1. Title: Continuous Values of ABI: Risk Factors for Lower Extremity Arterial Disease, and Possible Gender Differences


3. Timeline

   June - September, 1995: Initiation and completion of statistical analyses
   September - December, 1995: Preparation of manuscript

4. Rationale:

   In the majority of studies using low ankle-brachial index (ABI) as a marker of peripheral atherosclerosis, ABI has been dichotomized into disease versus no disease classes based on a cut-point of ABI. Frequently, ABI <= 0.90 has been used to categorically define disease, but other cut-points used include 0.95, 0.85, 0.80, and 1.0.

   The formulation of ankle-brachial ratio as a measure of impairment in the perfusion of the lower extremities lends itself to treatment on an interval or continuous scale. From this, it is postulated that degree of impairment, or severity of LEAD, can be determined, thus avoiding potential arbitrariness of categorical divisions into diseased/non-diseased groups. As a result of using ABI on an interval or continuous scale, a more appropriate modeling approach of the relationship between ABI and its correlates may be provided. Ultimately, this may be important in understanding potential differences in LEAD by sex. Within the small number of studies reporting mean ABI by gender, approximately half the studies showed lower mean ABI in women than men, suggesting higher prevalence of atherosclerosis in the lower extremities in women. This finding is a reversal of the other atherosclerotic vascular diseases found in men compared to women. An explanation to be explored in this analysis is whether the bio-physical properties of blood pressure waves as they travel from the heart to the leg, properties such as wave reflection and amplification, are influenced by gender differences in anatomy, thereby possibly creating low ABI measurements in women unrelated to atherosclerosis.

5. Purpose:

   Building on the categorical analysis already completed by Zheng and colleagues¹, the purpose of this study is to: (1) determine the association between cardiovascular disease risk factors and LEAD, using continuous or interval measurements of ABI as markers of disease, and (2) determine differences between men and women in the associations of these putative etiologic factors with severity of LEAD.

6. Data:

   a) Exposure variables, at Visit 1, singularly and in multivariable context -- cigarette smoking history, hypertension, diabetes mellitus, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, fibrinogen, presence of CHD or cerebrovascular disease at baseline, physical activity, alcohol intake, waist-to-hip ratio, body mass index, measures of socio-economic status, age, menopausal status, estrogen use, height - standing
and seated, presence of intermittent claudication, and variables related to renal function, such as creatinine.

b) Outcome Variable - LEAD, defined by continuous or interval scale measurements of ABI, taken at visit 1.

c) Focused Subgroup - males versus females

7. Analysis Strategy:

Graphic techniques - fit of the brachial systolic blood pressure vs ankle systolic blood pressure; population distributions of ankle sBP, brachial SBP, and ABI; shape and distribution of ABI by tertiles of arm BP; shape and distribution of ABI by risk factor strata, by gender.

Univariate statistics - mean ABI by quartiles or quintiles of potential risk factor, for continuous variables, or by strata of factor, for categorical variables, with and without stratification of arm blood pressure, and with and without stratification by gender.

Regression - regression models to regress putative risk factor on ABI; gender-specific models adjusted for age, alone; adjusted for age as well as for brachial SBP with the addition of an interaction term for risk factor -- brachial SPB; and adjusted for several risk factors simultaneously. Model combining gender, with the addition of a gender - risk factor interaction term.