Atrial Fibrillation and Risk of Dementia: A Prospective Cohort Study.

Background
The estimated cost of Alzheimer’s disease (AD) is $172 billion each year. Multiple risk factors are associated with AD and dementia. Atrial Fibrillation (AF) affects 3 million people in the US, 10% in age>80. AF is a known risk factor for stroke but could it lead to cerebral hypo-perfusion, or in combination with other neuro-pathological processes lower cognitive reserves and hasten the onset of dementia? Of eight longitudinal studies conducted, three have found that AF was associated with greater risk of dementia, whereas five found no association.

Objective
Determine whether AF is associated with risk of incident all-cause dementia or AD in older adults, independent of its effects on clinically recognized stroke.

Methods
• Inclusion criteria – 1 year of GH enrollment, one ACT follow up visit
• Exclusion criteria – history of stroke or TIA, inadequate follow-up
Study Measures
• AF considered present if two different visits in a 12-month period documented ICD-9 codes for AF or Atrial Flutter (Date of AF onset was second encounter).
• Primary outcomes were incident all-cause dementia and possible or probable AD identified through ACT procedures.
• Every 2 years patients were screened using CASI (Cognitive Abilities Screening Instrument). Also, any recent neuroimaging was reviewed if available.
• DSM-IV criteria was used to identify cases of dementia. NINCDS-ADRDA criteria to classify probably AD. Date of dementia onset defined as date halfway between the study visit that triggered dementia evaluation and prior visit.
• Incident strokes were determined from self-report and from inpatient and outpatient ICD-9 codes.
Statistical Analysis
• Used Chi-square test for categorical variables and Wilcoxon rank-sum test for continuous variables. Cox proportional hazards modeling used to estimate adjusted hazard ratios (aHRs) and 95% CI for association between AF and all-cause dementia or AD.
• Final covariates: education, sex, DM, HTN, SBP/DBP, CHD, incident stroke, CHF.

Results
• (Table 1), Median age 74.3, 60% female, 91% white, 38% completed college
• 132 had AF at study entry; additional 370 were diagnosed over a mean of 6.8 years.
• 391 people experienced a stroke (112 who had AF)
• 572 developed dementia (449 with possible/probable AD)
• aHR for all-cause dementia associated with AF was 1.38 adjusted for final covariates
• aHR for possible or probable AD in people with AF than in those without AF was 1.50
• aHR for dementia associated with AF was 1.32 in participants who experienced a stroke during follow up compared with 1.40 in those who did not.
Discussion
In this population study, AF was associated with 40-50% higher risk of AD and all-cause dementia. AF leads to incomplete atrial emptying, which may lead to thrombus formation in the left atrial appendage, which can result in brain embolization. It has been previously reported that cerebral microinfarcts are an important neuropathological predictor of clinical dementia. AF is associated with greater beat-to-beat variability, which may lead to cerebral hypoperfusion. Either of the above mechanisms in combination with neuropathological entities may produce clinical dementia. (Fortuhi’s ‘dynamic polygon’ hypothesis)
AF and AD may share common underlying mechanism, inflammation.

Limitations
1. Criteria for diagnoses of dementia and AD was based on clinical criteria, could have overlapped with Vascular of mixed dementia
2. Transient or asymptomatic cases of AF could have been missed
3. Timing of dementia onset was assumed to be halfway between first workup triggering visit and previous normal visit
4. No information about valvular heart disease or echographic findings was available; could lead to confounding.
5. Study population was predominantly white and well educated.

Summary
The idea of association between AF and AD is interesting because it could potentially be a treatable risk factor, possibly delaying the onset of AD, thus improving quality of life, decreasing caregiver burden, and decreasing healthcare costs. At this time, there is insufficient data from this study to change my practice. Future research should be aimed at comparing rate-controlled patients versus anticoagulated patients, factoring in CHADS2 scores. If this relationship is strong enough, what methods/protocols may be employed to screen and treat atrial fibrillation early to prevent development of dementia?