Κλινικά ερωτήματα στην Κολπική Μαρμαρυγή

ΝΙΚΟΛΑΟΣ ΦΡΑΓΚΑΚΗΣ
Αναπληρωτής Καθηγητής Καρδιολογίας ΑΠΘ
Γ' Κ/Δ Κλινική
Ιπποκράτειο Νοσοκομείο Θεσσαλονίκης
Πότε στέλνω τον ασθενή για ablation;
Catheter Ablation of AF

- Why catheter ablation in atrial fibrillation?

  The clinical outcome after catheter ablation is better as compared to AAD therapy.
Catheter Ablation and Antiarrhythmic Drug Therapy as First- or Second-Line Therapy in the Management of Atrial Fibrillation
Systematic Review and Meta-Analysis

Abdur Rahman Khan, MD; Sobia Khan, MBBS; Mujeeb A. Sheikh, MD; Sadik Khuder, PhD;
Blair Grubb, MD; George V. Moukarbel, MD

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Catheter Ablation</th>
<th>Anti-arrhythmic Drugs</th>
<th>Risk Ratio IV, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>2.1.1 Anti-arrhythmic Medication Naive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wazni 2005</td>
<td>4</td>
<td>33</td>
<td>22</td>
</tr>
<tr>
<td>Nielsen 2012</td>
<td>22</td>
<td>138</td>
<td>42</td>
</tr>
<tr>
<td>Morillo 2014</td>
<td>36</td>
<td>66</td>
<td>44</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>237</td>
<td>246</td>
<td>266</td>
</tr>
<tr>
<td>Total events</td>
<td>62</td>
<td>108</td>
<td>0.52 [0.30, 0.91]</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.16$; $\chi^2 = 7.24$, df = 2 ($P = 0.03$); $I^2 = 72$
Test for overall effect: $Z = 2.32$ ($P = 0.02$)

2.1.2 Previous Use of Anti-arrhythmic Medication

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Catheter Ablation</th>
<th>Anti-arrhythmic Drugs</th>
<th>Risk Ratio IV, Random, 95% CI Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>Total</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Krittayaphong 2003</td>
<td>3</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Stabile 2006</td>
<td>30</td>
<td>68</td>
<td>63</td>
</tr>
<tr>
<td>Pappone 2006</td>
<td>14</td>
<td>99</td>
<td>75</td>
</tr>
<tr>
<td>Oral 2006</td>
<td>25</td>
<td>77</td>
<td>53</td>
</tr>
<tr>
<td>Jais 2008</td>
<td>7</td>
<td>53</td>
<td>42</td>
</tr>
<tr>
<td>Follo 2009</td>
<td>7</td>
<td>35</td>
<td>20</td>
</tr>
<tr>
<td>Wilber 2010</td>
<td>35</td>
<td>103</td>
<td>47</td>
</tr>
<tr>
<td>Mont 2014</td>
<td>39</td>
<td>98</td>
<td>34</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>548</td>
<td>458</td>
<td>73.4%</td>
</tr>
<tr>
<td>Total events</td>
<td>160</td>
<td>343</td>
<td>0.37 [0.29, 0.48]</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.08$; $\chi^2 = 20.22$, df = 7 ($P = 0.005$); $I^2 = 65$
Test for overall effect: $Z = 7.48$ ($P < 0.00001$)

Total (95% CI) 785 | 696 | 100.0% | 0.40 [0.31, 0.52] |
Total events 222 | 451 | 0.40 [0.31, 0.52] |

Heterogeneity: $\tau^2 = 0.12$; $\chi^2 = 38.98$, df = 10 ($P < 0.0001$); $I^2 = 74$
Test for overall effect: $Z = 6.93$ ($P < 0.00001$)
Test for subgroup differences: $\chi^2 = 1.26$, df = 1 ($P = 0.26$), $I^2 = 20.8$
# Efficacy and safety of ablation for people with non-paroxysmal atrial fibrillation (Review)


<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Ablation</th>
<th>AADs</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forleo 2009</td>
<td>28/35</td>
<td>15/35</td>
<td></td>
<td>45.5%</td>
<td>1.87 [ 1.23, 2.83 ]</td>
</tr>
<tr>
<td>Monti 2014</td>
<td>69/98</td>
<td>21/48</td>
<td></td>
<td>51.9%</td>
<td>1.61 [ 1.14, 2.27 ]</td>
</tr>
<tr>
<td>Stabile 2006</td>
<td>13/26</td>
<td>0/19</td>
<td></td>
<td>2.6%</td>
<td>20.00 [ 1.26, 316.89 ]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>159</strong></td>
<td><strong>102</strong></td>
<td><strong>1.84 [ 1.17, 2.88 ]</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 110 (Ablation), 36 (AADs)
Heterogeneity: Tau² = 0.07, Chi² = 3.89, df = 2 (P = 0.14); I² = 49%
Test for overall effect: Z = 2.65 (P = 0.0080)
Test for subgroup differences: Not applicable

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Favours AADs    Favours 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

- Paroxysmal AF
  - IIa: AA Drugs
  - IIa: Catheter Ablation

- Persistent AF
  - IIa: AA Drugs
  - IIa: Catheter Ablation

- Long-standing Persistent AF
  - IIb: AA Drugs
  - IIb: Catheter Ablation

Recommend, reasonable, consider...
## 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter ablation of symptomatic paroxysmal AF is recommended to improve AF symptoms in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.</td>
<td>I</td>
<td>A</td>
<td>585–587, 713, 727</td>
</tr>
<tr>
<td>Catheter or surgical ablation should be considered in patients with symptomatic persistent or long-standing persistent AF refractory to AAD therapy to improve symptoms, considering patient choice, benefit and risk, supported by an AF Heart Team.</td>
<td>IIa</td>
<td>C</td>
<td>468,735, 777,831, 832, 1040</td>
</tr>
<tr>
<td>AF ablation should be considered in symptomatic patients with AF and heart failure with reduced ejection fraction to improve symptoms and cardiac function when tachycardiomyopathy is suspected.</td>
<td>IIa</td>
<td>C</td>
<td>185, 226–228, 720, 777–779, 828</td>
</tr>
<tr>
<td>AF ablation should be considered as a strategy to avoid pacemaker implantation in patients with AF-related bradycardia.</td>
<td>IIa</td>
<td>C</td>
<td>829, 830</td>
</tr>
</tbody>
</table>
The CASTLE-AF study

![Primary Composite Endpoint graph]

- Survival Probability vs Follow-Up Time (Months)
- Ablation and Conventional treatments compared
- HR, 0.62 (95% CI, 0.43-0.87); P=0.007
- Log-rank test: P=0.006
- Patients at Risk:
  - Ablation: 179, 141, 114, 76, 58, 22
  - Conventional: 184, 145, 111, 70, 48, 12

Marrouche, Brachmann et al. NEJM 2018
2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation

<table>
<thead>
<tr>
<th>B. Indications for catheter atrial fibrillation ablation in populations of patients not well represented in clinical trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
</tr>
</tbody>
</table>
Asymptomatic 40%\textsuperscript{4}

Failed Rx Ablation Candidate 30%\textsuperscript{3}

Rx Effective 30%

4% treated annually

Who is the Perfect Candidate for AF Ablation?

- Gender ?
- Age ?
- Type of AF ?
- LA size ?
- Comorbidities ?
The Impact of Age on 5-Year Outcomes After Atrial Fibrillation Catheter Ablation

T. JARED BUNCH, M.D.,†,‡ HEIDI T. MAY, Ph.D., M.S.P.H.,† TAMI L. BAIR, B.S.,† VICTORIA JACOBS, N.P.,† BRIAN G. CRANDALL, M.D.,† MICHAEL CUTLER, D.O., Ph.D.,† J. PETER WEISS, M.D.,† CHARLES MALLENDER, M.D.,† JEFFREY S. OSBORN, M.D.,† JEFFREY L. ANDERSON, M.D.,† and JOHN D. DAY, M.D.,†

J Cardiovasc Electrophysiol, 2016;27:141-146
Selected clinical trials of catheter ablation of atrial fibrillation and/or for FDA approval

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>Type</th>
<th>N</th>
<th>AF type</th>
<th>Ablation strategy</th>
<th>Initial time frame</th>
<th>Effectiveness endpoint</th>
<th>Ablation success</th>
<th>Drug/Control success</th>
<th>P value for success</th>
<th>Ablation complications</th>
<th>Drug/Control complications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Trials Performed for FDA Approval</td>
<td>2019</td>
<td>Randomized to RF ablation or AAD, multi-center</td>
<td>167</td>
<td>Paroxysmal</td>
<td>FVI, optional CFAE and lines</td>
<td>12 months</td>
<td>Freedom from symptomatic paroxysmal atrial fibrillation, acute procedural failure, or changes in specific drug regimen</td>
<td>66%</td>
<td>16%</td>
<td>&lt;0.001</td>
<td>4.9%</td>
<td>8.8%</td>
<td>FDA approval received</td>
</tr>
<tr>
<td>JACC 2013: 61: 1713-1723 (STOP AF)</td>
<td>2013</td>
<td>Randomized to cryoballoon ablation or AAD, multi-center</td>
<td>245</td>
<td>Paroxysmal</td>
<td>FVI</td>
<td>12 months</td>
<td>Freedom from any detectable AF, or non-study AAD, or non-protocol intervention</td>
<td>70%</td>
<td>7%</td>
<td>&lt;0.001</td>
<td>3.1%</td>
<td>NA</td>
<td>FDA approval received</td>
</tr>
<tr>
<td>Heart Rhythm 2014: 202-209 (TITOP)</td>
<td>2014</td>
<td>Randomized to phased RF 210</td>
<td>260</td>
<td>Persistent</td>
<td>FVI + CFAEs</td>
<td>6 months</td>
<td>Acute procedural success &gt;50% reduction in burden of AF</td>
<td>54%</td>
<td>26%</td>
<td>&lt;0.001</td>
<td>12.2%</td>
<td>NA</td>
<td>Not FDA approved</td>
</tr>
<tr>
<td>JACC 2014: 64: 647-656 (SMART-AF)</td>
<td>2014</td>
<td>Non-randomized multi-center study of contact force-sensing RF catheter, comparing to performance goals</td>
<td>172</td>
<td>Paroxysmal</td>
<td>FVI, optional CFAEs and lines</td>
<td>12 months</td>
<td>Freedom from symptomatic AF, flutter, tachycardia, acute procedural failure, or change in AAD</td>
<td>72.5%</td>
<td>N/A</td>
<td>&lt;0.0001</td>
<td>7.5%</td>
<td>NA</td>
<td>FDA approval received</td>
</tr>
<tr>
<td>Circulation 2015: 132: 907-915 (TOCCATA)</td>
<td>2015</td>
<td>Randomized to contact force-sensing RF catheter or approved RF catheter, comparing to treatment goals</td>
<td>300</td>
<td>Paroxysmal</td>
<td>FVI, optional triggers, CFAEs and lines in both arms</td>
<td>12 months</td>
<td>Freedom from symptomatic AF, flutter, tachycardia, acute procedural failure, or change in AAD</td>
<td>67.8%</td>
<td>49.4%</td>
<td>0.0071 for non-inferiority</td>
<td>7.2%</td>
<td>9.7%</td>
<td>FDA approval received</td>
</tr>
<tr>
<td>JACC 2015: 66: 1350-1360 (HeartLight)</td>
<td>2015</td>
<td>Randomized to interventional vs approved RF catheter, multi-center</td>
<td>335</td>
<td>Paroxysmal</td>
<td>FVI vs CTI ablation vs PIT, optional CFAEs, and lines</td>
<td>12 months</td>
<td>Freedom from symptomatic AF, flutter, tachycardia, acute procedural failure, or non-protocol intervention</td>
<td>61.1%</td>
<td>61.7%</td>
<td>0.003 for non-inferiority</td>
<td>5.3%</td>
<td>6.4%</td>
<td>FDA approval received</td>
</tr>
</tbody>
</table>
Ablation of persistent AF: STAR-AF II

single procedure success: Long-Standing Persistent AF

Follow-up: 56.3 (Q1,Q3: 49.1, 66.8) months

Sinus Rhythm in 20.3%
Different evolutions of AF in relation to substrate remodelling and trigger density

Nattel S et al., *Eur Heart J* 2014;35:1448–1456
Factors contributing to atrial damage

AF contributes to the remodeling progressing the AF disease – need to treat the AF.
AAD vs. ablation

Impact of catheter ablation on mortality
Data from Swedish health registries

Friberg L et al., Eur Heart J 2016;37:2478–87
Impact of catheter ablation on ischemic stroke – Data from Swedish health registries

Friberg L et al., Eur Heart J 2016;37:2478–87
The EAST study: redefining the role of rhythm control therapy in atrial fibrillation

EAST, the Early treatment of Atrial fibrillation for Stroke prevention Trial
The ITT analysis showed no differences in the primary endpoint or mortality, but the HR for the first occurrence of AF (after a blanking period) was 0.53 (95% CI, 0.46 - 0.61; \( P < .0001 \)) for ablation vs rate-control or rhythm-control drug therapy.

Patients younger than 65 years seemed to show a pronounced benefit from ablation, while patients older than 75 showed little. Patients with heart failure seemed to especially benefit.

In that "treatment-received" analysis of the trial, there was also a 40% drop in mortality (\( P = .005 \)) for patients who underwent ablation compared with those managed with drug therapy.
Με ποια κριτήρια επιλέγω μεταξύ ελέγχου συχνότητας (rate control) και ελέγχου ρυθμού (rhythm control) και ποια φαρμακευτική αγωγή χρησιμοποιώ αντίστοιχα

Κλινικά ερωτήματα στην Κολπική Μαρμαρυγή
No advantage of rhythm over rate control


Rhythm control only instituted for reduction of symptoms

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

Recommendations

Catheter ablation of symptomatic paroxysmal AF is recommended to improve AF symptoms in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.

Catheter ablation of AF should be considered as first-line therapy to prevent recurrent AF and to improve symptoms in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk.
Four reasons to consider rate control

- Background treatment in all patients with atrial fibrillation
- First choice treatment in patients with no or minor symptoms
- Treatment after failure of rhythm control
- Treatment when risks restoring sinus rhythm outweigh benefits
Optimum heart rate during AF

Rate control in atrial fibrillation

Isabelle C Van Gelder, Michiel Rienstra, Harry J G M Crijns, Brian Olshansky

Choice of drugs for rate control

Assess comorbidities

First-line treatment

None, Hypertension, or HFpEF
• β blocker or ND-CCA

HFrEF
• β blocker

Severe COPD or asthma
• ND-CCA

Pre-excited atrial fibrillation or atrial flutter
• Ablation

Second-line treatment

• Digoxin and/or β blocker and/or ND-CCA

Clinical reassessment*

Consider addition of other rate-controlling drug

• Digoxin and/or Amiodarone

IIa

Atrioventricular node ablation should be considered to control heart rate in patients unresponsive or intolerant to intensive rate and rhythm control therapy, accepting that these patients will become pacemaker dependent.

Lancet 2016; 388:818–28
Take home messages

Catheter ablation is an established treatment option for AF

Clinical predictors of a poorer outcome include

- non-PAF and particularly long-term persistent AF
- increased age
- sleep apnea, obesity, hypertension
- increased LA size (> 5 cm)
Take home messages

- Rate control is crucial in AF management
- It is background therapy for nearly all AF patients
- Rate control may be first choice therapy in elderly asymptomatic patients or when risks restoring sinus rhythm outweigh benefits
- A lenient strategy is safe, effective and easy to institute: it is reasonable to initiate first
- A stricter approach is indicated if symptoms persist or deterioration of cardiac function occurs
Ευχαριστώ για την προσοχή σας