ARIC Manuscript Proposal # 841

1.a. Full Title: Prevalence And Risk Factors Of Retinal Vein Occlusion And Retinal Arteriolar Emboli: Combined ARIC and CHS Study

b. Abbreviated Title (Length 26 characters): Retinal Occlusions And Emboli

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

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3. Timeline:

   This analysis is part of overall objective to investigate the prevalence and risk factors of retinal vascular disease, based on photographic grading during the ARIC third examination. The prevalence and correlates of retinal microvascular abnormalities and their association with CVD are underway (Klein et al, 1999, 2000, Wong et al, 2001). This proposal will now examine prevalence and risk factors of two uncommon retinal vascular conditions: retinal vein occlusions and retinal arteriolar emboli (Hollenhorst plaque). To increase the power of the analysis, we intend to combine the ARIC and CHS population.

   After approval, assembly of dataset will begin between Jan 2002 and March 2002, initial analyses and writing between April 2002 and October 2002, and final writing and submission of manuscript between November 2002 and Jan 2003.

4. Rationale:

   Retinal Vein Occlusions

   Retinal vein occlusions (RVO) are an important cause of loss of vision. Most of the information regarding RVO has come from clinical case series, case-control studies, and clinical trials. To date, information regarding the prevalence of RVO has been limited. In the population-based Blue Mountains Eye Study, the prevalence of RVO was 1.6%.1 In the Beaver Dam Eye Study, the prevalence of RVO was 0.6%.2 We are unaware of other population-based studies.

   Data from previous non-population-based studies have shown an inconsistent association of RVO with various vascular risk factors, including hypertension, prevalent CVD, diabetes
mellitus and rheological factors (hematocrit). Whether other vascular risk factors, such as inflammation, and carotid artery disease, are related to the development of RVO are unclear.

**Retinal Arteriolar Emboli**

Retinal arteriolar emboli are discrete plaque-like lesions lodged in the lumen of retinal arterioles. These lesions are pathologically heterogeneous, reflective emboli are believed to be composed of cholesterol crystals, whereas nonreflective types are composed of fibrin, platelets, calcium and other materials. Persons with retinal emboli appear to be at higher risk of stroke and mortality from CVD. Studies have reported associations between retinal emboli and atherosclerotic plaques in the carotid artery, cardiac mural thrombi and various systemic vascular and hematological disorders.

However, few population-based data on the epidemiology of retinal embolus and its risk factors are available. In the Blue Mountains Eye Study and the Beaver Dam Eye Study, 1.3 and 1.4% of the population had retinal emboli. The two studies reported associations with cardiovascular risk factors, such as hypertension and cigarette smoking, and less consistently, with diabetes. Associations with other vascular risk factors were not reported.

**Rationale For Combining ARIC And CHS Population**

In ARIC and CHS, RVO and retinal emboli were quantified based on standardized photographic evaluation by the same graders, at the University of Wisconsin, Madison. Combining the retinal data for the proposed study therefore seems a logical approach to increase the power of these analyses (Table).

<table>
<thead>
<tr>
<th>Number with condition</th>
<th>ARIC</th>
<th>CHS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinal vein occlusion</td>
<td>23</td>
<td>17</td>
<td>40</td>
</tr>
<tr>
<td>Retinal emboli</td>
<td>25</td>
<td>9</td>
<td>34</td>
</tr>
</tbody>
</table>

The purposes of the proposed report are to describe the prevalence of RVO and retinal emboli in the combined ARIC and CHS population, and to examine associated vascular risk factors.

5. **Main Hypothesis/Study Questions:**

1. To describe the prevalence of RVO and retinal emboli
2. To describe vascular risk factors of RVO and retinal emboli, including hypertension, diabetes, lipids, inflammatory markers, measures of carotid atherosclerosis and others.

6. **Data (variables, time window, source, inclusions/exclusions):**

1. Main outcome measures: RVO (Central and branch RVO), Retinal emboli (Hollenhorst plaques)
2. Demographic variables: age, sex, race, center, education
3. CVD risk factors: Hypertension status, diabetes status, systolic and diastolic BP, serum lipids (total, HDL and LDL cholesterol, TG, lp(a), apo A1 and B), fasting glucose levels, hemostatic function indicators (von Willebrand factor, factor VIII, fibrinogen, WBC), cigarette smoking indicators (ever/never, current/former/never, pack-years), alcohol indicators, hypertensive medications, diabetic medications, aspirin use, body mass index, waist to hip ratio, sports/leisure/work index, (variables from ARIC visit 1-3, except for lp(a), apo A1 and B, von Willebrand factor, factor VIIIc, and cigarette pack-years, available from ARIC visit 1 only)
Retinal vascular risk factors: Focal retinal microvascular changes include arteriovenous nicking, focal arteriolar narrowing, any retinopathy, retinal hemorrhage and type of hemorrhage (flame-shaped and blot hemorrhage), microaneurysm, soft exudates and hard exudates. Generalized arteriolar narrowing quantified as branch retinal arteriole-to-venular ratio (AVR), central retinal arteriolar equivalent, central retinal venular equivalent.

Prevalent CVD variables: Prevalent CHD, acute MI, silent MI, coronary artery bypass, carotid artery surgery

Exclusion criteria: From participants at ARIC third exam, exclude persons whose race is neither black nor white, if missing retinal photographs or upgradeable photographs.

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

b. If Yes, is the author aware that the file ICTDER01 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used?  ____ Yes  ____ No

(This file ICTDER01 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?  ____ Yes  _X_ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER01 must be used to exclude those with value RES_DNA = “No use/storage DNA”?  ____ Yes  ____ No

References