Cardiac Disease and Dementia Risk: From Clinical Events to Subclinical Brain Injury

Michelle C. Johansen, MD, PhD, FAHA, FANA
The Guy McKhann Associate Professor of Neurology
Division of Cerebrovascular Neurology
Associate Faculty, The Welch Center, Johns Hopkins University Bloomberg School of Public Health
Acting Director, George W. Comstock Center for Public Health Research and Prevention
mjohans3@jhmi.edu
www.johansenlab.org

Objectives

- Review the epidemiology of major clinical and subclinical cardiac conditions associated with cognitive decline and dementia.
- Describe plausible mechanisms linking cardiac disease to brain injury and dementia risk.
- Examine evidence for atrial cardiopathy as a dementia-risk phenotype beyond atrial fibrillation and clinical stroke.
- Describe the next steps in this developing field and the impact to patient care.

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Epidemiology of the Problem

- Projected increase in hypertension (51.2%→61.0%), diabetes (16.3%→26.8%), and obesity (43.1%→60.6%) rates by 2050.
- Prevalence of inadequate sleep projected to increase (40.3% to 42.1%).
- Better life's Essential 8 scores: Younger brain age, less subclinical vascular disease, slower cognitive decline, reduced dementia risk.

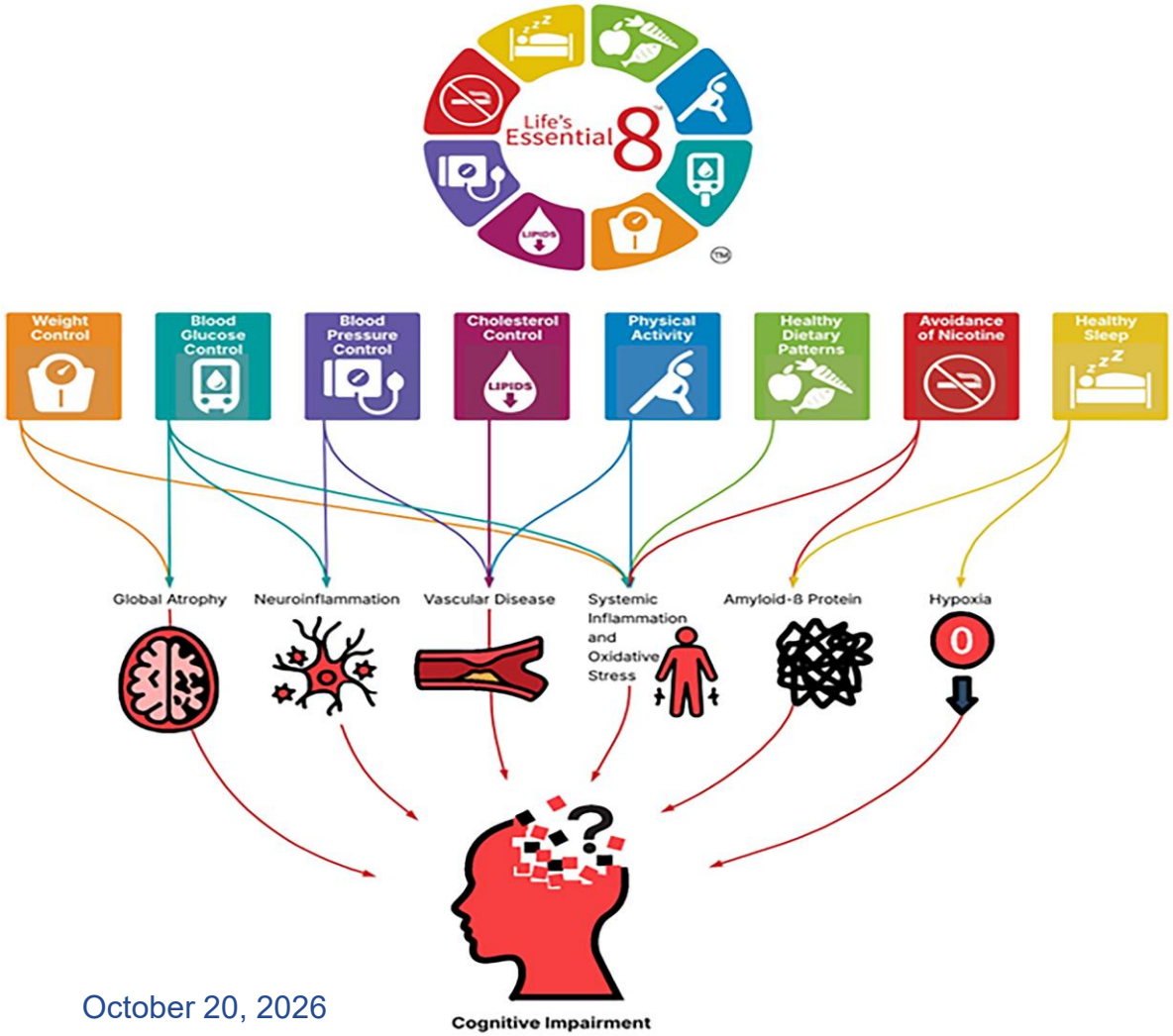


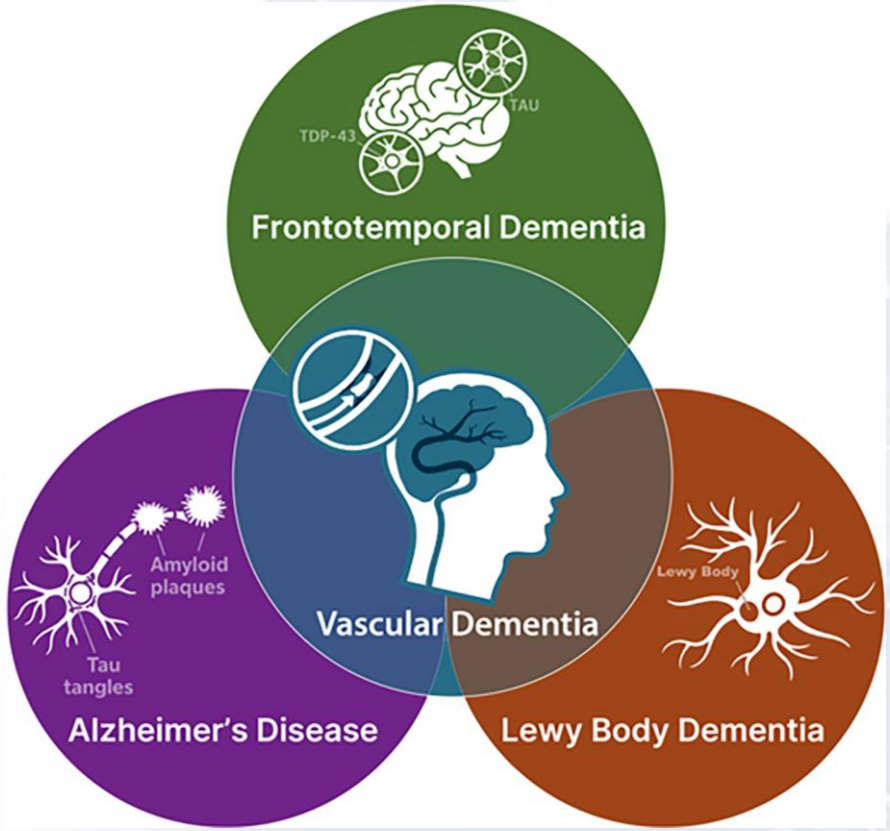
Palaniappan LP, Khan SS, Elkind MSV, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Committee. 2026 heart disease and stroke statistics: a report of US and global data from the American Heart Association. Circulation. 2026;153(9)

Epidemiology of the Problem

- In the US, optimal Life's essential 8 scores could avert approximately 40% of annual all-cause and CVD deaths.
- Total Cardiovascular Disease: The prevalence increases from 33.7% (M) and 19.6% (F) in young adults (20-39 yo) to 59.6% and 51.4% in mid-adulthood (40-59 yo), and 77.5% and 87.1% in adults ≥80 years of age.

How does prevalent cardiovascular disease translate to brain injury?

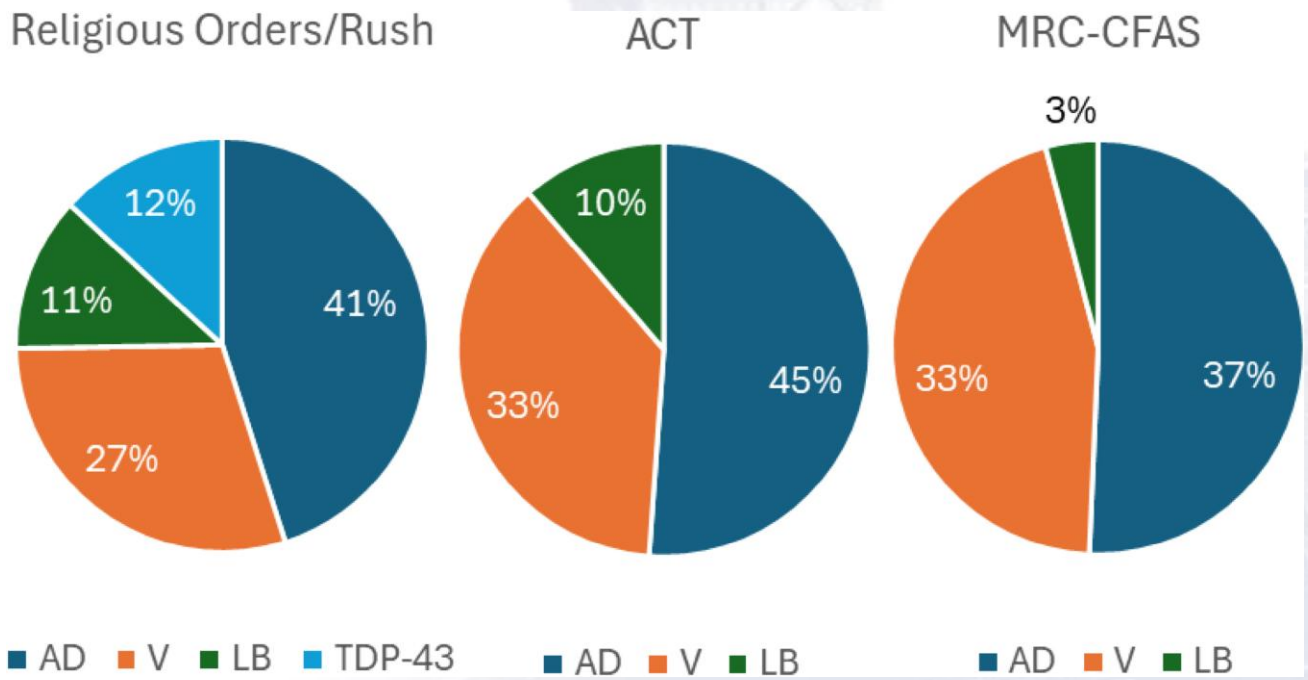




Gold ME, et al; Life's Essential 8: Essential for Brain and Cognitive Health. JAHA. 2026

Clinical and Pathological Overlap

- Dementia in later life is commonly multifactorial, not just traditional “AD” or “vascular dementia”
- Dementia is usually mixed pathology
  - AD neuropathology coexists with vascular brain injury
- Cardiac disease may contribute to this vascular burden while also potentially interacting with other dementia processes.



Smith EE, et al; Vascular Contributions to Cognitive Impairment and Dementia in the United States. Stroke. 2025

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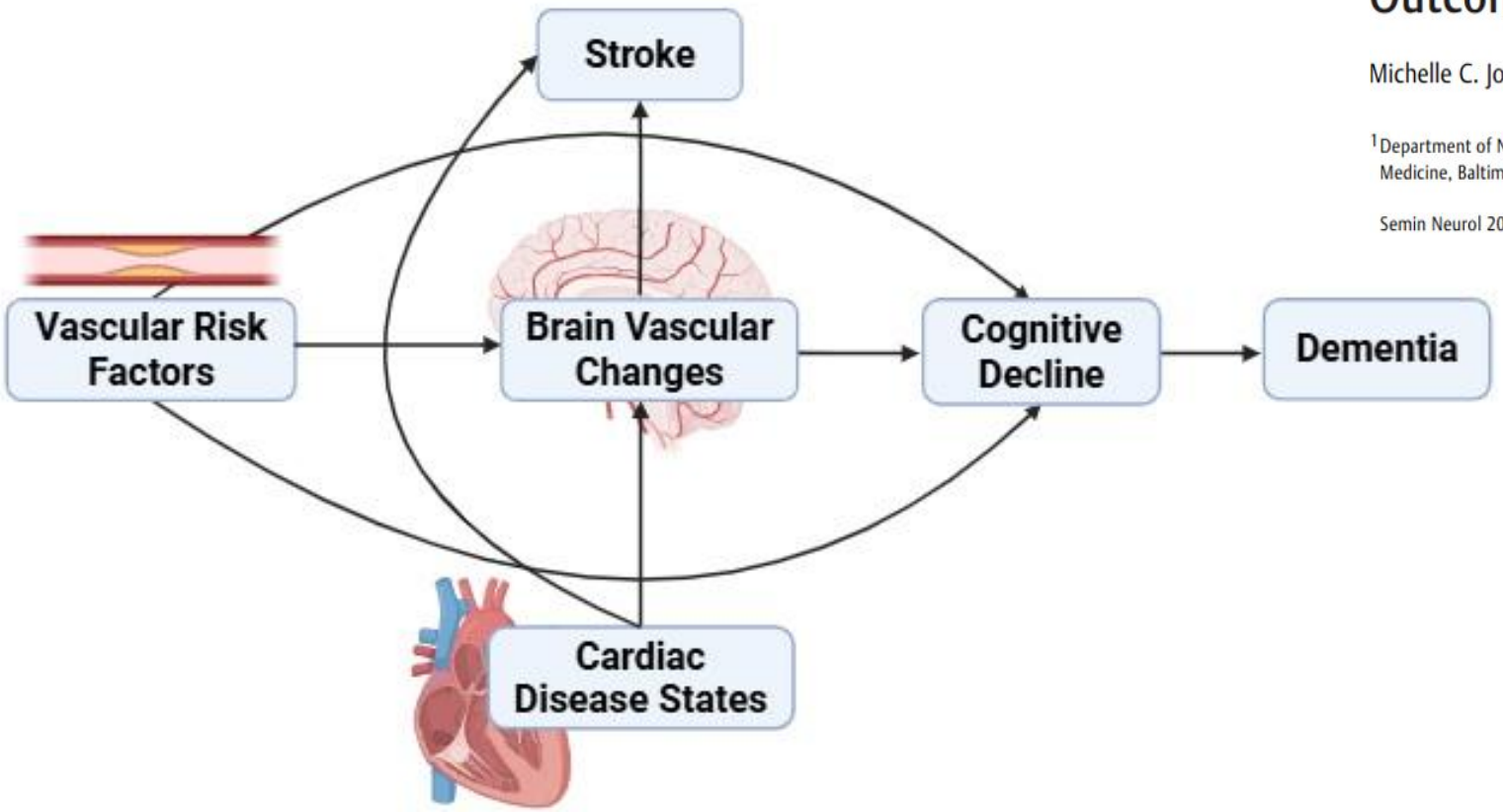
Cardiac disease states can affect the brain through more than one pathway



Cerebrovascular Disease and Cognitive Outcome in Patients with Cardiac Disease

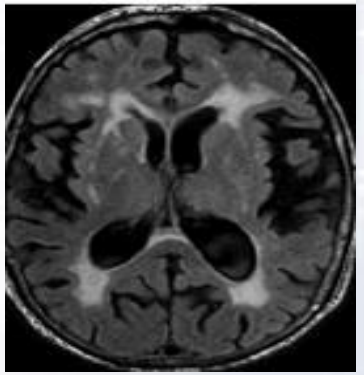
Michelle C. Johansen, MD[1] Rebecca F. Gottesman, MD, PhD[1]

[1]Department of Neurology, The Johns Hopkins University School of Medicine, Baltimore, Maryland

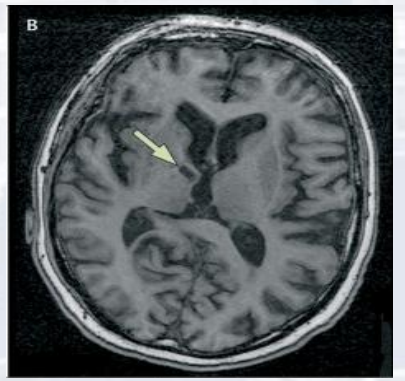
Address for correspondence Michelle C. Johansen, MD, 600 N. Wolfe Street, Phipps 4 Suite 446, Baltimore, MD 21287 (e-mail: mjohans3@jhmi.edu).

Semin Neurol 2021;41:463–472.

in Vascular Changes on imaging:



White matter disease/hyperintensity



Brain infarction

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Understanding the mechanisms linking cardiac disease to brain injury is essential for ultimate prevention

- Clinical stroke.
- Microembolization and subclinical infarction.
- Hemodynamic instability and hypoperfusion.
- Cerebral small vessel disease and microbleeds (including OAC-related).
- Systemic inflammation and endothelial dysfunction.
- Neurodegenerative pathways possibly amplified by cardiac/vascular milieu.

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Stroke and Dementia Risk

JAMA Neurology | Original Investigation

Association of Ischemic Stroke Incidence, Severity, and Recurrence With Dementia in the Atherosclerosis Risk in Communities Cohort Study

Silvia Koton, PhD, RN; James Russell Pike, MBA; Michelle Johansen, MD, PhD; David S. Knopman, MD; Kamakshi Lakshminarayan, MD, PhD; Thomas Mosley, PhD; Shalom Patole, MD; Wayne D. Rosamond, PhD; Andrea L. C. Schneider, MD, PhD; A. Richey Sharrett, MD, DrPH; Lisa Wruck, PhD; Josef Coresh, MD, PhD; Rebecca F. Gottesman, MD, PhD

JAMA Neurol. doi:10.1001/jamaneurol.2021.5080

Table 2. Association of Stroke Severity With General Cognitive Change in the Pooled Sample (N = 42 342)

	Model 1[a]			Model 2[b]		
Coefficient	β (SE)	*P* value	Age-standardized β[c]	β (SE)	*P* value	Age-standardized β[c]
Main effect sizes						
Stroke severity category (reference, no stroke)						
NIHSS 0-5 (minor)	−0.24 (0.16)	.13	1.28	−0.13 (0.16)	.42	0.69
NIHSS 6-10 (mild to moderate)	−0.66 (0.45)	.14	3.50	−0.40 (0.45)	.38	2.10
NIHSS ≥11 (moderate to severe)	0.05 (0.73)	.94	−0.28	0.21 (0.72)	.77	−1.09
Years since baseline	−0.18 (0)	<.001	0.96	−0.18 (0)	<.001	0.96
Interactions between time and stroke severity (reference, no stroke)						
Time × NIHSS 0-5	−0.18 (0.02)	<.001	0.93	−0.17 (0.02)	<.001	0.91
Time × NIHSS 6-10	−0.27 (0.06)	<.001	1.42	−0.28 (0.06)	<.001	1.50
Time × NIHSS ≥11	−0.39 (0.08)	<.001	2.07	−0.39 (0.08)	<.001	2.07

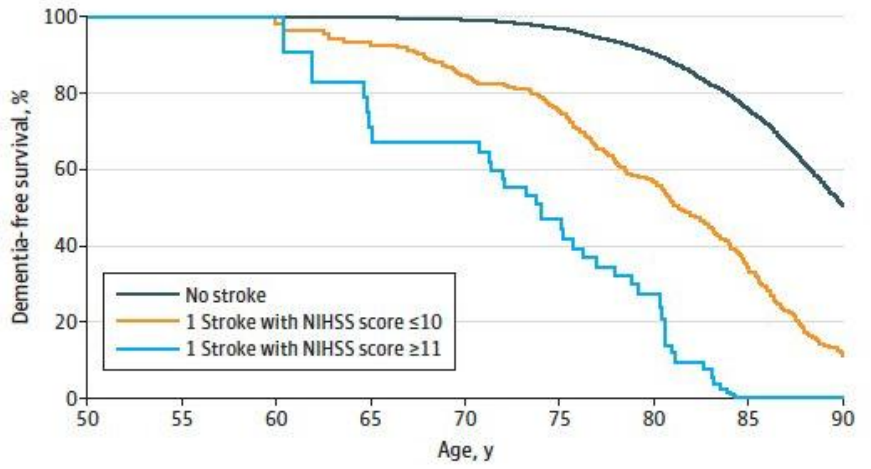
Abbreviation: NIHSS, National Institutes of Health Stroke Scale.

[a] Adjusted for cohort membership, baseline age, sex, race and ethnicity, education, and age-by-time interaction.

[b] Model 1 additionally adjusted for baseline BMI, systolic blood pressure, diastolic blood pressure, and blood glucose.

[c] Age-standardized β refers to the β coefficient divided by the corresponding coefficient for age in the model.

Figure 2. Extended Kaplan-Meier Curves of Dementia by National Institutes of Health Stroke Scale (NIHSS) Severity of Incident Ischemic Stroke (N = 15 379)



No. at risk								
No stroke	15 184	14 748	13 907	12 562	10 540	6305	2715	650
1 Stroke with NIHSS score ≤10	14	56	114	195	240	187	108	26
1 Stroke with NIHSS score ≥11	2	10	19	19	19	11	0	0

JAMA Network | Open

Original Investigation | Neurology

Ischemic Stroke Incidence and Severity and Poststroke Cognitive Decline and Incident Dementia

Silvia Koton, PhD, MOccH, RN; Alden L. Gross, PhD; Hugo J. Aparicio, MD; Alexa S. Beiser, PhD; Emily M. Briceño, PhD; Josef Coresh, MD, PhD; Mitchell S. V. Elkind, MD; Bruno J. Giordani, PhD; Rebecca F. Gottesman, MD, PhD; Rodney A. Hayward, MD; Virginia J. Howard, PhD; Michelle C. Johansen, MD, PhD; Ronald M. Lazar, PhD; Mellanie V. Springer, MD; Robert J. Stanton, MD; Jeremy Sussman, MD; Hang Wang, PhD; Rachael T. Whitney, PhD; Wen Ye, PhD; Deborah A. Levine, MD, PhD

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Cardioembolic stroke specifically appears to be a risk factor for cognitive decline

Effect of stroke type and ischemic stroke subtype on change in intercept after incident stroke		
Hemorrhagic stroke	−0.16 (−0.33 to 0.01)	0.07
Ischemic stroke		
Cardioembolic — Acute decline	−0.22 (−0.34 to −0.09)	0.001
Large vessel	−0.24 (−0.38 to −0.09)	0.001
Small vessel	−0.11 (−0.23 to 0.02)	0.09
Other	−0.27 (−0.57 to 0.03)	0.08
Unknown	−0.03 (−0.10 to 0.04)	0.38
Effect of stroke type and ischemic stroke subtype on change in slope after incident stroke		
Hemorrhagic stroke	−0.05 (−0.10 to −0.01)	0.03
Ischemic stroke		
Cardioembolic — Faster rate of decline	−0.05 (−0.09 to −0.01)	<0.01
Large vessel	−0.004 (−0.04 to 0.03)	0.83
Small vessel	−0.003 (−0.04 to 0.03)	0.85
Other	−0.07 (−0.18 to 0.03)	0.18
Unknown	−0.04 (−0.06 to −0.02)	<0.01
Log Likelihood	−153532.31	NA

Stroke
Volume 49, Issue 4, April 2018, Pages 987-994
https://doi.org/10.1161/STROKEAHA.117.018529



ORIGINAL CONTRIBUTIONS - CLINICAL SCIENCESCLINICAL SCIENCES

Risk Factors for Poststroke Cognitive Decline

The REGARDS Study (Reasons for Geographic and Racial Differences in Stroke)

Deborah A. Levine, MD, MPH, Virginia G. Wadley, PhD, Kenneth M. Langa, MD, PhD, Frederick W. Unverzagt, PhD, Mohammed U. Kabeto, MS, Bruno Giordani, PhD, George Howard, DrPH, Virginia J. Howard, PhD, Mary Cushman, MD, MSc, Suzanne E. Judd, PhD, and Andrzej T. Galecki, MD, PhD

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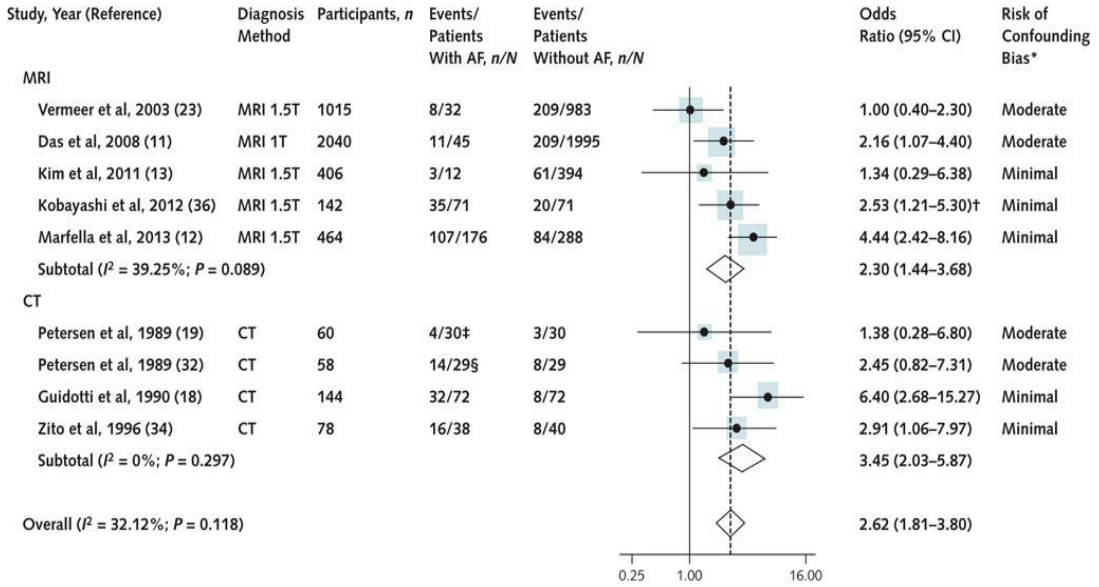
Cardiac disease is associated with silent cerebral infarction



Kalantarian, S et al; Associations between AF and SCI. Annals of Int Med. 2014

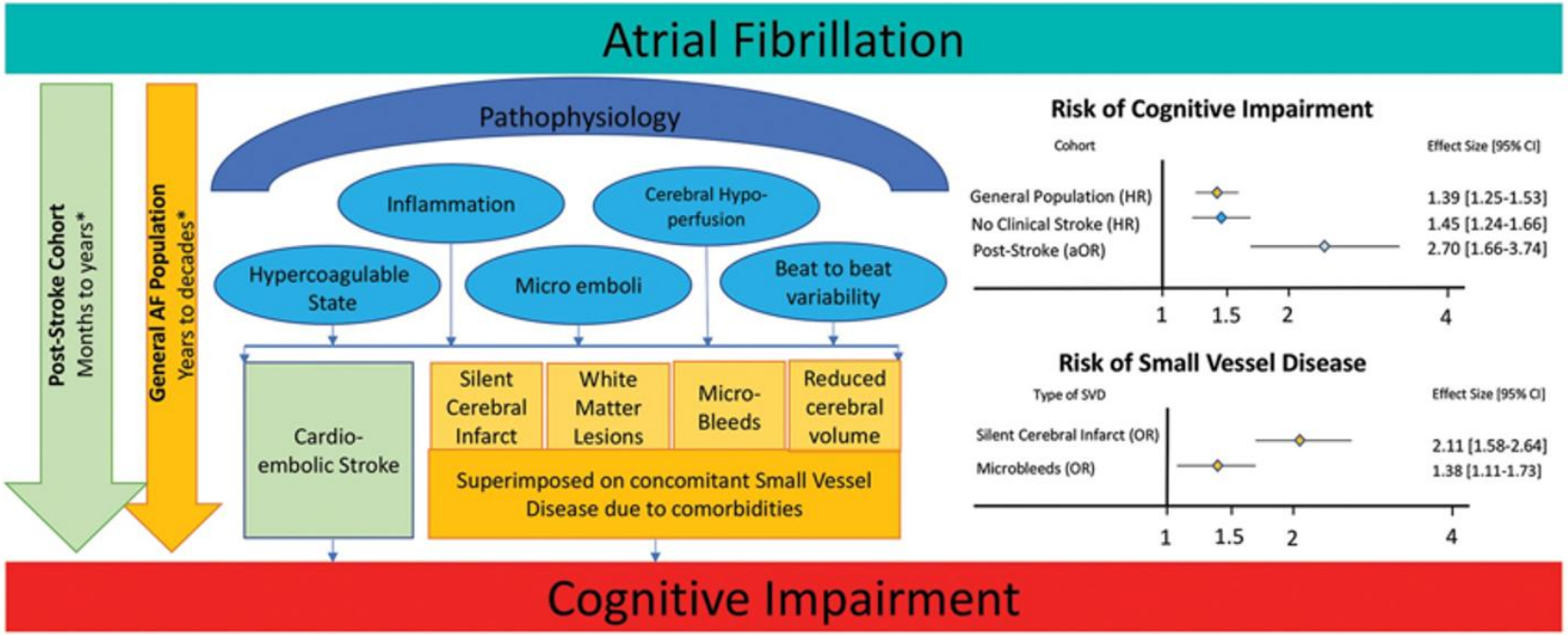
Table 1 | Associations between cardiac diseases and SCIs

Diagnosis	Reference	Study design (*n*)	Anticoagulation therapy (%)	Imaging modality	Rate of SCIs (%)	Rate of stroke (%)
AF						
Paroxysmal and persistent AF	Gaita *et al.* (2013)[26]	Case–control (90 paroxysmal AF, 90 persistant AF, 90 controls)	Aspirin: 24 OAC: 66 None: 11	MRI	Paroxysmal AF: 89 Persistent AF: 92 Controls: 46	Patients with previous CVA or TIA were excluded
Silent AF in patients with type 2 diabetes mellitus	Marfella *et al.* (2013)[27]	Case–control (176 with silent AF, 288 without silent AF)	Aspirin: 99	MRI	Silent AF: 61 No silent AF: 29	Silent AF: 17 No silent AF: 6 (3-year follow-up)
Nonvalvular AF	Kobayashi *et al.* (2012)[28]	Case–control (71 with AF, 71 controls)	Aspirin: 55 OAC: 31	MRI	AF: 80 Controls: 69	Patients with previous CVA or TIA were excluded
Symptomatic and drug-refractory paroxysmal or persistent AF	Neumann *et al.* (2011)[29]	Prospective pilot study (45 cryoballoon ablation, 44 radiofrequency energy technique)	Aspirin: 25 VKA: 51 Clopidogrel: 1 None: 25	MRI	12.3	Patients with previous CVA were excluded
Nonvalvular AF	Sato *et al.* (2004)[30]	Case–control (212 with AF, 78 controls)	None in the first year	MRI	AF: 86 Controls: 54 At 12-month follow-up, 21% of the patients with AF had new SCIs	Patients with previous CVA were excluded
Nonrheumatic AF with history (<3 months) of ischaemic stroke or TIA	EAFT Study Group (1996)[31]	Double-blind RCT of OAC treatment versus aspirin or placebo (*n*=985)	NA	CT	14 (at baseline, of whom 14% had additional SCIs at 2-year follow-up)	20
Nonrheumatic AF without history of stroke or TIA	Ezekowitz *et al.* (1995)[32]	RCT of warfarin versus placebo (*n*=516)	NA	CT	15 (on baseline CT)	7* (3-year follow-up)
Cardiomyopathy						
Ischaemic and nonischaemic DCM	Kozdag *et al.* (2008)[44]	Case–control (46 with ischaemic DCM, 26 with nonischaemic DCM, 56 controls)	Aspirin: 78	MRI	Ischaemic DCM: 39 Nonischaemic DCM: 27 Controls: 4	Patients with previous CVA or TIA were excluded
Cardiomyopathy with LVEF <20% being evaluated for heart transplantation	Siachos *et al.* (2005)[41]	Observational cohort (*n*=117)	Aspirin: 26 VKA: 27 None: 47	CT or MRI	34	Patients with previous CVA or TIA were excluded
PFO						
PFO	Di Tullio *et al.* (2013)[57]	Case–control (*n*=360)	Aspirin: 2	MRI	PFO: 17 Controls: 14	PFO: 9 Controls: 10 (in entire cohort of 1,100 participants)
Pulmonary embolism with or without a PFO	Clergeau *et al.* (2009)[50]	**Case–control (15 with PFO,** 45 without PFO)	NA	MRI	PFO: 33 No PFO: 2	2

*In the 307 patients for whom baseline and follow-up scans were available. Abbreviations: AF, atrial fibrillation; CVA, cerebrovascular accident; DCM, dilated cardiomyopathy; LVEF, left ventricular ejection fraction; NA, not available; OAC, oral anticoagulant; PFO, patent foramen ovale; RCT, randomized controlled trial; SCIs, silent cerebral infarcts; TIA, transient ischaemic attack; VKA, vitamin K antagonist.

Hassell,MEC et al; Silent Cerebral Infarcts associated with cardiac disease and procedures. Nat Rev Card. 2013

Atrial Fibrillation & Cognition: More than just a stroke risk factor



Europace, Volume 24, Issue 8, August 2022

- In the Rotterdam study, older individuals with AF had a 12% increased risk of dementia
- Two prospective AF trials found a 14% increased risk of cognitive decline
- A meta-analysis of stroke-free subjects found AF was associated with 40% greater risk of cognitive decline

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Atrial Fibrillation Subtype and Rapid Ventricular Response are Associated with Incident Dementia



Ryan Yue, Johns Hopkins Math Undergrad

Study Aim: To determine among AF patients in a large EMR cohort, those features most strongly associated with a higher risk of cognitive impairment, accounting for time and vascular risk, defined as a diagnosis of incident dementia or mild cognitive impairment (MCI).

- **Exposures:** AF subtype, RVR, and NT-proBNP after incident AF.
- **Main outcomes:** Incident cognitive impairment (ICD codes).

Conclusion:

- Greater AF burden and rapid ventricular response were associated with higher risk of incident cognitive impairment.

AF characteristic	N (%)	Incident cases of dementia/MCI	Adjusted HR (95% CI)*
AF subtype (N = 57,431)			
Paroxysmal (reference)	21,434 (37.3%)	640	1.00 (reference)
Persistent	8,366 (14.6%)	318	1.11 (1.01–1.22)
Long-standing persistent	973 (1.7%)	29	1.45 (1.07–1.95)
Permanent	1,135 (2.0%)	40	1.05 (0.81–1.35)
Other (unspecified + unclassified)	25,523 (44.4%)	1,041	0.95 (0.89–1.02)
RVR (N = 57,431)			
Rapid ventricular response (vs none)	5,564 (9.97%)	178	1.18 (1.05–1.33)
NT-proBNP (N = 8,527)			
NT-proBNP (per doubling)	8,527	306	0.99 (0.95–1.04)

Cardiac structure and function in dementia risk

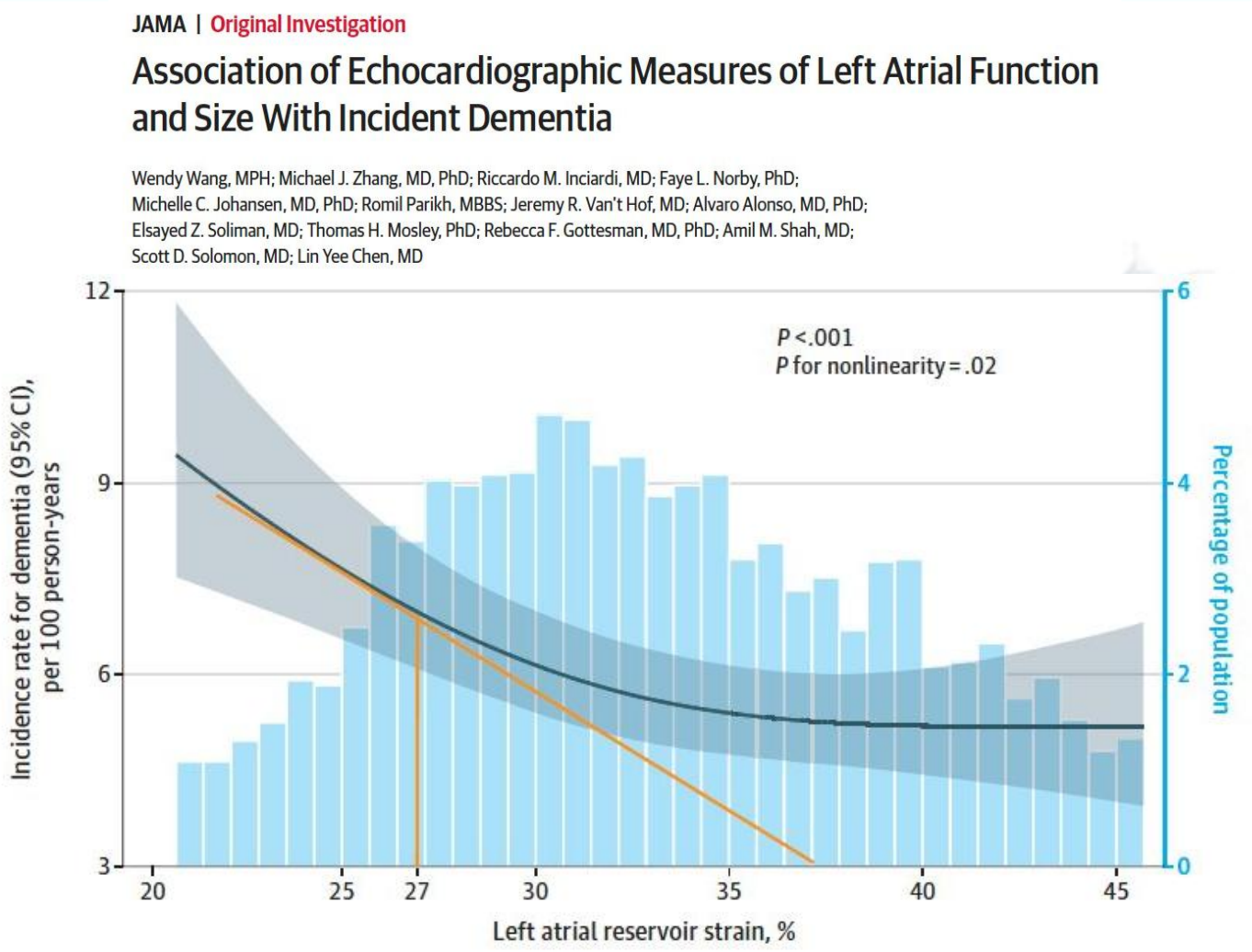
Study Aim: To examine the association of LA function and size with incident dementia (N=4096)

- **Exposures:** LA function (reservoir strain, conduit strain, contractile strain, emptying fraction, passive emptying fraction, and active emptying fraction), and LA size (maximal and minimal volume index) as evaluated by 2DE.
- **Main outcomes:** Dementia cases identified using in-person and phone cognitive assessments, hospitalization codes, and death certificates. Cox proportional hazards models were used.

Conclusion:

- Several ECG measures of lower LA function were significantly associated with an increased risk of subsequent dementia.
- Measures of LA size alone were not significantly associated with dementia risk.

Findings suggested that impaired LA function may be a risk factor for dementia.



Atrial cardiopathy and subclinical atrial disease

- Structural, functional, electrical biochemical atrial abnormalities that may predispose to thromboembolism even in the absence of documented AF
- Indicators: Left atrial enlargement, abnormal P-wave indices / P-wave terminal force, elevated NT-proBNP, impaired left atrial strain, atrial fibrosis on advanced imaging, frequent atrial ectopy

Is atrial cardiopathy associated with dementia?

- **5952** ARIC participants w/o prevalent dementia, **1709** met criteria for atrial cardiopathy
- Cox models to determine association between atrial cardiopathy and incident dementia
- Formal mediation analysis for stroke and AF
- Adjustment models: age, time-varying current smoking, time-varying hypertension, diabetes, low-density lipoprotein cholesterol, apolipoprotein E (apoE) genotype, prevalent stroke, prevalent heart failure, prevalent coronary heart disease, anticoagulation medication

Table 1. Participant Demographics, By Atrial Cardiopathy Status, At ARIC Visit 5 (2011–2013)

Participant demographic	Without Atrial Cardiopathy (n=3428)	With Atrial Cardiopathy (n=1735)	*P* value
Age, mean (SD)	74 y (4.6)	77 y (5.2)	<0.001
Female sex	2026 (60.1%)	955 (56.0%)	0.004
Black race	759 (22.5%)	334 (19.5%)	0.014
Education level (years of school)			<0.001
Basic education (≤11)	384 (11.4%)	246 (14.4%)	
Intermediate education (12–16)	1401 (41.6%)	739 (43.2%)	
Advanced education (>17)	1584 (47.0%)	724 (42.4%)	
Current cigarette smoker	193 (5.7%)	93 (5.4%)	0.68
Hypertension	2372 (70.4%)	1389 (81.3%)	<0.001
Diabetes	917 (27.2%)	466 (27.3%)	0.97
Low-density lipoprotein, mean (SD)	106mg/dL (34.0)	101mg/dL (34.5)	<0.001
Prevalent atrial fibrillation/flutter	88 (2.6%)	399 (17.5%)	<0.001
Prevalent stroke	77 (2.3%)	89 (5.2%)	<0.001
Prevalent coronary heart disease	328 (9.7%)	406 (23.8%)	<0.001
Anticoagulation use in the past 4 wks	83 (2.5%)	236 (13.8%)	<0.001
Mild cognitive impairment	641 (19%)	398 (23.3%)	<0.001

Hypertension defined as systolic >140 mm Hg, or diastolic >90 mm Hg, or use of hypertension medication. Diabetes defined as a hemoglobin A1c ≥6.5%. Two-sided $P<0.05$ was considered statistically significant. Presented as n (%) unless otherwise noted. ARIC indicates Atherosclerosis Risk in Communities Study.

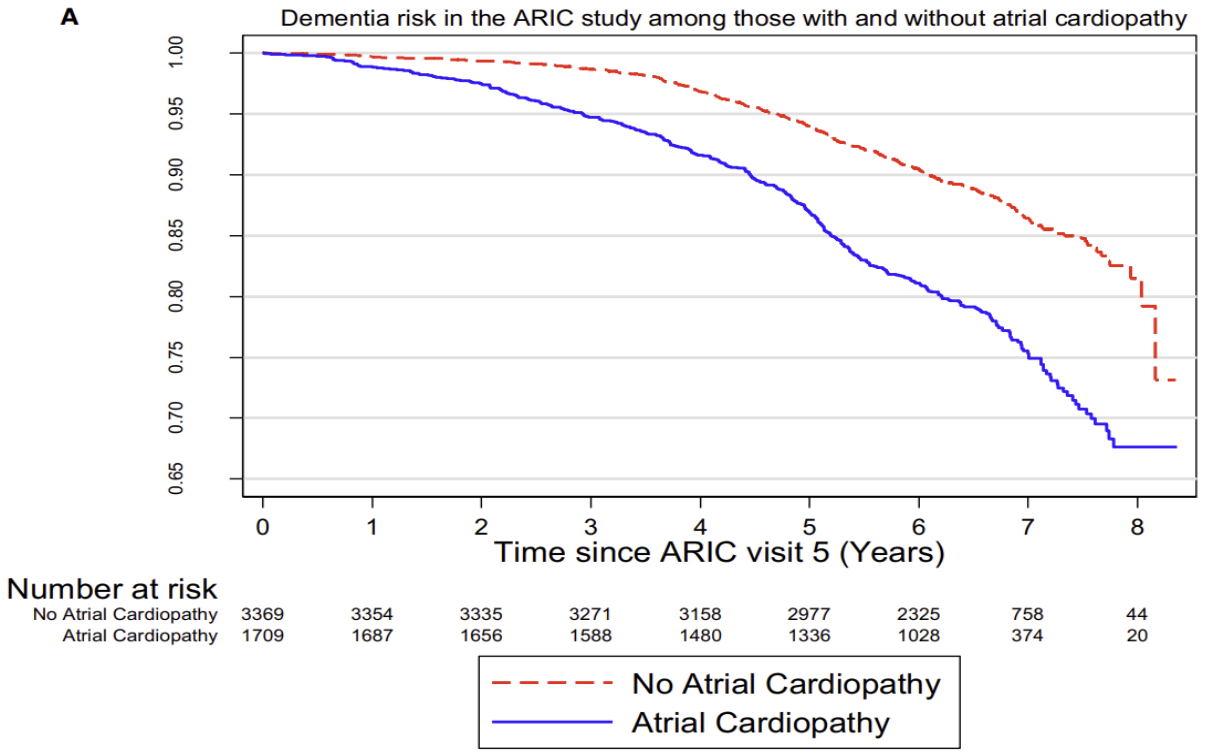
Atrial cardiopathy is associated with incident dementia

- 763 progressed to dementia over a mean time at risk of 6.12 years
- Adjusted HR 1.35 (1.16-1.58)
- Larger effect estimate with stricter definition of atrial cardiopathy [1.54 (1.25-1.89)]
- Only small proportion mediated by AF (4%) or stroke (9%)

Risk of Dementia Associated With Atrial Cardiopathy: The ARIC Study

Michelle C. Johansen, MD, PhD, Wendy Wang, MPH, Michael Zhang, MD, PhD, David S. Knopman, MD, Chiadi Ndumele, MD, PhD, Thomas H. Mosley, PhD, Elizabeth Selvin, MPH, PhD, Amil M. Shah, MD, MPH, Scott D. Solomon, MD, Rebecca F. Gottesman, MD, PhD, and Lin Yee Chen, MD, MS
AUTHOR INFO & AFFILIATIONS

Journal of the American Heart Association • Volume 11, Number 16 • https://doi.org/10.1161/JAHA.121.025646



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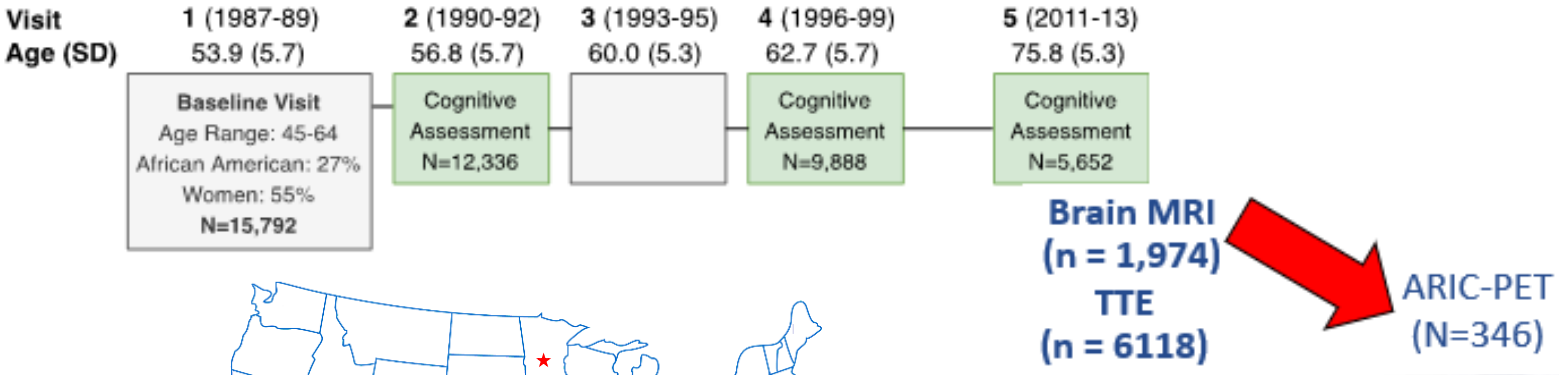
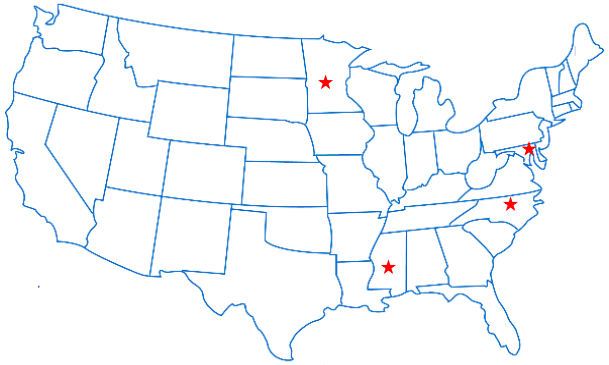
Atrial cardiopathy may be associated with other brain changes besides stroke

Atherosclerosis Risk in Communities (ARIC) study, ARIC-NCS and the ARIC PET Study



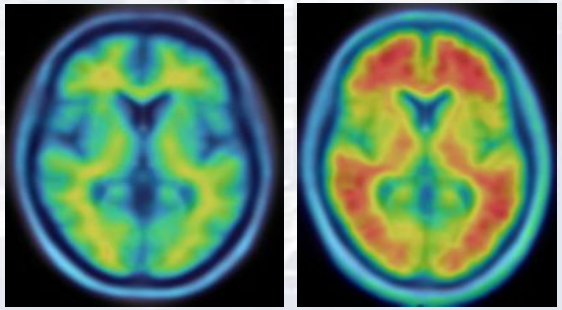




Rebecca Gottesman, MD PhD



Joe Coresh, MD PhD



- **Florbetapir PET** imaging allows for visualization of Aβ plaques
  - Typical AD: Neuron loss, neurofibrillary tangles, cerebral beta-amyloid plaques
- One avenue by which the association between cardiac structure and function, cognitive impairment and AD pathology might be explored

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Atrial cardiopathy may be associated with other brain changes besides stroke

ARIC

Atrial cardiopathy and an imaging marker of dementia pathology

➢ Study Aim:

To determine if the presence of atrial cardiopathy is associated with the presence of an imaging marker of aggregated β-amyloid among older adults without dementia

➢ Atrial cardiopathy was defined as ≥1: (1) left atrial volume index >34 mL/m2; (2) P-wave terminal force >5000 μV×ms; and (3) serum NT-proBNP (N-terminal pro-B-type natriuretic peptide) >250 pg/mL.

➢ Conclusion

- Atrial Cardiopathy, and left atrial volume, **were associated with elevated FBP SUVR (biomarker of aggregated Aβ)**
- Possible that atrial cardiopathy, and the cellular pathology that underlies it, may directly or indirectly impair brain integrity
- Limitations: reverse causation, unmeasured confounding, missed AF
- Plan is to repeat PET→ determine change over time

Odds of elevated global cortical cerebral amyloid by florbetapir PET (SUVR>1.2) by cardiac variable (N=316)

Cardiac Independent Variable	N with specified cardiac variable	Final Adjustment Model	
		OR	95% CI
LAVI (ml/m2) ≥34 ml/m2	50/316	**2.18**	**1.04-4.61**
P-wave terminal force >5000 uV x ms	21/316	0.79	0.29-2.14
serum NT proBNP>250 pg/mL	61/316	2.00	0.97-4.12
Atrial Cardiopathy	98/316	**1.81**	**1.02-3.22**
Prevalent Atrial fibrillation	17/316	0.73	0.24-2.17

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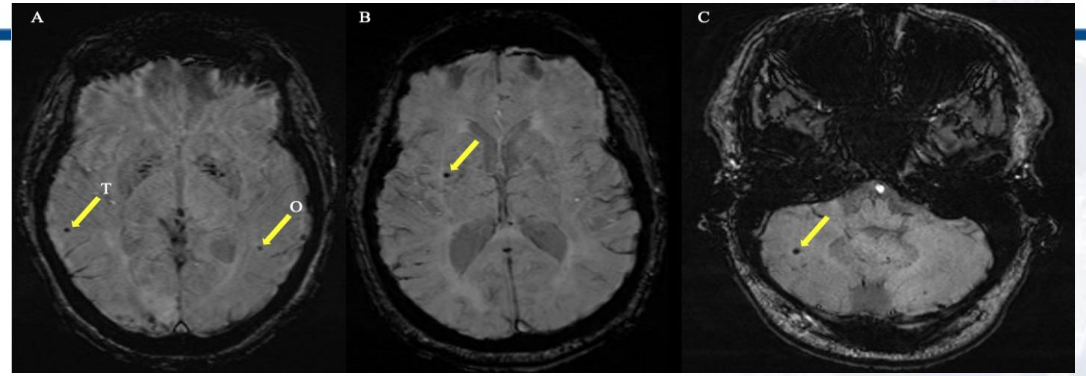
Johansen et al. JAHA 2020

Atrial Cardiopathy and Cerebral Microbleeds Among Stroke Patients Without Atrial Fibrillation



David Zhao, MD,
Harvard Residency

- Cerebral microbleeds (CMB) are associated with atrial fibrillation (AF), and cognitive decline
- Are CMB found in ischemic stroke (IS) patients w/ atrial cardiopathy, apart from AF?
- We found a significant association between atrial cardiopathy and CMB presence in nondemented IS patients w/o AF



Multivariable Logistic Regression Models Demonstrating the Association of Atrial Cardiopathy with CMB Presence, and CMB Location, Among Nondemented patients with Ischemic Stroke (IS) (N=120)*

Outcome	N	Univariate		Model 1		Model 2	
		OR	95% CI	OR	95% CI	OR	95% CI
CMB Presence	39	**2.61**	**1.19-5.74**	**2.47**	**1.01-6.07**	**2.50**	**1.02-6.15**
Lobar CMB	27	**2.50**	**1.04-5.99**	2.69	0.99-7.33	2.68	0.98-7.32
Deep CMB	13	0.69	0.20-2.38	0.47	0.11-1.95	0.46	0.11-2.01

*Adjustment models: Model 1= age, race, sex, ever smoker, history of hypertension, diabetes mellitus, low-density lipoprotein (mg/dL), and National Institutes of Health stroke scale. Model 2=Model 1 + anti-thrombotic medication use at time of admission (anti-coagulants and/or anti-platelet medications)

frontiers | Frontiers in Neurology

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Coronary Artery Atherosclerosis and White Matter Hyperintensity

Stroke
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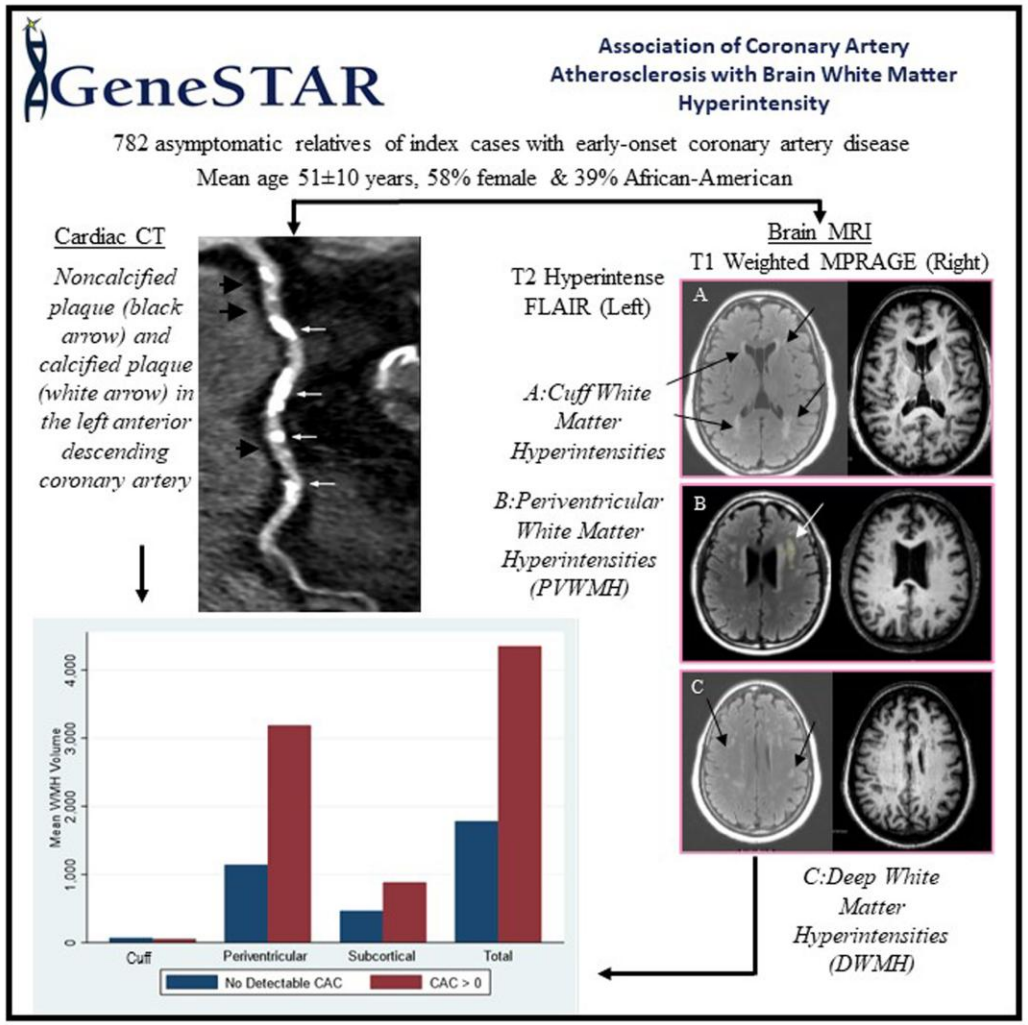
CLINICAL AND POPULATION SCIENCES

Association of Coronary Artery Atherosclerosis With Brain White Matter Hyperintensity

Michelle C. Johansen, MD, PhD, Rebecca F. Gottesman, MD, PhD, Brian G. Kral, MD, MPH, Dhananjay Vaidya, PhD, MPH, MBBS, Lisa R. Yanek, MPH, Lewis C. Becker, MD, Diane M. Becker, MPH, ScD, and Paul Nyquist, MD, MPH



- 782 adults underwent coronary CT angiography and brain MRI
- To determine the association between coronary plaque burden and WMH volumes and location
- Multilevel mixed-effects linear regression accounted for family structure and covariates
- Presence and volume of coronary plaque is associated with larger WMH volumes (vs. no plaque, or smaller volumes)
- Differential association based on location of WMH, with the largest effect estimate being the periventricular WMH
- Possibly due to different mechanism of injury based on location

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Myocardial Infarction is a risk factor for cognitive decline

Table 2. Adjusted Changes in Global Cognition, Executive Function, and Memory Acutely and in the Years Following Incident MI Among All 30 465 Individuals[a]

	Coefficient (95% CI)[b]					
	Global cognition (n = 30 465)		Executive function (n = 28 001)		Memory (n = 20 061)	
Measure	Model A	Model B	Model A	Model B	Model A	Model B
Baseline cognitive score	55.5 (55.3 to 55.8)	55.5 (55.3 to 55.7)	53.0 (52.8 to 53.3)	53.0 (52.8 to 53.3)	54.7 (54.5 to 55.0)	54.7 (54.5 to 55.0)
Baseline slope without incident MI, per y	−0.26 (−0.27 to −0.25)	−0.25 (−0.27 to −0.24)	−0.29 (−0.30 to −0.27)	−0.31 (−0.32 to −0.30)	−0.31 (−0.32 to −0.30)	−0.28 (−0.30 to −0.27)
Difference in baseline cognitive scores for every 10 y older age	−2.19 (−2.29 to −2.09)	−2.19 (−2.29 to −2.09)	−2.84 (−2.95 to −2.74)	−2.84 (−2.95 to −2.73)	−1.72 (−1.85 to −1.58)	−1.72 (−1.85 to −1.58)
Change in cognition slope for every 10 y older age	−0.16 (−0.16 to −0.15)	−0.16 (−0.16 to −0.15)	−0.12 (−0.13 to −0.11)	−0.12 (−0.13 to −0.11)	−0.18 (−0.20 to −0.17)	−0.18 (−0.20 to −0.17)
Acute change in cognition after incident MI	−0.70 (−0.99 to −0.40)	−0.18 (−0.52 to 0.17)	−0.68 (−0.97 to −0.39)	−0.17 (−0.53 to 0.18)	−0.01 (−0.55 to 0.52)	0.62 (−0.07 to 1.31)
Change in cognition slope after incident MI, per y	NA	−0.15 (−0.21 to −0.10)	NA	−0.14 (−0.20 to −0.08)	NA	−0.13 (−0.22 to −0.04)

Abbreviations: AF, atrial fibrillation; MI, myocardial infarction; NA, not applicable.

[a] For linear mixed-effects models, model A included a time-varying incident MI variable to estimate the association of incident MI with decline in cognitive function (intercept) at the time of the event (value changed from 0 to 1 at the time of incident MI). Model B included covariates in model A and added a time-after-MI covariate to estimate the association of incident MI with decline in cognitive function (slope) over the years following the event. Covariates in model A included time since the first cognitive assessment, time-varying incident MI, and baseline values (measured before or at the time of the first cognitive assessment) of sex, race and ethnicity, age, cohort study, years of education, current smoking, number of alcoholic drinks per week, body mass index, waist circumference, physical activity, cumulative systolic mean blood pressure, antihypertension medication use, fasting glucose level, low-density lipoprotein cholesterol level, history of AF (defined as history of AF at cohort baseline or incident AF before incident MI), age × follow-up time, race and ethnicity × follow-up time, sex × follow-up time. Covariates in model B included covariates in model A plus time after MI.

[b] All cognitive measures were set to a mean (SD) T score metric (50 [10]) at a participant's first cognitive assessment; a 1-point difference represented a 0.1-SD difference in the distribution of the specified cognitive domain across the 6 cohorts. Higher cognitive scores indicate better performance. Cognitive observations were censored after stroke.



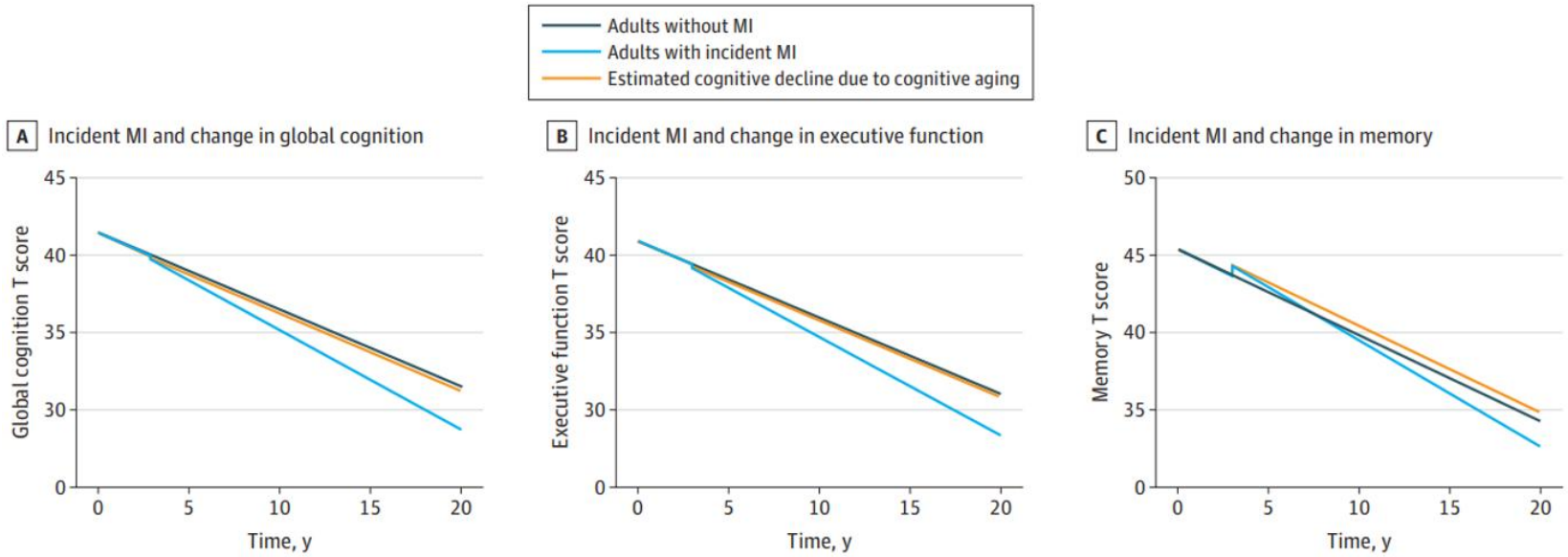
Myocardial Infarction is a risk factor for cognitive decline

JAMA Neurology | Original Investigation

Association Between Acute Myocardial Infarction and Cognition

Michelle C. Johansen, MD, PhD; Wen Ye, PhD; Alden Gross, PhD; Rebecca F. Gottesman, MD, PhD; Dehua Han, MPH; Rachael Whitney, PhD; Emily M. Briceño, PhD; Bruno J. Giordani, PhD; Supriya Shore, MD, MS; Mitchell S. V. Elkind, MD, MS; Jennifer J. Manly, PhD; Ralph L. Sacco, MD, MS; Alison Fohner, PhD; Michael Griswold, PhD; Bruce M. Psaty, MD, PhD; Stephen Sidney, MD, MPH; Jeremy Sussman, MD, MS; Kristine Yaffe, MD; Andrew E. Moran, MD, MPH; Susan Heckbert, MD, PhD; Timothy M. Hughes, MPH, PhD; Andrzej Galecki, MD, PhD; Deborah A. Levine, MD, MPH

Figure 1. Estimated Values of Cognition for the Association Between Incident MI and Change in Global Cognition, Executive Function, and Memory Acutely and in the Years Following the Myocardial Infarction (MI) Event Among 30 465 Participants



Global cognition measures global cognitive performance. All cognitive measures were set to a mean (SD) T score metric (50 [10]) at a participant's first cognitive assessment; a 1-point difference represented a 0.1-SD difference in the distribution of the specified cognitive domain across the 6 cohorts. Higher cognitive scores indicate better performance. Cognitive observations were censored after stroke. Graphs represent a patient who is aged 70 years with a high school education and is a nonsmoker with no alcohol use, no history of atrial fibrillation, no physical activity, no antihypertensive medication use, a body mass index of 27 (calculated as weight in kilograms divided by height in meters squared), a waist circumference of 96 cm, a fasting blood glucose level of 97 mg/dL (to convert to millimoles per liter, multiply by 0.0555), a low-density lipoprotein cholesterol level of 123 mg/dL (to convert to millimoles per liter, multiply by 0.0259), and a cumulative systolic blood pressure of 135 mm Hg.

Pooled data from 6 cohort studies found that incident MI was not associated with a decrease in global cognition, memory or executive function at the time of the event but was associated with faster declines over time.

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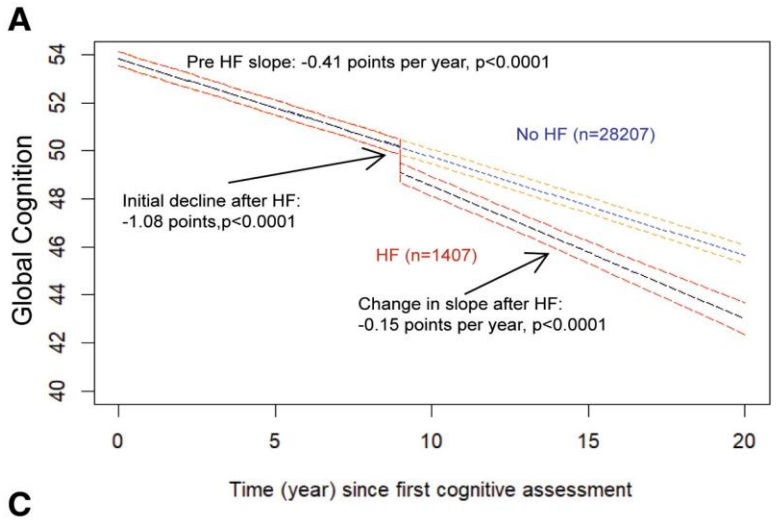
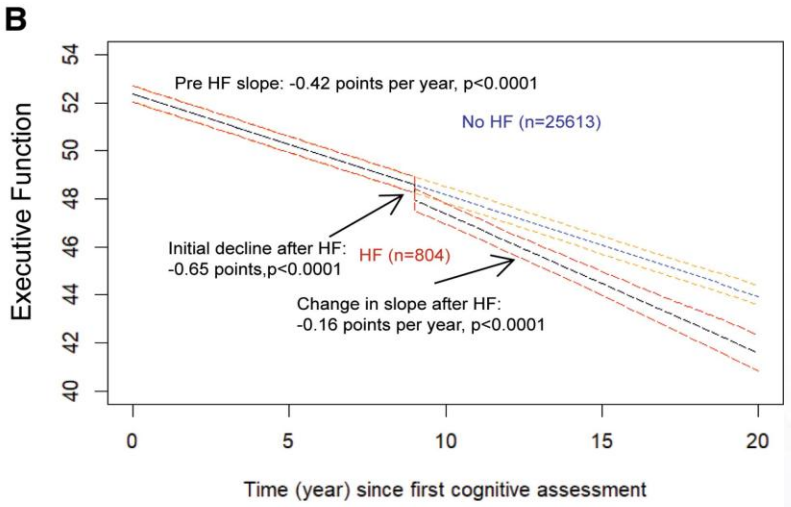
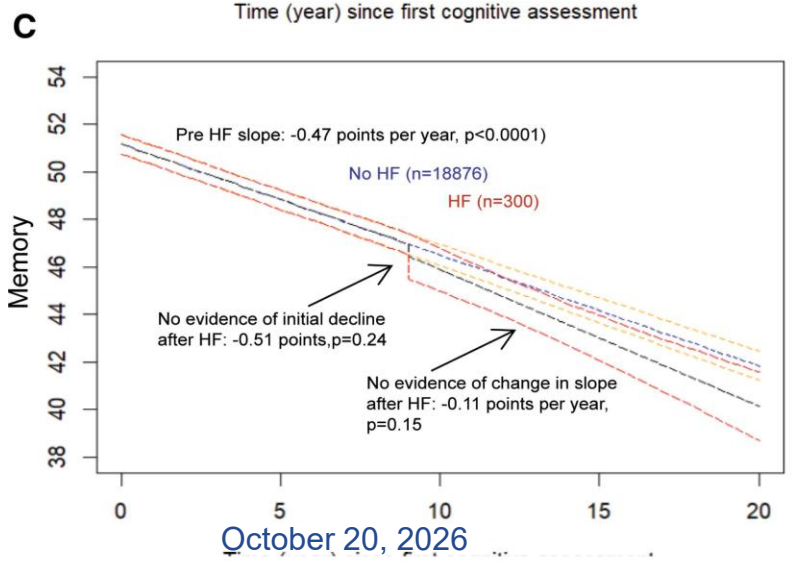
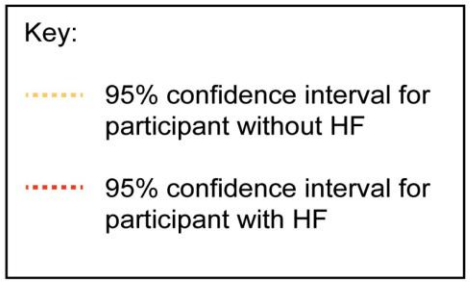
Predicted trajectory of change in cognitive function before and after heart failure









- Study design: Pooled cohort study of 29,614 adults from 6 U.S. population-based studies (1971–2019), excluding participants with baseline HF, stroke, or dementia.
- Methods: Examined cognitive change using linear mixed-effects models, adjusting for pre-HF cognitive trajectories and participant factors; outcomes were global cognition (primary), executive function, and memory.
- **Key findings**: Incident heart failure (5% of participants) was linked to an initial drop in global cognition and executive function, with faster long-term decline in both after HF diagnosis.
- Memory decline after HF was not statistically significant, but showed a similar downward trend.

Shore, et al; Trajectory of Cognitive Function After Incident Heart Failure. Circ Heart Fail. 2025

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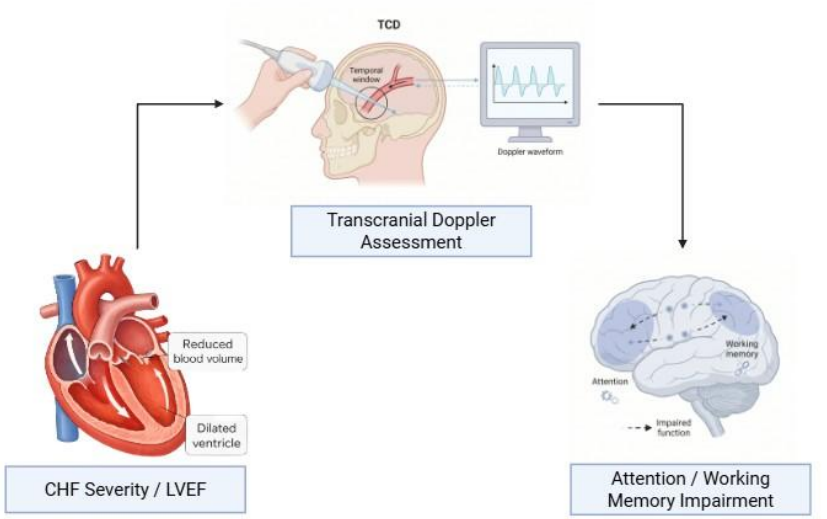
CHF severity, cerebral blood flow and cognition



Sandra Kong, MD
UCLA residency

- Objective: To examine whether markers of CHF severity are associated with domain-specific cognitive performance and cerebral blood flow velocity (CBFV).
- Cohort: Prospective single-center study of 138 decompensated CHF outpatients
- Cognitive outcomes: Standardized neuropsychological battery assessing executive function, attention/processing speed, memory, and visuospatial function.
- Key cognitive finding: Greater CHF severity by NYHA class was associated with poorer attention/working memory on cognitive batteries, but there were no consistent associations across other cognitive domains.
- Hemodynamic finding: Patients with LVEF 40–55% had higher TCD (ICA) CBFV than those with LVEF ≤40%, suggesting a possible relationship between cardiac function and cerebral perfusion.



Kong, et al; Congestive heart Failure and its associations with cognition and cerebral blood flow. Brain Circ. 2025

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Conclusions: A Unifying Framework

- Cardiac disease is strongly linked to cognitive decline and dementia risk through both clinical stroke, and likely cumulative subclinical brain injury
- Associations are seen across:
  - AF
  - atrial cardiopathy
  - heart failure / hemodynamic dysfunction
  - coronary disease and subclinical vascular injury
- Although distinct clinical entities, the associations likely reflect overlapping mechanisms, including:
  - embolism
  - hypoperfusion
  - small vessel injury
  - inflammation/endothelial dysfunction
  - interaction with AD pathology

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Conclusions: Why this Matters

- Cardiac disease should be viewed as part of a brain health prevention framework, not only a cardiovascular issue.
- Subclinical cardiac abnormalities may identify patients at elevated risk for cognitive decline, before overt neurologic disease.
- To move the field forward, we need:
  - improved cardiac phenotyping
  - biomarker-driven risk stratification
  - longitudinal imaging studies in cardiac disease cohorts
  - prevention trials targeting potential cardiac mechanisms of cognitive injury
- Cardiac disease may represent an upstream, potentially modifiable determinant of dementia risk.

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Collaborator & Funding Sources



ARIC



SCAN

JOHNS HOPKINS
WELCH CENTER *for*
PREVENTION, EPIDEMIOLOGY
& CLINICAL RESEARCH

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- American Heart Association
- NINDS, NIA
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- Clark Family
- ARIC study: NIH, NHLBI, NINS, NIA

THE JOHANSEN LAB

Division of Cerebrovascular Neurology
The Johns Hopkins University School of Medicine
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