ARIC Manuscript Proposal # 863

PC Reviewed: 02/13/02	**Status: __A__**	**Priority: __2__**
SC Reviewed: 02/14/02	**Status: __A__**	**Priority: __2__**

1.a. Full Title: The risk of left ventricular hypertrophy associated with moderate kidney dysfunction and anemia among African Americans

b. Abbreviated Title (Length 26 characters): Renal function, anemia and LVH

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

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3. Timeline: The data are available as part of ARIC visits 1 through 3. We project that analyses and manuscript preparation will take place over the next year.

4. Rationale:

The incidence and prevalence of kidney failure in the United States have increased substantially in the past 20 years, with the number of patients treated for kidney failure with dialysis or transplantation reaching over 300,000 by the end of 1997.[1] This number is projected to exceed 650,000 by 2010.[2] There is growing recognition of the much larger number of individuals with moderate kidney dysfunction, recently estimated at 5.6 million (serum creatinine levels 1.6 mg/dL or greater in men and 1.4 mg/dL in women).[3] We recently reported on the association between kidney function and hemoglobin levels in the general population, using data from NHANES III.[4] We found that below an estimated glomerular filtration rate (GFR) of 60 ml/min/1.73m^2, lower kidney function was strongly associated with lower hemoglobin levels and a higher prevalence of anemia. African Americans with moderate kidney dysfunction had an even higher risk of anemia than did their white counterparts. No prospective data are available on this association in patients without severe chronic kidney disease.

Kidney failure is known to cause anemia,[5] and anemia is associated with left ventricular hypertrophy (LVH) among patients receiving chronic dialysis.[6,7] Data on the association of kidney dysfunction and reduced hemoglobin levels with the presence or development of LVH among patients not receiving chronic dialysis are limited. Levin et al found higher serum creatinine and lower hemoglobin levels among patients with prevalent LVH in a cross-sectional

study of 175 patients with chronic kidney disease.[8] A Canadian prospective cohort study showed that lower hemoglobin levels predicted left ventricular growth one year after enrollment among 246 patients with chronic kidney disease.[9] The relationships between kidney function, anemia, and LVH among patients with milder kidney dysfunction have not been studied. Prospective data are especially needed to determine the levels of hemoglobin and kidney function at which individuals may be at increased risk of LVH. Other factors that may be related to LVH among individuals with moderate kidney dysfunction and/or anemia (e.g., sex, hypertension, diabetes mellitus, obesity) have not been identified. The higher prevalence of anemia and LVH among African Americans makes this an important subgroup to study.

ARIC provides an excellent opportunity to explore these associations prospectively. Serum creatinine, as measured at visits 1 and 2, will be used in conjunction with demographic information to estimate GFR as a measure of kidney function.[10] Hemoglobin was measured at each visit. Echocardiograms were performed on 2,445
African-American participants in Jackson, Mississippi at visit 3, providing a reliable measure of the primary outcome. Individuals with LVH at visit 1, as demonstrated by electrocardiographic results[11,12] or responses to the questionnaire, will be excluded from some analyses.

5. Main Hypothesis/Study Questions:

What is the prospective association between declining kidney function and hemoglobin levels among African Americans? What other factors influence this association?

What is the association between moderate kidney dysfunction, hemoglobin level, and the incidence of LVH among African Americans? What other factors influence this association?

Does the presence of both moderate kidney dysfunction and anemia interact to increase the risk of LVH among African Americans?

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

The following variables will be needed for these analyses: age, sex, race, center, serum creatinine, hemoglobin, electrocardiographic results to define LVH (S amplitude in lead V3 and R amplitude in lead aVL), echocardiographic results. Covariates of interest include blood pressure, anthropometric data, and diabetes status. All participants at the Jackson field center will be included.

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 ICTDER02 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 ICTDER02 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 ICTDER02 must be used to exclude those with value RES_DNA = "No use/storage DNA"? **____ Yes ____ 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

Reference List

(1) Excerpts from United States Renal Data System 1999 Annual Data Report. Am J Kidney Dis 1999; 34(2 Suppl 1):S1-176.

(2) Xue JL, Ma JZ, Louis TA, Collins AJ. Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. J Am Soc Nephrol 2001; 12(12):2753-2758.

(3) Coresh J, Wei GL, McQuillan G, Brancati FL, Levey AS, Jones C et al. Prevalence of high blood pressure and elevated serum creatinine level in the United States: findings from the third National Health and Nutrition Examination Survey (1988-1994). Arch Intern Med 2001; 161(9):1207-1216.

(4) Astor BC, Muntner PM, Levin A, Eustace JA, Coresh J. Association of kidney function with anemia: The Third National Health and Nutrition Examination Survey (1988-1994). Arch Intern Med 2001; in press.

(5) Eschbach JW, Adamson JW. Anemia of end-stage renal disease (ESRD). Kidney Int 1985; 28(1):1-5.

(6) Foley RN, Parfrey PS, Kent GM, Harnett JD, Murray DC, Barre PE. Long-term evolution of cardiomyopathy in dialysis patients. Kidney Int 1998; 54(5):1720-1725.

(7) Eschbach JW. The anemia of chronic renal failure: pathophysiology and the effects of recombinant erythropoietin. Kidney Int 1989; 35(1):134-148.

(8) Levin A, Singer J, Thompson CR, Ross H, Lewis M. Prevalent left ventricular hypertrophy in the predialysis population: identifying opportunities for intervention. Am J Kidney Dis 1996; 27(3):347-354.

(9) Levin A, Thompson CR, Ethier J, Carlisle EJ, Tobe S, Mendelssohn D et al. Left ventricular mass index increase in early renal disease: impact of decline in hemoglobin. Am J Kidney Dis 1999; 34(1):125-134.

(10) Levey AS, Greene T, Kusek JW, Beck GJ. A simplified equation to predict glomerular filtration rate from serum creatinine. J.Am.Soc.Nephrol. 11, 155A. 2000.

(11) Molloy TJ, Okin PM, Devereux RB, Kligfield P. Electrocardiographic detection of left ventricular hypertrophy by the simple QRS voltage-duration product. J Am Coll Cardiol 1992; 20(5):1180-1186.

(12) Arnett DK, Rautaharju P, Crow R, Folsom AR, Ekelund LG, Hutchinson R et al. Black-white differences in electrocardiographic left ventricular mass and its association with blood pressure (the ARIC study). Atherosclerosis Risk in Communities. Am Heart J 1994; 74(3):247-252.