Vascular Cognitive Impairment and Dementia (VCID)

Fifth Annual Stanford ADRC / UDall Participant Appreciation Day
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Assistant Professor
I have no disclosures
Outline

• Epidemiology of vascular risk, prevalence of vascular brain injury
• Definition of vascular disease
• Overlap between vascular disease and Alzheimer`'s disease
• Impact on cognition
• Vascular imaging
Estimated numbers of dementia patients worldwide

Future risk of stroke or dementia at age 65

What is cerebrovascular disease?

- Any disorder of cerebral blood vessels
  - Arteriolarsclerosis
  - Atherosclerosis
  - Cerebral amyloid angiopathy
  - CADSIL
What is cerebrovascular injury

• Hemorrhage
  • Large (stroke)
  • Microbleeds (clinically silent)
• Infarction – ischemic
  • Large vessel (stroke)
  • Small vessel (clinically silent)
• White matter hyperintensities
• Dilated Perivascular spaces
What are the vascular risk factors?

- Hypertension
- Hyperlipidemia
- Diabetes Miletus
- Smoking
- Drug abuse
- Obesity
- Traumatic brain injury
- Inflammatory or infectious disorders
- Age
- Sex
- Race and ethnicity
- Family history and genetics
- Bleeding disorders/blood thinners
- Sleep apnea
- Pollution
Evolution of the concept of cognitive impairment on vascular bases

Iadecola, Neuron, 2013
Vascular Cognitive Impairment and Dementia (VCID)

- Vascular Dementia
  - Post-stroke dementia
  - Vascular dementia without recent stroke
- Mixed Alzheimer’s disease with a vascular component
- VCI that does not meet dementia criteria

A group of syndromes that represent a clinicoradiologic and pathological spectrum.
The Neurovascular Unit

- Dementia
- Stroke
- Cerebral hypoperfusion
- Heart failure
- Artery stiffening
- Atrial fibrillation
- Disrupted neuronal activity
- Neurovascular unit uncoupling
- BBB breakdown
- Pericyte injury
- Endothelial dysfunction
- Astrocyte
- Neuron
- Microglia
Heterogenous pathology of dementia

- Multiple interacting and co-occurring pathologies
  - Neurodegenerative
    - Amyloid and tau
    - Lewy Bodies
    - TDP-43
  - Vascular
    - White matter changes
    - Infarcts
    - Microhemorrhages

Kapasi, et al., 2017
Heterogenous pathology of dementia

- Multiple interacting and co-occurring pathologies
  - Neurodegenerative
    - Amyloid and tau
    - Lewy Bodies
    - TDP-43
  - Vascular
    - White matter changes
    - Infarcts
    - Microhemorrhages

Attributable Risk of Alzheimer’s Dementia Attributed to Age-Related Neuropathologies

Kapasi, et al., 2017
Heterogenous pathology of dementia

Schneider 2007
Heterogenous pathology of dementia

With dementia

Without dementia

Schneider 2007

Much of Late Life Cognitive Decline Is Not due to Common Neurodegenerative Pathologies

Patricia A. Boyle, PhD,1,2 Robert S. Wilson, PhD,1,2,3 Lei Yu, PhD,1,3 Alasdair M. Barr, PhD,4 William G. Honer, MD,5 Julie A. Schneider, MD,1,3,6 and David A. Bennett, MD1,3

ANN NEUROL 2013;74:478–489

FIGURE 3: Variation in cognitive decline explained by the pathologic indices (gray) and the residual, unexplained variation in cognitive decline (white) derived from fully adjusted models. AD = Alzheimer disease; CVD = cerebrovascular disease; LBD = Lewy body disease.
Vascular risk scores

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Age, y</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–46</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>47–53</td>
<td>3</td>
<td></td>
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<tr>
<td>54–55</td>
<td>4</td>
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<table>
<thead>
<tr>
<th>Step 2</th>
<th>Education, y</th>
<th>Points</th>
</tr>
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<tbody>
<tr>
<td>0–6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>7–9</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>&gt;9</td>
<td>0</td>
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<thead>
<tr>
<th>Step 3</th>
<th>Sex</th>
<th>Points</th>
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<tbody>
<tr>
<td></td>
<td>Men</td>
<td>1</td>
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<tr>
<td></td>
<td>Female</td>
<td>0</td>
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<table>
<thead>
<tr>
<th>Step 4</th>
<th>Cholesterol, mg/dL</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;251</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>≥251</td>
<td>2</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 5</th>
<th>BMI, kg/m²</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0</td>
<td></td>
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<tr>
<td>≥30</td>
<td>2</td>
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<tr>
<th>Step 6</th>
<th>Systolic blood Pressure, mmHg</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;140</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>&gt;140</td>
<td>2</td>
<td></td>
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</tbody>
</table>

Add up points from steps 1 through 6, then look up predicted 40-years risk of dementia.

Exalto et al 2014
Vascular risk scores

Step 1
Age, y Points
40–46 0
47–53 3
54–55 4

Step 2
Education, y Points
0–6 3
7–9 2
>9 0

Step 4
Cholesterol, Points mg/dL
<251 0
≥251 2

Step 5
BMI, Points kg/m²
<30 0
≥30 2

Step 6
Systolic blood Pressure, mmHg Points
<140 0
≥140 2

Add up points from steps 1 through 6, then look up predicted 40-year risk of dementia.

Exalto et al 2014
White matter hyperintensities
White matter hyperintensity

Provenzano 2013
White matter hyperintensity

Provenzano 2013
Clinical Trials

SPRINT-MIND

![Graph showing cumulative incidence over follow-up years for two treatment groups: Standard treatment and Intensive treatment. The graph indicates the number at risk at different phases: Trial phase, Trial and cohort phase, and Cohort phase. The table below the graph lists the number at risk for each phase and group.]

<table>
<thead>
<tr>
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<th>Follow-up, y</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
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<tr>
<td><strong>No. at risk</strong></td>
<td></td>
</tr>
<tr>
<td>Standard treatment</td>
<td>4285</td>
</tr>
<tr>
<td>Intensive treatment</td>
<td>4278</td>
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</table>
Clinical Trials

SPRINT-MIND

FINGER
The glymphatic system

Jessen et al, Neurochem Res 2015
The glymphatic system

Jessen et al, Neurochem Res 2015
Expanded perivascular spaces (EPVS)
EPVS in Early and Late Age-of-onset AD

In prep
Function and cognition in AD and CO
Treatment of vascular cognitive impairment and dementia

- Antihypertensive therapy
- Diabetes management
- Statins
- Antithrombotic therapy
- Cholinesterase inhibitors
- Memantine
- Nonpharmacologic therapy
Cardiovascular Disease Deaths: 1950 to 2010

Nabel and Braunwald, NEJM 2012