Imaging of Intracranial Stenosis

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objectives & next steps

- collaterals offset ischemia
  - systematic evaluation of collaterals
- hemodynamic impact, not % stenosis
  - develop fractional flow measures
- collateral perfusion patterns distinct
  - establish noninvasive risk markers
collaterals offset ischemia
Collateral circulation in symptomatic intracranial atherosclerosis

Collateral grade (ASITN/SIR) variable, yet more robust with greater % stenoses and diminished antegrade (TICI) perfusion (p < 0.001)
WASID collaterals & outcome

“severe” – 70-99%

“moderate” – 50-69%
SAMMPRIS collaterals

424/451 cases with DSA available, collaterals in 376
- complete collaterals in 117 (31%)
- hemodynamic effects (partial TICI scores) in only 188 (50%), all in excess of 70% luminal stenosis

more robust collaterals (complete versus none/partial) associated with patients who at baseline were:
- younger (mean age 58.0 vs 61.5 years; p = 0.009)
- had higher serum HDL (40.0 vs 37.7 mg/dL, p = 0.035)
- participated in moderate exercise (43.1 vs 27.9%, p = 0.004)
- did not smoke (79.5 vs 69.4%, p = 0.042)
**SAMMPRIS collaterals**

- **Impaired perfusion** - partial TICI and none/partial collaterals
- **Normal perfusion** - complete TICI and no collaterals
- **Robust collaterals** - partial TICI and complete collaterals

376/424 of 451 subjects (186 medical, 190 stenting)

- early territorial stroke (SIT) in 6/186 (3.2%) medical, 20/190 (10.5%) stenting
- 0/66 (0%) SIT in medical, 0/51 (0%) SIT in stented when collaterals were complete

**Medical**
- partial TICI/partial collaterals (5/25 (20.0%))
- complete TICI/partial collaterals (1/95 (1.1%))
- partial TICI/complete collaterals (0/66 (0%)), p < 0.001

ICH within 30 days in 0/186 (0%) subjects

**Stenting**
- partial TICI/partial collaterals (11/46 (23.9%))
- complete TICI/partial collaterals (9/93 (9.7%))
- partial TICI/complete collaterals (0/51 (0%)), p < 0.001
Significance of Good Collateral Compensation in Symptomatic Intracranial Atherosclerosis

Alexander Y.L. Lau\textsuperscript{a,b}, Edward H.C. Wong\textsuperscript{a}, Adrian Wong\textsuperscript{a}, Vincent C.T. Mok\textsuperscript{a}, Thomas W. Leung\textsuperscript{a}, Ka-sing Lawrence Wong\textsuperscript{a}

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\begin{tabular}{|c|c|c|c|c|c|}
\hline
& Score & 0 & 1 & 2 & 3 & 4 \\
\hline
I. Antegrade grade & TICI & 0 & 1 & 2\textsuperscript{a} & 2\textsuperscript{b} & 3 \\
II. Collateral grade & ASITN/SIR & 0 & 1 & 2 & 3 & 4 \\
\hline
Composite circulation score = I + II. \\
\hline
\end{tabular}

\begin{tabular}{|c|c|c|c|}
\hline
& Good circulation score (n = 34) & Poor circulation score (n = 6) & p value \\
\hline
mRS 0–2 at 3 months & 31 (91\%) & 3 (50\%) & 0.051 \\
TIA/stroke in 12 months & 5 (15\%) & 2 (33\%) & 0.27 \\
\hline
\end{tabular}
36 cases, mean age 63.9±14.5 years, 28% female, and time from last symptomatic event to stenting was median 15.5 (IQR 27) days. Baseline degree of luminal stenosis ranged from 63 to 99% (median 85%). Collateral grade varied across cases (0-4). More robust collaterals linked with reduced rate of peri-procedural stroke (p=.04). Good collateral flow associated with in-stent restenosis on follow-up DSA.
perfusion angiography
next step

- collaterals offset ischemia
  - systematic evaluation of collaterals
hemodynamic impact, not % stenosis
percent stenosis?

A Standardized Method for Measuring Intracranial Arterial Stenosis

Owen B. Samuels, Gregg J. Joseph, Michael J. Lynn, Harriet A. Smith, and Marc I. Chimowitz

BACKGROUND AND PURPOSE: Atherosclerosis of the major intracranial arteries is an important cause of ischemic stroke. We established measurement criteria to assess percent stenosis of a major intracranial artery (carotid, middle cerebral, vertebral, basilar) and determined the interobserver/intraobserver agreements and interclass/intraclass correlations of these measurements.

METHODS: We defined percent stenosis of an intracranial artery as follows: percent stenosis = [(1 – (Dstenosis/Dnormal))] × 100, where Dstenosis = the diameter of the artery at the site of the most severe stenosis and Dnormal = the diameter of the proximal normal artery. If the proximal segment was diseased, contingency sites were chosen to measure Dnormal: distal artery (second choice), feeding artery (third choice). Using a hand-held digital caliper, three neuroradiologists independently measured Dstenosis and Dnormal of 24 stenotic intracranial arteries. Each observer repeated the readings 4 weeks later. We determined how frequently two observers’ measurements of percent stenosis of each of the 24 diseased arteries differed by 10% or less.

RESULTS: Among the three pairs of observers, interobserver agreements were 88% (observer 1 versus observer 2), 79% (observer 1 versus observer 3), 75% (observer 2 versus observer 3) for the first reading and were 75% (observer 1 versus observer 2), 100% (observer 1 versus observer 3), and 71% (observer 2 versus observer 3) for the second reading. Intraobserver agreement for each of the observers was 88%, 83%, and 100%. Interclass correlation was 85% (first reading) and 87% (second reading). Intraclass correlation was 92% (first and second readings combined).

CONCLUSION: This method shows good interobserver and intraobserver agreements for the measurement of intracranial stenosis of a major artery. If validated in subsequent studies, this method may serve as a standard for the measurement of percent stenosis of an intracranial artery.

historical translation
unique features
1D, not 2D or 3D
71-100% reliability
no subsequent validation
correlation with other features or clinical…?
used in WASID and SAMMPRIS
more than 12 years
percent stenosis and outcomes?

- **WASID** - 50-99%
- **SAMMPRIS** - 70-99%

**TABLE 3: Multivariate Associations of Baseline Characteristics with Stroke in the Territory of the Symptomatic Stenotic Artery**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaterals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None vs good</td>
<td>1.62 (0.52-5.11)</td>
<td>0.0019</td>
</tr>
<tr>
<td>Poor vs good</td>
<td>4.78 (1.55-14.7)</td>
<td></td>
</tr>
<tr>
<td>Age, ≥64 vs &lt;64 yr</td>
<td>0.54 (0.28-1.04)</td>
<td>0.067</td>
</tr>
<tr>
<td>Sex, female vs male</td>
<td>1.33 (0.67-2.63)</td>
<td>0.419</td>
</tr>
<tr>
<td>Race, other vs white</td>
<td>0.88 (0.45-1.71)</td>
<td>0.703</td>
</tr>
<tr>
<td>Qualifying event, stroke vs TIA</td>
<td>1.56 (0.67-3.62)</td>
<td>0.300</td>
</tr>
<tr>
<td>Symptomatic vessel, posterior vs anterior</td>
<td>1.36 (0.70-2.64)</td>
<td>0.370</td>
</tr>
<tr>
<td>Percent stenosis, ≥70% vs &lt;70%</td>
<td>1.54 (0.77-3.07)</td>
<td>0.222</td>
</tr>
<tr>
<td>On antithrombotic medication at qualifying event, yes vs no</td>
<td>1.20 (0.62-2.32)</td>
<td>0.582</td>
</tr>
<tr>
<td>Time from qualifying event, ≥17 vs &lt;17 days</td>
<td>1.59 (0.84-3.01)</td>
<td>0.150</td>
</tr>
<tr>
<td>NIH Stroke Scale, &gt;1 vs ≤1ª</td>
<td>1.72 (0.84-3.49)</td>
<td>0.136</td>
</tr>
</tbody>
</table>

*Only collaterals (p = 0.0003) and NIH Stroke Scale (p = 0.0152) were significant after removing nonsignificant characteristics.

HR = hazard ratio; CI = confidence interval; TIA = transient ischemic attack; NIH = National Institutes of Health.
atherosclerosis, not just stenosis

- Physical properties, length, architecture, surface irregularity, diffuse disease, tandem disease
- % stenosis is a poor descriptor of intracranial atherosclerosis, not accounting for complexity of lesions and diffuse disease

\[ Q = \frac{\pi \Delta P r^4}{8 L \eta} \]
fractional flow

\[ \text{FFR} = \frac{P_d}{P_a} \]

during maximal flow

\[ P_d / P_a = 60 / 100 \]

\[ \text{FFR} = 0.60 \]

Patient-Specific cCTA Data

Geometry

Myocardial Mass

CCTA

Equations of Blood Flow

\[ \rho u + p \nabla \cdot \mathbf{V} = -\mathbf{V} \cdot \mathbf{F} \]

\[ \nabla \cdot \mathbf{V} = 0 \]

Simulated physiologic conditions

- Aortic pressure
- Coronary flow at rest
- Effect of hyperemia on microcirculation
fractional flow

- Large, randomized trials established FFR for lesion-specific ischemia
- Fractional flow measures proven:
  - Enhance clinical decision-making
  - Improve event-free survival
  - Reduce unnecessary revascularization
  - Lower costs
- FAME, FAME II, DeFACTO

Anatomical luminal stenosis replaced by hemodynamics
TO F-MRA – SONIA to SINO A

- SONIA – % stenosis irrelevant
SONIA-WASID analyses

- Analyses included clinical variables, SIR, and invasive angiography measures (luminal stenosis, TICI score of antegrade flow, collateral grade) to identify predictors of stroke in the territory.
- 189 patients with 50-99% symptomatic IAD had TOF-MRA available.
- Univariate analysis, the hazard ratio (HR) for SIT of the symptomatic artery with SIR < 0.9 (SIR below median) was 5.2 (1.8, 15.3; p=0.001) as compared to SIR ≥ 0.9.
- Multivariate analysis correcting for baseline blood pressure, LDL, percent stenosis, recency of symptoms, TICI and downstream collaterals, the HR for SIR < 0.9 was 10.9 (2.0, 58.9; p=0.001).
- Only collaterals also had a significant independent association with stroke risk, HR 13.8 (3.4, 55.5; p<0.001).
- In patients with <70% stenosis, a SIR < 0.9 maintained a significant association with recurrent SIT (p=0.006), with a 2-year event rate of 17.3%, showing that even moderate stenoses can pose substantial ischemic risk.
from 2D to 3D...
CFD – Δ pressure
407 patients with 70-99% symptomatic stenosis DSA, biplanar views available for 3D reconstruction in 249, and CFD simulations in 188 (25 VA, 45 BA, 32 ICA, 86 MCA) under simulated normal inflow conditions (120/80 mm Hg), only 76/188 (40%) cases had low FF. During simulated hypertension, FF improved to normal in 10/188 (5%) cases. Simulated hypotension caused FF to worsen from normal in 12/188 (6%) cases. Other hemodynamic parameters including shear stress calculated and visually depicted.
CFD of CTA
CFD of MRA
periprocedural CFD
next step

- hemodynamic impact, not % stenosis
  - develop fractional flow measures
collateral perfusion patterns distinct
subtle signatures of stenosis
ASL signatures of stenosis
signatures of stenosis
collateral perfusion & sources
myriad mechanisms

recurrent stroke risk predicated on mechanisms
  - decreased flow due to arterial narrowing
  - impaired tissue perfusion
  - plaque instability with perforator occlusion and/or distal embolism
risk of collateral perfusion

Patient A (left) has low QMRA volumetric flow rate (28 mL/min) with impaired angiographic collaterals (ASITN grade 2), and partial angiographic perfusion (TICI grade 2B). Patient B (right) has normal QMRA flow (75 mL/min), complete angiographic perfusion (TICI grade 3), normal vasomotor reactivity (BHI 1.0), but 2 embolic signals were detected distal to the stenosis (1 ES noted by arrow).
next step

collateral perfusion patterns distinct
- establish noninvasive risk markers
conclusions

- systematic evaluation of collaterals
- develop fractional flow measures
- establish noninvasive risk markers