Κολπική Μαρμαρυγή: παρόν και μέλλον

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Conflict of interest

- Advisory board for Boehringer Ingelheim, Bayer
AF is a common supraventricular arrhythmia that is characterized by rapid and irregular activation in the atria without discrete P waves on the surface ECG.
Multiple wavelets hypothesis

Rapidly discharging automatic foci

Single reentrant circuit with fibrillatory conduction

Functional reentry resulting from rotors or spiral waves

Maintenance resulting from dissociation between epicardial and endocardial layers,
A Schematic Representation of the Natural History of AF

Guichard and Nattel. JACC 2017
Left Atrial Fibrosis and Risk of Cerebrovascular and Cardiovascular Events in Patients With Atrial Fibrillation

Jordan B. King, PharmD, MS, a,b Peyman N. Azadani, MD, b,c Prompong Suksaranjit, MD, MS, b
Adam P. Bress, PharmD, MS, d Daniel M. Witt, PharmD, e Frederick T. Han, MD, b Mihail G. Chelu, MD, PhD, b
Michelle A. Silver, MSPH, b Joseph Biskupiak, PhD, MBA, e Brent D. Wilson, MD, PhD, b Alan K. Morris, MS, b
Eugene G. Kholmovski, PhD, b,f Nassir Marroache, MD b

PA
Low Fibrosis <15%

AP
High Fibrosis >15%

Healthy tissue
Fibrotic
32 y old male with Persistent AF (SR during RF procedure)

Courtesy of Dr Efraimidis, Evaggelismos Hospital, Athens
46 y old pt with Persistent AF

Courtesy of Dr Efraimidis, Evaggelismos Hospital, Athens
Any complex of structural, architectural, contractile or electrophysiological changes affecting the atria with the potential to produce clinically-relevant manifestations.
EHRAS classification

Primarily Cardiomyocyte-dependent (Class I)
- lone AF
- genetic diseases
- diabetes mellitus

Primarily Fibroblast-dependent (Class II)
- aging
- cigarette smoking

Mixed Cardiomyocyte-Fibroblast-dependent (Class III)
- CHF
- valvular diseases

Primarily Non-Collagen Deposits (Class IV)
- isolated atrial amyloidosis
- granulomatosis
- inflammatory Infiltrates
- glycosphingolipids
Wavelet-based analysis of P waves identifies patients with lone atrial fibrillation: A cross-sectional pilot study

George Dakos\textsuperscript{a,\textasteriskcentered,\textasteriskcentered,1}, Yiannis S. Chatzizisis\textsuperscript{a,b,\textasteriskcentered,1}, Dimitrios Konstantinou\textsuperscript{a}, Ioanna Chouvarda\textsuperscript{1}, Dimitrios Filos\textsuperscript{c}, Stylianos Paraskevaidis\textsuperscript{a}, Lilian Mantziari\textsuperscript{a,d}, Nicos Maglaveras\textsuperscript{c}, Haralambos Karvounis\textsuperscript{a}, Ioannis Styliadis\textsuperscript{a}, Vassilios Vassilikos\textsuperscript{a,e}

Time-frequency representations of the wavelet transform on Z axis

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Comparison of time-frequency representations for control and AF patient.}
\end{figure}

\textit{Int J Cardiol. 2014 Jun 15;174(2):389-92}
P wave wavelet analysis parameters as independent predictors of lone AF prevalence

<table>
<thead>
<tr>
<th>Variables</th>
<th>B</th>
<th>SE</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Max3Zloc</td>
<td>0.061</td>
<td>0.019</td>
<td>0.003</td>
</tr>
<tr>
<td>Max3Z</td>
<td>53.773</td>
<td>29.715</td>
<td>0.030</td>
</tr>
<tr>
<td>PdurZ</td>
<td>70.609</td>
<td>21.102</td>
<td>0.008</td>
</tr>
<tr>
<td>Constant</td>
<td>-10.457</td>
<td>2.278</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Beat-to-beat P-wave morphology as a predictor of paroxysmal atrial fibrillation

Dimitrios Filos⁠¹,⁠², Ioanna Chouvarda⁠¹, Dimitris Tachmatzidis⁠², Vassilios Vassilikos⁠², Nicos Maglaveras⁠¹

¹Laboratory of Computing and Medical Informatics, Aristotle University of Thessaloniki, Box 323, 54124, Thessaloniki, Greece
²3rd Cardiology Department, Aristotle University of Thessaloniki, Greece
Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices

David T. Martin¹, Malcolm M. Bersohn², Albert L. Waldo³, Mark S. Wathen⁴, Wassim K. Choucair⁵, Gregory Y.H. Lip⁶, John Ip⁷, Richard Holcomb⁸, Joseph G. Akar⁹, and Jonathan L. Halperin¹⁰*, on behalf of the IMPACT Investigators

2718 patients with dual-chamber and biventricular defibrillators to start and stop anticoagulation based on remote rhythm monitoring vs. usual office-based follow-up with anticoagulation determined by standard clinical criteria.
20 (29.0%) followed AT by 1 to 489 days, and 9 (13.0%) preceded AT. 40 (58.0%) occurred without AT detected during the monitoring period. 69 thromboembolic events.
Rudolf Virchow

Hypercoagulability
Endothelial damage
Stasis
Are not directly related to the presence of absence of atrial fibrillation in the surface ECG.

Flow abnormalities, and endothelial changes must co-exist to induce thrombogenesis at the atrial endocardium.

Molecular alterations (oxidative stress pathways etc.) within myocytes and endothelial cells, and thereby, increase the expression of prothrombogenic factors.

Goette et al, Europace (2016) 18, 1455–1490
5004 pts, ARISTOTLE substudy

Hypercoagulability causes atrial fibrosis and promotes atrial fibrillation

Hypercoagulable state during AF promotes structural remodelling in the atria and contributes to the development of a substrate for AF by protease-activated receptors (PAR) activation
Effect of nadroparin on the development of a substrate for atrial fibrillation

Spronk et al, Eur Heart J 2017 (38) 38-50
Mechanical dyssynchrony of the left atrium during sinus rhythm is associated with history of stroke in patients with atrial fibrillation

Luisa Ciuffo¹, Yuko Y. Inoue¹, Susumu Tao¹, Esra Gucuk Ipek¹, Muhammad Balouch¹, Joao A.C. Lima¹,²,³, Saman Nazarian¹,³, David D. Spragg¹, Joseph E. Marine¹, Ronald D. Berger¹,⁴, Hugh Calkins¹, and Hiroshi Ashikaga¹,⁴

246 pts prior to RFA
23 Hx stroke or TIA

LA longitudinal strain and strain rate

Standard Deviation of the time to the peak longitudinal strain (SD-TPS).
Higher mechanical dyssynchrony of the LA during sinus rhythm is associated with a history of stroke/TIA in patients with AF.
Progression of Device-Detected Subclinical Atrial Fibrillation and the Risk of Heart Failure

Jorge A. Wong, MD, MPH, David Conen, MD, MPH, Isabelle C. Van Gelder, MD, William F. McIntyre, MD, Harry J. Crijns, MD, Jia Wang, MSc, Michael R. Gold, MD, Stefan H. Hohnloser, MD, C.P. Lau, MD, Alessandro Capucci, MD, Gianluca Botto, MD, Gerian Grönefeld, MD, Carsten W. Israel, MD, Stuart J. Connolly, MD, Jeff S. Healey, MD, MSc.

Subclinical atrial fibrillation (SCAF) (episodes lasting >6 minutes and ≤24 hours)

No progression of SCAF to episodes >24 hours

SCAF progression (incidence 8.8%/year)

Annual rate of heart failure (HF) hospitalization: 2.5%/year

Annual rate of HF hospitalization: 8.9%/year

SCAF progression associated with increased risk of HF hospitalization
[HR: 4.58; 95% CI: 1.64 - 12.8; p = 0.004]

Predictors of SCAF progression:
Older age
Greater BMI
SCAF episode duration: 1-hour increase in duration
13% increased risk of SCAF progression

4,103 patients experienced ischemic stroke  
89.4% delta>1  
54.6% delta>1
Table 2  The SAMe-TT₂R₂ score for assisting with decision-making for use of oral anticoagulants

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definitions</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>Sex (female)</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>Age (less than 60 years)</td>
<td>1</td>
</tr>
<tr>
<td>M</td>
<td>Medical history(^a)</td>
<td>1</td>
</tr>
<tr>
<td>T</td>
<td>Treatment (interacting drugs e.g. amiodarone for rhythm control)</td>
<td>1</td>
</tr>
<tr>
<td>T</td>
<td>Tobacco use (within 2 years)</td>
<td>2</td>
</tr>
<tr>
<td>R</td>
<td>Race (non-Caucasian)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><strong>Maximum points</strong></td>
<td>8</td>
</tr>
</tbody>
</table>

\(^a\)Two of the following: hypertension, diabetes mellitus, coronary artery disease/myocardial infarction, pulmonary artery disease, cardiac heart failure, previous stroke, pulmonary disease, hepatic or renal disease.
REVIEW

Ranolazine as a Promising Treatment Option for Atrial Fibrillation: Electrophysiologic Mechanisms, Experimental Evidence, and Clinical Implications

NIKOLAOS FRAGAKIS, M.D., Ph.D., KONSTANTINOS C. KOSKINAS, M.D., M.Sc., and VASSILIOS VASSILIKOS, M.D., Ph.D.
From the Third Department of Cardiology, Hippokrateion Hospital, Aristotle University Medical School, Thessaloniki, Greece

Currently available agents for pharmacologic management of atrial fibrillation (AF) are limited by their suboptimal efficacy and nonnegligible proarrhythmic risk. Ranolazine (RN) is a novel antianginal agent with increasingly appreciated antiarrhythmic properties that can suppress ventricular and supraventricular arrhythmias including AF. In this review, we describe the electrophysiological properties of RN, focusing on atrial-selective inhibition of a number of ion channels implicated in the development of AF, particularly the sodium current. We further summarize evidence from experimental studies that demonstrate a potent AF-suppressing effect of RN, alone or in combination with other antiarrhythmic drugs. Of clinical relevance, we present growing evidence from preliminary clinical investigations indicating the safety and efficacy of RN for prevention and treatment of AF in various clinical settings including prevention of AF in patients with acute coronary syndromes, prevention and conversion of postoperative AF after surgical coronary revascularization, sinus rhythm maintenance in drug-resistant recurrent AF, and facilitating of electrical or pharmacological cardioversion in cardioversion-resistant patients. While current experimental and clinical evidence points to RN as a potentially promising agent for suppression of AF, well-designed, large-scale trials will be required before RN can be considered for pharmacological treatment of AF in clinical practice. (PACE 2014; 37:1412–1420)

atrial fibrillation, ranolazine, clinical trials, pharmacology
Risk of Thromboembolism Associated With Atrial Fibrillation Following Noncardiac Surgery

Jawad H. Butt, MD, a Jonas B. Olesen, MD, PhD, b Eva Havers-Borgersen, MB, a Anna Gundlund, MD, b Charlotte Andersson, MD, PhD, b Gunnar H. Gislason, MD, PhD, b,e,d Christian Torp-Pedersen, MD, DMSc, c Lars Kober, MD, DMSc, a Emil L. Fosbøl, MD, PhD a

Gray's test p value = 0.26
Adjusted HR: 0.95; 95% CI: 0.85-1.07

Cumulative Incidence of Thromboembolism

Years After Index

Nonvalvular Atrial Fibrillation
Post-Operative Atrial Fibrillation Following Noncardiac Surgery

Electroporation Ablation

Circular Electroporation Ablation: method of delivery for pulmonary veins

The circular catheter is advanced to the ostium of the pulmonary vein.

The hoop of the catheter is at a 90° angle to the catheter shaft.

Another possible application of circular electroporation ablation: left ventricular epicardial lesions

LV lesions 3 weeks after electroporation ablation via the 12mm diameter circular catheter. The diameter of the transmural lesion is approximately 30mm.

Circumferential Ablation

- Ultra fast
- Great lesion depth
- Non-thermal
- Myocardial specificity:
  - No nerve damage
  - No coronary damage
  - No PV stenosis
  - Esophageal fistulas unlikely
  - LV transmularity with pericardial ablation

Advantages
- No power titration:
  - Not suitable for AVNRT
- Large lesions:
  - Not 1st choice for focal arrhythmias
- Myocardial stunning:
  - Endpoint misleading
  - High voltage:
    - Technical catheter challenge
    - Tiny gas bubbles

Disadvantages

Pulsed electric fields

Reddy et al JACC 2018
High-Power and Short-Duration Ablation for Pulmonary Vein Isolation

Biophysical Characterization

Eran Leshem, MD, MHA, a Israel Zilberman, DVM, b Cory M. Tschabrunn, PhD, a Michael Barkagan, MD, a Fernando M. Contreras-Valdes, MD, a Assaf Govari, PhD, b Elad Anter, MD a

Standard (25W/20 Sec) ablation

HP-SD (90W/4 Sec) ablation

Blood pool

Blood pool

Tissue

Tissue
Ablation Procedures (abs. values) in Greece during 2008-2017

Vassilikos et al, HJC 2018
**%AF ablation@volume**

<table>
<thead>
<tr>
<th>Year</th>
<th>&lt;100</th>
<th>&gt;100</th>
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<tbody>
<tr>
<td>2015</td>
<td>93</td>
<td>562</td>
</tr>
<tr>
<td>2016</td>
<td>201</td>
<td>610</td>
</tr>
<tr>
<td>2017</td>
<td>200</td>
<td>625</td>
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</table>

- 19 centers
- 7 centers >100

- 20 centers
- 6 centers >100

- 21 centers
- 7 centers >100
Smartwatch Algorithm for Automated Detection of Atrial Fibrillation

Joseph M. Bumgarner, MD, Cameron T. Lambert, MD, Ayman A. Hussein, MD, Daniel J. Cantillon, MD, Bryan Baranowski, MD, Kathy Wolski, MPH, Bruce D. Lindsay, MD, Oussama M. Wazni, MD, MBA, Khaldoun G. Tarakji, MD, MPH
The smartwatch strap with an electrode sensor that records heart rhythm

Patient places thumb on the sensor to record rhythm

The application utilizes an algorithm to differentiate sinus rhythm (SR) from atrial fibrillation (AF), or would label the recording as unclassified if it does not meet certain criteria

The app informs the patient if AF is detected; the results are transmitted to the patient’s physician

<table>
<thead>
<tr>
<th>Method for interpreting the recording:</th>
<th>% of patients with interpretable results</th>
<th>Accuracy of AF diagnosis compared to 12 lead electrocardiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>App algorithm only</td>
<td>66%</td>
<td>93% sensitivity; 84% specificity</td>
</tr>
<tr>
<td>Physician only</td>
<td>87%</td>
<td>99% sensitivity; 83% specificity</td>
</tr>
<tr>
<td>Recordings labeled as “unclassified” by the app algorithm when reviewed by physician</td>
<td>100%</td>
<td>100% sensitivity; 80% specificity</td>
</tr>
</tbody>
</table>

Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest) (ITT)

Ablation vs. Drug
Hazard ratio: 0.86 (95% CI, 0.65–1.15)
P=0.303

Number at risk
- Drug: 1096, 1036, 1006, 970, 880, 763, 652, 578, 499, 418, 312
- Ablation: 1108, 1045, 1021, 996, 915, 793, 700, 614, 535, 432, 309
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

Number at risk
Drug: 1096, 954, 860, 778, 680, 566, 464, 396, 330, 275, 204
Ablation: 987, 958, 937, 918, 849, 735, 648, 566, 494, 404, 291
CASTLE-AF Study

A Death or Hospitalization for Worsening Heart Failure

- Probability of Survival Free of Hospital Admission
- Months of Follow-up

Hazard ratio, 0.62 (95% CI, 0.43–0.87)
P=0.007 by Cox regression
P=0.006 by log-rank test

No. at Risk
Ablation          179  141  114  76  58  22
Medical therapy   184  145  111  70  48  12

Ablation according to the substrate, not according to paroxysmal versus non-paroxysmal AF
Take Home Messages

- The arrhythmia in certain cases is part of an atrial myopathy
- Imaging techniques are developing and seem to add valuable information for the future management and prognosis
- Anticoagulation
- Ablation techniques, ?Personalized approach
CAMERA-MRI Study

A. Primary Endpoint: Change in LVEF at Baseline and 6 Months by Treatment Arm

- Catheter Ablation
  - Mean difference = +14.0%, 95% CI: 8.5% to 19.5%
  - +18.3%
- Medical Rate Control
  - +4.4%

B. Catheter Ablation Lesion Set in Left Atrium: Pulmonary Vein and Posterior Wall Isolation

**A**

**ΔLVEF Stratified by LGE Status in Patients Following Catheter Ablation**

- **P = 0.0069**
- Mean difference = +10.7%
- 95% CI: 3.2% to 18.3%

<table>
<thead>
<tr>
<th>Status</th>
<th>Change in Absolute LVEF from Baseline (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LGE Positive</td>
<td>+11.6%</td>
</tr>
<tr>
<td>LGE Negative</td>
<td>+22.3%</td>
</tr>
</tbody>
</table>

**B**

**Correlation Between % of Ventricular LGE and ΔLVEF Following Catheter Ablation**

- **R = -0.67**
- **p = 0.0094**

![](image)