

ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #369

1. Title: Cigarette Smoking and MRI Abnormalities

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3. Timeline:

Immediate

4. Background:

Active cigarette smoking has been shown to be a potent risk factor for both clinical stroke¹ and atherosclerosis.^{2,3} ARIC has recently shown both active and passive smoking to be a risk factor for progression of carotid atherosclerosis,⁴ a major risk factor for stroke both through artery-to-artery emboli and thrombosis.^{5,6} There is no (known) data relating cigarette smoking to stroke defined by imaging, white matter abnormalities or atrophy in a bi-ethnic population sample of middle-aged adults.

5. Hypothesis:

That the cross-sectional prevalence of infarctions, white matter abnormalities, and atrophy will be larger with increasing exposure to cigarette smoke.

6. Analysis Plans/Variables:

Three primary outcome variables from the MRI data set will be used: (1) infarctions by MRI, (2) the white matter abnormality score, and (3) the atrophy score. For infarctions the outcome is dichotomous and logistic regression will be employed for analysis. The white matter abnormality scale and atrophy scale will be ranked (mean rank), and linear regression will be used for analysis. For infarctions, two separate analyses will be performed, one for large infarctions (those greater than 3 mm), and a separate analysis for large or small infarctions.

Smoking will be categorized into five categories: never smokers not exposed to passive smoke (N-E), never smokers exposed to passive smoke (N+E), past smokers not exposed to passive smoke (P-E), past smokers exposed to passive smoke (P+E), and current smokers (C). The primary analysis of the paper will focus on increasing prevalence of infarctions, and increasing mean rank score for white matter disease and atrophy, across these five smoking categories. In addition, the average passive smoking effect will be estimated for never plus past smokers. The differences between smoking categories will be estimated after adjustment for:

Smoking Effects Estimated After Adjustment For:

"Demographic Model"	age, race, sex
"Risk Factor Model"	age, race, sex, hypertension, HDL, diabetes
"Lifestyle Model"	age, race, sex, hypertension, HDL, diabetes, BMI, Key's Score, leisure time activity, educational level, alcohol use

This approach will estimate the smoking effect on MRI abnormalities, and then address if these differences are mediated by control for other factors which may differ between smoking groups.

Secondary analysis will address if there is a relationship between MRI abnormalities and: (1) pack-years of exposure in the P-E, P+E, and C groups, and (2) hours of ETS exposure in the N+E and P+E groups.

1. Shinton R, Beevers G. Meta-analysis of the relation between cigarette smoking and stroke. *BMJ* 1989;298:789-794.
2. McGill HC. The cardiovascular pathology of smoking. *Am Heart J* 1988;115:250-257.
3. Homer D, Ingall TJ, Baker HL, et al. Serum lipids and lipoproteins are less powerful predictors of extracranial carotid artery atherosclerosis than are cigarette smoking and hypertension. *Mayo Clin Proc* 1991;66:259-267.
4. Howard G, Burke GL, Szklo M, et al. Active and passive smoking are associated with increased carotid artery wall thickness: the ARIC study. *Arch Intern Med* 1994;154:1277-1282.
5. Dyken ML, Wolf PA, Barnett HJM, et al. Risk factors for stroke: a statement for physicians by the committee on risk factors and stroke of the stroke council. *Stroke* 1984;15:1105-1111.
6. Mas JL, Zuber M. Epidemiology of stroke. *J Neuroradiol* 1993;20:85-101.