COVADIS
Coronary Vasomotor Disorders International Study Group

Coronary Microvascular Dysfunction and the Brain: Is Small Vessel Disease a Link?

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Coronary Microvascular Dysfunction and the Brain: Is Small Vessel Disease a Link?

Introduction

- Small vessel disease of the heart and brain have far-reaching clinical and economic implications.
- Both organs **share common risk factors** (e.g., HTN, diabetes, dyslipidemia, aging, etc.) and are likely affected similarly by systemic inflammation, ischemia (atherosclerosis, vasospasm, micro-emboli) and neuroendocrine dysfunction. There is increasing awareness that sex differences modify interactions.
- Yet, **unclear whether the phenotype of myocardial ischemia resulting from coronary microvascular dysfunction (CMD) is linked with a similar brain condition, cerebral small vessel disease (CSVD).**

Microvascular Disease as a Multisystem Disorder

- Concept of microvascular disease as a multisystem disorder is not new and has been recently reviewed.
- The heart, brain, retina and kidney were included.
- However, considering the very high prevalence of diabetes, obesity, inactivity, etc. among these diseases- the multisystem microvascular disease concept may also extend to skeletal muscle microvasculature.

Coronary Microvascular Dysfunction (CMD)

- Mostly affects coronary arterioles, although more distal involvement (capillaries, venules, pericytes, membrane, etc.) is possible.
- First suggested in 1967 as a cause for angina/ischemia without obstructive CAD, 5-decades later very few labs (<5%) perform any functional testing.
- Barriers to testing are numerus and include lack of proven therapies to alter outcomes but, they will have to be addressed if the CMD field is to advance.
- Considering its very high prevalence, pathologic information is scarce.
- Prevalent in HTN, AS, cardiomyopathies (hypertrophic, nonischemic, and ischemic), DM, metabolic syndrome, CKD, after cancer chemotherapies and radiation.
- Increasingly recognized important contributor to ischemia, with and without epicardial coronary atherosclerosis.
- The latter, Ischemia and No Obstructive Coronary Arteries (INOCA), highly prevalent in middle-aged women: although reversable, effective treatment remains elusive.

Coronary Microvascular Disfunction (CMD)

- Causes myocardial ischemia, recurrent angina, shortness of breath, frequent ED visits, hospitalizations, and reduced QOL.
- Key Functional Changes-Reduced coronary endothelial dependent vasodilation (EDVD), enhanced vasoconstriction, spasm, limited CFR.
- Key Cardiac Imaging Features-reduced TIMI flow, “slow flow’ on invasive coronary angiography. Reduced coronary blood flow (Doppler velocity) or cardiac magnetic resonance imaging cMRI as MPRI to adenosine, also small scar by late gadolinium (LGE).
- Is reversable

Cerebral small vessel disease (CSVD)

- Mostly older women, closely correlated with age; prevalence increases from ~5% at age 50 to nearly 100% by age 90 years.

- Gait/balance disorders, risk of falls, CVAs, decreased QOL and contributes to cognitive decline or disrupt motor pathways.

- Brain imaging features- MRI as white matter hyperintensities (WMH), cerebral microbleeds (CMB), lacunar infarctions (LI), enlarged perivascular spaces (EPVS), and brain atrophy. Functional MRI and transcranial Doppler (TCD) alterations.

Cerebral small vessel disease (CSVD)

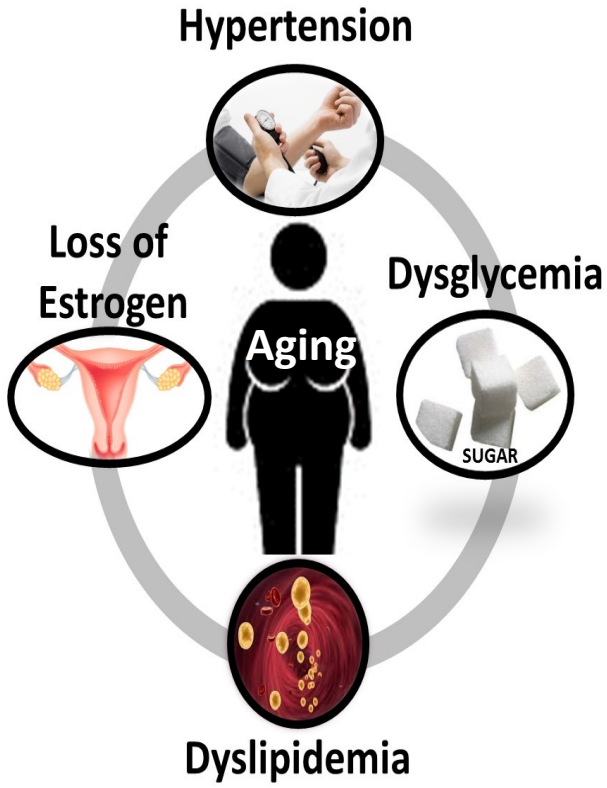
- Brain parenchymal lesions; either ischemic or hemorrhagic. Various etiologic classifications (e.g., Atherosclerosis, Cerebral amyloid angiopathy, Inherited or genetic (CADASIL, CARASIL, Fabry's disease, COL4A1 mutations, etc.), Inflammatory and immune-mediated, Venous collagenosis, others (post radiation angiopathy, nonamyloid microvessel degeneration in Alzheimer's disease).

- Some functional improvement with PhT, and exercise.

- Not reversable, at present.

Animal Models

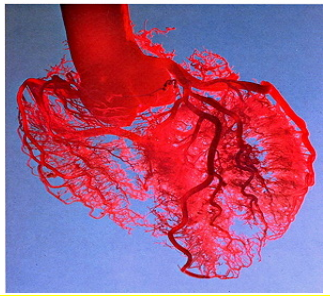
- Multiple animal models of CMD and CSVD provide pathways to enhance understanding of pathophysiology and therapies.
- Mechanisms of BBB damage and endothelial dysfunction.
- Also, insights into genetic and environmental basis of several human CSVDs.
- These models provided suggestions for functional, structural, and other alterations.



INFLAMMATION

OXIDATIVE STRESS

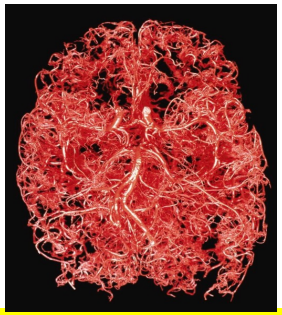
- Middle-aged women
- Myocardial ischemia
- Functional coronary angiography: ⬇EDVD, spasm, limited CFR
- cMRI: ⬇MPRI & LGE small scar
- **Reversible**



Coronary Microvascular Dysfunction (CMD)

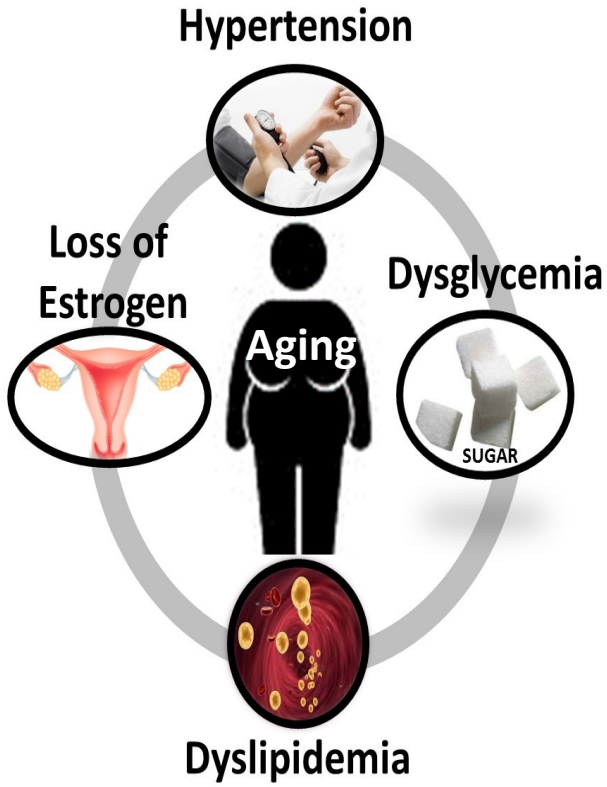
HFpEF

- Older women
- CVA, gait/balance disorders
- Cognitive impairment
- bMRI: WMH, CMB, LI, EPVS & Brain atrophy
- **Irreversible**



Cerebral Small Vessel Disease (CSVD)

ADRD



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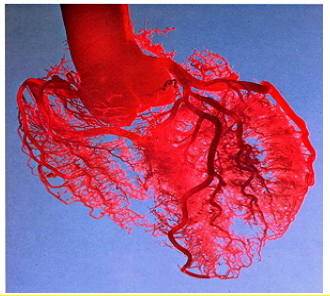

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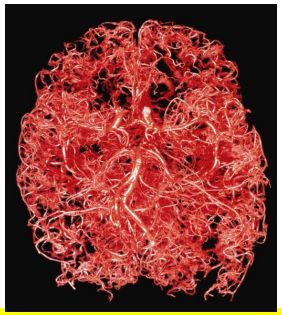

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