CardioEgypt 2010

Atrial Fibrillation: What to do when medical therapy fails

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“When medical therapy fails…”

- Patient symptoms or evidence of recurrent AF?
- Realistic assessment of each patient’s symptoms, response to treatment and likely long-term outcome
- What are the patient’s concerns?
  - Side-effects, e.g. bleeding on anticoagulants
  - Symptoms
  - Stroke risk
Non-pharmacological options

- Cardioversion
- Pacing
  - For sinus node disease
  - For “AF prevention”
- Ablation
  - AV node ablation + pacemaker
  - Pulmonary vein isolation / left atrial ablation

Ablation for Atrial Fibrillation
Main reference

Triggers

Substrate

Modulating Factors

Paroxysmal AF

Elimination of pulmonary vein triggers
Focal Ablation for Paroxysmal AF

- 45 patients with frequent episodes of atrial fibrillation (mean [±SD] duration, 344±32 minutes per 24 hours) refractory to drug therapy.
- Spontaneous initiation of atrial fibrillation was recorded
  - earliest electrical activity preceding onset of AF
- Single origin in 29 pts, multiple in 16
  - 94% of foci in pulmonary veins
- Follow-up period of 8±6 months after ablation
  - 62% had no recurrence of atrial fibrillation.

Ablation for Paroxysmal AF

- Electrogram-based pulmonary vein isolation versus anatomically-based wide area circumferential ablation
- PVI using RF energy, cryo, High-intensity focussed ultrasound, or other modalities
- WACA requires mapping system, e.g. Carto or NavX, + image integration with CT / MRI
Ablation for Paroxysmal AF

- Success rates 60-80%
- May require 2 or more procedures
- Complications include:
  - tamponade (1-5%)
  - stroke (0.5-1%)
  - PV stenosis (now rare)
  - atrio-oesophageal fistula (with extensive ablation procedures)

Ablation for Paroxysmal AF
Indications

- Symptomatic paroxysmal AF
  - Symptoms severe enough to warrant treatment
  - Not just “to get off drugs / warfarin”
- Drug-resistant
  - 1, 2 or more drugs?
  - Limited efficacy of multiple drug trials
  - Occasionally as “first-line” Rx
- Patients need to be aware of risks and of operator’s success rate
Persistent AF

Substrate modification
Circumferential left atrial ablation
Substrate modification
Clinical trials

### Ablation v Drugs as first-line Rx

- 70 patients with AF (at least 1 episode / month for 3 months; 96% paroxysmal, 4% persistent)
- Randomised to:
  - pulmonary vein isolation (PVI) guided by circumferential PV mapping catheter (n=33)
  - antiarrhythmic drugs (flecainide, propafenone, sotalol) (n=37)
- 1 year follow-up; primary end-point recurrence of symptomatic AF (or > 15 s of asymptomatic AF)
  - Loop recorder for 1st & 3rd months; 24 h Holters at 3,6 & 12 months

Wazni et al 2005; *JAMA* 293: 2634-40
Ablation v Drugs as first-line Rx
Results

- During initial 2 months:
  - 20 pts in drug-treated group had AF; 26 hospitalisations
  - 9 pts in PVI group had AF; no hospitalisations

- After 2 months:
  - 3 patients (2 AA drug, 1 PVI) lost to follow-up
  - Symptomatic recurrences in:
    - 22 (63%) of drug-treated pts
    - 4 (13%) of PVI-treated pts

Wazni et al 2005; *JAMA* 293: 2634-40

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Ablation v Drugs as first-line Rx
Results

- Asymptomatic AF in 16% of drug-treated pts and 2% of PVI-treated pts
- Initial drug used was flecainide in 77%, sotalol in 23%; drug changed in 16 pts
- Beta-blockers continued in 43% of PVI pts and 52% of AA-drug pts
- Hospitalisation in 19 (54%) of AA drug pts, 3 (9%) of PVI pts
- QOL scores (SF-36) better in PVI pts

Wazni et al 2005; *JAMA* 293: 2634-40
RF ablation as adjunct to antiarrhythmic drugs: Catheter Ablation for Cure of AF (CACAF Study)

- 137 pts with paroxysmal (67%) or persistent (33%) AF randomised to RF ablation and drugs or drugs alone
  - Amiodarone in 64%
- Primary end-point: any atrial arrhythmia lasting >30s (after 1-month “blanking period”)
- After 1 year, arrhythmia recurrences in
  - 63/69 (91.3%) control group (all AF)
  - 30/68 (44.1%) ablation group (P<0.001)
    - 26 AF, 4 A Flutter
- 3 major complications (4.4%)
  - 1 stroke, 1 tamponade, 1 transient phrenic paralysis

Results of wide area ablation for AF

- 1171 consecutive patients referred to a single centre in Milan for Rx of AF
  - 70% paroxysmal, 30% chronic
- 589 treated with ablation
- 582 received anti-arrhythmic drugs
  - Non-randomised
- Quality of life measured with SF-36 in 20% of patients

Pappone et al JACC 2003; 42: 185-97
Causes of Death and Adverse Events During Follow-Up

Pappone et al JACC 2003; 42: 185-97
p < 0.001

Pappone et al JACC 2003; 42: 185-97
APAF study

- 198 patients with paroxysmal AF, randomised to antiarrhythmic drugs v ablation
- Freedom from AF at 1 year:
  - 93% in ablation group
  - 35% in drugs group

Pappone et al JACC 2006; 48: 2340-7

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CPVA (n = 99)</th>
<th>ADT Group (n = 99)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>55 ± 10</td>
<td>57 ± 10</td>
<td>0.24</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>69/30</td>
<td>64/35</td>
<td>0.54</td>
</tr>
<tr>
<td>AF episode/month</td>
<td>6 ± 4</td>
<td>6 ± 6</td>
<td>0.81</td>
</tr>
<tr>
<td>Duration of AF (yrs)</td>
<td>6 ± 4</td>
<td>6 ± 6</td>
<td>0.81</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
<td>40 ± 6</td>
<td>38 ± 6</td>
<td>0.25</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5.1%</td>
<td>4%</td>
<td>1.00</td>
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<tr>
<td>Hypercholesterolemia</td>
<td>17%</td>
<td>21%</td>
<td>0.59</td>
</tr>
<tr>
<td>Hypertension</td>
<td>56%</td>
<td>57%</td>
<td>1.00</td>
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<tr>
<td>LVEF (%)</td>
<td>60 ± 8</td>
<td>61 ± 6</td>
<td>0.49</td>
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<tr>
<td>Coronary artery disease</td>
<td>2%</td>
<td>2%</td>
<td></td>
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<tr>
<td>Valvular heart disease</td>
<td>3%</td>
<td>1%</td>
<td>0.22</td>
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<tr>
<td>Congenital heart disease</td>
<td>2%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>No. of previously ineffective antiarrhythmic drugs</td>
<td>2 ± 1</td>
<td>2 ± 1</td>
<td>0.63</td>
</tr>
</tbody>
</table>
A

99 patients randomized to CPIA

- Stable SR (n = 65)
- Recurrent AF (n = 11)
- Post-ablation AT (n = 3)

ADT stopped (n = 86)
OAT stopped (n = 52)
ADT controlled (n = 5)
REDO (n = 6)
Gap-related (n = 2)
Macroreentrant (n = 1)

- Recurrent AF (n = 1)
- Stable SR (n = 3)

B

99 patients randomized to ADT

- AF suppression with the first tested ADT (n = 24)
- AF recurrence with the first tested ADT (n = 75)

Combination therapy

- Flecainide plus amiodarone (n = 26)
- Flecainide plus antiarrhythmic (n = 49)

- Stable SR (n = 11)
- Cross over to CAVR (n = 42)
- AF control (n = 33)

AF recurrence (n = 5)
No AF recurrence (n = 94)

Pappone et al JACC 2006; 48: 2340-7
Pappone et al. JACC 2006; 48: 2340-7

Pappone et al.
Randomised Non-randomised

JACC 2006; 48: 2340-7

JACC 2003; 42: 185-97
Ablation and Drugs

- Significance of early recurrences of AF (within first 2-3 months) is uncertain
- Some patients will have “partially successful” ablations
  - Arrhythmia controlled on drugs which were previously ineffective
- Many centres use antiarrhythmic drugs for 2-3 months post-ablation (and/or ignore early recurrences)
- Drugs may be useful to prevent early recurrences and promote “favourable electrical remodelling” (“SR begets SR”)

Conclusions

- Ablation for AF is generally considered appropriate for selected patients with severe symptoms despite antiarrhythmic drugs
- A few patients might be treated by ablation as first-line Rx
- Most patients are treated with antiarrhythmic drugs for 2-3 months post-ablation
- “Cure” rates vary between 50 – 80%
  - in most series, an additional 10% are controlled on antiarrhythmic drugs which were previously ineffective
AF ablation – indications 2010

1. Patients with documented paroxysmal AF, with:
   - symptoms clearly correlated to the documented arrhythmia
   - persistent symptoms resistant to at least two anti-arrhythmic drugs (or resistant to one drug, and with a strong contraindication to further drug trials)
   - symptoms occurring > every three months
   - symptoms that are severe enough to impair quality of life
   - structurally normal heart or mild structural heart disease
   - no contraindication to the catheterisation procedure
   - full understanding of risks / benefits of procedure

2. Patients who have recently progressed from recurrent paroxysmal atrial fibrillation to persistent atrial fibrillation (of less than six months’ duration) who fulfil the above criteria.
AF ablation – indications 2010

3. Rarely, patients with persistent atrial fibrillation or "permanent" atrial fibrillation (i.e. patients in whom cardioversion has failed) with:
   - severe symptoms in atrial fibrillation, not due solely to poor rate control
   - persistent symptomatic AF despite cardioversion on antiarrhythmic drugs
   - structurally normal heart or mild structural heart disease
   - no contraindication to the catheterisation procedure
   - a full understanding of the risks and benefits of the procedure
   - a reasonable expectation of a successful outcome (including, in practice, age <70)

Catheter Ablation for Arrhythmias

<table>
<thead>
<tr>
<th>WPW, SVT</th>
<th>Atrial flutter</th>
<th>Atrial fib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early 1990s</td>
<td>Mid 1990s</td>
<td>2000s</td>
</tr>
<tr>
<td>Uncommon</td>
<td>Moderate</td>
<td>Common</td>
</tr>
<tr>
<td>Relatively straightforward</td>
<td>Moderate</td>
<td>Difficult</td>
</tr>
<tr>
<td>Success &gt;95%</td>
<td>Success 90-95%</td>
<td>Success 50-70%</td>
</tr>
<tr>
<td>&quot;Esoteric&quot;</td>
<td>→</td>
<td>Mainstream</td>
</tr>
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</table>
Pacing to Prevent AF

- Sinus node disease + PAF
  - Atrial pacing superior to V pacing for reducing frequency of AF
- PAF without bradycardia
  - Pacing to reduce AF burden?
    - Some “industry-sponsored” trials showing reduction in AF burden
  - Pacing prior to ablation of AV conduction

Brady - Tachy Syndrome
Case study

L van B ♂  DoB 16/12/1770

- Professional musician
- Multiple medical problems
  - inflammatory bowel disease
  - deafness
  - psychiatric and social problems
  - palpitations since age 30 - detailed description:
PA³ Study

- Inclusion: symptomatic (antiarrhythmic drug-refractory) PAF in the absence of symptomatic bradycardia

- 2 study phases
  - Phase 1: Randomization between DDIR vs. no pacing (prior to ablation)
  - Phase 2: Randomization with crossover between DDDR vs. VDD (after ablation)
PA$^3$: Phase 2 - VDD vs. DDDR

- No difference between VDD and DDDR pacing in the prevention of AF