Κολπική μαρμαρυγή σε νεαρές ηλικίες

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ΓΝΘ “Γ. Παπανικολάου”
LONE AURICULAR FIBRILLATION

BY

WILLIAM EVANS AND PETER SWANN

From the Cardiac Department of the London Hospital

Received December 22, 1953

Factors not yet identified

Age

Hypertension

Structural heart disease

Genetic factors

Increased alcohol consumption

Extensive sports

Personality traits
AF Etiology in the Young

AF incidence and prevalence \(<0.1\%/y\) in pts younger than 40 y. up to \(>20\%\) in pts beyond 80 years

1. Familial form - Channelopathies
2. Alcohol
3. Obesity
4. Sports and Physical Activity
5. Behavioural or Emotional Triggers, increased Coffee and Nicotine consumption
6. Cardiac Pathologies (CHD, HOCM, WPW, Myocarditis)
IDENTIFICATION OF A GENETIC LOCUS FOR FAMILIAL ATRIAL FIBRILLATION

Ramon Brugada, M.D., Terry Tapscott, B.S., Grazyna Z. Czernuszewicz, M.S., A.J. Marian, M.D., Anna Iglesias, B.S., Lluís Mont, M.D., Josep Brugada, M.D., Josep Girona, M.D., Anna Domingo, M.D., Linda L. Bachinski, Ph.D., and Robert Roberts, M.D.

We identified a small family in whom atrial fibrillation segregated as an autosomal dominant trait; chromosome 10q in the region of 10q22–q24

(F Engl J Med 1997;336:905-11.)

Familial Aggregation of Lone Atrial Fibrillation in Young Persons

Nina Øyen, MD, MPH, DrMED,*† Mattis F. Ranthe, MD,* Lisbeth Carstensen, PhD,* Heather A. Boyd, PhD,* Morten S. Olesen, PhD,§ Søren-Peter Olesen, MD, DrMED,|| Jan Wohlfahrt, MSc, DrMED,* Mads Melbye, MD, DrMED

A family history of lone AF is associated with substantial risk of lone AF, with the strongest risks associated with young age at onset, multiple affected relatives, and in first-degree relatives.

(J Am Coll Cardiol 2012;60:917–21)

A novel mutation in LAMIN A/C is associated with isolated early-onset atrial fibrillation and progressive atrioventricular block followed by cardiomyopathy and sudden cardiac death

Hubert Pan, M.S.1, Ashleigh A. Richards, M.D.1, Xiaohui Zhu, M.S.3, Jose A. Joglar, M.D.2, Helen L. Yin, Ph.D.3, and Vidy Garg, M.D.1,4,5,#

Here, we present a large family in which a novel mutation of LMNA segregates with affected members with cardiac disease. The phenotype consists of early-onset AF and progressive AVB that is followed by DCM and SCD. In this report, we discuss the clinical and genetic findings and emphasize that LMNA mutations are a potential cause of early-onset AF and progressive conduction system disease.

Atrial fibrillation in inherited cardiac channelopathies: From mechanisms to management

Andres Enrquez, MD,* Charles Antzelevitch, PhD, FHRSc,† Verda Bismah, Bsc, ‡ Adrian Baranchuk, MD¶

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
<th>Pathophysiology</th>
<th>Risk factors</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long QT syndrome</td>
<td>2%–29%</td>
<td>Loss-of-function K channels mutations or gain-of-function Na channel mutations</td>
<td>LQT1, male sex, longer QT interval</td>
<td>Beta-blockers, mexiletine, flecainide (LQT3)</td>
</tr>
<tr>
<td>Brugada syndrome</td>
<td>6%–53%</td>
<td>SCN5A mutation with reduction in Na inward current ($I_{Na}$) and atrial transmural repolarization dispersion</td>
<td>Spontaneous Brugada ECG pattern, previous ventricular tachycardia / ventricular fibrillation, P-wave duration and dispersion</td>
<td>Quinidine, bepridil, catheter ablation</td>
</tr>
<tr>
<td>Short QT syndrome</td>
<td>18%–70%</td>
<td>Gain-of-function mutations in genes encoding for K channels</td>
<td>Positive genotype, KCNQ1 mutation (SQTS2)</td>
<td>Propafenone, quinidine</td>
</tr>
<tr>
<td>Catecholaminergic polymorphic</td>
<td>11%–37%</td>
<td>Ryanodine receptor dysfunction with Ca leak from sarcoplasmic reticulum, cytosolic Ca overload, and delayed afterdepolarizations</td>
<td>Not reported</td>
<td>Beta-blockers, flecainide, propafenone, catheter ablation</td>
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<tr>
<td>ventricular tachycardia</td>
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*(Heart Rhythm 2016;13:1878–1884)*
AF may be the first manifestation → proper diagnosis has prognostic importance (risk of SCD)

A high suspicion index if young patients with “lone AF”, previous syncopal episodes, or a family history of SCD

The presence of AF in BS has been associated with a more malignant course, with a greater incidence of syncope and VF, thus being a marker of more advanced disease
Atrial fibrillation in inherited cardiac channelopathies:

- **Pharmacologic therapy is challenging**
  1. Rare conditions, case reports
  2. AADs used for AF control are **contraindicated in particular conditions**, such as Class I agents in BS or QT-prolonging drugs in congenital LQTS. Amiodarone adverse effects in the long-term

- **Candidates for ICD** → ICD programming to avoid inappropriate shocks and atrial lead to increase discrimination capabilities (if AF present or with LQTS with expected beta-blocker bradycardia)
Alcohol Consumption and Risk of Atrial Fibrillation

A Meta-Analysis

(J Am Coll Cardiol 2011;57:427–36)
The role of obesity in atrial fibrillation

Chrishan Joseph Nalliah\textsuperscript{1,2,3}, Prashanthan Sanders\textsuperscript{3}, Hans Kottkamp\textsuperscript{4}, and Jonathan M. Kalman\textsuperscript{1,2*}

**Clinical evidence**

1. Weight loss results in decreased AF duration and burden.\textsuperscript{33}
2. Weight loss is associated with cardiac remodelling.\textsuperscript{48, 49}
3. Long-term weight loss is associated with lower recurrent AF.\textsuperscript{45}
4. Weight loss is associated with improved AF-free survival after AF ablation.\textsuperscript{44}
5. Weight fluctuation is associated with AF recurrence.\textsuperscript{45}

**Epidemiological evidence**

1. Obesity is associated with higher rates of incident AF (increase per unit BMI)\textsuperscript{7,19-22}
2. Weight increase is associated with increased AF risk.\textsuperscript{38}
3. Increased weight is associated with AF progression.\textsuperscript{23}

**Mechanistic evidence**

1. Obese patients have electrophysiologic and structural atrial changes.\textsuperscript{7,6}
2. Weight gain results in electrophysiologic, structural and histological change.\textsuperscript{9,96}
3. Pericardial fat is associated with incident AF, AF severity and freedom from AF.\textsuperscript{61,95}
4. Both are AF and obesity associated with diastolic impairment.\textsuperscript{8,77}
5. Weight loss is associated with freedom from AF and a concomitant decline in inflammatory markers.\textsuperscript{46,87}

Causative relationship between obesity and AF
AF Prevalence and Age
AF was common in our study population, with a prevalence of 22% and incidence of 2% new cases annually. Thus, HCM patients appear to have a 4- to 6-fold-greater likelihood of developing AF compared with the general population.
Atrial Fibrillation in Patients with Congenital Heart Disease

Tabitha G Moe$^{1,2}$, Victor A Abrich$^2$, Edward K Rhee$^1$

**Figure 4:** Prevalence of atrial fibrillation by age and defect
Paroxysmal AF up to 50% of patients with WPW, and is the presenting arrhythmia in 20%
The relationship between personality, socio-economic factors, acute life stress and the development, spontaneous conversion and recurrences of acute lone atrial fibrillation

Anna Vittoria Mattioli *, Silvia Bonatti, Mauro Zennaro, Giorgio Mattioli

Conclusions Type A behaviour pattern and acute life stress affect the development and spontaneous conversion of atrial fibrillation. Patients with acute stress showed the highest probability of spontaneous conversion followed by patients with Type A behaviour. Other socio-economic factors affect spontaneous conversion and recurrences of lone atrial fibrillation to a lesser extent.

Anger and Hostility Predict the Development of Atrial Fibrillation in Men in the Framingham Offspring Study

Elaine D. Eaker, ScD; Lisa M. Sullivan, PhD; Margaret Kelly-Hayes, EdD, RN; Ralph B. D’Agostino, Sr, PhD; Emelia J. Benjamin, MD, ScM

Conclusions—This is the first study to examine and demonstrate a predictive relation between measures of anger and hostility to the development of AF in men. As opposed to type A behavior, measures of anger and hostility may be more productive avenues for research in studying the risk of arrhythmias and total mortality in men. (Circulation. 2004;109:
<table>
<thead>
<tr>
<th>Pathophysiologial process</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Atrial remodelling</td>
<td>AV valve disease (e.g., rheumatic fever)</td>
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<tr>
<td></td>
<td>Ventricular systolic and/or diastolic dysfunction</td>
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<td>Ventricular hypertrophy (e.g., outflow obstruction, systemic hypertension, hypertrophic cardiomyopathy)</td>
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<td>Primary or secondary pulmonary hypertension</td>
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<td>Sleep apnea</td>
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<td></td>
<td>Atrial wall ischemia</td>
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<td>Age-related fibrosis</td>
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<tr>
<td>Inflammatory or infiltrative disease</td>
<td>Pericarditis</td>
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<td></td>
<td>Myocarditis</td>
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<td></td>
<td>Amyloidosis</td>
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<td></td>
<td>Celiac disease</td>
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<td></td>
<td>Other systemic inflammatory diseases</td>
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<tr>
<td>Endocrine disorder</td>
<td>Hyperthyroidism</td>
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<td></td>
<td>Pheochromocytoma</td>
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<td></td>
<td>Diabetes</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome/obesity</td>
</tr>
<tr>
<td>Mechanical</td>
<td>Intracardiac tumor</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Intracardiac catheters or leads</td>
</tr>
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<td></td>
<td>Alcohol</td>
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<tr>
<td></td>
<td>Drugs (e.g., cocaine, amphetamines, stimulants)</td>
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<td></td>
<td>Postoperative (cardiac, pulmonary, or esophageal)</td>
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<td></td>
<td>Neurogenic</td>
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<tr>
<td></td>
<td>Changes in autonomic tone (e.g., vagal stimuli, swallow-induced)</td>
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<td>Electrophysiologic abnormalities</td>
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Clinical Features

- In the young (<50y), the initial presentation is usually with paroxysmal AF
- Persistent AF (<50y) is often associated with identifiable causes like structural heart disease, hyperthyroidism or alcohol excess
- “Typical” symptoms of irregular palpitations, with or without chest pain, breathlessness, or dizziness
- Palpitations are reported in 80% of young with paroxysmal AF

Ruigómez A. BMC Card. Dis. 2005
Kerr C. AHJ 2005
AF Treatment in the Young

1. Rate control
2. Rhythm Control
   I. AAD
   II. Ablation
Rate Control in the Young

- No data available
- Young pts do not tolerate rate control medication
- Physically active, with faster conducting AV nodes → high ventricular rates at rest and even more during exercise
- Compared with older patients, b-blockers are more often associated with side effects leading to lower acceptance
- Even at higher doses they are often incapable of achieving heart rates <110 bpm during AF

Kerr C. EHJ 1996
Wasner K. EHJ 2014
Rhythm control in the young

• In young patients and in patients with a first detected AF episode
• This was independent of AF-related symptoms: 60% of centers used a rhythm control strategy in all patients after a first detected episode and almost 50% in young patients even if AF was well tolerated
## Rhythm control with antiarrhythmic drugs

<table>
<thead>
<tr>
<th>Potential benefits</th>
<th>Potential problems</th>
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<tbody>
<tr>
<td>Arrhythmia suppression (at least for some time, especially in patients with low AF burden)</td>
<td>Use over prolonged period time expected if effective; arrhythmia suppression, no definitive treatment AF recurrence 44–67% at 1 year</td>
</tr>
<tr>
<td>Easy to take</td>
<td>No proven benefit in mortality</td>
</tr>
<tr>
<td>Relatively safe, particularly in healthy individuals</td>
<td>More withdrawals due to adverse effects than controls</td>
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Rhythm control with catheter ablation

2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation

Indications for Catheter Ablation of Symptomatic Atrial Fibrillation

Symptomatic AF
- Paroxysmal AF
  - IIa: AA Drugs
  - Catheter Ablation
- Persistent AF
  - IIa: AA Drugs
  - Catheter Ablation
- Long-standing Persistent AF
  - IIb: AA Drugs
  - Catheter Ablation
Catheter ablation of atrial fibrillation in the young: insights from the German Ablation Registry

Chun KR. Clin Res Cardiol 2013
Safety and Efficacy of Atrial Fibrillation Ablation in Young Patients

Jane Dewire, BA1, Sunil Agarwal, MD2, Irfan K. Khurram, MD1, Joseph E. Marine, MD, FHR1, Ronald Berger, MD, PhD, FHR1, David Spragg, MD, FHR1, Hiroshi Ashikaga, MD, PhD1, John Rickard, MD1, Saman Nazarian, MD, PhD, FHR1, Hugh Calkins, MD, FHR1

**Figure 1: Age of Patients**

34.1 (5.6) years.

(62.5%) patients had paroxysmal AF

25 (62.5%) patients were free of AF without antiarrhythmic drugs (AAD)

40 (100%) patients experienced > 95% reduction of AF burden on or off AADs

No major complications or adverse events occurred during the study.
Catheter ablation of atrial fibrillation in very young adults: a 5-year follow-up study

Ardan M. Saguner†, Tilman Maurer‡, Erik Wissner, Francesco Santoro, Christine Lemes, Shibu Mathew, Christian Sohns, Christian H. Heeger, Bruno Reißmann, Johannes Riedl, Thomas Fink, Kentaro Hayashi, Peter Wohlmut, Karl-Heinz Kuck, Feifan Ouyang, and Andreas Metzner§

85 consecutive young adults (mean age 31 ± 4 years; 69% men) with symptomatic paroxysmal AF (PAF, n = 52) and persistent (Pers) AF (n = 33)

Recurrence-free survival (index / last procedure)

What’s new?

- The outcome after catheter ablation for atrial fibrillation (AF) in very young adults is not well defined
- Catheter ablation (± antiarrhythmic drugs) in adults ≤35 years of age with symptomatic AF can restore sinus rhythm in 84% at 5-years follow-up
- Structural heart disease and obesity independently predict AF recurrence in this population

Major complications occurred in 6/122 (4.9%)

Europace (2018) 20, 58–64
### Indications for catheter atrial fibrillation ablation in populations of patients not well represented in clinical trials

<table>
<thead>
<tr>
<th>Indication</th>
<th>Recommendation</th>
<th>Evidence Grade</th>
</tr>
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<tbody>
<tr>
<td>Congestive heart failure</td>
<td>It is reasonable to use similar indications for AF ablation in selected patients with heart failure as in patients without heart failure.</td>
<td>IIa B-R</td>
</tr>
<tr>
<td>Older patients (&gt;75 years of age)</td>
<td>It is reasonable to use similar indications for AF ablation in selected older patients with AF as in younger patients.</td>
<td>IIa B-NR</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>It is reasonable to use similar indications for AF ablation in selected patients with HCM as in patients without HCM.</td>
<td>IIa B-NR</td>
</tr>
<tr>
<td>Young patients (&lt;45 years of age)</td>
<td>It is reasonable to use similar indications for AF ablation in young patients with AF (&lt;45 years of age) as in older patients.</td>
<td>IIa B-NR</td>
</tr>
<tr>
<td>Tachy-brady syndrome</td>
<td>It is reasonable to offer AF ablation as an alternative to pacemaker implantation in patients with tachy-brady syndrome.</td>
<td>IIa B-NR</td>
</tr>
<tr>
<td>Athletes with AF</td>
<td>It is reasonable to offer high-level athletes AF as first-line therapy due to the negative effects of medications on athletic performance.</td>
<td>IIa C-LD</td>
</tr>
<tr>
<td>Asymptomatic AF**</td>
<td>Paroxysmal: Catheter ablation may be considered in select patients. **</td>
<td>IIb C-E0</td>
</tr>
<tr>
<td></td>
<td>Persistent: Catheter ablation may be considered in select patients. **</td>
<td>IIb C-E0</td>
</tr>
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## Arguments pro and contra rhythm control in young asymptomatic patients

<table>
<thead>
<tr>
<th><strong>Pro</strong></th>
<th><strong>Contra</strong></th>
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<tbody>
<tr>
<td>May prevent long-term consequences of AF as stroke, heart failure, increased mortality</td>
<td>AF by itself has not been shown to increase mortality in younger patients unless they have concomitant cardiovascular disease</td>
</tr>
<tr>
<td>Patients may become symptomatic later on</td>
<td>Stroke risk is independent of rhythm control strategies and at this point no data support discontinuation of anticoagulation with a rhythm control strategy</td>
</tr>
<tr>
<td>Rhythm control is easier to achieve at an early stage in younger patients and those with paroxysmal AF</td>
<td>Antiarrhythmic drugs are no good choice in young patients as they would have to take medication for many years with risk of side effects</td>
</tr>
<tr>
<td>Catheter ablation is superior to antiarrhythmic medication and may prevent recurrence and progression to persistent AF in the majority of younger patients</td>
<td>Catheter ablation still has a significant risk of complications. Its main benefit is improvement of symptoms (which is already the case in asymptomatic patients). Atrial fibrillation may still recur despite repeat procedures</td>
</tr>
</tbody>
</table>
Prevention of AF-related complications

- Only **anticoagulation** has proved **survival benefit** in the overall AF population.
- Pts (≤65 years) without comorbidities (CHA2DS2-VASc 0) have a very low annual risk of thromboembolic events and do not require OAC.
- Retrospective studies → may be safe to discontinue OAC after successful catheter ablation but no prospective data.
- AF frequently recurs after RFA or AADs → discontinuation of OAC beyond a CHA2DS2-VASc score of ≥1 based on a rhythm control strategy is most likely not a safe option.
Young and Atrial Fibrillation

- Etiology – Lone AF ???
- PV triggers - usually typical symptoms
- Rhythm control preferred - if symptomatic
- No AADs (moderate efficacy – side effects)
- Catheter Ablation encouraging results in young symptomatic – in asymptomatic ?? (AT post-ablation)