Background

- Vascular Cognitive Impairment (VCI) is defined as cognitive impairment attributable to vascular risk factors and vascular pathologies.¹
- Diagnosis of VCI: (i) history of stroke or evidence of vascular disease on neuroimaging (2) neuropsychological testing should demonstrate cognitive deficits.²
- In 2006 the National Institute of Neurologic Disorders and Stroke and the Canadian Stroke Network (NINDS-CSN) developed the Vascular Impairment Harmonization Standards (VCIHS), a neuropsychological assessment of cognition that evaluates language, memory, visuospatial, and executive functions.³
- English, French, Chinese, and Korean adaptations of the VCIHS have been developed and their utilities have been assessed.⁴
- However, validation of the VCIHS using extensive MRI guided brain volumetric analyses to assess the influences of vascular neuro-pathology on each facet of cognition have not been explored.

Methods

1. Study Participants
- 60 participants with acute ischemic stroke to:
  - (i) Achieve MRI guided validation of the Korean-VCIHS;
  - (ii) Determine neuropathologic substrates of VCI on MRI by investigating the associations between (i) brain atrophy, (ii) infarct volume, and (iii) degree of white matter hyperintensity (WMH) and the Korean-VCIHS.

2. Magnetic Resonance Imaging
- T1-weighted, T2-weighted, Diffusion Weighted Imaging (DWI), and FLAIR images were acquired on 1.5T Philips MRI scanner at Hallym University Hospital in South Korea within four days of stroke event.

3. Image Processing
- Acutely infarcted tissues (hyperintensity on DWI) and previous co-occurring infarcts (hypoedema on T1) were traced using ANALYZE 8.0 software.
- WMH on FLAIR images were assessed using a semi-automated fuzzy lesion extractor (FLEX) pipeline.
- T1-based brain tissue segmentation was achieved using a modified in-house Semi-Automatic Brain Region Extraction (SABRE) Pipeline ⁵ See Figure 1.

4. Neuropsychological Assessment
- 3 months after stroke, MMSE (Mini-Mental Status Exam) and the VCIHS were administered.
- The VCIHS was comprised of 10 tests across 4 Cognitive Domains:
  - Memory Function
    - i. Hopkins Verbal Learning Test (Immediate Recall, Delayed Recall and Recognition)
  - Executive Function
    - i. Trails Making Test-Part A and Part-B
    - ii. Controlled Oral Word Association Test (Phonemic)
    - iii. Digit Symbol Coding
  - Visuospatial Function
    - i. Ray Complex Figure Task Copy
  - Language Function
    - i. Boston Naming Test
    - ii. Controlled Oral Word Association Test (Animal)

Results

5. Statistical Analysis
- Using Microsoft SPSS 20.0 Software Multiple linear regression analyses with backwards elimination of non-significant variables were performed.
- Brain Parenchymal Fraction (BPF), stroke volume, WMH volume, and the ARWMC scale as predictors of (i) Executive Function (ii) Memory (iii) Visuospatial Function and (iv) Language Function
- Age, sex, education and stroke location were controlled for in all analyses.

Table 1: Demographic and Cognitive Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>74.5 ±7.2</td>
</tr>
<tr>
<td>Gender (Male/female)</td>
<td>35/25</td>
</tr>
<tr>
<td>T1WMH Volume (cc)</td>
<td>23.6 ±7.2</td>
</tr>
<tr>
<td>T2 Volume (cc)</td>
<td>27.2 ±7.2</td>
</tr>
<tr>
<td>T1WMH (mm)</td>
<td>4.2 ±1.2</td>
</tr>
<tr>
<td>VCIHS - Total Score</td>
<td>1.2 ±0.2</td>
</tr>
</tbody>
</table>

Table 2: Volumetric Data*

<table>
<thead>
<tr>
<th>Volume</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Matter Volume (cc)</td>
<td>23.6 ±7.2</td>
</tr>
<tr>
<td>T2 Volume (cc)</td>
<td>27.2 ±7.2</td>
</tr>
<tr>
<td>T1WMH Volume (cc)</td>
<td>23.6 ±7.2</td>
</tr>
<tr>
<td>T1WMH (mm)</td>
<td>4.2 ±1.2</td>
</tr>
</tbody>
</table>

Discussion and Conclusion

- Executive dysfunction was the most common feature in this cohort with VCI, suggesting that VCI oriented global cognitive measures should adequately assess executive function.
- The K-VCIHS Global Score (Average of 10 Tests) attains 40% of its score to executive function, while each cognitive domain in the K-VCIHS Global Score (Average of 4 Cognitive Domains), has a 25% contribution to the overall cognitive score.
- Executive function in the whole sample of stroke patients (model 1), was related to ischemic infarction volume. However, in patients with supratentorial strokes (model 2;Figure 2A), executive function was also related to global WMH volume.
- This study also has implications for calculating global cognitive scores from individual test scores, as different brain behavior relationships were noted depending on how the Global VCIHS Z-score was calculated:
  - While the K-VCIHS Global Score (Average of 4 Cognitive Domains), was associated with brain atrophy (model 8), the K-VCIHS Global Score (Average of 10 Tests) was associated with infarction volume (model 7).
- Overall, these results suggest that the Korean adaptation of the NINDS-CSN VCIHS-NP is reflective of the varying effects of brain atrophy, white matter hyper-intensities and stroke lesions on cognition.
- We also identify plausible neuroimaging substrates of VCI:
  - Brain Atrophy: Global cognition and visuospatial function
  - White Matter Hyperintensity: Executive function in those with supratentorial stroke
  - Infarction Volume: Global cognition, memory, executive function, visuospatial function

Acknowledgements

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References

5. Rabinstein AA, et al. Executive dysfunction is the most common feature in this cohort with VCI. 2019;504. PMCID: PMC5776059.
8. Vinters HV, et al. The NINDS-CSN VCIHS-NP is reflective of the varying effects of brain atrophy, white matter hyper-intensities and stroke lesions on cognition.
9. We also identify plausible neuroimaging substrates of VCI:
  - Brain Atrophy: Global cognition and visuospatial function
  - White Matter Hyperintensity: Executive function in those with supratentorial stroke
  - Infarction Volume: Global cognition, memory, executive function, visuospatial function

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