Vascular Dementia or Dementia with Cerebro-Vascular Disease: Changes in Concepts

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Current concepts on dementia

Excessive emphasis on memory disturbances:

- Based on the cortico-hippocampic type (AD)
- Not applicable to the sub-cortical and fronto-temporal types, more frequent in VaD

The DSM-IV definition is loose:

- 1) memory loss + 2) cognitive impairment x and y (+ z…)
  = dementia if (and only if) there is 3) a functional loss
- Executive dysfunction is often prominent in VaD:
  alternative to memory loss as first criterion? It drives the early functional loss…

WHO ICD-10: Dementia is not only a dysmnesia
VaD is an etiological category of dementia in ICD-10
- Includes dementia resulting from cerebral ischemia or hemorrhage (post-stroke dementia)
- Much rarer: dementia from global hypoperfusion (post-CABG or post-CHF)
- BUT: the definition of dementia needs to be clarified: phenocopy of AD or broader definition?
Diagnosis of VaD: NINDS-AIREN criteria

Dementia
- Impaired memory (?)
- ≥2 other cognitive domains impaired

+Cerebrovascular disease
- History of CVD (3-month)
- Neurological examination
  - Neuroimaging

Probable/Possible diagnosis
- Temporal relationship between CVD and dementia
  - Abrupt onset/stepwise progression
  - Absence of disorders that could account for deficits (eg, AD)

Diagnosis of VaD

Román GC et al. Neurology. 1993;43:250-60
**Alternative Definitions**

**Vascular cognitive disorder (VCD):** a diagnostic category that includes any degree of cognitive impairment resulting from cerebrovascular disease [CVD]. Includes:

**Vascular cognitive impairment (VCI):** isolated cognitive dysfunction, not qualifying as dementia, and

**Vascular Dementia (VaD):** cognitive impairment causing dementia, both resulting from ischemic or hemorrhagic CVD (post-stroke dementia); or from hypoperfusion (hypotension, post coronary artery bypass graft [CABG] or post congestive heart failure [CHF])

*Roman et al, J Neurol Sci, 2004*
Executive Control Functions

“Command and control” of complex goal-directed action
Examples include initiation, sequencing and monitoring of complex behavior
Executive dysfunction is expressed as disorganized thought, behavior, or emotions
ECF was added to the DSM-IV definition of dementia in 1994

Executive dysfunction in vascular dementia

Is a characteristic feature of VaD\(^1\) although not mandatory in current criteria

Includes difficulties in planning, organization, problem-solving, conceptualization, mental flexibility

Leads to difficulties in performing instrumental activities of daily living (IADL)\(^2\) Such as managing finances, phoning, transportation, medication, engaging in hobbies\(^3\)

\(^1\)Román GC, Royall DR. Alzheimer Dis Assoc Disord. 1999;13:S69-80
\(^3\)Dartigues et al, PAQUID Study, 1994
## Key differentiating factors

<table>
<thead>
<tr>
<th>Alzheimer’s disease</th>
<th>Vascular dementia</th>
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<tbody>
<tr>
<td>Insidious onset</td>
<td>Sudden onset</td>
</tr>
<tr>
<td>Progressively</td>
<td>Fluctuating, stepwise</td>
</tr>
<tr>
<td>deteriorating course</td>
<td>course with plateaus</td>
</tr>
<tr>
<td>No early focal</td>
<td>Early focal neurological</td>
</tr>
<tr>
<td>neurological signs</td>
<td>symptoms &amp; signs</td>
</tr>
<tr>
<td>No vascular damage</td>
<td>Evidence of relevant vascular</td>
</tr>
<tr>
<td>on brain imaging</td>
<td>brain damage</td>
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</tbody>
</table>

### Epidemiology: Prevalence of AD + CVD in the elderly

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Population (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester^1</td>
<td>1987</td>
<td>9</td>
</tr>
<tr>
<td>Appiganano^2</td>
<td>1990</td>
<td>13</td>
</tr>
<tr>
<td>Gothenburg^3</td>
<td>1993</td>
<td>8.2</td>
</tr>
<tr>
<td>Canadian IVIC^4</td>
<td>2000</td>
<td>7.5</td>
</tr>
<tr>
<td>Canadian SHA1 (VCI/AD)^5</td>
<td>2000</td>
<td>8</td>
</tr>
<tr>
<td>Campo Grande^6</td>
<td>2002</td>
<td>37</td>
</tr>
<tr>
<td>Cardiovascular Health Study^7</td>
<td>2003</td>
<td>16</td>
</tr>
</tbody>
</table>

**Overall: 10–20%**

Worldwide, stroke has affected ≈31 million people\(^1\)

25% to 41% may develop VaD\(^2\)

≈8 to 13 million people with VaD caused by stroke

Poststroke Dementia Prevalence

Helsinki: 6% to 25.5%
New York City: 27% to 41%
USA: 1 million cases
Europe: 800,000 VaD cases
Global prevalence of VaD in Europe:
  16/1000 after age 65
  52/1000 after age 90

EURODEM. Neurology. 2000; 54 (suppl 5).
Poststroke Dementia Incidence

United States: 150,000 new cases/y
1/3 of the 360,000 incident cases of AD

Europe: 134,000 new cases/y

Incident stroke cases: → 536,000/y

EURODEM. Neurology. 2000; 54 (suppl 5).
VaD Is More Than MID…

Strategic single strokes: thalamic dementia, inferior genu lacune, caudate stroke

White matter incomplete ischemia: Binswanger’s disease, CADASIL*

Subcortical Ischemic Vascular Dementia: small-vessel disease with multiple lacunar strokes

CADASIL = cerebral autosomal dominant arteriopathy + subcortical infarcts & leukoencephalopathy.
1) Large-Vessel Disease

=> Large ischaemic areas

Discrete infarcts in strategic locations

- Frontal lobe
- Hippocampus, basal forebrain
- Gyrus angularis
- Parietal-occipital lobes

- Aphasia, apraxia, disinhibition, apathy
- Amnesia
- Constructional problems
- Alexia, agraphia, apraxia

Cortical type of dementia - MID
Large vessel infarctions

Cortical VaD

Left cortico-subcortical occipito-temporal infarct

Soubcortical VaD

Left thalamic infarct
Disruption of Cortico-Subcortical Circuits

- Small-vessel disease
- Subcortical infarcts in strategic locations: thalamus, caudate nucleus, internal capsule
- Disruption of specific fronto-subcortical circuits or nonspecific thalamocortical projections
  - Executive dysfunction
  - Apathy
  - Attentional deficit
  - Personality change

Subcortical type of dementia
Subcortical ischemic VaD
Thalamic VaD

Bilateral medial thalamic ischemic strokes
(L) anterior thalamus - polar thalamic from PCoA
Medial and central thalamus: CM nucleus - mamillothalamic tract - paramedian thalamic artery from basilar-PCA occlusion

The critical lesion in thalamic amnesia is damage of the mamillothalamic tract, which projects into the anterior nuclei of the thalamus, and then to the cingulate cortex.

PCoA = posterior communicating artery. PCA = posterior cerebral artery.
Thalamic VaD Imaging

CT

MRI
Binswanger’s Disease
(Illustrated in Kraepelin’s *Psychiatrie* 1910)

Figur 127. Subkortikale Encephalitis.
B=Balken; H=Herdartige Markatrophie.
Sub-cortical VaD at MRI

- White matter lesions predominance
- Lacunar infarct predominance
Lacunes Are *Not* Benign Lesions

Silent lacunes, particularly in the thalamus, more than double the risk of dementia [HR=2.26; 95% CI, 1.09-4.70]

5-year mortality in patients with lacunes reaches 27.4%

One or more silent lacunes occurred in about one fourth of 3660 participants in the Cardiovascular Health Study (CHS), age ≥65

Extensive Metabolic and Neuropsychological Abnormalities Associated With Discrete Infarction of the Genu of the Internal Capsule

On 18FDG positron emission tomography (PET) images of the brain, decreased metabolic activity is apparent in the left temporal lobe (long arrows), occipito-temporal lobe (long arrows), and right cerebellar hemisphere (short arrow) 2 weeks after stroke.

Comorbid AD + CVD is frequent in autopsy series in the old-old
Vascular risk factors increase AD risk (?)
Pure AD, without CVD, occurs in only 20% of postmortem studies in patients with dementia
There is a significant inverse relationship between severity of CVD and Braak & Braak’s stages of AD => interaction?
CVD may exteriorise preclinical AD to “Alzheimer’s dementia”
Many patients with “AD” actually have low Braak’s lesions + CVD
Many cases diagnosed as “AD” are in fact cases of VaD
Treatment of vascular risk factors may therefore prevent dementia onset and progression

AD : Alzheimer’s disease; CVD : cerebrovascular disease; VaD : vascular dementia.
Probability of Clinically Diagnosed Dementia as a Function of AD Pathology

**Summary Measure of AD Pathology**

- **Probability of Dementia**
  - 1.0
  - 0.5
  - 0.0

**Probability of Dementia**

- **With Cerebral Infarction**
- **Without Cerebral Infarction**

*Schneider et. al., Neurology. 2003;60:1082-1088*
AD vs VaD: difference in course

Prospective results from clinical trials
Placebo group progressions in VaD and AD: ADAS-cog in donepezil trials

Historical comparisons from pivotal studies

Management of VaD

- Identify patients at risk of dementia due to CVD
  - Control vascular risk factors and disease
    - Stabilization of CVD
  - Control of concomitant conditions
    - Improvement in patients’ outcomes and caregiver QoL
  - Targeted dementia therapy
    - Improvement in dementia symptoms

Sachdev et al. 1999; Nyhenuis and Gorelick, 1998
Primary Prevention of VaD

Target

Brain at risk of CVD

Action (treatment of risk factors)

Arterial hypertension
Cardiac abnormality
Lipid abnormality: DIET, statins
Diabetes mellitus
Homocysteine

Secondary Prevention of VaD

Target
  CVD brain at risk of VCI/VaD

Action
  Treatment of acute stroke (tPa)
  Prevention of stroke recurrence
  Slow progression of VaD related changes
  Treatment of vascular risk factors
  Neuroprotection?

VCI = vascular cognitive impairment.

Diagnostic criteria for Dementia

A1 : Memory impairment

Impaired ability to learn new information or to recall previously learned information (1)

(1) From DSM IV-TR
Diagnostic criteria for Dementia

A2 : Disturbance in executive functioning

Planning, organizing, sequencing, abstracting (1)

(1) From DSM IV-TR
A3: One (or more) cognitive disturbances:

(a) Impairment in abstract thinking, as indicated by inability to find similarities and differences between related words, difficulty in defining words and concept, and other similar tasks (2)

(b) Impaired judgment, as indicated by inability to make reasonable plans to deal with interpersonal, family, and job-related problems and issues (2)

(c) Aphasia (language disturbance) (1)

(1) From DSM IV-TR  (2) From DSM III-R
Diagnostic criteria for Dementia

A3 : One (or more) cognitive disturbances:

(d) Apraxia (impaired ability to carry out motor activities despite intact motor function) (1)

(e) Agnosia (failure to recognize or identify objects despite intact sensory function) (1 & 2)

(f) Constructional difficulty (e.g., inability to copy three-dimensional figures, assemble blocks, or arrange sticks in specific designs) (2)

(1) From DSM IV-TR   (2) From DSM III-R
Dementia with new relevant Cerebro-vascular lesion(s) - Definition

Dementia

Occurring within 3 months after a recurrent stroke

and/or

With at least 1 out of 3 types of new lesions on brain imaging:

- Strategic stroke > 1.5 cm diameter
- More than 2 supratentorial lacunes
- More than 25% ischaemic white matter changes
Conclusion

VaD and vascular cognitive impairment may become the most common cause of cognitive loss and behavioral changes in the elderly, particularly in the older-old, causing a major public health problem.