Update on Percutaneous PFO Closure

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Embolus Crossing a PFO

- Peripheral embolism
- Death
- Stroke

... but the discussion is still ongoing
Stroke is associated with PFO

Lechat 1988
Webster 1988
De Belder 1992
Di Tullio 1992
Hausmann 1992
Cabanes 1993

Cryptogenic Stroke  Control
Not only in young patients
Prevalence of Patent Foramen Ovale in cryptogenic stroke

- Prospective examination of 503 consecutive stroke patients
- 227 patients with cryptogenic stroke and 276 control patients with stroke of known cause

There is general agreement...

- ... that there is a risk of recurrence after the first paradoxical embolism due to a PFO
- ... that after a paradoxical embolism there is a need for some preventive treatment
- ... that having a PFO does not have any advantages
Meta-analysis of Event Rates in Patients with Cryptogenic Stroke

- 12 studies with 943 medically treated cryptogenic stroke pts (mean age 45 years, mean F/U 34 mos)
- 12 studies with 1,430 stroke pts after PFO closure (mean age 46 years, mean F/U 18 mos)
Update on Randomized Trials
Closure I (NMT)
PFO-Closure vs Medical Therapy

- Age 18-60 yrs
- Prior TIA/stroke
- 1600 patients planned
  - in April 2007 reduced to 800
- 95 centers (US, Canada, UK)
- Enrolment completed 2008 (900 patients)
  - Results to be reported at AHA 2010
RESPECT (Amplatzer) PFO-Closure vs Medical Therapy

- Age 18-55 yrs
- Prior stroke/TIA
- 500 pts planned
  - >500 enrolled in Dec 2008
  - Enrolment is ongoing
PC Trial
PFO-Closure vs Medical Therapy

- PC Trial
  - Plan: 450 patients
    - randomized closure with Amplatzer PFO occluder vs medical therapy,
      FU 5 yrs
  - Study started in 2000
  - Enrolment finished?
What are the problems with these randomized trials?

- Some centers had limited experience with the procedure when they started
- Patient numbers are rather small
- Patients with a clear paradoxical embolism got their PFO closed outside of the trials
- Follow-up is rather short
- Technology outdated
So what if these trials are …

• positive, i.e. PFO closure is better than medical therapy
  - Neurologist will not believe it

• negative, i.e. medical therapy is better than PFO closure
  - Cardiologists will not believe it

• Patients will prefer PFO closure anyway
  - because they just do not want to take anticoagulation therapy forever
PFO and Migraine
Many case series and also prospective non-randomized trials have shown a benefit of PFO closure in migraine …

… in particular if the PFO was closed to prevent recurrent stroke
The MIST trial was the first randomized trial PFO closure vs sham procedure in migraine patients who did not have a stroke ...

... and it was negative
MIST: Very high prevalence of PFO in migraine

<table>
<thead>
<tr>
<th>result</th>
<th>total #</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>total studied</td>
<td>432</td>
<td>100</td>
</tr>
<tr>
<td>small shunts (atrial and pulmonary)</td>
<td>72</td>
<td>16.7</td>
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<tr>
<td>large pulmonary shunt</td>
<td>22</td>
<td>5.1</td>
</tr>
<tr>
<td>ASD</td>
<td>3</td>
<td>0.7</td>
</tr>
<tr>
<td>large PFO</td>
<td>163</td>
<td>37.7</td>
</tr>
<tr>
<td>large shunts (all types)</td>
<td>188</td>
<td>43.5</td>
</tr>
<tr>
<td>total shunts</td>
<td>260</td>
<td>60.2</td>
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</table>

Prevalence of large shunts was approximately six times greater than in the general population.
# MIST - Cure of Migraine

**Primary Endpoint**

<table>
<thead>
<tr>
<th>% of patients</th>
<th>PFO Closure</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.1</td>
<td>4.1</td>
</tr>
<tr>
<td>n.s.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are not significantly different (n.s.).
50% Reduction in Headache Days

Exploratory analysis

PFO Closure: 42% reduction
Sham: 23% reduction

% of patients

n.s.
PRIMA

- Amplatzer PFO occluder for migraine therapy
- Randomized multicenter study, unblinded
- Primary endpoint: Reduction of migraine days
- Ongoing
3 other migraine trials have been stopped due to slow enrolment and/or lack of funding

- MIST II
- ESCAPE US
- ESCAPE EU
So should we close PFOs to prevent migraine?

Not yet!
How to Close the PFO?
CSI – Catheter Interventions in Congenital & Structural Heart Diseases

www.csi-congress.org
A variety of different devices have been used for PFO closure.
Morphology of PFO varies

• Location
  - Close to or away from the aorta
• Size
  - Up to 28mm
• Tunnel length
  - 0 to 25mm
• Single – multiple perforations
• Additional septal membranes
• Septum aneurysm
• Eustachian valve, Chiari network
The tailored approach

• Certain PFO designs fit better to certain anatomic conditions
• Others fit better to certain patient conditions
  - Clotting disorder
  - Atrial fibrillation
New Devices for PFO Closure
How can new devices and techniques improve outcome?

- Lower profile and less foreign material could reduce risk of thrombus formation.
- Softer devices and in tunnel devices could reduce distortion of the septum and risk of atrial fibrillation.
- Bioresorbable devices and non device closure techniques could prevent unknown long-term complications.
New Devices and Techniques

• New umbrella devices
• Suture based techniques
• Non device closure
• Bioresorbable devices
• In-tunnel devices
New Devices and Techniques

- New umbrella devices
- Suture based techniques
- Non device closure
- Bioreabsorbable devices
- In-tunnel devices
Solysafe®

- Self-centering
- Phynox wires
- Polyester patches
- In the defect, wire holders are moved towards each other
- Clicking mechanism keeps the wire-holders together
- Short 10 F introducer

New version for PFO under development
Occlutech PFO Occluder

Single layer PFO  Double layer PFO
Similar to Amplatzer but no left atrial hub
Nitocclud PFO (PFM)

- Nitinol
- One single wire
- Fabric on the left side
- Very flexible delivery system
  - No tension between delivery cable and device before release
Nitocclud PFO (PFM)

EU trial has finished enrolment
Results to be presented at CSI

Courtesy F Freudenthal
Spider (Lifetech)

- Right Disc: Nitinol mesh frame with ePTFE membrane
- Left Disc: Nitinol braid wire anchors covered with ePTFE patch
New Devices and Techniques

• New umbrella devices
• Suture based techniques
• Non device closure
• Bioreosorbable devices
• In-tunnel devices
Suture Techniques

- Less foreign material
- Mimic surgery
Edwards E2E System

Therapy Catheter
Vacuum port, needles, suture
Suture based PFO Closure

Animal trials very promising

In humans this did not work
The Sutura SuperStitch® EL Arms and Needles

• Based on a puncture site closure technique
• Profile: 12 Fr
• Working length: 90 cm
• Suture type: Polypropolene 4-0

Courtesy C. Ruiz
NobleStitch Suture Mediated PFO Closure

Introduce NobleStitch

Suture Septum Primum

Suture Septum Secundum

FIM results to be presented at CSI
New Devices and Techniques

- New umbrella devices
- Suture based techniques
- Non device closure
- Bioreabsorbable devices
- In-tunnel devices
Non device closure

• Offer a psychological advantage

• Avoid all device related long-term complications including those not known yet
PFX™
Radiofrequency Closure System

- First implant free device for intracardiac defect closure
- Leaving no foreign body behind
PFO Closure by Radiofrequency

Immediately after
CoAptus: A New Approach of Non-device Closure

- Using radiofrequency
- Septum primum and septum secundum are coapted mechanically
- Then energy is applied
- Thereafter, the device is removed leaving nothing behind
28 day

RA

LA
New Devices and Techniques

- New umbrella devices
- Suture based techniques
- Non device closure
- Bioreorbable devices
- In-tunnel devices
Resorbable devices

- Offer a psychological advantage
- Avoid all device related long-term complications including those not known yet
BioSTAR (NMT)

- CardioSEAL® framework
- STARFlex® self-centering mechanism
- Bioresorbable collagen matrix, heparin coating
- CE mark
BioTREK™ Bioabsorbable Septal Repair

- 100% absorption over time
- novel bioabsorbable polymer (P4HB)
  - absorbs as a non-inflammatory natural metabolite
- easily repositionable and retrievable
- radiopaque and echogenic
- currently in pre-clinical studies

6 months

Explant photo courtesy of Aaron V. Kaplan, MD and Ebo D. de Muinck, M.D. Ph.D., Dartmouth Medical School (USA)
New Devices and Techniques

- New umbrella devices
- Suture based techniques
- Non device closure
- Bioresorbable devices
- In-tunnel devices
In-tunnel devices

- Minimize surface area
- Minimize risk of thrombus formation
- Minimize risk of atrial fibrillation
- Less foreign material in the body
In-Tunnel Devices

SeptRX
In clinical trials

CohereRX FlatStent RX
CE mark

Not FDA approved
The SeptRx- System

- Nitinol frame and Nitinol wire mesh
- Small left and right atrial anchors
- Sits almost completely within the PFO tunnel
- FIM trial finished
Coherex EF

Designed to "Stent" the PFO tunnel
Nitinol and Polyurethane
Coherex

- PFO closure from inside

Results of FIM to be presented at PCR and CSI
Which will be the best PFO closure device?

- There will be no "best device"
- Each PFO has its own best device
- The tailored approach is the way to go
Take Home Messages

• PFO is a frequent cause of "cryptogenic" stroke
• PFO closure prevents paradoxical embolism and stroke
  - Randomized trials will be finished very soon
• There is a need for more randomized PFO closure trials in migraine patients
• Many new PFO closure devices are under development