Session: Why do stroke patients need a cardiologist?

PREVALENCE OF CORONARY ATHEROSCLEROSIS IN PATIENTS WITH CEREBRAL INFARCTION

The Asymptomatic Myocardial Ischemia in Stroke and Atherosclerotic Disease (A.M.I.S.T.A.D.) study

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DECLARATION OF CONFLICT OF INTEREST

• none
What is the frequency of CAD in patients with ischemic stroke?

Which consequence in terms of risk of major vascular events?
Vascular Prognosis in Stroke Patients

- Patients with stroke had a high risk of recurrent vascular event
- The most frequent event after a stroke is having another stroke

* Stroke patient subgroup only (n = 6,431)

Vascular Prognosis in Stroke Patients

- The risk of Myocardial Infarction increases with time

Cumulative risk of Non Fatal and Fatal Stroke and Cardiac events in the NOMAS Study

Vascular Prognosis in Stroke Patients

Cumulative risk of Fatal Cardiac events in the NOMAS Study

Cerebrovascular Disease

Patient Profile: REACH registry

- Total: N=63,129
- TIA: N=8,741 (48%)
- Stroke: N=13,650 (73%)

- Of the total CVD population:
  - 40.2% have more than 1 disease location
    - 34.3% have 2 disease locations
    - 5.9% have 3 disease locations

--> Polyvascular disease
1-year cardiovascular event rates as function of number of symptomatic disease locations

All p values <0.001

*Pts with ≥3 risk factors but no symptoms are counted as 0, even in the presence of asymptomatic carotid plaque or reduced ABI

**TIA, unstable angina, other ischemic arterial event including worsening of peripheral arterial disease

Steg PG et al. JAMA. 2007
Acute Coronary Syndrome Following Stroke: Data from RCTs

- Acute phase of Stroke/TIA (IST, ECASS-I, TOAST):  
  - Risk of Fatal ACS: 2 to 5% at 90 days

- Among 846 ischemic stroke patients in the Virtual International Stroke Trials Archive, 35 (4.1%) died from cardiac causes at 12 weeks (Prosser J et al. Stroke 2007;38:2295-302)

- Long-term prevention trials:
  - Risk of Fatal ACS:  
    - 2 to 2.5% between day-30 and month-24 post stroke (ESPS-2)  
    - 5% at 3 years in TASS
Vascular Prognosis in Stroke Patients

CHD and Vascular Death Risk After a Stroke
Meta-Analysis of RCTs and Epidemiological Studies

Relationship Between Stroke and Major Coronary Event Risk

Amarenco P et al. Stroke. 2010
Stroke Subtypes and Any CHD Event Risk

<table>
<thead>
<tr>
<th>Estimated Risk per Person-Year (%)</th>
<th>Atorvastatin N=2365</th>
<th>Placebo N=2366</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Subjects</td>
<td>1.1</td>
<td>1.9</td>
</tr>
<tr>
<td>Entry Event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA</td>
<td>1.0</td>
<td>1.8</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2</td>
<td>2.0</td>
</tr>
<tr>
<td>Ischemic</td>
<td>1.2</td>
<td>2.0</td>
</tr>
<tr>
<td>Cardioembolic or Large Vessel</td>
<td>1.4</td>
<td>1.9</td>
</tr>
<tr>
<td>Small Vessel</td>
<td>1.3</td>
<td>2.1</td>
</tr>
<tr>
<td>Other Ischemic</td>
<td>1.0</td>
<td>1.7</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>1.0</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Amarenco P et al. Stroke. 2010
Identification of Presymptomatic CAD Individuals Among Stroke Patients

Exercise T1-201 Myocardial Scintigraphy

Rokey: positive in 41% of 34 stroke patients without cardiac symptoms

Di Pasquale: positive in 26% of 190 stroke/TIA patients without cardiac symptoms
Identification of Presymptomatic CAD Individuals Among Stroke Patients

Coronary Angiography in 420 Carotid Stenting
Past CAD n=166 ; No past CAD n=254

<table>
<thead>
<tr>
<th>Disease Type</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-vessel disease</td>
<td>70</td>
<td>17%</td>
</tr>
<tr>
<td>Two-vessel disease</td>
<td>64</td>
<td>15%</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>93</td>
<td>22%</td>
</tr>
<tr>
<td>Left main stenosis</td>
<td>31</td>
<td>07%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>258</strong></td>
<td><strong>61%</strong></td>
</tr>
</tbody>
</table>

Clinical symptoms with st    100        24%
No clinical symptoms with st   158       38%
Clinical symptoms without st   66        16%

Heart 2005
Identification of Presymptomatic CAD Individuals Among Stroke Patients

Multiple Atherosclerotic Sites in Stroke (MASS) Autopsy study

• Coronary artery plaque: 72.2% (254/352)
• Coronary artery stenosis: 38.1% (131/344)

Plaque: OR Stroke= 3.62 (95% CI, 2.54-5.16, p<0.0001)
Stenosis: OR Stroke= 2.59 (95% CI, 1.72-3.89, p<0.0001)

MASS Autopsy Study: Prevalence of CAD in 808 Patients with Fatal Stroke


* P<.001 for the comparison with patients with cerebrovascular disease
MASS Autopsy Study: 381 Patients With Stroke

Autopsy Prevalence of Coronary Plaque, Stenosis, or Myocardial Infarction in Case of Brain Artery Stenosis

Any Segment of the Cerebral Arteries

Internal Carotid Artery Origin

Prevalence of Asymptomatic Coronary Artery Disease Among 315 Patients with no History of Coronary Heart Disease

**Coronary Plaque**

- 31% 
- 38% 
- 16% 
- 15%

**Coronary Stenosis ≥ 50 %**

- 74%
- 15%
- 6%
- 5%

Number of vessel disease

PRECORIS study

- Using 64-section Coronary CT angiography
- 20% of 274 patients with noncardioembolic stroke or TIA have coronary artery stenosis ≥50%

Calvet et al. Circulation. 2010
In summary:
- Asymptomatic coronary atherosclerosis is highly prevalent in stroke patients

However, in stroke patients:

Do we have to actively search for asymptomatic CAD?

Does asymptomatic coronary atherosclerosis predict a higher risk of major vascular event?

Can we further interfere with this risk?
AMISTAD STUDY DESIGN

• Consecutive inclusion
• All ischemic stroke over 3.5 years (between June 2005 and December 2008)
• 405 patients (regardless of ischemic stroke subtype)
  – 63 with known CHD (15.6%)
  – 342 with no known CHD
  • 315 (92.1%) had coronary angiography within a median 8 (interquartile range, 6 to 11) days after stroke onset
  • 27 either refused CA after inclusion or had a contra-indication
• Informed consent signed by all patients
• IRB approval
AMISTAD STUDY DESIGN

• Risk Factor Evaluation

• Standardized Etiological Investigations

• Evaluation of Extra Coronary Atherosclerosis Disease Burden
  • US examination of both extracranial carotid arteries
  • US examination of both femoral arteries
AMISTAD STUDY DESIGN

• **Follow-up**:
  - 3 months, 6 months, 1 and 2 years
  - Face to face interview by stroke neurologist or structured telephone interview (patient, close relative or family doctor)
  - Blood pressure, Lipid profile, Treatment and Outcome Event

• **Outcome Event**: TIME TO FIRST MAJOR VASCULAR EVENT
  - Vascular Death (Fatal stroke, Fatal MI, Other Cardiovascular death)
  - Non Fatal Stroke
  - Non Fatal Cardiac Event (MI, resuscitation after cardiac arrest, hospitalization for unstable angina or cardiac insufficiency)
  - Major Peripheral Event (non cervicocephalic or cardiac disease leading to hospitalization or revascularization)
AMISTAD STUDY RESULTS : Baseline characteristics

- 378 Patients included in the FU analysis, 6 had no information

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (n=372)</th>
<th>Coronal Artery Disease Subgroups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Absence (n=119)</td>
</tr>
<tr>
<td>Age, y, mean ± SD</td>
<td>62.3 ± 13.1</td>
<td>55.5 ± 13.2</td>
</tr>
<tr>
<td>Male gender</td>
<td>278 (74.7)</td>
<td>79 (66.4)</td>
</tr>
<tr>
<td>BMI, kg/m², mean ± SD</td>
<td>26.1 ± 4.5</td>
<td>25.9 ± 4.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>304 (81.7)</td>
<td>75 (63.0)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>82 (22.0)</td>
<td>26 (21.9)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>161 (43.3)</td>
<td>36 (30.3)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>143 (38.5)</td>
<td>38 (31.9)</td>
</tr>
<tr>
<td>Personal history of stroke</td>
<td>31 (8.4)</td>
<td>6 (5.0)</td>
</tr>
<tr>
<td>Family history of stroke</td>
<td>85 (22.9)</td>
<td>31 (26.1)</td>
</tr>
<tr>
<td>Family history of CHD</td>
<td>96 (25.8)</td>
<td>24 (20.2)</td>
</tr>
</tbody>
</table>
AMISTAD STUDY RESULTS:

Mean Baseline and Follow-up SBP and LDL-C Levels by Baseline Coronary Artery Disease Subgroups. 95% Confidence Intervals are plotted.

- Average decrease of 9 mm Hg
- Average decrease of 40 mg/dL (1 mmol/L)
AMISTAD STUDY RESULTS:

Cumulative Incidence Curves of Composite End Point of Major Vascular events in the Baseline Coronary Artery Disease Subgroups

![Graph showing cumulative incidence curves for different subgroups.](image)

**No. at Risk by Coronary Artery Disease subgroups**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence</td>
<td>119</td>
<td>111</td>
<td>106</td>
<td>101</td>
<td>96</td>
</tr>
<tr>
<td>Silent stenosis &lt;50%</td>
<td>112</td>
<td>111</td>
<td>106</td>
<td>99</td>
<td>90</td>
</tr>
<tr>
<td>Silent stenosis ≥50%</td>
<td>80</td>
<td>71</td>
<td>66</td>
<td>63</td>
<td>56</td>
</tr>
<tr>
<td>Known coronary heart disease</td>
<td>61</td>
<td>51</td>
<td>44</td>
<td>40</td>
<td>39</td>
</tr>
</tbody>
</table>

Log-rank, p<0.0001
**AMISTAD STUDY RESULTS:**

**Association of Two-Year Vascular Risk with Presence and Severity of Asymptomatic Coronary Artery Disease Diagnosed at Baseline.**

<table>
<thead>
<tr>
<th>Asymptomatic CAD at baseline</th>
<th>Age-sex-adjusted</th>
<th>Age-sex-adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N (KM %)*</td>
<td>HR (95%CI)</td>
</tr>
<tr>
<td><strong>Coronary plaque †</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No disease</td>
<td>4/119 (3.6)</td>
<td>1.00 (ref.)</td>
</tr>
<tr>
<td>1-vessel disease</td>
<td>3/46 (6.8)</td>
<td>2.05 (0.45-9.32)</td>
</tr>
<tr>
<td>2-vessel disease</td>
<td>5/52 (9.7)</td>
<td>3.25 (0.84-12.60)</td>
</tr>
<tr>
<td>3-vessel disease</td>
<td>14/94 (15.5)</td>
<td>5.65 (1.70-18.80)</td>
</tr>
<tr>
<td>≥ 1 vessel disease</td>
<td>22/192 (11.8)</td>
<td>3.72 (1.22-11.37)</td>
</tr>
<tr>
<td><strong>Coronary stenosis ≥50% †</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No disease</td>
<td>13/231 (6.0)</td>
<td>1.00 (ref.)</td>
</tr>
<tr>
<td>1-vessel disease</td>
<td>6/47 (12.9)</td>
<td>2.60 (0.94-7.18)</td>
</tr>
<tr>
<td>2- or 3 vessel disease §</td>
<td>7/33 (22.3)</td>
<td>4.96 (1.81-13.65)</td>
</tr>
<tr>
<td>≥ 1 vessel disease</td>
<td>13/80 (16.7)</td>
<td>3.43 (1.48-7.93)</td>
</tr>
</tbody>
</table>

* Number of events/number of patients (Kaplan-Meier estimates).
† Regardless of stenosis severity.
§ Plaque with arterial lumen reduction ≥50% in diameter.
§§ pooled since only 1 event occurred among 16 patients with 3-vessel disease.
Impact of arterial atherosclerotic burden of coronary, extracranial carotid and femoral arteries on Vascular Risk Recurrence

AMISTAD STUDY RESULTS:

* coronary, extracranial carotid and femoral arteries
CONCLUSIONS:

In patients with recent non-fatal cerebral infarction:

- Asymptomatic CAD is highly predictive of any future major vascular event within 2 years after stroke.

- The risk of major vascular events increased with the extent of atherosclerotic disease:
  - Number of coronary arteries involved
  - Number of vascular beds involved

- Long-term follow-up is in progress to confirm these results.

- Further studies are required to test more aggressive preventive strategies in stroke/TIA patients.