Clinical features and long-term outcomes of moyamoya disease (MMD) in China

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**Epidemiology**

**Prevalence in Japan:**
6.03-10.5/100,000 persons

**Annual incidence:** 0.54-0.94/100,000

**Prevalence in Korea:**
8-16.1/100,000 persons

**Annual incidence:** 1.7-2.3/100,000

Epidemiology of MMD in China

- 1976: Four MMD patients were first reported by Li Shu-Xing
- 1978: STA-MCA bypass was first reported by Yang De-Juan
- 2012: Duan Lian et al reported 802 cases of MMD
- Relatively, papers about Chinese MMD in English 50/2700 (2%)

There is still no national epidemiological and multiple centers surveys on MMD!
Epidemiology of MMD in China

Estimation Prevalence 1.61-3.92/100,000 person

50000 patients

Epidemiological and clinical features of Moyamoya disease in Nanjing, China

Epidemiology of moyamoya disease in Taiwan: a nationwide population-based study.

Clin neuro neurosurg 2010 112(3):199-203
Stroke. 2014 May;45(5):1258-63
MMD in Tiantan hospital during past 25 years (n=528)
Status and questions

Surgical revascularization with direct, indirect, and combined methods remains the preferred procedure for patients with moyamoya disease.

Questions!

There are still lack multicenter, randomized studies and no national standard Guide line!

There are still controversial about surgical treatment of hemorrhagic MMD!

There is a lack of multicenter reports regarding clinical characteristic, natural history and long-term outcome of in the Chinese MMD.
Methods

1. Registration study
Consecutive patients admitted in 18 neurosurgical centers from 2007 to 2011 in China were reviewed

2. Follow-up study
Clinical features and long-term outcome of moyamoya disease: a single-center experience of 528 cases in China

This study was supported by ‘11th Five-Year Plan’ National Science and Technology supporting plan (2006BAI01A13). Beijing Municipal S&T Commission (D101107049310001)
Methods 1 - registration study

China

North

Beijing

Beijing

TianTan hospital

Liaoning

Hospital of CMU

Shanghai

Huashan hospital

Fujiang

Union hospital

South

...
Methods 1-Patient selection

Inclusion criteria:

The diagnostic criteria for MMD was based on the guideline reported in 1997 and 2012 by Research committee of Japan

(1) stenosis or occlusion of the terminal internal carotid and the proximal middle and anterior cerebral arteries.

(2) unilateral or bilateral involvement.

(3) patients with any other disease that might explain the arterial steno-occlusive disease were excluded.

Methods 1-Patient selection

Exclusion criteria:

(1). Patients with any other disease that might be responsible for the observed vasculopathy: including atherosclerosis, systemic vasculitis, neurofibromatosis, meningitis, sickle-cell disease, Down syndrome, and prior skull-base radiation therapy

(2). Patients who did not complete informed consent
Methods 1–Data collection

Standard workbook and network platform

(Each patient have completed informed consent)

1. Basic information:
   Age, sex, ethnicity, native place, telephone, et al

2. Baseline stroke risk factors:
   hypertension, cerebral aneurysm, familial MMD, hyperlipidemia, diabetes, hyperthyroidism, hypertensive heart disease, significant alcohol and/or tobacco use parental stroke history
Standard workbook and network platform

3. Clinical records: hospital charts (mRS, type), radiographic data (CT, MRA/ CTA/DSA stage, CBF(CTP /SPECT)

4. Treatments: direct, indirect, conservative, combined treatment

5. Outcomes: complications, morbidity, mortality, CBF changes, mRS
We have established a database and platform of MMD in a multiple-center in China.

A total of 704 patients were collected. Follow up 10-15 years
Regional distribution 704 patients
Results 1

General information

<table>
<thead>
<tr>
<th>Age and sex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: female</td>
<td>358:346</td>
</tr>
<tr>
<td>(1.04:1)</td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>28.98 ± 15</td>
</tr>
<tr>
<td>Age ≤18 years</td>
<td>225 (31.9%)</td>
</tr>
<tr>
<td>Age &gt;19 years</td>
<td>479 (68.1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Han</td>
<td>696 (99%)</td>
</tr>
<tr>
<td>Tibetan</td>
<td>2</td>
</tr>
<tr>
<td>Korea</td>
<td>3</td>
</tr>
<tr>
<td>Mongolian</td>
<td>2</td>
</tr>
<tr>
<td>Huizu</td>
<td>1</td>
</tr>
</tbody>
</table>
## Results 1

<table>
<thead>
<tr>
<th></th>
<th>TIA</th>
<th>Infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic type</td>
<td>242 (57.2%)</td>
<td>181 (42.7%)</td>
</tr>
<tr>
<td>Hemorrhagic type</td>
<td>IVH (38.1%)</td>
<td>ICH (31.3%)</td>
</tr>
<tr>
<td></td>
<td>107</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>SAH (11.7%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IVH and ICH</td>
<td>53</td>
</tr>
</tbody>
</table>

**1.5** VS **1**
## Results 1

### General information

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family MMD</td>
<td>23 (3.3%)</td>
</tr>
<tr>
<td>Hyperthyroidson</td>
<td>10 (1.4%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>21 (3.0%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>73 (10.3%)</td>
</tr>
<tr>
<td>Aneurysms</td>
<td>26 (3.7%)</td>
</tr>
<tr>
<td>Smoking alcohol</td>
<td>66 (9.4%)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>32 (4.5%)</td>
</tr>
</tbody>
</table>
Results 1

DSA stage distribution

![Bar chart showing distribution of DSA stages (I-VI) with stage III having the highest count and stages I and VI having the lowest counts.]
Results 1

Age distribution
Results 1

Age distribution for two types

- Hemorrhagic
- Ischemic
## Results 1

### Treatments

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conservative</td>
<td>135 (19%)</td>
</tr>
<tr>
<td>STA-MCA</td>
<td>243 (34.5%)</td>
</tr>
<tr>
<td>Indirect bypass</td>
<td>326 (46.3%)</td>
</tr>
<tr>
<td>EDAS (102)</td>
<td></td>
</tr>
<tr>
<td>Multiple bur hole (97)</td>
<td></td>
</tr>
<tr>
<td>EMS (28)</td>
<td></td>
</tr>
<tr>
<td>EDAMS (22)</td>
<td></td>
</tr>
<tr>
<td>Combined bypass</td>
<td>31 (5%)</td>
</tr>
</tbody>
</table>
Results 1- STA-MCA VS Indirect bypass

### Postoperative complications: total 55 (9.7%)

<table>
<thead>
<tr>
<th></th>
<th>STA-MCA</th>
<th>Indirect</th>
<th>T/X² value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound infection</td>
<td>6</td>
<td>2</td>
<td>3.489</td>
<td>0.06</td>
</tr>
<tr>
<td>hematomas</td>
<td>8</td>
<td>3</td>
<td>4.144</td>
<td>0.04</td>
</tr>
<tr>
<td>New infarction</td>
<td>4</td>
<td>6</td>
<td>0.031</td>
<td>0.861</td>
</tr>
<tr>
<td>subdural hydromas</td>
<td>5</td>
<td>6</td>
<td>0.034</td>
<td>0.853</td>
</tr>
<tr>
<td>Seizure</td>
<td>3</td>
<td>3</td>
<td>0.122</td>
<td>0.726</td>
</tr>
<tr>
<td>Second operation</td>
<td>5</td>
<td>4</td>
<td>0.609</td>
<td>0.435</td>
</tr>
<tr>
<td>Total</td>
<td>31(12.7%)</td>
<td>24(7.3%)</td>
<td>4.641</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Discussions 1

Clinical features of MMD in mainland China

- Two types
- Two peak distributions
- Familiar history

Same with Japan and Korea
**Discussions 1**

**Own characteristics of MMD in mainland China**

1. There was no difference in sex distribution in Chinese MMD

<table>
<thead>
<tr>
<th></th>
<th>China</th>
<th>Japan</th>
<th>Korea</th>
<th>USA and European</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male :</td>
<td>1:1 - 1:1.1</td>
<td>1:1.8 - 1:2.2</td>
<td>1:1.8 - 1:1.94</td>
<td>1:1.8 - 1:4.25</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>202-802</td>
<td>3900-7700</td>
<td>2539-8154</td>
<td>35-7473</td>
</tr>
</tbody>
</table>

Discussions 1

Own characteristics of MMD in mainland China

2. A younger-age peak was found in Chinese MMD compared with Japan and Korea

First peak: 6-15 y
Second peak: 30-40y
Discussions 1

Own characteristics of MMD in mainland China

3. Relatively lower proportion of familiar MMD in this group: 23 (3.3%)
   Other reported from China: 1.48-7%

Familiar MMD Japan: 12.1-16%

May not be the actual incidence!
Duan L et investigated 527 MMD patients family members by TCD: proportion of familiar MMD was increased from 7% to 15%
Methods 2: a follow-up study

528 patients screened

332 cases of ischemic MMD

- 302 received revascularizations
  - 30 lost to follow up
  - 37 followed up less than 1 year

- 30 treated conservatively
  - 18 lost to follow up
  - 12 followed up less than 1 year

196 cases of hemorrhagic MMD

- 104 received revascularizations
  - 38 lost to follow up
  - 22 followed up less than 1 year

- 92 treated conservatively
  - 20 lost to follow up
  - 12 followed up less than 1 year

331 patients assessed
Follow-up
331 patients (62.6%) had at least 1 year follow up. The median follow-up was 39 months (range 12 to 300).

Types
the initial symptom of presentation was ischemia in 227 hemorrhage in 104.

Treatments
- Revascularization (n=271)
- Direct (n=177)
- Indirect (n=94)
- Conservative (n=60)
- Hemorrhagic MMD
Results 2

Follow up events:

There were 33 (9.9%) intracranial hemorrhages, 68 (20.5%) TIs, (43 new infarctions) during follow up.

Twenty-five of 60 (41.6%) conservatively treated patients and eight of 271 (2.9%) surgically treated patients experienced a rebleeding event (OR=23.4; 95% CI 9.8 to 56.1; P <0.01).

<table>
<thead>
<tr>
<th></th>
<th>Surgical</th>
<th>Conservative</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>New bleeding</td>
<td>8(2.95%)</td>
<td>25(41.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Death due to bleeding</td>
<td>2(0.7%)</td>
<td>4(6.6%)</td>
<td>0.010</td>
</tr>
<tr>
<td>Ischemic events</td>
<td>51(18.8%)</td>
<td>17(28.3%)</td>
<td>0.099</td>
</tr>
</tbody>
</table>
Results 2

Kaplan Meier Cumulative hazard curve for rebleeding comparing surgical and conservative treatment
Results 2

Kaplan Meier Cumulative hazard curve for ischemic events comparing surgical and conservative treatment
## Results 2

### Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Surgical</th>
<th>Conservative</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Improvement in mRS</strong></td>
<td>177 (65.3%)</td>
<td>27 (45%)</td>
<td>0.03</td>
</tr>
<tr>
<td>mRS = 0 — 2</td>
<td>238 (87.8%)</td>
<td>42 (70.0%)</td>
<td>0.001</td>
</tr>
<tr>
<td>mRS = 3 — 5</td>
<td>31 (8.3%)</td>
<td>14 (23.3%)</td>
<td>0.015</td>
</tr>
<tr>
<td><strong>Perfusion (1 months)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased</td>
<td>164/224 (73.2%)</td>
<td>7/43 (16.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Decreased</td>
<td>29</td>
<td>13</td>
<td>0.004</td>
</tr>
<tr>
<td>No change</td>
<td>31</td>
<td>23</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Conclusions

1. There was no difference in sex distribution in Chinese MMD, with 2 age peaks (6-15 years, and 36-40 years) noted, and ischemic symptoms as the main presentation.

2. Adult patients have a higher rate of hemorrhagic presentation than children.

3. Hemorrhagic MMD had a much higher rate of rebleeding and poorer prognosis than ischemic type.

4. Surgical revascularizations can improve cerebral perfusion and have greater efficacy at preventing rebleeding than conservative treatment.
Limitations

1. This study is a non-randomized retrospective study, data are collected over 25 years during which many diagnostic and therapeutic things have changed, therefore, selection bias may exist and results cannot completely reflect the epidemiology of MMD in China.

2. There are 20% of patients lost to follow-up and direct imaging follow-up was incomplete for some patients.

3. Scientific comparisons between varying revascularization interventions cannot be made due to the retrospective and nonrandomized nature of this study.

4. Long-term follow-up angiographic data were not obtained in most of these patients, although 1 year follow-up imaging were available.
Thank you!