August 25-29, 2018), a wide range of papers related to the diagnosis and treatment of atrial fibrillation were presented ([esc365.escardio.org](http://esc365.escardio.org)). I have chosen to focus on a small number of these papers, which, in my opinion, represent topics of major importance as relates to the epidemiology, pathophysiology, and the management of this persistent and very common arrhythmia.

## DO ALL CASES OF ATRIAL FIBRILLATION QUALIFY FOR ANTICOAGULATION?

Pieter Vandervoort (BE) presented the paper “Results from a real-life digital population screening for atrial fibrillation using only a smartphone. Device-detected and subclinical atrial tachyarrhythmias.” This talk focused on an important and common question: do all cases of atrial fibrillation qualify for anticoagulation? The following conclusions were made during the talk:

- Atrial high-rate episodes and subclinical atrial fibrillation (nonsustained atrial tachycardia) occur often. If they persist for more than 24 hours, they are associated with an increased thromboembolic risk. Shorter episodes are less consistent as a predictor of stroke, while very short episodes only require monitoring.
- There is no consensus regarding a minimum or optimum threshold that could be used as an indication for anticoagulation; this may vary from patient to patient.
- Though the results of further studies are still awaited, there is so far no good clinical evidence to confirm the efficacy of anticoagulation for atrial high-rate episodes and subclinical atrial fibrillation. Therefore, these patients require an individual approach to the evaluation of their thromboembolic risk.
- We do not yet know whether atrial high-rate episodes and subclinical atrial fibrillation may serve as risk factors or markers. Further refinement of these criteria may be necessary in order to derive useful parameters for risk

stratification (eg, atrial high-rate episodes burden and density, markers of atrial myopathy or hypercoagulability, etc).

### LEFT ATRIAL APPENDAGE OCCLUSION

In his presentation, Dariusz Dudek (PL) asked the question “Who is an LAA occlusion [exclusion] candidate?” and presented the selection criteria and current data. According to the author, the clinical and technical challenges involved in left atrial appendage closure include the following: (i) device-related thrombosis; (ii) postprocedural leaks; and (iii) device embolization. More specifically, we could focus on the following items:

- Device-related thrombosis:
  - The incidence with endocardial devices ranges from 3% to 7.2%.<sup>1</sup>
  - For epicardial left atrial appendage exclusion, the risk of a thrombus appears to be comparable.
  - Independent predictors of thrombosis include a history of transient ischemic attack or stroke, permanent atrial fibrillation, large left atrial appendage diameter, and a low left ventricular ejection fraction.<sup>2</sup>
- Postprocedural leaks
  - Leaks are reported for both endocardial and percutaneous endo-epicardial closure, as well as exclusion system closure. The incidence ranges from 0% to 63%, depending on the type of left atrial appendage device and the modality of monitoring.
  - The consequences of postprocedural leaks remain unclear, with studies reporting conflicting results regarding the risk of stroke.
  - The contradictions in reported data expose the limitations of imaging modalities and device selection.
  - Continued surveillance with transesophageal echocardiography and temporary initiation of anticoagulation are recommended if a leak occurs.

Dariusz Dudek made the following conclusions:

- Stroke prevention remains a major goal in patients with atrial fibrillation. Although anticoagulation remains the first choice, the low compliance is alarming.
- Left atrial appendage closure devices will continue to evolve as an alternative strategy, as new technologies are developed, appropriate patient populations are identified, and operator skills and periprocedural techniques are improved.
- Catheter ablation with left atrial appendage closure offers a new clinical perspective. More studies are needed to address patients who are ineligible for

(new) oral anticoagulants—(N)OAC, ie, those patients with a high risk of a cardioembolic event, but who have exhibited major bleeding, and those patients with very high CHA<sub>2</sub>DS<sub>2</sub>-VASC scores who are at risk of stroke despite (N)OAC therapy.

### **ANTICOAGULATION IN PATIENTS WITH ATRIAL FIBRILLATION**

Renato D. Lopes (US), in his lecture on “Anticoagulation in atrial fibrillation: what the trials tell us and gaps in current knowledge,” recognized the following data gaps in atrial fibrillation/NOAC trials: (i) patients with atrial fibrillation and renal impairment (including end-stage renal disease); (ii) subclinical (device-detected) atrial fibrillation; (iii) patients undergoing atrial fibrillation ablation; (iv) new-onset atrial fibrillation and acute cardioversion; and (v) patients with atrial fibrillation and ACS (on DAPT plus OAC).

The author concluded by saying that:

- NOACs should be recommended in preference to warfarin for stroke prevention in atrial fibrillation; however, this transition from warfarin to NOACs has been slow.
- We need more data concerning various subgroups of patients with atrial fibrillation.
- Ongoing research hopes to deliver optimal management to all patients.

### **STROKE PREVENTION IN PATIENTS WITH ATRIAL FIBRILLATION**

In addition to the foregoing, still focusing on stroke prevention in atrial fibrillation, Stuart J. Connolly (CA) summarized, in his lecture “ANNEXA-4 - andexanet alfa for reversal of Factor Xa inhibitors in patients with acute major bleeding,” some of the central findings that have emerged from the relevant studies so far, as follows:

- Antiplatelet therapy works.
- Anticoagulation works better.
- NOACs are even better, especially regarding safety.
- Bleeding matters a lot, perhaps a bit less than ischemic stroke prevention.
- The dose of NOAC matters too.

### **ATRIAL FIBRILLATION AND HEART FAILURE**

Sidney C. Smith (US), in his very comprehensive lecture, focused on the important feedback relationship between atrial fibrillation and heart failure. The author identified certain factors that contribute to this dangerous association, including

more atrial and ventricular remodeling, greater neurohormonal activation, more advanced heart failure, more frequent hospital admissions and stroke, smaller reverse remodeling response to cardiac resynchronization therapy, more frequent cognitive dysfunction in atrial fibrillation.

The author concluded that:

- Atrial fibrillation and heart failure frequently coexist, which can lead to a vicious cycle.
- Atrial fibrillation affects heart failure outcomes via hemodynamic effects, risk of thromboembolic events, and exposure to adverse effects of therapy (anticoagulants, antiarrhythmics, and ablation).
- Growing evidence shows that rhythm control of atrial fibrillation in patients with heart failure, via catheter ablation, is of particular benefit.
- Patient selection is vital.

### **RADIOFREQUENCY CATHETER ABLATION FOR ATRIAL FIBRILLATION**

Klaus Kettering (DE) and Felix Gramley (DE) focused on another very important issue: long-term outcomes of radiofrequency catheter ablation for atrial fibrillation, with a specific focus on the long-term outcomes of redo procedures after pulmonary vein isolation with the cryoballoon technique (first- vs second-generation cryoballoon). This very important study included 80 patients (59 with paroxysmal atrial fibrillation and 21 with persistent atrial fibrillation) who had to undergo a redo procedure after an initially successful circumferential pulmonary vein isolation with the cryoballoon technique. In 40 patients (group A), the Medtronic Arctic Front Balloon was used, while, in another 40 (group B), the Arctic Front Advance cryoballoon was employed. The redo ablation procedures were performed using a segmental approach or a circumferential ablation strategy (CARTO; Biosense Webster) depending on the intra-procedural findings.

During the redo procedure, reconducting pulmonary veins were detected (mean, 1.8) using a circular mapping catheter (group A, 2.3; group B, 1.3). There was a slightly higher incidence of chronic pulmonary vein reconnections related to the left-sided pulmonary vein ostia than to the right-sided pulmonary veins in both groups. In addition, more sites of chronic pulmonary vein reconnection were found in the inferior parts of the pulmonary vein ostia than in the superior parts. In 35 patients in group A, a segmental approach was sufficient to eliminate the residual pulmonary vein conduction because only a few pulmonary vein fibers had recovered (1 to 3 reconnected pulmonary veins; group A1). In the remaining 5 patients in group A, a circumferential ablation strategy was used to treat complete recovery of the pulmonary vein to left atrium conduction of all four pulmonary

veins (group A2). In group B, a segmental approach was sufficient in all patients because there was only a minor reconnection of 1 to 2 pulmonary veins. All recovered pulmonary veins were again isolated successfully. At the 24-month follow-up, 76.3% of all patients (61/80) were free from arrhythmia recurrence (group A, 29/40 [72.5%]; group B, 32/40 [80%]). No major complications were seen in either group.

The investigators concluded that, for patients who underwent initial circumferential pulmonary vein isolation using the cryoballoon technique, a repeat ablation procedure could be performed safely and effectively using radiofrequency catheter ablation. Since only a few reconducting pulmonary vein fibers were found in the majority of patients (especially those treated with the second-generation cryoballoon), a segmental re-ablation approach appeared to be sufficient.

### **CABANA TRIAL**

Another extremely important study, the CABANA trial, examined the recurrence of atrial arrhythmias after catheter ablation vs antiarrhythmic drug therapy for atrial fibrillation. The CABANA investigators randomized 2204 symptomatic patients with paroxysmal or persistent atrial fibrillation 1:1 to either percutaneous left atrial catheter or medical therapy. More specifically, the patients were classified according to age  $\geq 65$  or  $< 65$  years with  $\geq 1$  risk factor for stroke) and to those who were eligible for ablation and  $\geq 2$  drugs for rhythm or rate control.

The primary end point was a composite of death, disabling stroke, serious bleeding, or cardiac arrest. After a median 48.5-month follow-up, there was a nonsignificant 14% difference in favor of ablation, as assessed by an intention-to-treat (ITT) analysis (HR, 0.86; 95% CI, 0.65-1.15;  $P=0.30$ ). The secondary end point was all-cause mortality. A nonsignificant 15% difference was observed in favor of ablation (ITT; HR, 0.85; 95% CI, 0.60-1.21;  $P=0.377$ ). Analyses by treatment received and per protocol showed significant benefits of ablation for both the primary end points for mortality.

The following conclusions were made:

- Catheter ablation was associated with a significant reduction ( $\approx 50\%$ ) in the relative risk for the recurrence of atrial arrhythmias.
- The Holter-determined atrial fibrillation burden was significantly lower in patients randomized to catheter ablation compared with those who received drug therapy across the 5-year follow-up.
- Atrial fibrillation was the dominant first recurrent rhythm after the 90-day blanking period.
- No treatment-related difference was observed in recurrent atrial flutter/atrial tachycardia.

### TOP TEN MESSAGES FROM THE 2016 ESC GUIDELINES

John Camm (UK), in his striking lecture on “Atrial fibrillation, the big picture,” focused on the top ten messages from the 2016 ESC guidelines. Specifically, he advised:

1. Using ECG screening in populations at risk for atrial fibrillation, especially stroke survivors and the elderly.
2. Proposing lifestyle changes to all suitable patients with atrial fibrillation to make their management more effective.
3. Using oral anticoagulation in all patients with atrial fibrillation unless they are at a low risk for stroke based on the CHA<sub>2</sub>DS<sub>2</sub>-VASc score or have true contraindications for anticoagulant therapy.
4. Reducing all modifiable bleeding risk factors in all patients with atrial fibrillation on oral anticoagulation, eg, by treating hypertension, minimizing the duration and intensity of concomitant antiplatelet and NSAID therapy, treating anemia, and eliminating causes of blood loss, maintaining stable INR values in patients on vitamin K antagonists, and moderating alcohol intake.
5. Checking the ventricular rate in all patients with atrial fibrillation and using rate-control medications to achieve lenient heart rate control (initially <110 bpm at rest).
6. Selecting antiarrhythmic drugs based on their safety profile and considering catheter or surgical ablation when antiarrhythmic drugs fail.
7. Not using antiplatelet therapy for stroke prevention in patients with atrial fibrillation.
8. Not permanently discontinuing oral anticoagulation in patients with atrial fibrillation at an increased risk of stroke unless such a decision is taken by a multidisciplinary team.
9. Not using rhythm-control therapy in patients with asymptomatic atrial fibrillation or in patients with permanent atrial fibrillation.
10. Not performing cardioversion or ablation without anticoagulation unless an atrial thrombus has been ruled out by a transesophageal echo.

### THE FUTURE FOR ATRIAL FIBRILLATION MANAGEMENT

Finally, Nassir F. Marrouche (US), in a futuristic lecture, focused on a very important issue: “The next 10 years in atrial fibrillation – my crystal ball.” In particular, he stressed that the outline of management is:

- Early detection of the substrate.
- A personalized path.

- Standardization of ablation lesions.
- Real-time MRI.
- Robotics.

Starting with genetics, metabolism, and risk factors, we progress to advanced imaging, aiming at the outcomes of early detection and prevention, treatment, and monitoring of progression. The futuristic approach begins with the patient's risk profile (MRI image analysis, fibrosis, shape, and function). The findings will be processed by machine learning until the algorithms become sufficiently sophisticated for these outcomes to be attained.

The more futuristic VytronUS robotics system will allow the automatic detection of endocardial and epicardial borders, 3D evaluation of tissue thickness, automated or manually defined dosing and automated therapy delivery. Using the VytronUS system, in combination with machine learning, we will be able to perform preablation tissue characterization and intraoperative ultrasound tissue analysis. The big data from these measurements will be sent to a machine learning system, which may eventually yield a methodology for lesion prediction.

## CONCLUSIONS

In conclusion, at the annual conference of the European Society of Cardiology, the topic of atrial fibrillation certainly had a leading role because of its epidemiology and its major complications. The particular scientific community that deals with this topic, namely arrhythmologists, specialists in heart failure, and stroke specialists, are continuing to uncover unknown and obscure features of this arrhythmia associated with the theory of chaos, but the same experts also acknowledge the enormous difficulties that remain in clarifying important aspects of this problem. ■

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