Left atrial appendage occlusion: Ready for prime time?

David Hildick-Smith
Sussex Cardiac Centre
Brighton, UK
Proctor: AGA, NMT, Gore
Advisory Board: Coherex
• 500,000 strokes/year in U.S.
• Up to 20% of ischemic strokes occur in patients with atrial fibrillation

Percent of Total Strokes Attributable to Atrial Fibrillation

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>10</td>
</tr>
<tr>
<td>60-69</td>
<td>15</td>
</tr>
<tr>
<td>70-79</td>
<td>20</td>
</tr>
<tr>
<td>80-89</td>
<td>30</td>
</tr>
</tbody>
</table>
Non-Valvular Atrial Fibrillation Stroke Prevention
Medical Rx

- Warfarin cornerstone of therapy
- Assuming 51 ischemic strokes/1000 pt-yr
- Warfarin prevents 28 strokes at expense of 11 fatal bleeds
  - 60-70% risk reduction vs no treatment

Cooper: Arch Int Med 166, 2006
Non-Valvular AF Stroke Prevention
Warfarin Rx

- Narrow therapeutic window
- Multiple interactions
- Repeat blood tests
- Compliance
Non-Valvular Atrial Fibrillation Warfarin Use in AF Patients by Age
Non-Valvular Atrial Fibrillation Stroke Pathology

- Insufficient contraction of LAA leads to stagnant blood
- 90% of thrombus found in LAA

Johnson: Eur J Cardiothoracic Surg 17, 2000
Fagan: Echocardiography 17, 2000
WATCHMAN® LAA Closure Technology
PROTECT AF Clinical Trial Design

• Prospective, randomized study of WATCHMAN LAA Device vs long-term warfarin therapy
• 2:1 allocation ratio device to control
• 800 patients enrolled from Feb 2005 to Jun 2008
  – Device group (463)
  – Control group (244)
  – TEE follow-up at 45 days, 6 months and 1 year
  – Clinical follow-up biannually up to 5 years
  – Regular INR monitoring while taking warfarin
Intent-to-Treat
Primary Safety Results

Event-free probability

900 patient-year analysis

Days

365 730 1095

143 51 11

261 87 19

Device
Control
Intent-to-Treat Primary Efficacy Results

Event-free probability vs. Days for WATCHMAN and Control groups.

900 patient-year analysis

Days: 365, 730, 1095

WATCHMAN:
- 365 days: 147 events
- 730 days: 52 events
- 1095 days: 12 events

Control:
- 365 days: 270 events
- 730 days: 92 events
- 1095 days: 22 events
Continued access Registry (n=460)

<table>
<thead>
<tr>
<th></th>
<th>Registry</th>
<th>Protect AF</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>3.3%</td>
<td>7.7%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>2.2%</td>
<td>5.0%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Reddy et al Circulation 2011
• READY FOR PRIME TIME?
• Not yet
  – Inexperience with implantation
  – Procedural complications
  – Patient acceptability
  – Expense and potential volume
  – Multiple devices in development
  – Philosophical aspects
• Inexperience with implantation
  – few operators in UK have done >10 cases
  – more demanding than ASD closure
  – operators need to be experienced with
    • transseptal puncture
    • device placement
• Procedural complications
  – transseptal puncture
  – large calibre catheters
    • air embolism, clot delivery
    • LAA thin-walled
  – robust devices
    • retaining hooks
    • risk of embolisation (circular device, elliptical os)
• Patient acceptability
  – patients usually have no symptoms
  – 3% procedural risk
  – potential of long-term benefit
  – “take my chances”
• Expense and volume
  – up-front costs for long-term “savings”
  – commissioners sensitised by TAVI
  – lab time and operator availability
• Multiple devices in development
  – Watchman
  – Amplatzer ACP
  – Coherex waveform
  – GORE
  – Pericardial lasso
  – Surgical approaches (AF abln plus LAA removal)
• Philosophical issues:
  – When does “primary prevention” stop being sensible?

• Antihypertensives for octogenarians?
• Statins for nonagenarians?
• Devices for the asymptomatic over-80’s?
• Imaginary asymptomatic patient aged 85:
  – ACE-I and statin for HT and cholesterol?
  – TAVI for asymptomatic severe AS?
  – Mitraclip for asymptomatic severe MR?
  – EVAR for asymptomatic AAA?
  – LAAO for asymptomatic AF?
  – What are we trying to achieve?
• If not for prime time, then for whom?
  – patients with contraindications to warfarin
    • e.g. severe haemorrhagic episode on warfarin
  – patients with strong personal preference
• For the future:
  – lower risk
  – softer devices
  – mould to LAA
  – repositionable
  – redeliverable
Parallels with other technologies:

- TAVI initially for surgical turn-downs
  - equivalent to warfarin-contraindicated
- Now TAVI for surgical high risk
  - equivalent to LAAO for higher CHADS score AF
- In 10 years TAVI for 50% of all AVR
  - in ten years, LAAO for 25% of all AF