Pial Synangiosis in Patients with Moyamoya Less Than 2 Years of Age

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Overview

- Progressive arteriopathy characterized by stenosis and occlusion of the distal intracranial ICA
- 6% of all pediatric strokes

Scott and Smith, NEJM, 2009
# Treatment Options of Moyamoya

## Medical Therapy
- Anti-platelet drugs
- Calcium channel blocker
- Does not alter natural history
- Many ended up having surgery in long-term

## Direct Bypass
- Immediately improved perfusion
- Technically challenging
  - vessel size
  - proximal stenosis
- Requires vessel clamping

## Indirect Bypass
- Delayed perfusion
- Simpler surgery
- No clamping time
- Potentially broader revascularization

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**Moyamoya Is A Surgical Disease**

AHA Scientific Statement

Management of Stroke in Infants and Children
A Scientific Statement From a Special Writing Group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the Young

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Recommendations for Treatment of Moyamoya in Children

Class I Recommendations

1. Different revascularization techniques are useful to effectively reduce the risk of stroke resulting from moyamoya disease (Class I, Level of Evidence B). However, despite a vast literature on moyamoya, there are no controlled clinical trials to guide the selection of therapy.

2. Indirect revascularization techniques are generally preferable and should be used in younger children whose small-caliber vessels make direct anastomosis difficult, whereas direct bypass techniques are preferable in older individuals (Class I, Level of Evidence C).

3. Revascularization surgery is useful for moyamoya (Class I, Level of Evidence B). Indications for revascularization surgery include progressive ischemic symptoms or evidence of inadequate blood flow or cerebral perfusion reserve in an individual without a contraindication to surgery (Class I, Level of Evidence B).
Surgical Technique: Pial Synangiosis
Why look at (very) young kids with moyamoya?

Young children have higher anesthetic risks and natural history of moyamoya progression is more aggressive.
Moyamoya in Very Young Children

• Associated with more major strokes and carries a more fulminant clinical course as compared to older children and adults
  – Need aggressive surgical treatment

Moyamoya disease among young patients: its aggressive clinical course and the role of active surgical treatment. Neurosurgery 54:840-844

• Present with advanced steno-occlusive lesions and less transdural collaterals than older children
  – More limited cerebrovascular reserve

Posterior circulation and high prevalence of ischemi stroke among young pediatric patients with moyamoya disease. AJNR, Jan 2011; 32: 192-198

• Therefore, very young children with moyamoya have worse disease, more aggressive natural history, and are more fragile surgical candidates—can we treat them successfully?
Study Design

• Retrospective review

• Study population:
  – Pediatric patients with Moyamoya treated between 1994-2005
  – Only patients < 2 years of age were included

• Moyamoya confirmed radiographically by neuroradiologists per Japanese guidelines

• Standardized surgical treatment (pial synangiosis)

• Outcome evaluation
  Angiographic - 1-year post-operative angiography
  Clinical - Modified Rankin scale (mRS) during follow-up and stroke rate
### Summary of functional grades in a mRS

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>no symptoms, neurologically intact</td>
</tr>
<tr>
<td>1</td>
<td>some neurological symptoms or headache, but no significant disability &amp; performing at age level &amp; all usual activities</td>
</tr>
<tr>
<td>2</td>
<td>mild neurological deficit; some difficulty performing at age level on all previous activities; independent</td>
</tr>
<tr>
<td>3</td>
<td>moderate neurological deficit, requiring some help with activities of daily living; delay in developmental milestones; walking unassisted</td>
</tr>
<tr>
<td>4</td>
<td>moderate-to-severe neurological deficit; requires help in self-care; unable to walk unassisted</td>
</tr>
<tr>
<td>5</td>
<td>severe neurological disability or vegetative</td>
</tr>
<tr>
<td>6</td>
<td>dead</td>
</tr>
</tbody>
</table>
Results

• Patient population (from a series of 456 operations)
  – 19 children (11 female, 8 male)
  – Mean age at presentation: 1.1 years (2 months – 1.7 years)
  – Mean age at time of 1\textsuperscript{st} surgery: 1.4 years (6 months - 1.9 years)

• Total treated hemispheres: 36 (34 included in analysis)
  – 12 patients had bilateral pial synangiosis during one anesthesia
  – 5 patients had staged bilateral surgeries
  – 2 patients had unilateral procedures

• Mean Length of follow-up: 7 years (1-14 years)
## Clinical Presentation

### Associated disease/conditions

<table>
<thead>
<tr>
<th>Association</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Graves Disease</td>
<td>2</td>
</tr>
<tr>
<td>Noonan Syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Alagille syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Facial AVM</td>
<td>1</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>2</td>
</tr>
<tr>
<td>NF1</td>
<td>3</td>
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</tbody>
</table>

### Clinical presentation

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA</td>
<td>18</td>
</tr>
<tr>
<td>Stroke</td>
<td>17</td>
</tr>
<tr>
<td>Seizure</td>
<td>4</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>0</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>1</td>
</tr>
</tbody>
</table>
Peri–operative and Delayed Complications

• Peri-operative complications:
  – 3 unanticipated staged procedures
    • 2 due to EEG changes after 1\textsuperscript{st} procedure
    • 1 due to significant brain swelling
  – 2 peri-operative strokes (10.5\% per patient, 5.6\% per treated hemisphere)

• Delayed complications:
  – 3 patients had additional surgeries
    • 1 subdural collection evacuation
    • 2 re-do synangiosis for ACA symptoms
  – 1 delayed infarction
Long-term Angiographic Outcome

• 10 patients (19 hemispheres) had post-operative angiography
  – Matsushima A (>2/3 MCA territory): 11 (57.9%)
  – Matsushima B (1/3-2/3 MCA territory): 6 (31.6%)
  – Matsushima C (<1/3 MCA territory): 2 (10.5%)

• In summary, 90% of treated hemispheres had Grade A-B revascularization
Long-term Clinical Outcome

- Majority of the patients (68%) had favorable long-term outcome (mRS = 0-2) and 94% were stable or improved from preop mRS (despite arteriopathy progression)
Stroke Outcome

- Total strokes postop per hemisphere over 5 year window
  - 6% stroke risk per hemisphere over 5 years
- Compared to natural history of 65-82% stroke per hemisphere over 5 years.
- 10-fold rate of improved protection afforded by surgery

Hallemeier 2006, Kuroda and Houkin 2008
Conclusions

• Very young children (<2 years of age) with moyamoya present with significant disease burden and ischemia.

• Pial synangiosis is a safe and effective method of treating these patients, with low peri-operative complication rate.

• Surgery – in marked contrast to the documented natural history of untreated patients - provides long-term, durable angiographic and clinical protection from stroke as measured by mRS and annual stroke rate.