Vascular Dementia

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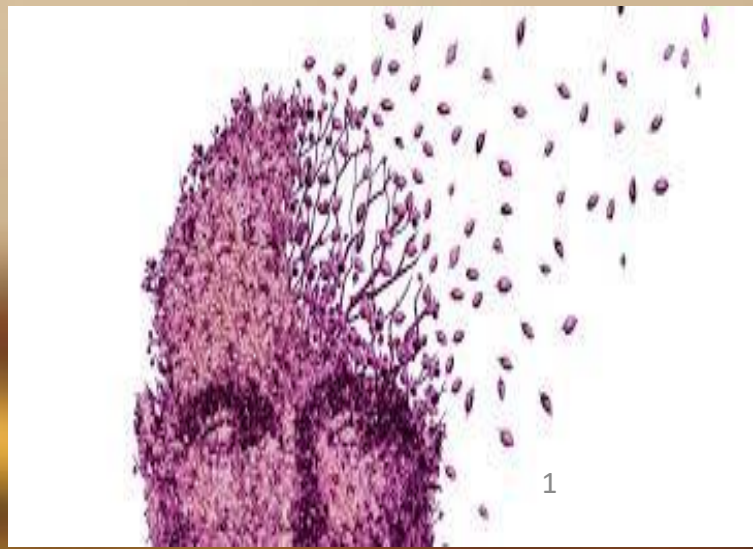

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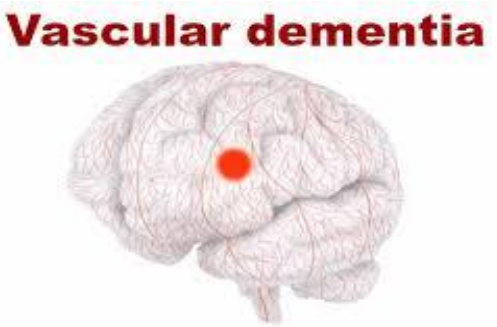
Vascular cognitive impairment (VCI)

- Is a term which emphasizes the vascular contribution to any degree of cognitive function, from subtle or mild deficits to prodromal and fully developed dementia (van der Flier et al., 2018).

- Cerebrovascular diseases in the large (e.g., stroke) and small vessels are the primary cause of VCI (Kalaria, 2016).

- **The most serious form of VCI is called vascular dementia**.

Vascular Dementia (VaD)



- is the second most common cause of dementia,
  after Alzheimer's disease (AD) .

- is a chronic progressive disease of the brain & a common post-stroke problem which **affects cognitive function or thinking abilities**.

- **Executive functions** of brain (Planning)→ more predominantly affected than **memory**

- Motor and mood changes→ often seen early

Vascular Dementia (VaD) Cont'

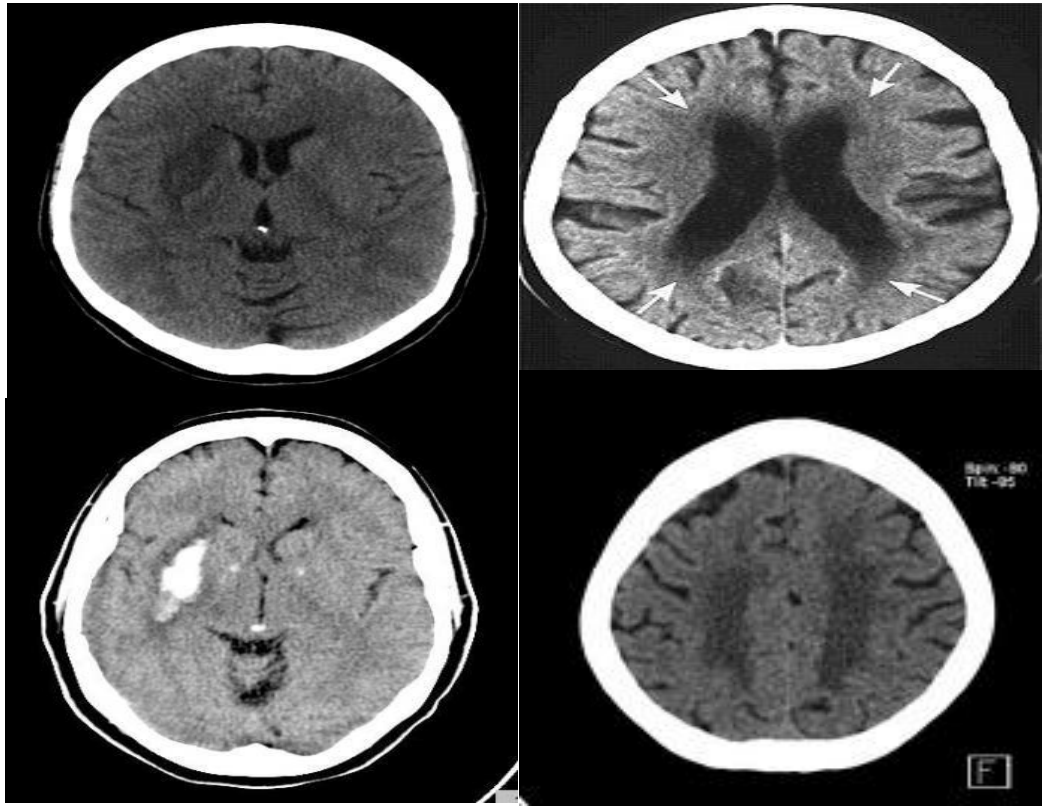
- Depending on the location and size of damaged brain area, onset of dementia following a stroke differs from person to person

- ❑ problems with episodic memory→ infarct in the hippocampus

- ❑ slow thinking and problems with executive function → infarct in the frontal lobe

- **Damage to both white and grey matter due to vascular cause**

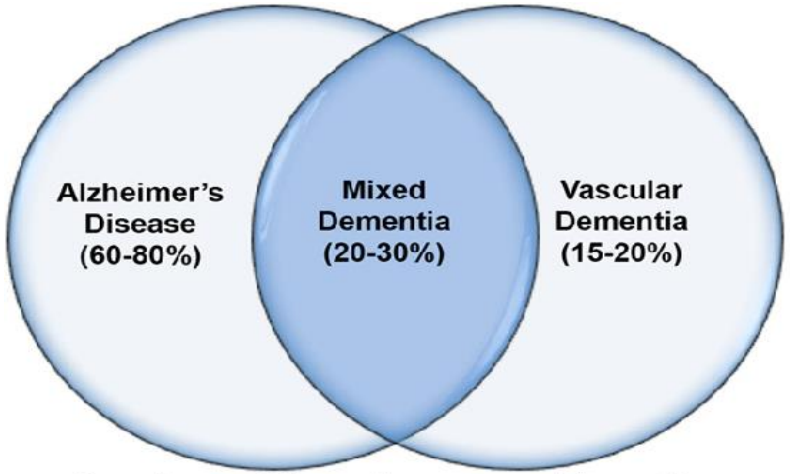
1. Infarction
2. Leukoaraiosis
3. Hemorrhage
4. Small vessel changes



Prevalence of Vascular dementia

- In some **Asian** countries, VaD appears to be more prevalent than AD.

- **For every 100 people with dementia, 20 of those will have vascular dementia** (**20% of the cases**)

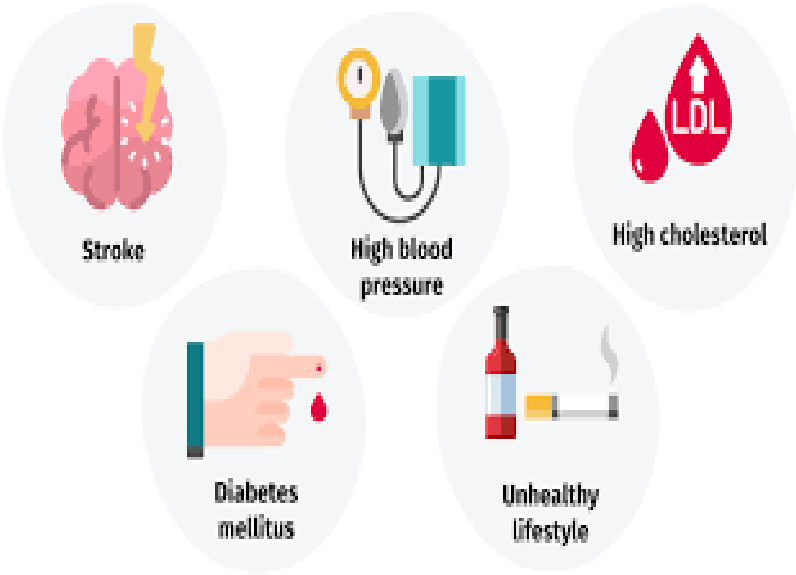


Prevalence of the major causes of dementia

(Dichgans and Leys, 2017)

Etiology of VaD

- Stroke
- Hypertension /Hypotension
- Hyperlipidaemia (in some studies)
- Diabetes (& ‘metabolic syndrome’)
- Smoking (and probably other risk factors)
- Genetic causes (rare)
- But **age** is strongest ‘risk factor’



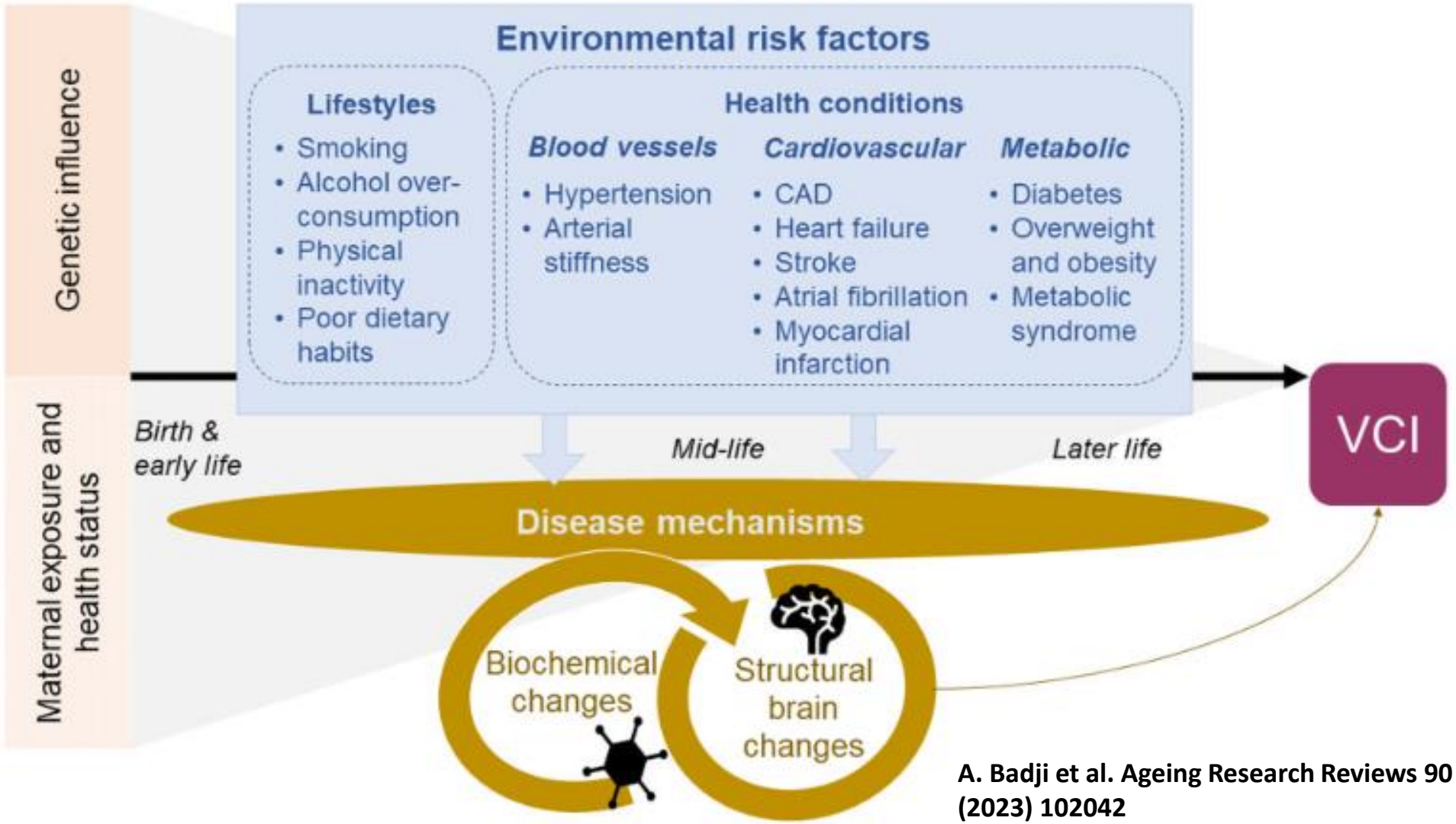
Types of VaD

- Sub-cortical ischemic VaD (**Binswanger's disease**)
- Post Stroke dementia
- Multi-infarcts dementia
- Mixed dementia

Differential Diagnosis of VaD

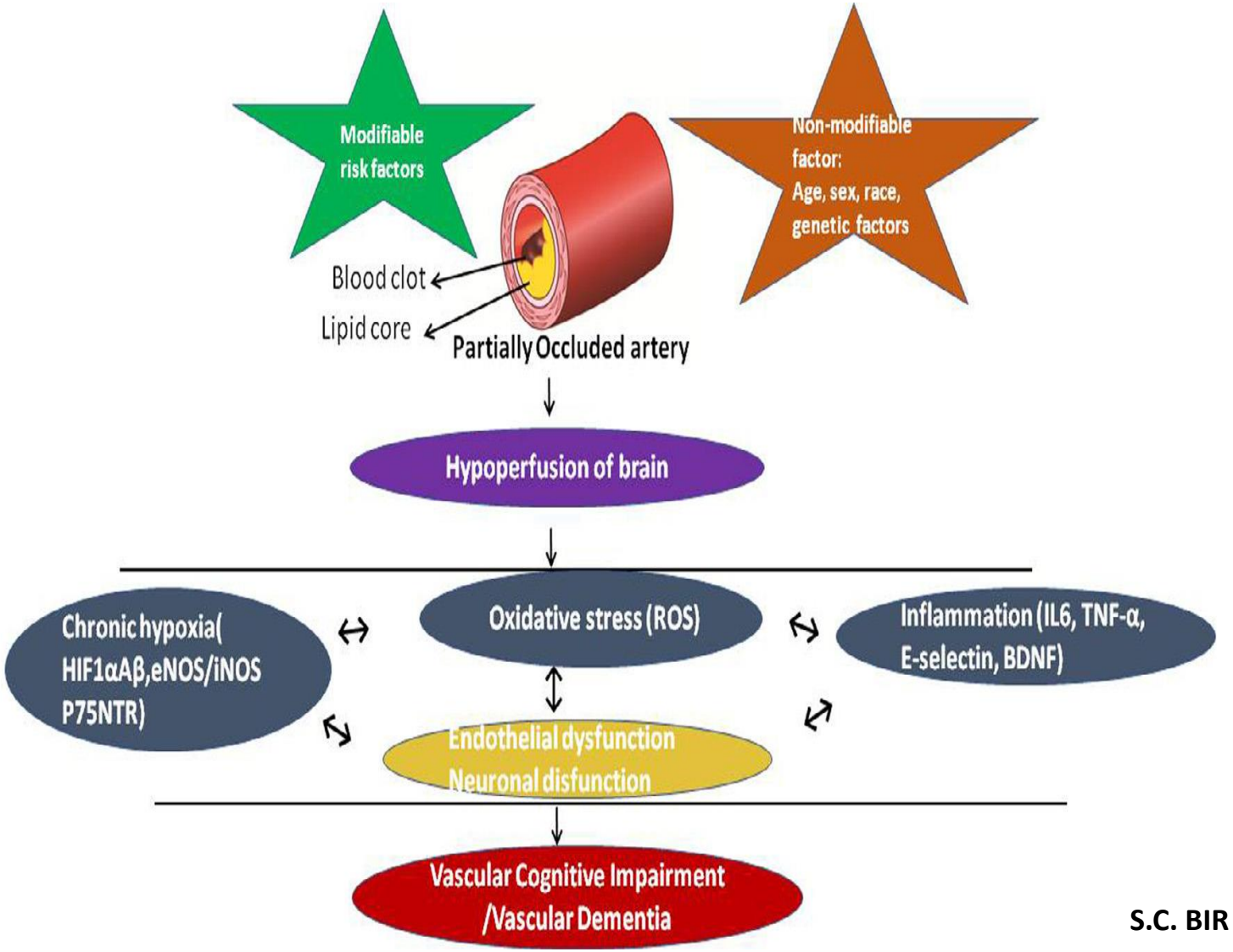
- Alzheimer Disease
- Mixed dementia
- Normal pressure Hydrocephalus
- Excessive alcohol consumption
- Bipolar and other mood disorders
- Metabolic derangement(B12 and homocystine)

Disease Mechanism of VCI



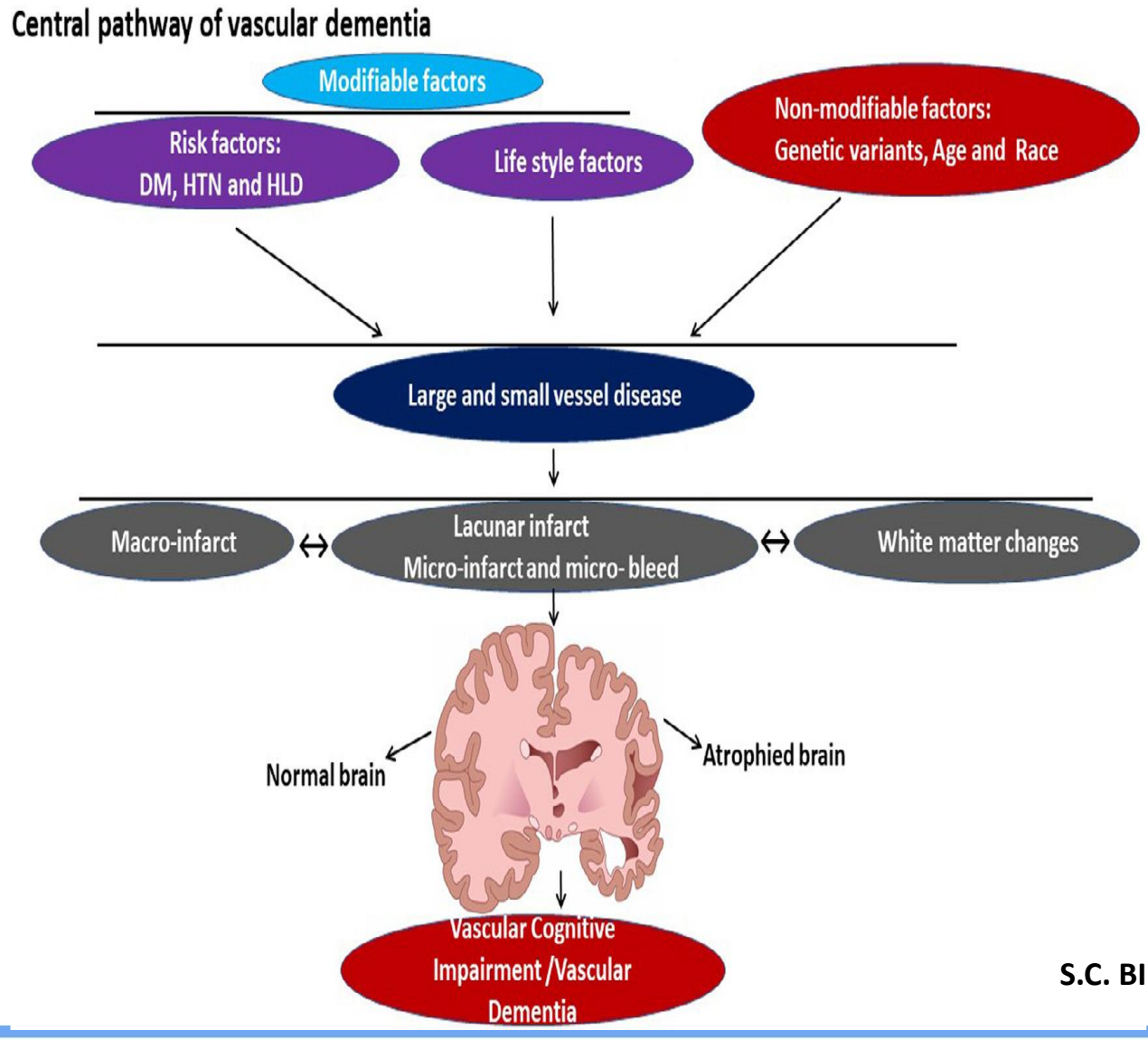
A. Badji et al. Ageing Research Reviews 90 (2023) 102042

Potential cellular and molecular mechanism of VaD



S.C. BIR ET AL., 2021

Pathophysiology of vascular dementia



S.C. BIR ET AL., 2021

Pathophysiology of VaD

- **Atherosclerosis** of large feeding arteries, often associated with **smoking and hyperlipidemia**, → territorial infarcts via cerebrovascular arterial occusion or thromboembolism, resulting in the classic "step-wise" cognitive and functional decline of VaD .

- **Arteriolosclerosis**, mainly linked to **hypertension**→ occlusive disease of small arteries that feed deep, penetrating structures, → lacunar infarcts, central hemorrhage, and cerebral microbleeds.

- **Microvascular disease**, most closely associated with **diabetes**, commonly disrupts metabolic function at the capillary level.

Pathophysiology of VaD Con't

- **Finally, the *APOE* ε4** genotype and **cerebral amyloid angiopathy** in which amyloid-β accumulates primarily in pial and cortical arteries and capillaries →

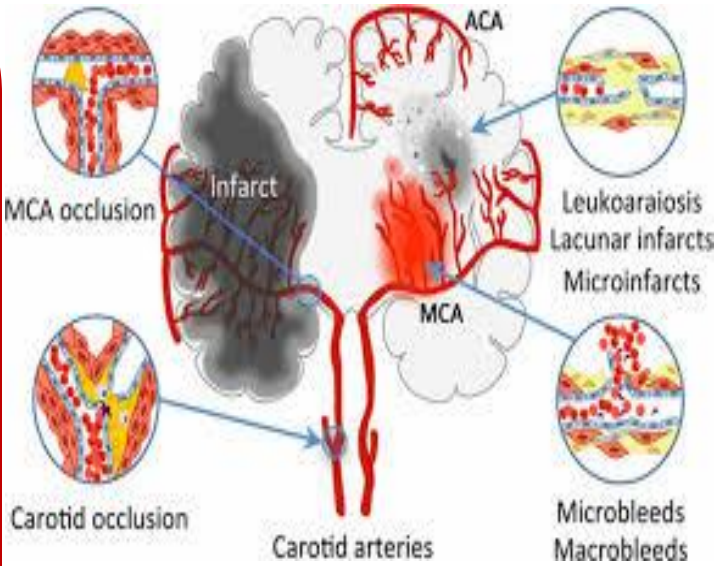
  - lobar hemorrhage
  - cortical microinfarcts, and
  - white matter hyperintensities → also risk factors for vascular cognitive impairment and dementia.

- **Mixed vascular disease** is more likely to cause cognitive and functional decline than pure atherosclerosis or arteriolosclerosis.

Amy E. Sanders; Caroline Schoo; Virginia B. Kalish. October 22, 2023

Forms of pathology that may contribute to vascular dementia

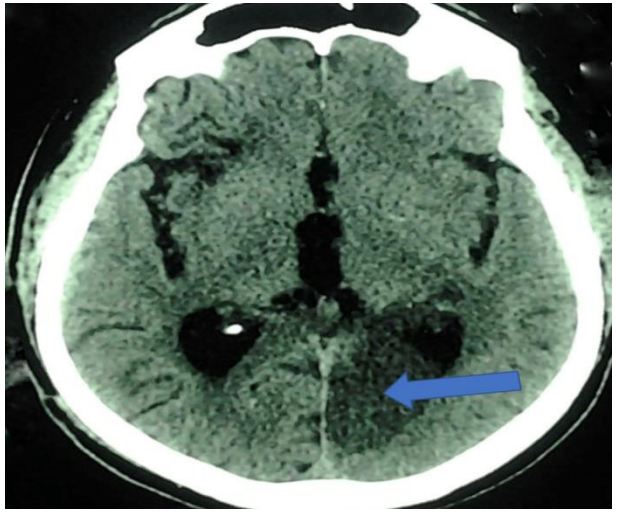
- Large-vessel disease/ Major stroke
- Lacunar stroke
- Microinfarcts
- Diffuse subcortical small vessel disease
- Cerebral amyloid angiopathy
- Mixed or multiple forms of vascular pathology



Dementia due to large vessel disease

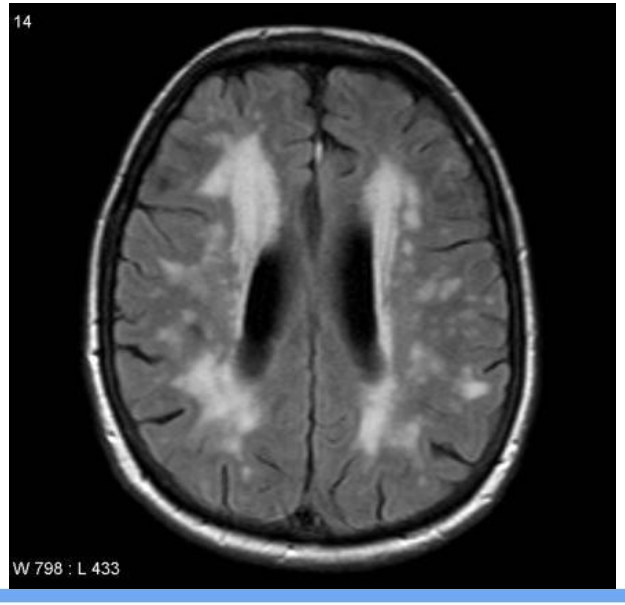
1. **Single strategic infarct dementia**

   - in main artery territories, or in the watershed zones between the main arterial territories



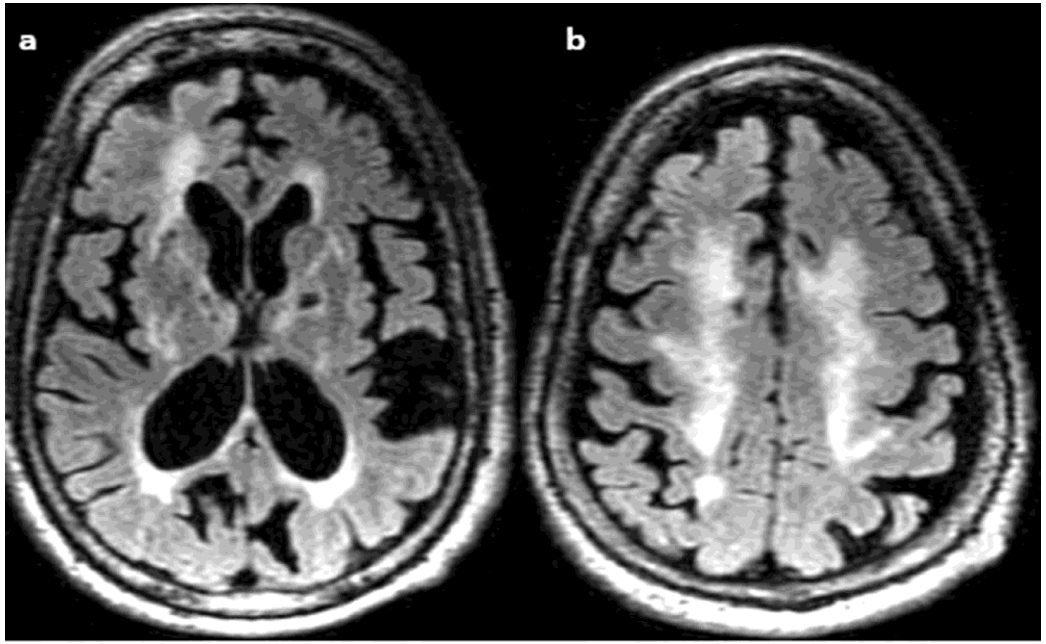
2. Micro-infarcts (seen by CT or MRI)

   - most are probably due to embolic occlusion of small arteries by microemboli.



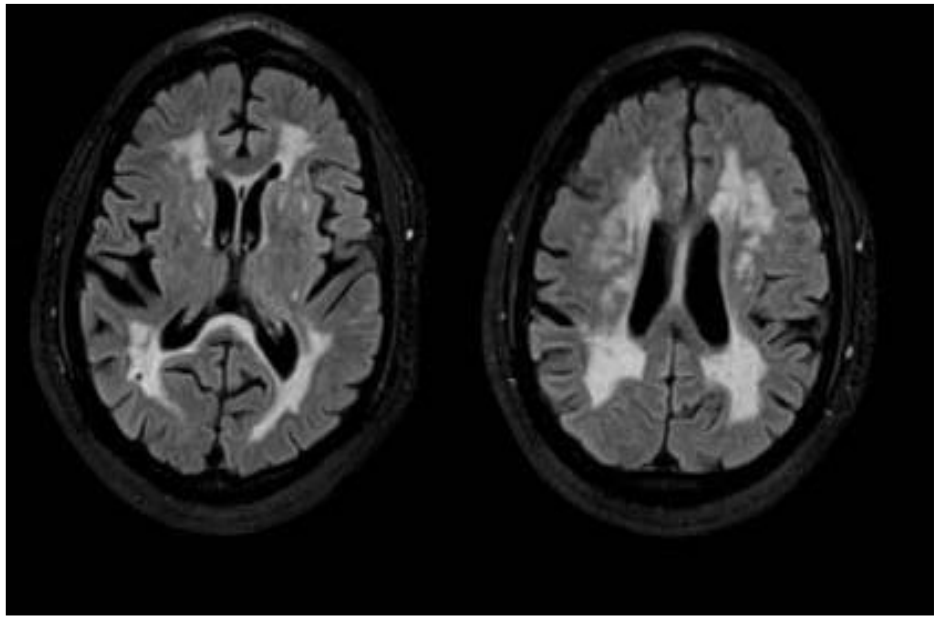
Lacunar stroke

- small, round or oval subcortical infarcts from 3 to 20mm in size
- may be clinically silent/ TIA or stroke
- Lacunar infarcts in thalamus can cause prominent cognitive problems
- often multiple and bilateral
- associated with disease affecting the small arteries and arterioles subserving deep grey and white matter



Small Vessel Diseases

- Small vessel disease (SVD) of the brain accounts for ~25% to 30% of strokes
- damage to the small subcortical vessels → supply deep grey matter and white matter
- The vessels affected →small arteries and arterioles that branch from proximal parts of the major cerebral arteries to supply the basal ganglia and thalamus, and penetrating arterioles



Symptoms associated with SVD

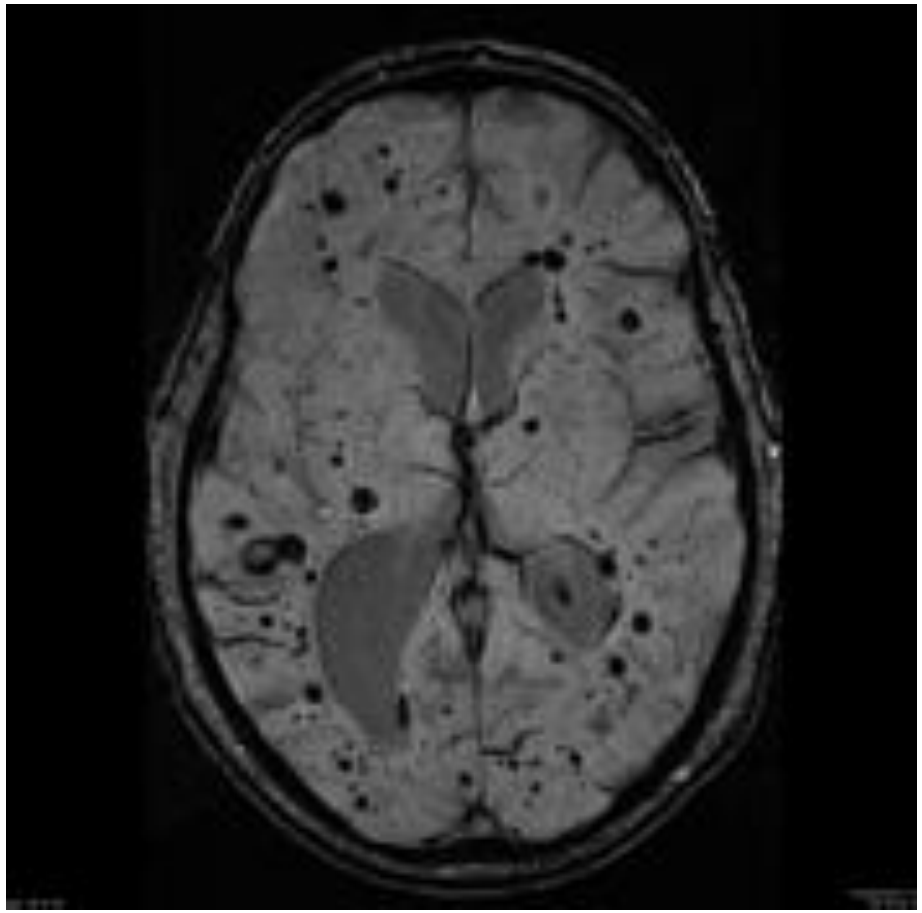
	Initial stage	Intermediate stage	Terminal stage
Cognitive performance	Mild deficits (eg, in executive functions, attention, set-shifting abilities) appreciable only with appropriate cognitive tests	Clinically obvious cognitive deterioration not reaching the severity of dementia (corresponds to vascular subcortical mild cognitive impairment)	Dementia with associated memory deficits (ie, subcortical vascular dementia)
Mood	Depressive symptoms	Depression	Not assessable
Sphincteric functions	From normal to urgency	Urinary incontinence episodes	Complete urinary incontinence, sometimes also faecal incontinence
Gait	From normal to mild slowing, subjective postural instability	Apraxic gait*	Bedridden
Pseudo-bulbar signs	Absent (primitive reflexes† on neurological examination can be present)	Dysphagia, dysarthria, pathological laughing, and crying	Severe dysphagia (PEG might be required), unintelligible speech
Daily living functions	Independence, small difficulties in some IADL might be present	Functional impairment; notable alterations in IADL and some alterations in BADL	Complete loss of autonomy

PEG=percutaneous endoscopic gastrostomy. IADL=instrumental activities of daily living. BADL=basic activity of daily living. *Notably slowed, short-stepped, wide-based, shuffling gait (lower body parkinsonism clinical picture). †Sucking reflex, palmar grasp reflex, palmomental reflex, snout reflex, glabellar reflex, or "tap".

Lancet Neurol 2010; 9: 689-701

Cerebral amyloid angiopathy

- Principally affects the leptomeningeal and cortical vessels
- A key feature of cerebral amyloid angiopathy is **microbleeds**
- A high number of CMBs are associated with an increased risk of cognitive deficit including dementia



Clinical characteristics

- Greater variability in presentation due to the pathophysiological heterogeneity of VaD

- Cognitive impairment is dependent upon the location of vascular lesions

- **Depression and apathy** are not un**common** in VaD while hallucinations and delusions are less prominent.

Clinical characteristics Con’t

- Common presentation is executive dysfunction featured as predominant deficits in

❑ attention

❑information processing

❑difficulties in complex activities

❑disorganized thought and

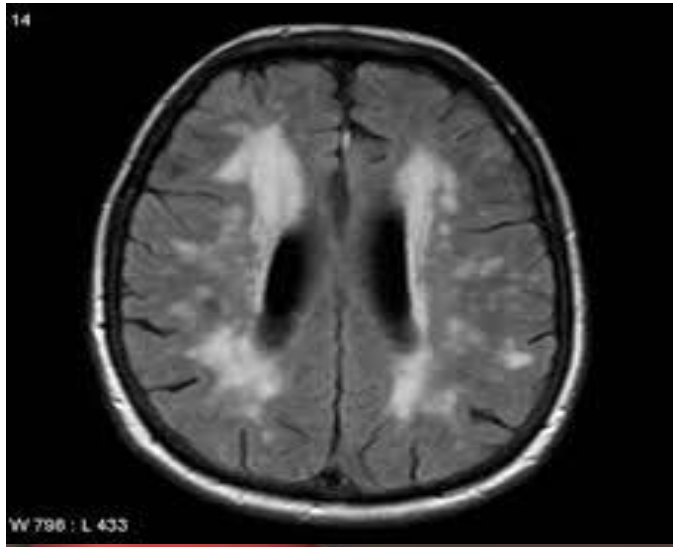
❑ behavior.

Clinical features consistent with Vascular Dementia

- Early gait disturbances, frequent falls
- Parkinsonian features
- Early urinary symptoms
- Personality change, mood disorders (vascular depression), psychomotor retardation
- Predominant abnormal executive function (Affects subcortical & frontal lobes)
- Memory and language deficits less obvious & occur late
- Behavioural & Psychiatric symptoms

Clinical Characteristics of Vascular Dementia

	Vascular dementia
Age of onset	>65
First changes	Variable, focal neurologic symptoms
Progression	Abrupt or gradual, stepwise
Motor symptoms	Focal weakness
Imaging	Strokes, lacunar infarcts
Pathology	Arterioles with thickened vessel wall



Single strategic infarct

Anatomy Location	Dysfunction
ACA (Inferomedial frontal infarct)	Abulia, memory impairment, language impairment
Lt MCA infarct (Dominant parieto-temporal, temporo-occipital association, angular gyrus)	Aphasia with cognitive impairment
Rt MCA (Non- Dominant pareito-temporal , temporo-occipital association)	Visuo-spatial functions
PCA (Bilateral inferomedial temporal or thalamic infarct)	Amnesia
Lacunar infarcts (Bilateral thalamic)	Amnesia

Clinical assessment

History

- Relation to stroke, transient ischemic attack, myocardial infarction, AF

- vascular risk factors present- diabetes, hypertension, hyperlipidaemia
  - duration
  - severity
  - response to current pharmacologic treatment
  - lifestyle changes
- previous cardiac surgeries or interventions for peripheral vascular disease.

Clinical assessment

- Time and mode of onset of **cognitive impairment**

- **patterns** of cognitive difficulty

  - VaD→ dysexecutive patterns or problems with attention

  - AD→ memory & word-finding difficulty usually predominate

- **Progression pattern** → slow progression suggestive of subcortical vascular disease or possible AD / mixed pathology

- **a pattern of step-wise progression** → suggestive of possible underlying lacunar or territorial infarction

Clinical assessment Con't

- Temporal association between cognitive/functional change and any ischemic/hemorrhagic insult
- **Mood** → symptoms of anxiety or depression.
- depression at **midlife** can act as a **risk factor for later-life dementia**
- **later-life depression** can be seen as a **dementia prodrome**.

Clinical assessment Con't

- **Functional ability** for both **instrumental** (ie, cooking, driving, financial assistance, and medication management)

- more basic **activities of daily living** (ie, dressing, bathing, and toileting) should be assessed

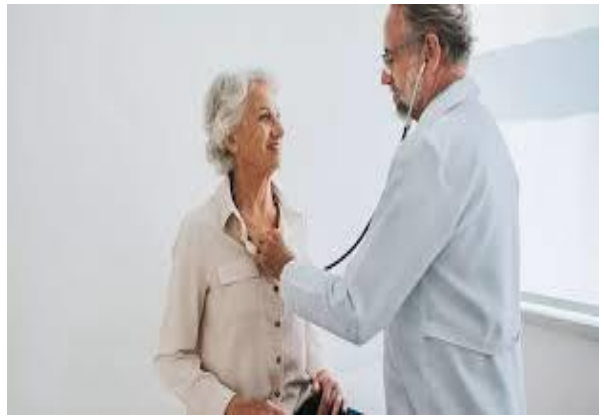
Clinical assessment Con't

- Social history →past or current tobacco use, alcohol, drugs, obesity, physical activity habits, and social networks.

- Family history → any form of dementia, but especially if thought to have been related to cerebrovascular disease. any cardiovascular or other neurological diseases.

- Medication →use of medications to modify vascular risk factors & contraindicated in older adults with cognitive concerns

Clinical assessment Con't



Physical examination

- significant underlying cardiovascular disease→ Pulse and blood pressure
- arrhythmia (especially the irregularly irregular rhythm that indicates atrial fibrillation),
- carotid bruit indicating possible atherosclerosis
- evidence of fluid overload on pulmonary examination

signs of relevant systemic disease such as diabetes mellitus

Clinical assessment Con't

- Extremities → signs of peripheral vascular disease eg:
  - decreased skin temperature
  - brittle/shiny skin on the legs and feet
  - weak pulses in the legs and feet

- pitting lower extremity edema may indicate heart failure

- Examination of the fundus may reveal signs of hypertensive, diabetic retinopathy.

Clinical assessment Con't

On neurological examination

- signs of focal neurological deficit: most commonly encountered are
    - upper motor neuron patterns of facial weakness
    - hemiparesis
    - hemisensory loss
    - visual field defects.

Clinical assessment Con't

- Extra-pyramidal signs
- Evidence of gait impairment, bradykinesia, and rigidity
- Associated degenerative disorders
- **Classic' physical signs** associated with vascular dementia include
  - dysarthria
  - pseudobulbar palsy
  - gait abnormalities and
  - emotional lability.

- the Montreal Cognitive Assessment (MoCA)
- the Mini-Mental State Examination (MMSE)

Diagnostic criteria

Modified Hachinski Ischemic Scale

Score	Feature
0 1 2	Abrupt onset
0 1	Stepwise deterioration
0 1	Somatic complaints
0 1	Emotional incontinence
0 1	History of hypertension
0 1 2	History of stroke
0 1 2	Focal neurologic symptoms
0 1 2	Focal neurologic signs

A score of 4 or more on this modified scale indicates that cerebrovascular disease is thought to make a significant contribution to the dementia.

Hachinski VC, Lassen NA, Marshall J. Multi-infarct dementia. A cause of mental deterioration in the elderly. Lancet 1974;2: 207–210

NINDS-AIREN Criteria (Roman et al, 1993)

I Probable vascular dementia:

1 dementia syndrome not due to delirium, psychosis, aphasia or sensorimotor impairment, and

2 cerebrovascular disease defined by presence of focal neurological signs and evidence of relevant cerebrovascular disease by brain imaging (further specified), and

3 a relationship between 1 and 2 such as dementia occurring within 3 months of a stroke, or abrupt deterioration, or fluctuating stepwise progression.

II Features consistent with probable vascular dementia include early gait disturbance, frequent falls, early urinary symptoms, pseudobulbar palsy, personality and mood changes, subcortical deficits such as psychomotor retardation and abnormal executive function.

III Features making vascular dementia unlikely include clinical symptoms in the absence of focal neurological signs or cerebrovascular lesions on brain CT or MRI.

IV Possible vascular dementia may be diagnosed in the absence of brain imaging studies or clear temporal relationship of dementia to stroke.

V Definite vascular dementia requires clinical criteria for probable vascular dementia and pathological evidence of cerebrovascular disease in the absence of tangles and plaques or other types of dementia pathology.

The term 'Alzheimer's disease with cerebrovascular disease' refers to patients fulfilling criteria for possible Alzheimer's disease who also have clinical or imaging evidence of cerebrovascular disease. Avoid the term 'mixed dementia'.

(After Román 1993)

highest specificity, although lower sensitivity

DSM-IV Criteria for VaD

1. Multiple Cognitive Deficits including amnesia

2. Significant impairment in social or occupational functioning which is a change

3. Presence of focal neurological signs and symptoms or laboratory evidence of cerebrovascular disease judged to be aetiologically related to dementia (stepwise decline dropped)

4. Deficits not only during a delirium

Three basic features (analysis of many criteria)

- The presence of a stroke temporally related (within 3 months) to the onset or marked worsening dementia.
- The presence of bilateral gray matter infarcts in the frontal, temporal, or parietal cortices, basal ganglia, or thalamus.
- Symptoms or physical examination evidence of neurologic signs consistent with prior strokes.

Investigations

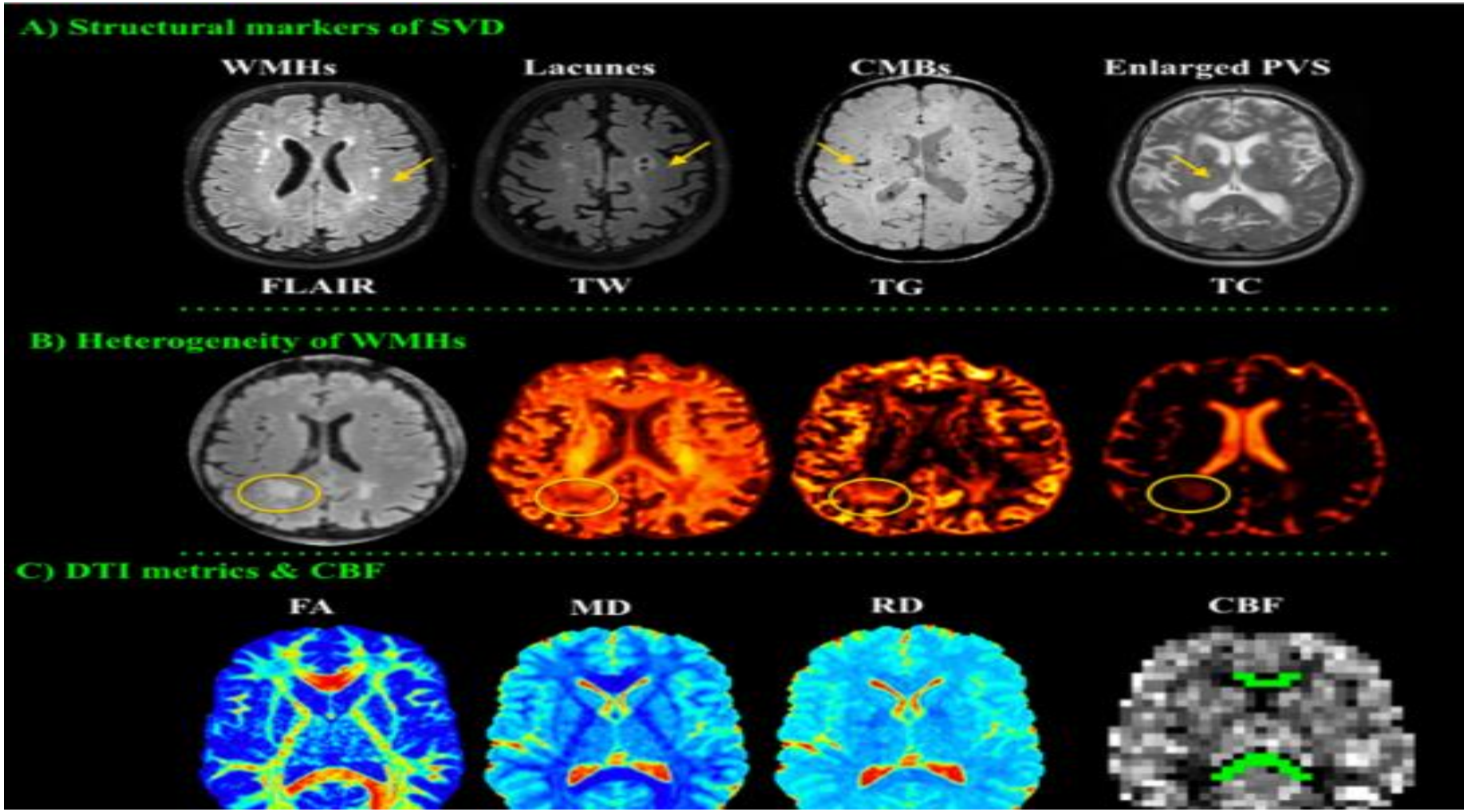
- complete blood count, ESR
- a comprehensive metabolic panel: RBS, Lipid profile, TFT
- c-reactive protein, HIV, or treponemal antibodies
- vitamin B12 and homocysteine levels
- ECG, CxR, USG(Abd), Carotid Doppler USG, Echo
- Computed tomography (CT)
- FDG-PET scan
- Electroencephalogram (EEG)
- Magnetic resonance imaging (MRI)
- amyloid-, or tau PET

Investigations Con’t

- utility of biomarkers—whether in CSF or blood—in vascular dementia lags behind that of Alzheimer disease at this time.

- interleukin 6 is a biomarker with the potential for discriminating between Alzheimer disease and vascular dementia

Structural MRI markers of cerebrovascular pathology underlying VCI



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MRI

- **T1-weighted sequence**: Atrophy
- **FLAIR** (fluid-attenuated inversion recovery sequences):White matter ischemia
- **Gradient echo (GRE) or susceptibility-weighted imaging (SWI)**: cerebral microbleeds in deep subcortical, along cortex (superficial siderosis), asso: underlying CAA
- **Diffusion-weighted imaging (DWI)**: brightly and whitely highlights acute stroke

Complications

- delusions, visual hallucinations, and paranoia.
- Care partner counseling is essential here
- problems with
  - gait
  - aspiration
  - falls
  - pressure sores or ulcers, and
  - burdensome hospitalizations

Case study

- A 65-year-old right-handed male

- acute onset of behavioral problems such as disorientation, confusion, and agitation

- His word output appeared decreased and his words did not have real meaning, difficulty in word findings

Case study

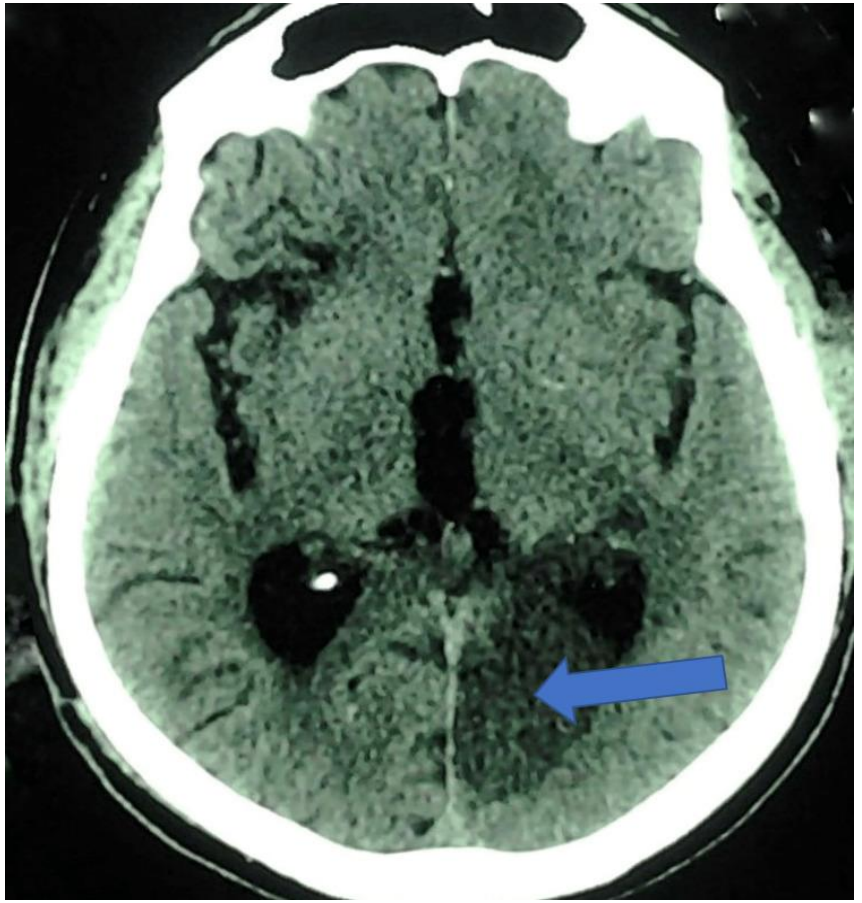
- He also had incontinence and gait apraxia

- He was a smoker for the past 30 years and did not have any other significant medical history

- nervous system (CNS) examination appeared withdrawn, with decreased word output, with mild focal deficits, and the fundus showed no papilledema

Case study

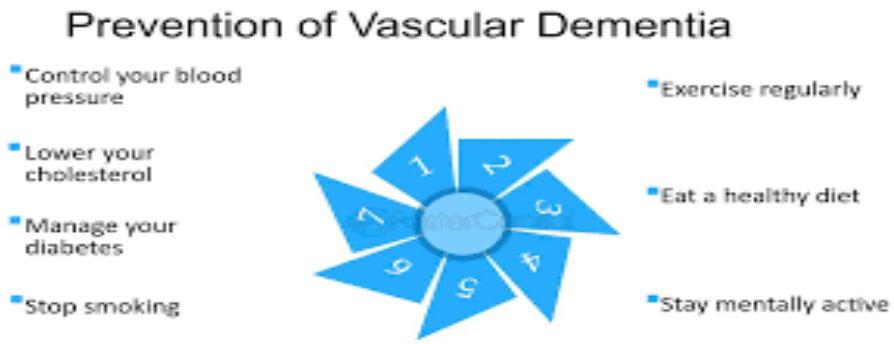
- CT scan of the brain showed a focal ischemic lesion involving the left medial occipital area with bilateral periventricular ischaemia



- **Left posterior cerebral artery (PCA) infarct** involvement of the thalamus, hippocampus, and parahippocampus explains his memory loss and confabulation

- medical management was initiated with anti-platelet medications and statins

Prevention



- **Primary Prevention**

➢optimal control of hypertension and diabetes mellitus

➢a healthy lifestyle (Diet, active physical and mental exercise program)

➢Control of risk factors for stroke, such as AF

- **Secondary Prevention**

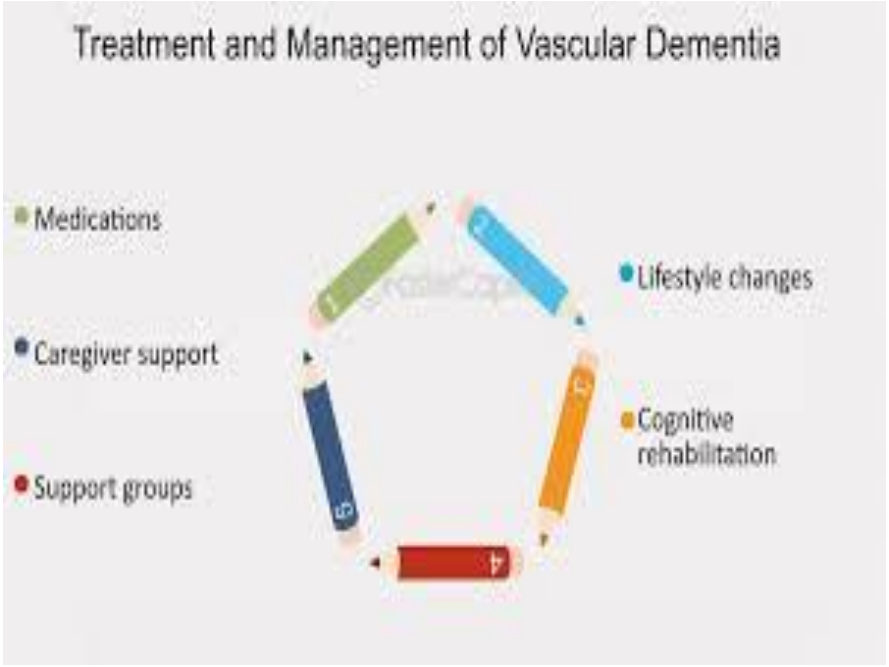
➢Treatment of acute stroke (rtPA)

➢Prevention of stroke recurrence: antiplatelet agents for secondary prevention of cerebrovascular events but not primary prevention.

➢Slow progression of VaD related changes

➢Treatment of vascular risk factors

Treatment



Treatment of cognitive changes

1. Cholinesterase inhibitor agents

- are used rather commonly for AD
- They are also not uncommonly used in VaD, but with less evidence to support their use.
- These agents are generally well tolerated but have the potential for significant gastrointestinal side effects and can promote clinically significant bradycardia

Treatment Con't

2. Memantine, an N-methyl D-aspartate (NMDA) receptor antagonist

• Two randomised controlled studies have tested the effects of memantine in vascular dementia and both found only modest efficacy (Orgogozo 2002; Wilcock 2002)

Neither memantine nor any of the cholinesterase inhibitors is licensed in vascular dementia.

Treatment Con’t

Symptomatic treatment

- Anti depressants (specifically SSRIs)
- Atypical antipsychotics

Control of vascular risk factors

- hypertension is the strongest treatable risk factor

Nonpharmacologic approaches

- the collaboration of nutritionists
- clinical social workers
- cognitive rehabilitation: improvements in global cognitive function, attention, and working memory
- therapists (physical, occupational, and speech/language)
- audiologists

Nonpharmacologic approaches Con’t

- companion care services and
- geriatric case managers to improve patient care.
- later or end stages→ referral for palliative care or hospice.
- Whether to offer these interventions necessitates carefully conversing with patients and caregivers, weighing the benefits and adverse effects, and individualizing recommendations to achieve realistic goals and optimize patient outcomes.

Take Home Messages

- Vascular dementia is not a single entity but any form of dementia arising from a wide variety of impairments in the cerebrovascular circulation
- Pure vascular dementia is rare: vascular dementia is most commonly associated with Alzheimer's disease
- Treatment of vascular risk factors is appropriate, although the evidence is small
- Cholinesterase inhibitors have only a small benefit and are not licensed for use in vascular dementia

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Thank You