ARIC Manuscript Proposal #801

PC Reviewed: 06/05/01 **Status: A** **Priority: 1**
SC Reviewed: _____ **Status: _____** **Priority: _____**

1.a. Full Title: Risk Factors for Peripheral Arterial Disease (PAD), CHD, and carotid atherosclerosis

b. Abbreviated Title (Length 26 characters): PAD, CHD, IMT risk factors

2. Writing Group (list individual with lead responsibility first):

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3. Timeline: First draft by 12/01

4. Rationale: PAD measured by ankle-brachial index (ABI) is a result of atherosclerosis in the lower aorta, the iliac, superficial femoral or popliteal arteries (1). Little is known about whether risk factor patterns differ for atherosclerosis of different major arterial beds. Patterns are similar for CHD and carotid IMT (2), but a substantial body of literature suggests that smoking and diabetes may be more important for severe PAD. For example, smoking appears to be more important for intermittant claudication than for CHD (3). Smoking and diabetes are clearly the primary risk factors for amputation and other manifestations of severe PAD 1515}. Smoking relative risks are also known to be much higher for death from aortic aneurysm than CHD (4). This study will investigate whether smoking or diabetes are more important for asymptomatic PAD than for CHD or carotid thickening. Recent reviews also suggest that triglycerides may be particularly important for PAD (5).

Since atherosclerotic endpoints (PAD, CHD and carotid IMT) are measured with different degrees of accuracy, one cannot compare directly the relative strength of associations of a risk factor like smoking with these different endpoints. The relative strength of risk factors can be compared however, as was done for carotid IMT vs. CHD (2). Mean ABI differs by gender(6), and this clouds the interpretation of gender differences related to ABI. Thus all analyses will be stratified by gender.

Risk factor associations from exam 1 can also be examined in cross-sectional analyses of PAD data from exams 3 and 4.

This proposal does not overlap with previous ARIC publications relating PAD to clinical diseases (7), plasma fatty acids (8), or glutathione S-transferase genes (9). The only previous ARIC proposal relating to major risk factors (243B) has been withdrawn. This proposal does not overlap with proposals for laboratory-based nested case-control studies.

5. Main Hypothesis/Study Questions: (1) Relative to lipids, smoking and diabetes are more strongly associated with PAD measured by ABI than with CHD or carotid IMT. (2) Relative to LDL-cholesterol, triglycerides are more strongly associated with PAD than CHD or carotid IMT**.**

6. Data (variables, time window, source, inclusions/exclusions): PAD, major risk factors, CHD, carotid IMT. Exclude baseline prevalent CHD, non visualized carotid IMT.

7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes _X__ No

8.a. Will the DNA data be used in this manuscript? _Yes __X_ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

___X__ Yes _____ No

References

{1} Carter SA. Indirect systolic pressures and pulse waves in arterial occlusive diseases of the lower extremities. Circulation 1968; 37(4):624-637.
{2} Sharrett AR, Sorlie PD, Chambless LE, Folsom AR, Hutchinson RG, Heiss G, Szklo M. Relative importance of various risk factors for asymptomatic carotid atherosclerosis versus coronary heart disease incidence; the ARIC Study. Am J Epidemiol 1999; 149:843-852.
{3} Gordon T, Kannel WB. Predisposition to atherosclerosis in the head, heart, and legs. The Framingham study. JAMA 1972; 221(7):661-666.
{4} Hammond EC, Garfinkel L. Coronary heart disease, roke, and aortic aneurysm. Factors in the etiology. Arch Environ Health 1969; 19(2):167-182.
{5} Fowkes FG. Epidemiology of peripheral vascular disease. Atherosclerosis 1997; 131 Suppl:S29-31.:S29-S31.
{6} Hiatt WR, Hoag S, Hamman RF. Effect of diagnostic criteria on the prevalence of peripheral arterial disease. The San Luis Valley Diabetes Study. Circulation 1995; 91(5):1472-1479.
{7} Zheng Z-J, Sharrett AR, Chambless LE, Rosamond WD, Nieto FJ, Sheps DS, Dobs A, Evans G , Heiss G. Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis: the ARIC Study. Atherosclerosis 1997; 131:115-125.

{8} Zheng Z-J, Folsom AR, Shahar E, McGovern PG, Eckfeldt JH. Association of plasma fatty acid composition with lower extremity arterial disease: the ARIC Study. Nutrition, Metabolism and Cardiovascular Disease 1997; 7:360-370.
{9} Li R, Folsom AR, Sharrett AR, Couper D, Bray M, Tyroler HA. Interaction of the glutathione S-transferase genes and cigarette smoking on risk of lower extremity arterial disease: the Atherosclerosis Risk in Communities (ARIC) study. Atherosclerosis 2001; 154(3):729-738.