What is the Patent Foramen Ovale (PFO)?
When and How to Treat

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Causes of Stroke

750,000 recognized strokes annually in US
The leading cause of disability
Third leading cause of death (200,000/yr)

15% Hemorrhagic
>95% Lacunar
<5% Large vessel

85% Ischemic
25% Thrombotic
~40% Cryptogenic
~30% Arch, Large Vessel

Atrial Fibrillation
~30% Cardiac Source

Akinetic segment
Cardiomyopathy
Mitral Stenosis
Other
Patent foramen ovale (PFO) is a flap-like opening between the primum and secundum atrial septum at the level of fossa ovalis that may persist after birth.
Anatomy and Physiology
Incidence
Connection with cryptogenic stroke
Closure devices
Closure procedure
Randomised trial

Normal Fetal Circulation

From Body/Placenta

LUNGS

Right Atrium

Left Atrium

Body/Placenta
Anatomical closure
(∼70%)

Functional closure
(∼30%)

Laminar thrombosis
(fibrosis)

Δ transatrial pressure
gradient
(PFO)
Functional Closure

In most individuals fragile adhesions form between septum secundum superiorly and thin flap like septum primum inferiorly and close the foramen permanently.

In some an oblique tunnel like opening persists between the septa called patent foramen ovale (PFO).

Size of PFO varies between 1 – 19 mm with a mean diameter of 4.9 mm.
The concept of preferential flow

Blood flow from IVC is directed against fossa ovalis and blood from SVC is directed towards tricuspid

Clockwise Rotation of Blood Flow
Physiology of PFO

Usually allows right to left shunt during.....

Physiological conditions like blowing nose, straining at stool, coughing, trumpet playing, sporting event, sexual intercourse, diving

Pathological conditions with increased RA pressure like RVMI, cardiomyopathy, PEEP ventilation, pulmonary embolism, pulmonary stenosis, COPD, high altitude pulmonary edema, tricuspid valve disease

Pathological conditions with normal RA pressure but abnormal blood flow like RA mass, post-pneumonectomy or multifactorial like platypnea-orthodeoxia syndrome

Anatomic Variation

Location of PFO

Central Defect Position

Superior

Anterior

Posterior Defect Position

Inferior

Anterior Defect Position

Posterior

Zone of Fusion
PFO: Imaging Modalities

TEE  ICE

Anatomic Variability of PFO

Nature of septum primum
Nature of septum secundum
Degree of septal overlap (tunnel length)
Location of PFO
Presence of additional atrial septal defects
Anatomic Variation

Septum Primum

Presence of rigid versus redundant, hypermobile septum primum “Atrial Septal Aneurysm (ASA)”

Variable Separation from Septum Secundum

Anatomic Variation

Septum Primum: “Aneurysm”

No  Yes

TEE Image

“Thicker”, non-compliant septum primum

TEE Image

“Soft”, compliant septum primum
Anatomic Variation
Septum Primum: “Separation”

Variable length of septum secundum

Variable thickness of septum secundum
Anatomic Variation

Septum Secundum: “Length”

Virtually Absent secundum  Longer septum secundum

Anatomic Variation

Septum Secundum: “Thickness”

Thin  Thick
Anatomic Variation
Septal Overlap/Tunnel Length

- Length of tissue overlap
- Length of septal attachments
- Complexity of overlap
Anatomic Variation
Septal Attachments in Tunnel

- Long Septal Overlap with Short Septal Attachment
- Long Septal Overlap with Long Septal Attachment

Unattached
Attached

Anatomic Variation
Complexity of Septal Attachments/Tunnel

Complex Septal Overlap
**Prevalence of PFO**

| General population by autopsy       | 27%   |
| Cryptogenic ischemic stroke (age<55) | 46%   |
| Cryptogenic ischemic stroke (age>55) | 21%   |
| Healthy adults by contrast TTE      | 10-18%|
| Healthy adults by contrast TEE      | 26%   |


**Incidence of PFO**

**Prevalence in Autopsies 19 - 36%**

**Average According to Age (27%)**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>&lt; 30 years</td>
<td>33%</td>
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<tr>
<td>30 – 80 years</td>
<td>25%</td>
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<tr>
<td>&gt; 80 years</td>
<td>20%</td>
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</table>
PFO with ASA

Prevalence 1%

1.9% excursion > 10mm

0.22% excursion > 15mm

The link between stroke and Atrial Septal Aneurysm

Table showing incidence of cardioembolic events in patients with ASA

<table>
<thead>
<tr>
<th>Investigator</th>
<th>year</th>
<th>Pts with ASA</th>
<th>Incidence of cardioembolic events (%)</th>
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<tbody>
<tr>
<td>Galet</td>
<td>1985</td>
<td>10</td>
<td>20</td>
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<td>Hanley</td>
<td>1985</td>
<td>80</td>
<td>20</td>
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<td>Belkin</td>
<td>1987</td>
<td>36</td>
<td>28</td>
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<td>Schneider</td>
<td>1990</td>
<td>23</td>
<td>52</td>
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<tr>
<td>Mugge</td>
<td>1995</td>
<td>195</td>
<td>44</td>
</tr>
<tr>
<td>Marazanoff</td>
<td>1995</td>
<td>259</td>
<td>58</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>49,5</td>
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</table>
Table showing prevalence of ASA in CVA patients

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Year</th>
<th>Number of pts</th>
<th>Prevalence of ASA</th>
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<tr>
<td></td>
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<td>Stroke (N)</td>
<td>Control (C)</td>
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<tr>
<td>Pearson</td>
<td>1991</td>
<td>133</td>
<td>277</td>
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<td>Ilercil</td>
<td>1997</td>
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<td>Agmon</td>
<td>1998</td>
<td>355</td>
<td>363</td>
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<tr>
<td>Lamy</td>
<td>2002</td>
<td>581</td>
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</table>

Diagnostic criteria for Atrial Septal Aneurysm

- **a:** Protrusion of interatrial (IAS) septum ≥15 mm beyond plane of septum
- **b:** Phasic excursion of IAS ≥15 mm in amplitude
- **c:** Diameter of base of aneurysmatic IAS ≥ 15 mm

Agmon Y et al. Circulation 1999
PFO: The Pathology

TIA – Cryptogenic stroke
Migraine
Orthodeoxia – platypnea syndrome
Obstructive sleep apnea
Decompression sickness in divers

PFO: The Mechanism

Paradoxal venous embolism
Chemical mediators?
Increased right – left shunting of venous blood
Idem (PHT induced)
Gas passage
Diseases linked to PFO

Ischemic stroke
Decompression illness in divers
Platypnea – orthodeoxia syndrome
Perioperative hypoxemia
Pulmonary embolism, COPD, OSA
Migraine, transient global amnesia

Importance of the problem relating PFO with stroke

Annual incidence of stroke in US is 750,000 out of which about 75% or 600,000 are ischemic

About 31% (mean) or 200,000 of these ischemic strokes are cryptogenic in nature

About 70,000 of these cryptogenic strokes are associated with PFO

If we add TIA’s or peripheral embolism about 100,000 patients per year may have paradoxical embolism associated with PFO

Meier B et al Circulation 2003
Cryptogenic Stroke

Cerebral infarction which cannot be classified as strokes of determined cause despite a complete diagnostic work-up and are labeled as “cryptogenic strokes”

**AVERAGE 35%**

Mechanism of Stroke

*Paradoxical embolism from thrombus formation in systemic veins*

*Thrombus formation in PFO itself*

*Paroxysmal atrial arrhythmias*
### Paradoxical Embolism

10 patients with known PFO underwent radionuclide venography using Valsalva maneuver followed by (99m) Tc–macro aggregated albumin (MAA) brain SPECT to see the fate of emboli originating in the lower extremities.

Counts were measured in the region of interest (ROI) in anterior and posterior circulation territory of the brain.

Brain SPECT with MAA was sensitive in detecting right to left shunt and higher posterior circulation counts indicate an increased likelihood of cerebral emboli originating from lower extremities.

*Hayashida K et al J Nucl Med 2001*

### Risk for Embolic Stroke

- **PFO** 9 X
- **PFO + ASA** 30 X

Prevalence of PFO is 50% in patients with cryptogenic stroke.
Risk for Embolic Stroke

Presence of Eustachian valve PFO oriented

Presence of Chiari reticulum

Primary hematic diathesis:
C and S proteins, AT III defect,
Lupus anticoagulant factor,
Anticardiolipin antibodies, Leiden's factor V

Association of PFO related stroke with DVT e Thrombophilia

Prothrombin gene mutation G20210A and Factor V mutation G1691A have been found to represent risk factors for PFO related stroke Pezzini A et al Stroke 2003

In another study on 17 patients 31% patients had hematological risk factors for venous thrombosis including activated protein C resistance and increased anticardiolipin antibodies Chaturvedi S et al J Neurol Sci 1998

Frequency of DVT estimated at 10% only by venography Lethen H et al Am J Cardiol 1997
Risk for Embolic Stroke

**Thrombus stuck in PFO**

Srivastava NEJM 337:681,1997

46-year-old man

[Image of sonogram showing a thrombus in the atrium]
Risk for Embolic Stroke

Thrombus stuck in PFO

Risk for Embolic Stroke

Thrombus stuck in PFO
Obstructive Sleep Apnea

PFO Prevalence is ± 70%
Decompression sickness in divers

In type II decompression sickness (DCS) there is a possible five fold increase risk in PFO vs Control

Platypnea - Orthodeoxia syndrome

Described as increased dyspnea and hypoxemia on erect position that is relieved by assuming a recumbent position

Disorders associated with platypnea-orthodeoxia syndrome:

- Intracardiac shunt (PFO)
- Pulmonary vascular shunt (Anatomic PA to PV communications, COPD, post-pneumonectomy)
- Extra thoracic disorders (Liver disease)  
  
  Laybourn et al, J Thorac Cardiovasc Surg 1997
PFO & Platypnea – Orthodeoxia Syndrome

Exact mechanism in PFO is unclear: Interplay of mean interatrial gradient, RV compliance and anatomic relation between IVC & PFO

During early diastole and isovolumetric RV contraction RA pressure may be higher than LA pressure

Unequal diastolic compliance has been proposed to be a mechanism of shunting. Conditions that decrease RV compliance may lead to enhancement of right to left shunt

Anatomic displacement of the heart may cause distortion of interatrial septum causing it to widen. May also accentuate preferential flow from IVC to PFO

Detection

PFO cannot be diagnosed by history, physical exam or CXR. No reliable electrocardiographic sign

Right heart catheterization is invasive and catheter passage of defect may not be achieved

Dye dilution method no longer used

TTE / transcranial doppler (TCD) can be used for diagnosis but is less sensitive than TEE

Gold standard of diagnosis is TEE
**TEE**

Can use contrast (air-saline microbubbles, galactose or oxypolygelatin suspensions) or doppler technique

Provocative measures such as coughing or Valsalva maneuver may be necessary if RLS is not visible in resting condition

If shunt is right → left, the contrast passes from RA to LA in the first 3 beats. In left → right shunt (conditions where LAP is high) negative contrast in RA may be demonstrated

Doppler can identify R→L, L→R or bidirectional shunt

Can diagnose associated Atrial Septal Aneurysm

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**Transcranial doppler**

Transcranial doppler ultrasound detects microbubble induced embolic signals within intracranial arteries usually middle cerebral artery. Usually requires intravenous contrast at rest and after Valsalva maneuver

Sensitivity: 68% - 89%

Specificity: 92 - 100%
Treatment of PFO

Medical therapy: Aspirin, Warfarin

Surgical closure of PFO

Percutaneous catheter closure

Conclusion

On medical therapy, presence of PFO regardless of size or presence of Atrial Septal Aneurysm does not increase ischemic stroke or death

There was a tendency to improved outcome with warfarin versus aspirin in cryptogenic stroke cohort with or without PFO but it was not statistically significant

Homma S et al Circulation 2002
Results

Aspirin therapy may be adequate for secondary prevention in young patients with isolated PFO and cryptogenic stroke

Patients with cryptogenic stroke and the presence of both PFO & septal aneurysm constitute a high risk subset and preventive strategies other than aspirin should be considered

Mas JI et al N Engl J Med 2001

Surgical therapy
First percutaneous closure of an ASD was first performed in 1974 and reported by King in 1976.

In 1980's Rashkind developed Clamshell occluder. Subsequently CardioSEAL, StarFlex device, Buttoned device, ASDOS device, Monodisc, Angel-Wings device and Amplatzer ASD closure device were introduced.

Bridges first proposed that PFO closure would reduce incidence of recurrent strokes.

1990's: appearance of devices dedicated solely to PFO's.

September 10, 1997 1° PFO implantation done by Bernhard Meier with PFO Amplatzer PFO occluder.

**Transcatheter Closure of PFO**

**Amplatzer PFO Occluder : AGA Medical**

**Device Advantages:**
- Simple delivery/release
- Easy retrieval before final release
- Reusable device after retrieval
- Conforms anatomy to device
Transcatheter Closure of PFO
CardioSeal/STARFlex : NMT Medical

Device Advantages:
Simple delivery/release

STARFlex is self-centering

Most flexible device, no anatomic distortion

Images: Courtesy of NMT Medical
Self-Centering STARFlex Device

Helex Device
Currently Available Devices

Intrasept

Transcatheter Closure of PFO

Intrasept Device: Cardia

Device Advantages:
- Simple delivery/release
- Easy retrieval even after release
- Reusable after retrieval
- Some adjustment to the anatomy
- Lowest profile after delivery
Transcatheter Closure of PFO
Premere Device: St. Jude Medical

Device Advantages:
- Two piece device adjusts to any tunnel length
- 90% less surface area in LA
- Easy retrieval until final release
Transcatheter Closure of PFO
Premere Device: St. Jude Medical

Solysafe Device: Phynox Wires

Basic idea of Dr. Laslo Solymar
Solysafe Device: Phynox Wires

Double-Disc Occluder made of:
8 Phynox Wires
2 Polyester Membranes

Percutaneous transcatheter closure of PFO

Contraindications
These include thrombus at site of implant, intracardiac mass or vegetation, active endocarditis or bacteremia
Others include pts unable to take antiplatelet or anticoagulants

Complications
Device migration, infective endocarditis, thrombus formation on device, residual shunt, air embolism, cardiac tamponade, access site problems

Advantages
Outpatient procedure, short recovery time, minimally invasive, no need for long term anticoagulation, reduces stroke events

Meier B et al Circulation 2003
### Studies of percutaneous PFO closure showing recurrence of embolic events

<table>
<thead>
<tr>
<th>Investor</th>
<th>Year</th>
<th>N</th>
<th>Mean age (yrs)</th>
<th>Follow-up</th>
<th>CVA</th>
<th>TIA</th>
<th>Peripheral emboli</th>
<th>CVA + TIA + periph emboli</th>
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<tbody>
<tr>
<td>Martin</td>
<td>2002</td>
<td>110</td>
<td>47</td>
<td>2.3 yrs</td>
<td>1 pt</td>
<td>1 pt</td>
<td>-</td>
<td>0.9 per yr</td>
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<tr>
<td>Braun</td>
<td>2002</td>
<td>276</td>
<td>45</td>
<td>15.1±5. mths</td>
<td>0%</td>
<td>1.7%</td>
<td>0%</td>
<td>-</td>
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<tr>
<td>Du</td>
<td>2002</td>
<td>18</td>
<td>42</td>
<td>2.2±1.8 yrs</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-</td>
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<tr>
<td>Wahl</td>
<td>2001</td>
<td>132</td>
<td>51</td>
<td>1.8±1.6 yrs</td>
<td>0</td>
<td>6</td>
<td>2 pt</td>
<td>-</td>
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<tr>
<td>Sievert</td>
<td>2001</td>
<td>281</td>
<td>46.8</td>
<td>12 mths</td>
<td>2 pt</td>
<td>7 pt</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Butera</td>
<td>2001</td>
<td>35</td>
<td>47.8</td>
<td>12.3±8 mths</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Windecker</td>
<td>2000</td>
<td>80</td>
<td>52</td>
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<tr>
<td>Hung</td>
<td>2000</td>
<td>63</td>
<td>46</td>
<td>2.6±2.4 yrs</td>
<td>1 pt</td>
<td>3 pt</td>
<td>-</td>
<td>3.2 per yr</td>
</tr>
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</table>

### Comparison of stroke recurrence during natural course versus PFO closure (Non randomized & non matched comparison)

![Graph showing comparison of stroke recurrence](image)

Meier B et al Cardiology Rounds 1999
Transcatheter Closure of PFO

**Procedural Risks**

- Serious complications ~1/500 cases, include:
  - Stroke, air to coronaries, cardiac perforation, embolized device, infection, anesthesia complications.
- Minor complications:
  - Intra-operative arrhythmia (<2%), hematoma at cath site

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**Late Risks**

- Device Thrombosis:
  - Risk unknown, probably < 2%
  - Many pts asymptomatic: echo finding only
- Late Arrhythmia:
  - Transient PAC’s: probably 50%
  - Paroxysmal Atrial Fibrillation: probably 3 - 8%
- Device Erosion:
  - Risk unknown, probably device/anatomy specific
Transcatheter Closure of PFO

Potential Procedural Benefits

- The “Good News”:
  - 30-60 minute procedure
  - Less pain than surgery, no scar
  - No long term anti-coagulation
  - Return to full activity (including gym) in 5 days

Transcatheter Closure of PFO

Device Endothelialization: CardioSEAL

Device thoroughly endothelialized by 6 months
Anatomic Variation
Which may complicate PFO closure

Presence of additional septal fenestrations

Presence of long non-compliant tunnel

Presence of hypermobile septum primum
Anatomic Variation
Presence of Additional Septal Fenestrations

LAO/Cranial

RAO

Anatomic Variation
Complications of Long, Non-Compliant Tunnel

1
2
3

RA
LA
IVA
LA
RA
LA
RA

Anatomic Variation

Complications of Long, Non-Compliant Tunnel

Transseptal Puncture Approach

Balloon Eversion Technique
Anatomic Variation

Long Tunnel: Transseptal Technique

![TEE Image]

Anatomic Variation

Long Tunnel: Transseptal Technique

![Diagram with labeled sites]

Site of Puncture
Long Tunnel: Balloon Eversion

Anatomic Variation

Anatomic variation
Impact of Hypermobile Septum Primum

Even with extreme septal excursions, focus on the separation between septum primum and septum secundum.
Summary

In patients aged < 55 years cryptogenic stroke is strongly associated with PFO and Atrial Septal Aneurysm and some causality may be inferred.

In patients > 55 yrs heterogeneous results are found in literature and the association and causality is less clear.

Medical therapy with aspirin or warfarin are both viable alternatives for secondary prevention although in one study aspirin was not found to be effective for secondary prevention in young cryptogenic stroke patients with both PFO and Atrial Septal Aneurysm.

Follow-up

- Acetylsalicylic acid 100 mg and clopidogrel 75 mg (3 - 6 months)
- Prophylaxis against endocarditis (for 3 - 6 months)
- Echocardiography
  - transthoracic before discharge
  - transesophageal 6 months after implantation
- Clinical follow-up
  - physician visit 6 months after procedure
  - neurological examination in case of suspected recurrence
Summary

Percutaneous PFO closure is safe, convenient, and effective and has largely supplanted surgical procedures. A trend towards better outcomes may emerge with better devices and increasing skill.

Surgical closure is well established, safe and successful but needs thoracotomy, heart-lung machine, longer hospitalization, and is not free from wound and scar problems, residual shunts and recurrent events.

There is no published large randomized study comparing medical therapy versus PFO closure.

Conclusion

At the present time the unequivocal indication for closure is patients with PFO & recurrent cryptogenic stroke despite medical therapy (raises an ethical question: Should we wait for a second stroke?)

Presently, it seems acceptable to attempt percutaneous closure in patients who desire it after complete explanation of the advantages and disadvantages.

Patients with a high risk of recurrent events like multiple previous embolic events, PFO + Atrial Septal Aneurysm, thrombophilia, professional divers, or those unable to tolerate prolonged anticoagulation may benefit from closure. Patient selection criteria continue to evolve.....
OUR STUDY

Percutaneous PFO closure

From September 2004:
- 75 patients
- Age from 16 to 69 (mean 49)

Devices implanted:
- 28 Premere
- 20 Amplatzer
- 6 Amplatzer cribriform
- 13 Atriasept
- 3 BioSTAR
- 2 Solysafe
- 1 double BioSTAR
- 1 double Amplatzer

OUR STUDY

PFO closure – Follow-Up

- 1 month: Echocardiogram
- 3 months: Echocardiogram
- 6 months: Echocardiogram – Transcranial Echodoppler
- 1 year: Echocardiogram
- 2 years: Echocardiogram – M R I
- 3 years: Echocardiogram
- 4 years: Echocardiogram
- 5 years: Echocardiogram
OUR STUDY

PFO closure – Where we are

Successful device deployment 100% of pts without any periprocedural major complication.

Two pts atrial arrhythmia have occurred.

All pts was discharged within 3 days in good overall conditions. In all pts a double antiplatelet regimen was adopted.

The follow-up was complete in 100% of the cases (median 36, range 3-58 months).

At five years, there was no recurrent stroke or TIA, and no new cerebral lesions developed by MRI in those patients with residual shunt.

In 73 of them the Rankin scale reduced to 0 whereas only in 2 pts score 1 was reached.

In 19 of the 31pts with concomitant migraine, the intensity and the frequency of the attacks decreased over time.

At the TCD, 5 pts resulted positive for microembolic signals.

The TTE evaluation showed however an optimal sealing of all the devices without signs of erosion, incomplete closure and thrombus formation around the device.
**Future Perspectives**

1. **Self-check of the study via HRQL** to ensure the continuous improvement of the outcomes.

2. **Introduction of an MRI study** after 2 years of f-u to assess the relation between PFO and cryptogenic stroke.

**OUR STUDY**

**HRQL**
- 49 pts (2008-2009)
- Age 13 – 68 yrs
- Symptomatic (TIA or Stroke)
- ICE
- QOL

**EURO QoL**
**SF36**
**PS**
Statistical Analysis

- Verifica delle normalità delle variabili PCS-MCS: KOLMOGOROV – SMIRNOV, SHAPIRO - WILK
- Analisi della correlazione tra diverse variabili: RHO di SPEARMAN, T di STUDENT
- Verifica della differenza dei livelli di PCS-MCS: WELCH, WELCH MULTIPLO
- Verifica della significatività delle relazioni in tabelle a doppia entrata: Test esatto di FISHER, ANOVA
- Analisi esplorative sulla struttura dei dati: CLASSIFICATION TREES

Results

- SF36
- Indici sintetici
  - Componente fisica standardizzata
  - Componente mentale standardizzata
  - PCS
  - MCS

\( \alpha = 0.05 \)
Relational Analysis

\[ p < 0.05 \]

- PCS and PS → (risultato positivo dopo il trattamento)
- PCS-MCS and EURO QoL

\[ p < 0.002 \]  \[ p < 0.03 \]

PCS, MCS and SF36

Healthy Status  Improvement

Cut off?
Classification trees

Cut off PCS = 33,528
Cut off MCS = 44,785

PCS

<table>
<thead>
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<th>Risultato del trattamento sui problemi</th>
<th>Livello PCS</th>
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<th>&gt; cutoff</th>
<th>Totale</th>
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<tr>
<td>Risolti solo in parte</td>
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<td>6</td>
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<td>Risolti poco</td>
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<td>Totale</td>
<td></td>
<td>7</td>
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**p < 0,0001**
### MCS

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<td>6</td>
<td></td>
</tr>
<tr>
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<td>2</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Per nulla risolti</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Totale</strong></td>
<td><strong>23</strong></td>
<td><strong>26</strong></td>
<td><strong>49</strong></td>
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</table>

\[ p < 0,03 \]

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**OUR STUDY**

**MRI Study**

[Images of MRI scans]
OUR STUDY

MRI Study
ONGOING TRIALS

**Cryptogenic Stroke**

- **PC-Trial** to compare efficacy of percutaneous closure of PFO using the Amplatzer PFO occluder with medical treatment in pts with presumed paradoxical embolism
- **RESPECT** to investigate whether percutaneous PFO closure (AMPLATZER) is superior to current standard of care medical therapy in the prevention of recurrent embolic stroke
- **CLOSURE 1** to determine whether the STARFlex will safely and effectively prevent recurrent embolic stroke compared with medical therapy

**CARDIA** to determine whether the CARDIA system will safely and effectively prevent recurrent embolic stroke compared with anticoagulation therapy
MIST and MIST II (Migraine intervention with Starflex Technology).

The study will evaluate safety and effectiveness of Starflex implant technology for the prevention of migraine attack in pts with PFO.

ONGOING TRIALS

Migraine

FORMAT (INTRASEPT)
PRIMA (AMPLATZER)
ESCAPE (PREMERE)
SUMMARY

Transluminal Closure of PFO

Easy
Safe
Good thing for doctor and patient

SUMMARY

NO EVIDENCE BASED MEDICINE DATA ON THIS PROCEDURE
BUT

THE ONLY GOOD PFO

IS A CLOSED PFO

CONCLUSION

The Future of PFO Closure

Separation of indications
Definitive data on clinical trials
Predictive algorithm for first stroke prevention
The Future of PFO Closure

Bio-absorbable device materials
(BioSTAR – NMT)

Non-device alternatives
(Radiofrequency, Clips, etc.)

In-tunnel devices (Coherex, SeptRx, etc.)

Bio-absorbable device BioSTAR
Bio-absorbable device BioSTAR

In-tunnel Device

- Treat only the tunnel, not the whole septum
- Minimize surface area exposed to LA / RA
  - Minimize risk of thrombus formation
- Lower risk of erosion, septal distortion
- Lower risk of atrial fibrillation
- Leave much less foreign material in the body
In-tunnel Device

In Tunnel Devices need a Tunnel!

For simple PFO’s, determining tunnel length is straightforward

In aneurysmal PFO, some interrogation is required

For example......

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Functional Tunnel Length

- Simple PFO with tunnel and no ASA

TEE easily shows if functional tunnel length is 4mm or greater (Type I)
Functional Tunnel Length

- PFO with Aneurysm
  - Various excursions and attachments to septum secundum require additional evaluation to determine tunnel length

Attachment to secundum can vary in length from a single point of contact to long segments

for example......

Functional Tunnel Length

- PFO with septal Aneurysm and adequate (≥ 4mm) tunnel length (Type II tunnel)

Attachment at septum secundum is continuous, and ≥ 4mm
Functional Tunnel Length

- PFO with septal Aneurysm and inadequate (< 4mm) tunnel length for in tunnel device (Type III).

**Tunnel Type III**

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Functional Tunnel Length

- Much more important than the anatomical tunnel length
- It is important to be thorough in your review
- Evaluation adds only a few minutes to the procedure
- It predicts outcome of in-tunnel PFO closure
In-tunnel Device

- Nitinol lattice
- Integrated polyurethane foam
- Micro-tined anchors
- 13 and 19 mm widths

The Coherex FlatStent™ EF PFO Closure System is the first and only in-tunnel PFO closure system to gain CE mark approval.
In-tunnel Device

Lateral expansion by the FlatStent creates apposition between septum primum and septum secundum

In-tunnel Device

Simple delivery
Recapture
Minimal material exposure
In-tunnel Device

Clinical results with Coherex Flatstent EF
PFO Closure System

13mm FlatStent EF
Type 0: 0/0; N/A
Type I: 11/12; (91%)
Type II: 3/4; (75%)
Type III: 1/2; (50%)

19mm FlatStent EF
Type 0: 0/0; N/A
Type I: 8/8; (100%)
Type II: 9/9; (100%)
Type III: 4/7; (73%)

Clinically effective closure at 6 months, defined as no residual flow or trivial (<10 bubbles on Valsalva) residual flow based on TEE.
In-tunnel Device

The SeptRx- System

- Nitinol frame and Nitinol wire mesh
- Left and right atrial anchors
- Sits within the PFO tunnel

- EU trial with the Gen-2 device will start this year

Radiofrequency – CoAptus solution

Mechanical Coaption + Bipolar radiofrequency = Acute Seal
**Key Factors for Clips, Sutures & RF**

Reasonable overlap (tunnel)
Centering device!

**For clips:** strong enough to hold material together as well as strength to translate movement with the heart

**For sutures:** capture the septum secundum and primum

**For RF:** creating enough energy without thermal dispersion

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**THANK YOU!**