AASK Why Is Left Ventricular Hypertrophy So Deleterious?

Lawrence R. Krakoff

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Hypertension, kidney disease, and enlarged hearts have been intertwined since Richard Bright’s observations in the early 19th century. In recent decades, a sequence of epidemiological surveys have revealed that the black population is disproportionately burdened by hypertension, left ventricular hypertrophy (LVH), and chronic progressive renal disease progressing to death, stroke, heart failure, and end-stage renal disease that requires renal replacement therapy, most often dialysis. Once clinical trials established the importance of reducing arterial pressure to prevent both fatal and nonfatal cardiovascular disease and progression of chronic kidney disease, it became imperative to define optimal antihypertensive drug therapy for the many blacks at risk for these diseases. Could any effective antihypertensive drug class do the job? Or would any 1 class, for example, angiotensin-converting enzyme inhibitors, be superior for reducing the disastrously high rate of fatal and nonfatal disease in blacks with hypertensive chronic renal disease, so many of whom had enlarged hearts (LVH) early in their course? The African-American Study of Kidney Disease (AASK) was designed and implemented to provide much needed evidence bearing on these questions.

AASK was a randomized, double-blinded trial enrolling nondiabetic blacks with hypertension with established chronic kidney disease assigned to therapy with a β-blocker, metoprolol, or an angiotensin-converting enzyme inhibitor, ramipril, or a calcium blocker, amlodipine plus other agents to achieve either of 2 blood pressure goals: mean arterial pressure 102 to 107 mm Hg or <92 mm Hg. In 2001, AASK demonstrated that ramipril was clearly superior to amlodipine concerning several renal end points, proteinuria, change in estimated glomerular filtration rate, end-stage renal disease, and death. It was not certain (and remains controversial) as to whether a lower goal for antihypertensive management was superior to the usual goal of <140/90 mm Hg. One could anticipate that AASK would have a high incidence of fatal and nonfatal cardiovascular events, and this expectation was met. Neither antihypertensive drug class nor on-treatment blood pressure level (usual or low) was related to cardiovascular outcomes, but duration of hypertension and electrocardiographic abnormalities were related to these events.

Echocardiography has proven to be far superior to electrocardiography for detection of both LVH and prediction of future cardiovascular disease, but was not included at entry for AASK. The AASK Cohort study enrolled those who completed the original trial without having a renal end point and added echocardiography to the new baseline measurements. Left ventricular dimensions, systolic and diastolic function were derived from the echo assessments to provide far more information about cardiac function than had been previously available. The relationship between the various echocardiographic parameters and either cardiovascular or renal outcomes after a follow-up period of 5 years is reported in this issue of Hypertension. In brief, presence of echo LVH was positively related with cardiovascular outcomes, including heart failure, but not to renal outcomes during this period of observation. Furthermore, abnormal left ventricular diastolic function was significantly related to heart failure admissions.

What accounts for the importance of LVH in predicting higher rates of cardiovascular disease in this and other studies? At baseline, those with LVH in this report had significantly higher systolic blood pressure throughout the entire day compared with those without LVH as revealed by 24-hour ambulatory blood pressure monitoring. The LVH cohort also had higher urinary albumin excretion and previous cardiovascular events. So, the explanation may be that the predictive value of LVH is only the expression of higher arterial pressure and antecedent burden of cardiovascular disease. One alternate view, however, is to suggest that LVH reflects more generalized vascular growth and structure, somewhat independent of arterial pressure. Is the vascular structure and modeling of those with LVH such that current antihypertensive medications are less effective than in those without LVH? I suggest here that LVH as a phenotype be explored as a cause of resistant hypertension, rather than only as a consequence of it.

An association between LVH and increased downstream disease is not new, but the pathways linking the 2 are not well defined by the AASK results. It would be useful to know more about the events constituting the primary cardiovascular outcomes. Death or hospitalization for cardiovascular disease covers much ground. LVH has been linked to sudden cardiac death, ischemic heart disease, atrial fibrillation, and heart failure with either systolic or diastolic dysfunction. Which of these were similar or different in the outcomes for those with or without LVH or diastolic dysfunction in the AASK Cohort? Comparison might be valuable in considering how the results of the AASK Cohort might be translated into therapy directed specifically to LVH apart from antihypertensive medication.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Cardiovascular Center, Icahn School of Medicine at Mount Sinai, New York, NY.

Correspondence to Lawrence R. Krakoff, Cardiovascular Center, Icahn School of Medicine at Mount Sinai, 5 E 98th St, Box 1030, New York, NY 10029. E-mail Lawrence.krakoff@mountsinai.org


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