Hemorrhagic Transformation of Ischemic Stroke Caused by Acute Basilar Artery Occlusion

The Basilar Artery Stroke International Cooperation Study (BASICS)

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Author Disclosures

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Introduction

- **Aim:** analyze the frequency and predictors of hemorrhagic transformation (HT) of ischemic stroke after acute basilar artery occlusion (BAO) using the BASICS registry.

- **Why:** Hemorrhagic transformation (HT) in ischemic strokes is associated with poor outcome.

- **Risk factors:** studied in trials of ischemic stroke but the large majority of these patients had an anterior circulation stroke:
  - Stroke severity, Lytic Dose, Mode of txt (IV vs IA), Early CT changes, DWI size, prior ASA use, Age, Hyperglycemia, Timing, Heparin.
BASICS Background

- The Basilar Artery International Cooperation Study (BASICS) is the largest prospective observational registry of patients with imaging confirmed basilar artery occlusion.
- Basilar artery occlusion is a rare cause of stroke.
- Aim: Collect preliminary data that will help direct future treatment trial design.
- Prospective, observational, multi-center, international registry – symptomatic & radiologically confirmed basilar artery occlusion.
- Total Patients 619
Methods

- HT was reported by the treating physician. Defined as any reported intracerebral hemorrhage on imaging in the posterior circulation and/or symptomatic intracerebral hemorrhage reported by the investigator.

- Evaluated association between predefined baseline and risk factors and the occurrence of HT in univariate analysis.

- Univariate analysis: chi square (Fisher Exact where appropriate) for categorical, T-test for continuous variables.

- Once risk factors with $P < 0.2$ were identified in the univariate analysis, a multivariate regression analysis, using these variables, was used to determine the independent predictors.
Variables in the Univariate analysis

- Initial imaging findings (CT findings, location of occlusion), NIHSS, deficit at presentation, age, vascular risk factors, stroke mechanism, time to diagnosis, recanalization status, and treatment modality.
Univariate analysis: Imaging

- Initial CT Scan
  - Early Ischemic Changes
  - Old Posterior Circulation Stroke
  - Dense Basilar Artery Sign
  - Normal

- Location of occlusion: Proximal, Middle, or Distal

- Recanalization (TCD’s, CTA, Angio): Patent, Severe Stenosis, or Occluded

- TIMI Score for IA txt:
  - TIMI 0,1 = no recanalization, TIMI 2,3= recanalization

- Post treatment Imaging CT/MRI: HT or No HT
Univariate analysis: Non-imaging

- Severity
  - Initial NIHSS
  - Presenting symptoms: None/TIA, Minor Stroke, Tetraplegia, Locked In, or Coma

- Time to Diagnosis

- Age

- Vascular Risk Factors: Age, DM, HTN, Atrial Fibrillation, Valvular heart disease, Hyperlipidemia, Peripheral Vascular Disease, Coronary Artery Disease, Alcohol use, Current smoking.

- Presumed Etiology: Unknown, Embolic, Atherosclerosis, or Dissection
Univariate analysis: Treatment

- Treatment Modality
  - Anti-thrombotics
  - IV tPa alone
  - IV tPa + IA tPa
  - IA tPa alone
  - IA Mechanical thrombectomy + IA tPa
  - IA Mechanical thrombectomy alone
Results

Univariate analysis revealed, treatment modality (p<0.001), stroke severity (deficit) (P=0.034), NIHSS at time of treatment (P=0.005), recanalization (p=0.008), peripheral vascular disease (p=0.042), and alcohol use (p=0.049) as risk factors for HT in basilar artery ischemic strokes.

Used all variables with P<0.2 for multivariate analysis which also included: early ischemic changes on CT scan (p=0.166), hyperlipidemia (p=0.149), and location of occlusion (p=0.176).
Results

- HT was reported in 79/619 (13%) patients.
- The percentage of patients with HT was 11% after IV alone, 17% after IA alone, 22% after treatment with IV+IA tPA, 27% after IA plus mechanical thrombectomy, and 20% for mechanical alone.
- HT occurred in 21% of those with locked in state, 16% of those in coma, and 27% of those with PVD.
## Tabulated Univariate

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>HT with Variable</th>
<th>HT without Variable</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT Early Ischemia</td>
<td>16% (26/164)</td>
<td>12% (53/455)</td>
<td>0.166</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Deficit</td>
<td></td>
<td></td>
<td>0.034</td>
</tr>
<tr>
<td>Recanalization</td>
<td></td>
<td></td>
<td>0.008</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>27% (8/30)</td>
<td>12% (71/589)</td>
<td>0.042</td>
</tr>
<tr>
<td>Alcohol</td>
<td>27% (6/22)</td>
<td>12% (73/597)</td>
<td>0.049</td>
</tr>
<tr>
<td>NIHSS</td>
<td>24 ± 9*</td>
<td>21 ± 11*</td>
<td>0.018*</td>
</tr>
</tbody>
</table>

* NIHSS are patients’ with HT vs No HT
## Treatment Modality

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombotic Therapy (AT)</td>
<td>2% (3/210)</td>
</tr>
<tr>
<td>IV TPA alone</td>
<td>11% (9/80)</td>
</tr>
<tr>
<td>Combined txt (IA + IV TPA)</td>
<td>22% (9/41)</td>
</tr>
<tr>
<td>IA TPA alone</td>
<td>17% (31/179)</td>
</tr>
<tr>
<td>Combined txt (IA + Mech)</td>
<td>27% (21/79)</td>
</tr>
<tr>
<td>Mechanical Thrombectomy</td>
<td>20% (6/30)</td>
</tr>
</tbody>
</table>

P < 0.001
## Treatment Modality

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HT</th>
<th>P Value (compared to AT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombotic Therapy (AT)</td>
<td>2% (3/210)</td>
<td>N/A</td>
</tr>
<tr>
<td>TPA alone (IV or IA)</td>
<td>15% (40/259)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Combined treatment (IA + IV TPA) or (IA + Mech) or Mechanical Thrombectomy</td>
<td>24% (36/150)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P = 0.032 comparing TPA alone vs Combined Treatments

* P values not adjusted for multiple comparisons*
### Deficit at Presentation

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA or Minor Stroke</td>
<td>8% (20/246)</td>
</tr>
<tr>
<td>Tetraplegia</td>
<td>11% (6/57)</td>
</tr>
<tr>
<td>Locked in</td>
<td>21% (9/44)</td>
</tr>
<tr>
<td>Coma</td>
<td>16% (44/272)</td>
</tr>
</tbody>
</table>

\[ P = 0.034 \]
## Recanalization

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patent</td>
<td>18% (52/294)</td>
</tr>
<tr>
<td>Severe Stenosis</td>
<td>11% (2/18)</td>
</tr>
<tr>
<td>Occluded</td>
<td>9% (14/164)</td>
</tr>
<tr>
<td>No Imaging (unknown)</td>
<td>8% (11/138)</td>
</tr>
</tbody>
</table>

\[ P=0.008 \]
Results

*Multivariate logistic regression analysis* showed that the following variables were independent predictors: *CT_early ischemic changes* (P=0.009), *treatment modality* (p<0.001), *stroke severity* (deficit at presentation) (p=0.092) and *peripheral vascular disease* (p=0.034).
Multivariate Analysis Odds Ratios

- **Treatment modality**
  - TPA alone vs AT: 15.8 (4.7-53.3) P<0.001
  - Combined vs AT: 29.2 (8.5-100.9) P<0.001
  - TPA alone vs Combined: 0.54 (0.3-0.9) P=0.03 / (1.85)

- **Stroke Severity (Deficit)**
  - Minor stroke vs Coma: 0.59 (0.3-1.1) P=0.09 / (1.7)
  - Locked in vs Coma: 2.43 (0.97-6.1) P=0.06

- **Peripheral Vascular Disease**: 3.3 (1.3-8.5) P=0.011

- **CT Early Ischemic change**: 2.3 (1.3-4.1) P=0.004

- Interactions were not significant.
Discussion / Limitations

- Retrospective, observational registry, no randomization
- Investigator reported symptomatic bleeds without central review
  - Risk for overcalling hemorrhagic transformation in patients who have received intra-arterial contrast agents.
- We did not look at risk factors for HT in individual treatment modalities.
  - ie HT risk factors for IA treated patients only
Conclusion

- Stroke severity, aggressive treatment (combined use of IV + IA tPa, IA tPa + mechanical thrombectomy, or mechanical thrombectomy), CT early ischemic changes, and history of peripheral vascular disease are associated with HT of ischemic stroke caused by basilar artery occlusion.

- We highly recommend participation in BASICS 2 to randomize patients to IV vs IA treatment as the registry did not reveal a difference in outcome (and more HT in the more aggressively treated patients).
Acknowledgements

- Participating Centers of the BASICS Study
- Dr Schonewille for organizing this massive effort & study.
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