

AMERICAN SOCIETY OF NEPHROLOGY-ASP JUNIOR DEVELOPMENT AWARD IN GERIATRIC NEPHROLOGY



AWARD RECIPIENT

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PROJECT

"THE EFFECT OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS ON AORTIC STIFFNESS IN ELDERLY PATIENTS WITH CHRONIC KIDNEY DISEASE"

MENTORSHIP TEAM

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Individuals with chronic kidney disease (CKD) are 10 to 100 times more likely to experience cardiovascular (CV) morbidity and mortality, depending on their age and gender. In a sample of patients aged 65 years and older without previous CV complications, it was demonstrated that increased arterial stiffening significantly predicts future CV complications. Worsening CKD (stages 3 to 5) is associated with increased aortic stiffness.

The prevalence of CKD is higher among the elderly. Although more than 7 million people have moderate CKD (stage 3) in the US, only 500,000 survive to the dialysis stage (stage 5), as the majority die of CV complications. Early markers of CV disease would enable clinicians to intervene earlier to prevent and treat risk factors for CV disease in patients with CKD.

Due to the effects of the intimal portion of the vasculature during the normal aging process, the elderly have an increased risk of CV disease. In addition, those with CKD have additional vascular pathology with increased collagen deposition and subsequent decreased elasticity of the medial aspect of their vasculature. This possible additive effect on the vasculature could cause a significant increase in the CV morbidity and mortality in persons over age 65.

Histological findings associated with aortic stiffening are a result of increased collagen deposition. Angiotensin II is involved in increased collagen deposition and release of growth factors in the vascular wall. Inhibitors of angiotensin II, including angiotensin converting enzyme inhibitors (ACE-I), are currently used to control hypertension and delay disease progression of CKD. These well characterized inhibitors present an opportunity to target arterial stiffness.

The goal of this proposal is to investigate the potential for ACE-I to prevent or delay CV disease in older adults with CKD by examining their impact on aortic stiffness in people with stage 3 CKD in a randomized, controlled study. This goal will be achieved by:

1. Comparing vascular stiffening in patients over age 65 with stage 3 CKD to age matched controls.
2. Evaluating the effect of ACE-inhibitors on aortic stiffness as measured by pulse wave velocity at baseline and 12 months in patients older than 65 years of age with stage 3 CKD.
3. Evaluating the effects of ACE-I on clinical and subclinical markers of CV disease in stage 3 CKD.

My long term career goal is to become an academic nephrologist leading a clinical research program investigating vascular stiffness in patients with CKD. Aortic stiffness in the geriatric population is the first step for further evaluation of the cardiovascular abnormalities unique to this population of CKD patients. Not only can this concept be expanded into a larger clinical trial, but it can also evolve into translational research with investigation into the pathophysiology of uremic changes in the vasculature at a cellular and molecular level. Reaching these long-term career goals are attainable through the American Society of Nephrology-ASP Junior Career Development Award in Geriatric Medicine and the continued support of my expert mentoring team of Bryan N. Becker, MD, Molly Carnes, MD, and Nancy Sweitzer, MD, PhD.