# Biomarkers Associated with Cardiovascular Risk in the Texas Alzheimer's Research Consortium (TARC) Cohort

Rachelle Doody[1], Wenyaw Chan[1], Christie Ballantyne[1], Valory Pavlik[1], Robert Barber[4], Sid O'Bryant[3], Eveleen Darby[1], Ramon Diaz-Arrastia[2],Thomas Fairchild[4], Donald Royall[5], Perrie Adams[2], and the TARC Investigators

## Background

- Risk factors for vascular disease and AD overlap
- There are scant data regarding the role of LpPLA2, a risk for cardiovascular disease even in the absence of hypercholesterolemia, in AD
- Elevated homocysteine is a powerful risk factor for vascular disease, and is known to be increased in AD. Homocysteine and LpPLA2 may interact to increase AD risk.

## Hypotheses

- TARC participants with probable AD will have a significantly different LpPLA2 levels than non-demented controls
- Homocysteine and LpPLA2 interact to alter the risk of AD
- Prevalent CVD or its risk factors (hypertension, diabetes, smoking) may additionally interact with these markers to affect AD risk.

## Methods

- Case-control design with 197 AD cases and 198 normal controls enrolled in the TARC cohort and examined using standardized procedures.
- Diagnosis of AD based on NINCDS-ADRDA criteria . Controls performed within normal limits on psychometric assessment.
- Serum total Homocysteine (tHcy) concentrations measured using the recombinant enzymatic cycling assay (Roche Hitachi 911).
- LpPLA2 determined using the diaDexus PLAC® sandwich enzyme immunoassay (diaDexus, Inc, San Francisco, CA)
- CVDE classified according to Adult Treatment Panel III guidelines (see Table 1)
- Fischer's exact test (unadjusted) and logistic regression analysis (adjusted) used to assess the association of the CVD risk biomarkers (dichotomized at the median) with case-control status, and interactions among biomarkers and CVDE. Models adjusted for age, sex, and BMI.

**Table 1. Characteristics of Cases and Controls**

| | AD Cases (n=197) | Controls (n=198) | p |
|---|---|---|---|
| | Mean (±SD) or Percent | Mean (±SD) or Percent | |
| **Covariates** | | | |
| Age at Visit | 77.41 (8.29) | 70.42 (8.89) | **<.001** |
| Sex (% female) | 34.52 | 31.82 | .750 |
| BMI (kilos/meters²) | 25.68 (5.06) | 27.48 (4.82) | **<.001** |
| CVD Equivalent* | 48.22 | 46.46 | .726 |
| MMSE | 19.18 (6.22) | 29.42 (0.88) | **<.001** |
| **Biomarkers** | | | |
| Homocysteine | 16.2 (9.01) | 13.3 (5.03) | **< .001** |
| LpPLA2 | 297.0 (71.6) | 281.1 (65.7) | **.02** |

*CVD Equivalent calculated according to Adult Treatment Panel III guidelines (history of MI, stent placement, CHF, diabetes, or any two of HTN, hyperlipidemia, or current smoking)

## Results

- Mean LpPLA2 and homocysteine were both higher in cases than controls.
- Both biomarkers significantly predicted case-control status in adjusted logistic regression models (Figure 1).
- There was no interaction between LpPLA2 and homocysteine in predicting AD status.
- There was a significant LpPLA2 and CVDE interaction (p=.012) in predicting AD status (Figure 2).

## Conclusion

- LpPLA2 may be an independent risk factor for AD.
- Homocysteine was elevated in cases, as expected, but did not interact with LpPLA2 in increasing AD risk.
- The effect of LpPLA2 was mediated by presence of CVDE. Individuals with low LpPLA2 and prevalent CVDE were less likely to have AD, whereas LpPLA2 was not predictive of AD in the absence of CVDE.

**Figure 1. Proportion of Cases and Controls Above the Median for Each Biomarker**

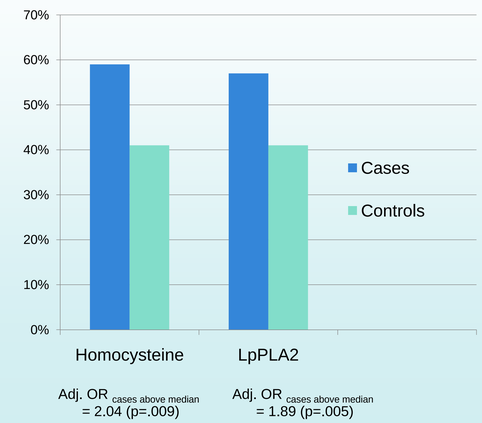
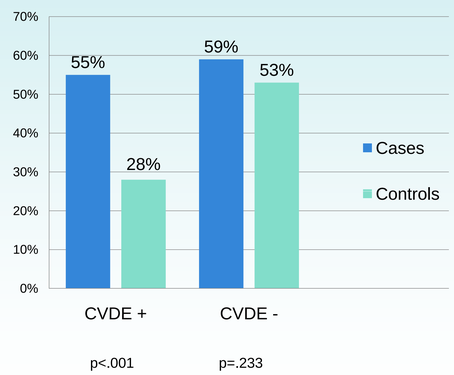



**Figure 2. Proportion of Patients with LpPLA2 Above the Median, by Presence or Absence of CVDE**




TARC Consortium Members: [1]Baylor College of Medicine, [2]UT-Southwestern Medical Center, [3]Texas Tech Health Sciences Center, [4]University of North Texas Health Science Center, [5]UT Health Science Center—San Antonio