What Evil Lurks in the Hearts of Men?

Neal S. Gaither, MD, FACC, FSCAI

The Sonographer Knows...
Definition of Stroke

“sudden death of brain cells in a localized area due to inadequate blood flow”

- Annually, 500,000 new cases in U.S.
- One in three events is fatal
- Third leading cause of death
- Leading cause of disability
- 3 Million Americans currently permanently disabled
Overview of Stroke

- **Hemorrhagic stroke:**
  - Intracerebral hemorrhage (Hypertension most common cause)
  - Subarachnoid hemorrhage

- **Ischemic stroke** (can undergo hemorrhagic conversion):
  - Atherothrombotic infarct – local occlusion of an artery
  - Embolic infarct –
    - Material causing infarct travels from elsewhere
  - Hypoperfusion – global decrease in brain blood flow
Hemorrhagic stroke:
- Intracerebral hemorrhage (Hypertension most common cause)
- Subarachnoid hemorrhage

Ischemic stroke (can undergo hemorrhagic conversion):
- Atherothrombotic infarct – local occlusion of an artery
- Embolic infarct – Material causing infarct travels from elsewhere
- Hypoperfusion – global decrease in brain blood flow

Lacunar stroke – “empty space”
- Small infarcts in deep brain structures due to occlusion of a deep penetrating artery
- Less closely associated with cardiac sources of embolism
<table>
<thead>
<tr>
<th>Stroke type</th>
<th>Clinical course</th>
<th>Risk factors</th>
<th>Other clues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracerebral Hemorrhage</td>
<td>Gradual progression during minutes or hours</td>
<td>Hypertension, Trauma, Bleeding diatheses, Illicit drugs (cocaine), Vascular malformations, Blacks and Asians</td>
<td>Precipitated by sex or other physical activity. Patient may have reduced alertness.</td>
</tr>
<tr>
<td>Subarachnoid Hemorrhage</td>
<td>Sudden, severe headache, Focal brain dysfunction less common than with other types.</td>
<td>Smoking, hypertension, alcohol, genetic susceptibility (e.g., polycystic kidney disease, family history), Drugs (cocaine)</td>
<td>Precipitated by sex or other physical activity. Patient may have reduced alertness.</td>
</tr>
<tr>
<td>Ischemic (thrombotic)</td>
<td>Stuttering progression with periods of improvement</td>
<td>Atherosclerotic risk factors (age, smoking, diabetes mellitus, etc.). Men &gt;&gt; women</td>
<td>History of TIA, Neck bruit</td>
</tr>
<tr>
<td>Ischemic (embolic)</td>
<td>Sudden onset with deficit maximal at onset. Clinical findings may improve quickly.</td>
<td>Atherosclerotic risk factors, Heart disease (valvular, atrial fibrillation, endocarditis). Men &gt;&gt; women</td>
<td>Can be precipitated by getting up at night to urinate, or sudden coughing or sneezing.</td>
</tr>
</tbody>
</table>
Causes of Ischemic Stroke

- 50% - Cerebral /cervical vasculature
- 20% - High-risk cardiac abnormalities
- 30% - “Cryptogenic” (many have embolic features suggesting a possible cardioaortic origin)

Computed tomography scan in a patient with atrial fibrillation, showing a hyperdensity in the right middle cerebral artery consistent with thromboembolism (arrow). Figure illustrations by Rob Flewell

J Am Coll Cardiol 2008; 51:1049–59
Characteristics of Cardioembolic Stroke

- 14-30% of all strokes
- Increases with age
- Cardiac emboli are often large
  - Larger strokes
  - High incidence of morbidity and mortality compared with other types of stroke
- Recurrent events are common but *may be prevented* with appropriate recognition and treatment
Characteristics of Cardioembolic Stroke

- Clinical diagnosis
  - No gold standard
  - Potential cardiac source coupled with absence of other obvious cause

- Neuroimaging findings suggestive of cardioembolic stroke:
  - Simultaneous/sequential strokes in different territories
  - Predominate in carotid and middle cerebral artery territories
  - Hemorrhagic transformation may be more common
Characteristics of Cardioembolic Stroke

How does this happen?
- Blood stasis in a left-sided cardiac chamber
- Release of material from an abnormal structure
- Abnormal passage from venous to arterial circulation (paradoxical embolism)
Cardiac source of embolism

- Atrial fibrillation
- Ischemic Heart Disease
  - Recent Myocardial infarction
  - Ischemic cardiomyopathy/LV aneurysm
- Paradoxical Emboli
- Valvular Heart Disease
  - Mechanical prosthetic valve
  - Rheumatic mitral stenosis
  - Endocarditis
- Dilated cardiomyopathy
- Cardiac tumors

Pie chart showing:
- Atrial Fibrillation: 45%
- Acute MI: 15%
- Ventricular Aneurysm: 10%
- Rheumatic Heart Disease: 10%
- Prosthetic Cardiac Valves: 10%
- Other: 10%

# Cardiac Sources of Embolism

<table>
<thead>
<tr>
<th><strong>High Risk</strong></th>
<th><strong>Intermediate or Uncertain Risk</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Atrial arrhythmias</td>
<td>- Interatrial septal abnormalities</td>
</tr>
<tr>
<td>- Left atrial thrombus</td>
<td>- Patent foramen ovale, ASD</td>
</tr>
<tr>
<td>- Left ventricular thrombus</td>
<td>- Atrial septal aneurysm</td>
</tr>
<tr>
<td>- Primary cardiac tumors</td>
<td>- Septal pouch</td>
</tr>
<tr>
<td>- Metastatic cardiac tumors</td>
<td>- Pulmonary arteriovenous malformation</td>
</tr>
<tr>
<td>- Cardiac vegetations</td>
<td>- Spontaneous echo contrast “smoke”</td>
</tr>
<tr>
<td>- Prosthetic cardiac valve</td>
<td>- Mitral valve prolapse</td>
</tr>
<tr>
<td>- Aortic atheroma</td>
<td>- Valvular calcification</td>
</tr>
<tr>
<td></td>
<td>- Valvular strands</td>
</tr>
</tbody>
</table>
Transesophageal Echo

- More sensitive for detecting intracardiac source of embolism:
  - 57% vs. 15% by TTE**
- More likely to be helpful
  - Younger patients with stroke
  - Non-lacunar stroke
- Weaknesses:
  - LV apex

Transesophageal Echo

- Higher sensitivity for:
  - Left atrial thrombus
  - Abnormal prosthetic valve (esp. Mitral)
  - Aortic arch atheroma
  - Patent Foramen Ovale (PFO)
  - Spontaneous Echo Contrast ("smoke")
  - Valvular strands

** Pearson, et. al. JACC 1991; 17(1):66.**
## Distribution of Cerebral Infarctions According to Age in the Sagrat Cor Hospital of Barcelona Stroke Registry

<table>
<thead>
<tr>
<th>Subtype of Cerebral Infarction (n = 1840)</th>
<th>Years of Age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 65 (n= 314)</td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>46 (14.6)</td>
</tr>
<tr>
<td>Atherothrombotic</td>
<td>66 (21.0)</td>
</tr>
<tr>
<td>Lacunar</td>
<td>93 (29.6)</td>
</tr>
<tr>
<td>Unknown cause</td>
<td>61 (19.4)</td>
</tr>
<tr>
<td>Unusual cause</td>
<td>48 (15.3)</td>
</tr>
</tbody>
</table>
Cardiac Disorders Associated with Cardioembolic Stroke in 402 Patients

<table>
<thead>
<tr>
<th>Cardiac source of Embolism</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial Fibrillation without structural heart disease</td>
<td>89 (22.1%)</td>
</tr>
<tr>
<td>Isolated Structural Heart Disease</td>
<td>81 (20.1%)</td>
</tr>
<tr>
<td>Atrial Fibrillation Complicating Structural Heart Disease</td>
<td>232 (57.7%)</td>
</tr>
</tbody>
</table>
# 402 Patients in the Barcelona Stroke Registry

<table>
<thead>
<tr>
<th>Cardiac Source of Embolism</th>
<th>Total Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>318 (79.1%)</td>
</tr>
<tr>
<td>Lone atrial fibrillation</td>
<td>88</td>
</tr>
<tr>
<td>Associated with structural cardiac disease</td>
<td>230</td>
</tr>
<tr>
<td>Hypertensive left ventricular hypertrophy</td>
<td>120 (29.8%)</td>
</tr>
<tr>
<td>Associated with atrial fibrillation</td>
<td>118</td>
</tr>
<tr>
<td>Associated with atrial flutter</td>
<td>2</td>
</tr>
<tr>
<td>Left ventricular systolic dysfunction</td>
<td>91 (22.6%)</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>59</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>32</td>
</tr>
<tr>
<td>Rheumatic mitral valve disease</td>
<td>50 (12.4%)</td>
</tr>
<tr>
<td>Mitral annular calcification</td>
<td>40 (9.9%)</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>5 (1.2%)</td>
</tr>
<tr>
<td>Atrial septal aneurysm with patent foramen ovale</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Degenerative heart valve disease</td>
<td>4 (1%)</td>
</tr>
</tbody>
</table>
Cardiogenic Stroke: Causes

- Atrial fibrillation
- Ischemic Heart Disease
  - Recent Myocardial infarction
  - Ischemic cardiomyopathy/LV aneurysm
- Paradoxical Emboli
- Valvular Heart Disease
  - Mechanical prosthetic valve
  - Rheumatic mitral stenosis
  - Endocarditis
- Dilated cardiomyopathy
- Cardiac tumors
Age Distribution of People With AF Compared With US. General Population

Atrial Fibrillation and Stroke

- Approximately 80,000 strokes per year are associated with AF
- Risk of stroke is 5% per year
- Atrial Remodeling in AF:
  - Electrical remodeling
  - Histologic remodeling
  - Anatomic remodeling - "Atrial Cardiomyopathy"
- 90% of Left Atrial Thrombi develop in the Left Atrial Appendage

TEE: LA Appendage Thrombus

Doufekias, E. et al. J Am Coll Cardiol 2008;51:1049-1059
A Look Inside the Appendage
Left Atrial Appendage: Normal rhythm Vs. Chronic AF

Left: Cast from a 52-year-old man with antemortem sinus rhythm. Volume is 5.88 cm². Cast has 20 to 40 twigs and is densely covered with fine structures.

Right: Cast from a 76-year-old man with antemortem AF. Volume is 18.67 cm². Cast has more than 40 twigs and no fine structures.

- LAA area >6 cm² clear risk factor for arterial emboli in the SPAF-II study
- Patients may have LAA surgically ligated during valve surgery to prevent cardioemboli
- Percutaneous LAA occlusion device available for patients in whom anticoagulation may be contraindicated

SPAF = Stroke Prevention in Atrial Fibrillation.
Atrial Remodeling: “Atrial Cardiomyopathy”

Normal LA Appendage

LA Appendage in AF
Dilated Cardiomyopathy

Left Atrial Appendage Thrombus seen with TTE (rare)
3-D Left Atrial Appendage Thrombus
Left Atrial Appendage Thrombi – not always evident!
A Tale of Two Thrombi
LAA Closure: Postop TEE
Cardiogenic Stroke: Causes

- Atrial fibrillation
- **Ischemic Heart Disease**
  - Recent Myocardial infarction
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- Dilated cardiomyopathy
- Cardiac tumors
LV Thrombi and Embolic Risk

Increased embolic risk in patients with left ventricular thrombi

John R. Stratton, M.D., and Arthur D. Resnick, M.D.

TABLE 5
Comparison of patients in the thrombus group with and without embolization during follow-up

<table>
<thead>
<tr>
<th></th>
<th>Patients with emboli (n = 11)</th>
<th>Patients without emboli (n = 74)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>58 ± 7</td>
<td>61 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>91</td>
<td>86</td>
<td>NS</td>
</tr>
<tr>
<td>Interval from MI to echo exam (months)</td>
<td>50 ± 76</td>
<td>29 ± 47</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction (n = 67)</td>
<td>0.34 ± 0.18</td>
<td>0.30 ± 0.14</td>
<td>NS</td>
</tr>
<tr>
<td>Chronic or paroxysmal atrial fibrillation (%)</td>
<td>18</td>
<td>13</td>
<td>NS</td>
</tr>
<tr>
<td>MI during follow-up (%)</td>
<td>18</td>
<td>8</td>
<td>NS</td>
</tr>
<tr>
<td>Echocardiographic features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular aneurysm (%)</td>
<td>73</td>
<td>75</td>
<td>NS</td>
</tr>
<tr>
<td>Thrombus thickness (cm)</td>
<td>2.8 ± 1.0</td>
<td>2.8 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>Thrombus protrusion (%)</td>
<td>90</td>
<td>49</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>Thrombus mobility (%)</td>
<td>70</td>
<td>20</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

MI = myocardial infarction; NS = not significant (p > .05).

Anterior Apical MI
Cardiogenic Stroke: Causes

- Atrial fibrillation
- Ischemic Heart Disease
  - Recent Myocardial infarction
  - Ischemic cardiomyopathy/LV aneurysm
- Paradoxical Emboli
- Valvular Heart Disease
  - Mechanical prosthetic valve
  - Rheumatic mitral stenosis
  - Endocarditis
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- Cardiac tumors
Basic physiology:

- In fetal life, blood is shunted from the right to left atrium through the foramen ovale.
- After birth, the PFO closes in 75%.
- But may be patent in up to 75% of patients with unexplained stroke.

Strong association between PFO and stroke in patients under 55 years of age:

- Stroke can occur due to
  - Paradoxical embolism
  - In-situ thrombosis?
**Definition:**

A systemic embolism (stroke or other) due migration of thrombus, air, or tumor particle from the venous to the arterial circulation, usually due to the presence of an intracardiac communication with right to left shunting.

**Right to Left Shunts:**
- Patent foramen ovale
- ASD or VSD (rare)
- Pulmonary AVM
PFO: Gross Anatomy
**Patent Foramen Ovale**

- Diagnosis by echo with agitated saline contrast:
  - PFO judged present if microbubbles seen within left sided chambers within 3 heartbeats from maximal right atrial opacification
  - TEE more sensitive than TTE
  - Lower extremity injections more likely to be positive
  - Doppler color flow less sensitive
  - Transcranial Doppler (not specific for PFO)
Bubbles in agitated saline are **22-144** microns Vs. pulmonary capillaries **5.5** microns

Magnitude of the observed contrast shunt influenced by

- Position of patient
- Choice of and route of administration of contrast agent
  - Blood from SVC → Tricuspid valve
  - Blood from IVC → Fossa ovalis
- Provocative maneuvers
- Patient compliance

PFO: 3-D Transesophageal Echo

Patent foramen ovale -
PFO: Transesophageal Echo
Paradoxical Embolism

- Venous source (usually thrombus) travels to the right heart chambers and ultimately finds its way to the arterial circulation,
- Not truly cardiogenic embolism since the heart is an innocent bystander which permits passage of embolic material.
PFO: Paradoxical embolus in transit
Thrombus in PFO... in situ formation?
Positive “Bubble” Study: TTE
AMPLATZER PFO Occluder

- Percutaneous, transcatheter device
- Self-expanding, double-disc design
- Nitinol wire mesh with polyester fabric/thread
- Radiopaque marker bands
- Sizes: 18, 25, 35 mm
- Recapturable and repositionable

*CAUTION: Investigational device in the United States. Limited by Federal (or U.S.) law to investigational use. Not available for sale in the U.S.*
Subject Distribution

Enrolled
N=980

Randomization stratified by site and presence/absence of atrial septal aneurysm

Randomized to device group
N = 499

Study device implant attempted
N = 464

Post Implant: clopidogrel 1 month and aspirin 6 months. After 6 months, antiplatelet therapy at discretion of site investigator

TEE with bubble study at 6 months

Randomized to medical group
N = 481

Medical treatment specified pre-randomization by site neurologist

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin only</td>
<td>46.5%</td>
</tr>
<tr>
<td>Warfarin only</td>
<td>25.2%</td>
</tr>
<tr>
<td>Clopidogrel only</td>
<td>14.0%</td>
</tr>
<tr>
<td>Aspirin + dipyridamole</td>
<td>8.1%</td>
</tr>
<tr>
<td>Aspirin + clopidogrel(^1)</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

1. Aspirin + clopidogrel was removed from the protocol in 2006 based on changes to the AHA/ASA treatment guidelines
Primary Endpoint Analysis – ITT Cohort
50.8% risk reduction of stroke in favor of device

- **3/9** device group patients did not have a device at time of endpoint stroke

HR: 0.492
Log-rank P-value: 0.0825
(95% Confidence interval = 0.217 - 1.114)
Primary Endpoint Analysis – As Treated Cohort
72.7% risk reduction of stroke in favor of device

- The As Treated (AT) cohort demonstrates the treatment effect by classifying subjects into treatment groups according to the treatment actually received, regardless of the randomization assignment

HR: 0.273
Log-rank P-value: 0.0067
(95% Confidence interval = 0.100 - 0.747)

Device Group
n=5

Medical Group
n=16

Time to Event (years)
### Totality of Evidence

**46.6% - 72.7% risk reduction of stroke in favor of device**

#### Totality of Evidence

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Risk Reduction</th>
<th>P-Value $^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent to Treat Raw Count</td>
<td>46.6%</td>
<td>0.157</td>
</tr>
<tr>
<td>Intent to Treat KM</td>
<td>50.8%</td>
<td>0.083</td>
</tr>
<tr>
<td>Per Protocol KM</td>
<td>63.4%</td>
<td>0.032</td>
</tr>
<tr>
<td>As Treated KM</td>
<td>72.7%</td>
<td>0.007</td>
</tr>
</tbody>
</table>

#### Number Needed to Treat (NNT)

<table>
<thead>
<tr>
<th></th>
<th>NNT $^2$</th>
<th>Device Group Event Rate $^3$</th>
<th>Medical Group Event Rate $^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Year</td>
<td>250</td>
<td>1.33%</td>
<td>1.73%</td>
</tr>
<tr>
<td>2 Year</td>
<td>70.4</td>
<td>1.60%</td>
<td>3.02%</td>
</tr>
<tr>
<td>5 Year</td>
<td>23.9</td>
<td>2.21%</td>
<td>6.40%</td>
</tr>
</tbody>
</table>

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1. P-values: ITT Raw Count is calculated using Fisher’s Exact test; all other P-values are calculated using log-rank test
2. The NNT is the average number of subjects that need to be treated with the AMPLATZER™ PFO Occluder in order to prevent one stroke in the respective time intervals. The NNT is calculated as the reciprocal of the difference between the control arm and device arm event rates
3. Calculated using the Kaplan-Meier estimated event rates for each treatment group

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[23]
### Subpopulation Differential Treatment Effect

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Device Group</th>
<th>Medical Group</th>
<th>Hazard Ratio and 95% CI</th>
<th>Pvalue (Log Rank)</th>
<th>Interaction Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no. of patients/total number (%)</td>
<td>9/499 (1.8%)</td>
<td>16/481 (3.3%)</td>
<td>0.492 (0.217, 1.114)</td>
<td>0.0825</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.5155</td>
</tr>
<tr>
<td>- 18-45</td>
<td>4/230 (1.7%)</td>
<td>5/210 (2.4%)</td>
<td>0.698 (0.187, 2.601)</td>
<td>0.5901</td>
<td></td>
</tr>
<tr>
<td>- 46-60</td>
<td>5/262 (1.9%)</td>
<td>11/266 (4.1%)</td>
<td>0.405 (0.140, 1.165)</td>
<td>0.0828</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.7312</td>
</tr>
<tr>
<td>- Male</td>
<td>5/268 (1.9%)</td>
<td>10/268 (3.7%)</td>
<td>0.448 (0.153, 1.311)</td>
<td>0.1321</td>
<td></td>
</tr>
<tr>
<td>- Female</td>
<td>4/231 (1.7%)</td>
<td>6/213 (2.8%)</td>
<td>0.571 (0.161, 2.024)</td>
<td>0.3789</td>
<td></td>
</tr>
<tr>
<td><strong>Shunt Size</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0667</td>
</tr>
<tr>
<td>- None, trace or moderate</td>
<td>7/247 (2.8%)</td>
<td>6/244 (2.5%)</td>
<td>1.034 (0.347, 3.081)</td>
<td>0.9527</td>
<td></td>
</tr>
<tr>
<td>- Substantial</td>
<td>2/247 (0.8%)</td>
<td>10/231 (4.3%)</td>
<td>0.178 (0.039, 0.813)</td>
<td>0.0119</td>
<td></td>
</tr>
<tr>
<td><strong>Atrial septal aneurysm</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.1016</td>
</tr>
<tr>
<td>- Present</td>
<td>2/180 (1.1%)</td>
<td>9/169 (5.3%)</td>
<td>0.187 (0.040, 0.867)</td>
<td>0.0163</td>
<td></td>
</tr>
<tr>
<td>- Absent</td>
<td>7/319 (2.2%)</td>
<td>7/312 (2.2%)</td>
<td>0.889 (0.312, 2.535)</td>
<td>0.8259</td>
<td></td>
</tr>
<tr>
<td><strong>Index infarct topography</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.3916</td>
</tr>
<tr>
<td>- Superficial</td>
<td>5/280 (1.8%)</td>
<td>12/269 (4.5%)</td>
<td>0.366 (0.129, 1.038)</td>
<td>0.0487</td>
<td></td>
</tr>
<tr>
<td>- Small Deep</td>
<td>2/57 (3.5%)</td>
<td>1/70 (1.4%)</td>
<td>1.762 (0.156, 19.93)</td>
<td>0.6429</td>
<td></td>
</tr>
<tr>
<td>- Other</td>
<td>2/157 (1.3%)</td>
<td>3/139 (2.2%)</td>
<td>0.558 (0.093, 3.340)</td>
<td>0.5157</td>
<td></td>
</tr>
<tr>
<td><strong>Planned medical regimen</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.1966</td>
</tr>
<tr>
<td>- Anticoagulant</td>
<td>4/132 (3.0%)</td>
<td>3/121 (2.5%)</td>
<td>1.141 (0.255, 5.098)</td>
<td>0.8628</td>
<td></td>
</tr>
<tr>
<td>- Antiplatelet</td>
<td>5/367 (1.4%)</td>
<td>13/359 (3.6%)</td>
<td>0.336 (0.120, 0.944)</td>
<td>0.0299</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

- For carefully selected patients with history of cryptogenic stroke and PFO, the RESPECT Trial provides evidence of benefit in stroke risk reduction from closure with the AMPLATZER PFO Occluder over medical management alone.
  - Primary analysis of ITT cohort was not statistically significant but trended towards superiority while secondary analyses suggested superiority.
  - Stroke risk reduction was observed across the totality of analyses with rates ranging from 46.6% - 72.7%.

- PFO closure with the AMPLATZER PFO Occluder exposes patients to a very low risk of device- or procedure-related complications.

- Results of the RESPECT Trial have substantial import for the treatment of patients with a history of cryptogenic stroke and PFO.

- Follow-up of patients is on-going and will continue to provide additional longer term information regarding benefits, risks, and differential treatment effects in sub-populations.
ASD Closure – Amplatzer Device
Apical 4-Chamber - Amplatzer
Alternate Pathway for Paradoxical Embolism

Pulmonary AVM – the lungs ordinarily act as a filter to trap particulates from the venous circulation and prevent arterial embolization
Cardiogenic Stroke: Causes

- Atrial fibrillation
- Ischemic Heart Disease
  - Recent Myocardial infarction
  - Ischemic cardiomyopathy/LV aneurysm
- Paradoxical Emboli
- **Valvular Heart Disease**
  - Mechanical prosthetic valve
  - Rheumatic mitral stenosis
  - Endocarditis
- Dilated cardiomyopathy
- Cardiac tumors
Rheumatic Mitral Stenosis
Case Presentation: 56 year old man

Acute right-sided weakness, impaired speech, reduced level of consciousness, possible seizure

Reduced left brachial and radial pulses

Head CT: large left parietal, bilateral posterior frontal intraparenchymal hemorrhages

Arterial Duplex Left Upper extremity: occluded left axillary artery

Echocardiogram
2D Echocardiogram

Differential Diagnosis:
- Primary cardiac tumor (Myxoma, Fibroelastoma)
- Endocarditis (esp. fungal)
Subacute Bacterial Endocarditis
Subacute Bacterial Endocarditis
56 Year-old Woman with Stroke
A 66-year-old, previously healthy woman presented with an acute onset of weakness on the left side of the body.

Mechanical MV Thrombosis
Mechanical MV Thrombosis: 3-D
Mechanical MV Thrombosis: Postop
Cardiogenic Stroke: Causes

- Atrial fibrillation
- Ischemic Heart Disease
  - Recent Myocardial infarction
  - Ischemic cardiomyopathy/LV aneurysm
- Paradoxical Emboli
- Valvular Heart Disease
  - Mechanical prosthetic valve
  - Rheumatic mitral stenosis
  - Endocarditis
- Dilated cardiomyopathy
- Cardiac tumors
Cardiogenic Coronary Embolism:
38-year-old female with acute chest pain

- Transposition of the great vessels diagnosed at birth
- Mustard procedure at age 4
Cardiogenic Coronary Embolism:
38-year-old female with acute chest pain

- Transposition of the great vessels diagnosed at birth
- Mustard procedure at age 4
Cardiogenic Coronary Embolism: 38-year-old female with acute chest pain
Dilated Cardiomyopathy
Dilated Cardiomyopathy: Layered Apical Thrombus
Cardiogenic Stroke: Causes

- Atrial fibrillation
- Ischemic Heart Disease
  - Recent Myocardial infarction
  - Ischemic cardiomyopathy/LV aneurysm
- Paradoxical Emboli
- Valvular Heart Disease
  - Mechanical prosthetic valve
  - Rheumatic mitral stenosis
  - Endocarditis
- Dilated cardiomyopathy
- Cardiac tumors
Atrial Myxomas: Symptoms related to embolization

☑️ CNS Embolization:

☑️ In a review of 113 cases of atrial myxoma with neurologic presentation:
  ☑️ 83% of patients presented with ischemic stroke, most often in multiple sites (43%).
  ☑️ 12% of patients presented with seizures.

☑️ In a retrospective review of 74 patients with atrial myxoma:
  ☑️ 12% had neurologic manifestations.

  ☑️ Cerebral infarction was present in 89% of the cases and most myxomas (89%) demonstrated a mobile component on transesophageal echocardiography.

☑️ Other complications

  ☑️ Myxoma-induced cerebral aneurysm
  ☑️ Myxomatous metastasis mimicking vasculitis or endocarditis.
32 year-old Woman with Simultaneous TIA’s and NSTEMI
32 year-old Woman with Simultaneous TIA's and NSTEMI
62 year-old woman with stroke
Negative TTE
Metastatic Lung Cancer
Left Ventricular mass: TEE
Mobile Aortic Atheroma
79-year-old male with Stroke Symptoms

- Nonischemic cardiomyopathy (EF 20%) – moderate CAD
- Class III congestive heart failure, biventricular ICD
- Sudden onset:
  - Confusion
  - Weakness
  - Diaphoresis
  - Dizziness
  - Left-sided facial droop
  - Shortness of breath
  - Precordial chest pressure
79-year-old male with Stroke Symptoms