Noninvasive characterization of high-risk ICAS plaque & patient

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Presenter Disclosure Information

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Non-invasive characterization of high-risk ICAS plaque & patient

FINANCIAL DISCLOSURE:

No disclosures to be done relevant to attendance and content of talks in 2013 SVIN Conference.

UNLABELED/UNAPPROVED USES DISCLOSURE:
None
Intracranial Atherosclerosis

A major cause of stroke worldwide
Translational research priorities

- Intracranial vulnerable plaque characterization
- Vulnerable ICAS patient characterization
- Monitoring basic processes and response to therapies
Classical approach

Focus on intracranial stenosis
(Angiographic & Haemodinamic)
Limitations of classical approach

Restricted to advanced and stenoocclusive stage

Makowski, Radiology 2013
Limitations of classical approach

Arterial remodelling and plaque composition
New approach to ICAS: Plaque imaging

Plaque morphology & activity

Turan et al, J Neuroimaging 2010

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Vulnerable plaque characterization

Outward vs. inward remodelling

Plaque surface irregularity

Fig. 4. Plaque surface irregularity on a color map of high resolution MR in a 47-year-old man with multifocal infarctions of the right middle cerebral artery territory. (A) T2-weighted high resolution MR imaging shows the ill-defined plaque margin (arrow). (B) Color map imaging of T2-weighted high resolution MR shows the luminal irregularity of the plaque’s inner margin, suggestive of plaque surface irregularity (arrow).

Table 3
Predictors of symptomatic disease with MCA stenosis.

<table>
<thead>
<tr>
<th></th>
<th>Univariate regression</th>
<th>Multivariate regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Degree of MCA stenosis (%)</td>
<td>1.07 [1.01–1.15]</td>
<td>0.02</td>
</tr>
<tr>
<td>Remodeling ratio</td>
<td>1.11 [1.03–1.20]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Outward remodeling</td>
<td>5.50 [1.15–26.41]</td>
<td>0.03</td>
</tr>
<tr>
<td>Inward remodeling</td>
<td>0.05 [0.01–0.45]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Plaque surface irregularity</td>
<td>9.33 [1.52–57.66]</td>
<td>0.008</td>
</tr>
</tbody>
</table>

OR = odds ratio; CI = confidence interval; MCA = middle cerebral artery. The univariate columns show results for each variable fit separately while the multivariate columns show results from a single model fitting all variables simultaneously.

Chung et al, Eur J Radiol 2012
Intraplaque hemorrhage more frequent in symptomatic MCA plaques (19.6% vs 3.2%)
Vulnerable plaque characterization

Intracranial Atherosclerotic Plaque Enhancement in Patients with Ischemic Stroke

M. Skarpathiotakis, D.M. Mandell, R.H. Swartz, G. Tomlinson, and D.J. Mikulis

Correlation with histology

Intracranial-Derived Atherosclerosis Assessment: An In Vitro Comparison between Virtual Histology by Intravascular Ultrasonography, 7T MRI, and Histopathologic Findings


AJNR 2013

Very good identifying presence of plaque

Still limitations regarding plaque components

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Basic mechanisms?

In vivo monitoring of basic mechanisms and molecular pathways determining high-risk ICAS

- Inflammatory infiltration, Thrombogenic potential
- Response to therapies: Plaque stabilization and regression
- Development of collateral circulation (Angiogenesis, Arteriogenesis)
Biomarkers: Inflammation

C-Reactive Protein Predicts Further Ischemic Events in First-Ever Transient Ischemic Attack or Stroke Patients With Intracranial Large-Artery Occlusive Disease
Juan F. Arenillas, MD; José Álvarez-Sabín, MD, PhD; Carlos A. Molina, MD, PhD; Pilar Chacón, MD, PhD; Joan Montaner, MD, PhD; Àlex Rovira, MD; Bernardo Ibarra, MD; Manuel Quintana

Progression of Symptomatic Intracranial Large Artery Atherosclerosis Is Associated With a Proinflammatory State and Impaired Fibrinolysis
Juan F. Arenillas, MD, PhD; José Álvarez-Sabín, MD, PhD; Carlos A. Molina, MD, PhD; Pilar Chacón, MD, PhD; Israel Fernández-Cadenas, PhD; Marc Ribó, MD, PhD; Pilar Delgado, MD, PhD; Marta Rubiera MD, PhD; Anna Penalba; Àlex Rovira, MD; Joan Montaner, MD, PhD

Association between Inflammatory Biomarkers and Progression of Intracranial Large Artery Stenosis after Ischemic Stroke
Kanako Shimizu, MD, Kana Shimomura, MD, Yoshiaki Tokuyama, MD, Kenzo Sakurai, MD, PhD, Kenji Isahaya, MD, PhD, Satoshi Takaishi, MD, PhD, Bunta Kato, MD, PhD, Noriko Usuki, MD, Takahiro Shimizu, MD, Koji Yamada, MD, PhD, and Yasuhiro Hasegawa, MD, PhD

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Biomarkers: Inflammation

BIOSIS

Biomarkers of Ischemic Outcomes in Symptomatic Intracranial Stenosis

NIH Grant# 1 R01 NS064162
PI: Michael Frankel, MD
Institution: Emory University
Biomarkers: Inflammation LpPLA2


N= 75
18 recurrent events
(10 ischemic stroke)
Biomarkers: PAI-1

Predictive value of ankle-brachial index and PAI-1 in symptomatic intracranial atherosclerotic disease recurrence (new ischemic stroke)

Massot A, Arenillas J et al, under review
Biomarkers & advanced imaging

Oomics approach
Refine statistical analysis to improve predictive power

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Next step: Molecular imaging in ICAS

Following coronary & carotid literature

Makowski et al, Radiology 2013
Conclusion

- Noninvasive identification of high-risk ICAS plaque & patient as a main research priority
- HRMIR shows first evidence of differential ultrastructural characteristics of symptomatic intracranial ath plaque in vivo
- Biomarker studies suggest involvement of inflammation and PAI-1, further studies needed

Intracranial stenosis  Intracranial ath PLAQUE
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