Relationship of femoral artery ultrasound measures of atherosclerosis with chronic kidney disease

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ABSTRACT

Background: Chronic kidney disease (CKD) is strongly associated with peripheral artery disease (PAD). Detection of subclinical PAD may allow early interventions for or prevention of PAD in persons with CKD. Whether the presence of atherosclerotic plaque and femoral intima-media thickness (IMT) are associated with kidney function is unknown.

Methods: We performed a cross-sectional observational study of 1029 community-living adults. We measured superficial and common femoral artery IMT and atherosclerotic plaque presence by ultrasound. Estimated glomerular filtration rate (eGFR; continuous) and eGFR <60 mL/min/1.73 m^2 (binary) were evaluated as outcomes.

Results: Mean age was 70 ± 10 years, mean eGFR was 78 ± 17 mL/min/1.73 m^2, and 156 (15%) individuals had eGFR <60 mL/min/1.73 m^2; 260 (25%) had femoral artery plaque. In models adjusted for demographics and cardiovascular risk factors, individuals with femoral artery plaque had mean eGFR approximately 3.0 (95% confidence interval, −5.3 to −0.8) mL/min/1.73 m^2 lower than those without plaque ($P < .01$). The presence of plaque was also associated with a 1.7-fold higher odds of eGFR <60 mL/min/1.73 m^2 (95% confidence interval, 1.1-2.8; $P < .02$). Associations were similar in persons with normal ankle-brachial index. The directions of associations were similar for femoral IMT measures with eGFR and CKD but were rendered no longer statistically significant with adjustment for demographic variables and cardiovascular disease risk factors.

Conclusions: Femoral artery plaque is significantly associated with CKD prevalence in community-living individuals, even among those with normal ankle-brachial index. Femoral artery ultrasound may allow evaluation of relationships and risk factors linking PAD and kidney disease earlier in its course. (J Vasc Surg 2018;67:1855-63.)

Chronic kidney disease (CKD) is associated with peripheral artery disease (PAD).[1] CKD and PAD both independently increase the risk for cardiovascular disease (CVD) events and contribute significantly to morbidity and mortality.[2-5] PAD prevalence in patients with end-stage renal disease is high even after adjusting for traditional CVD risk factors. Yet, the mechanisms linking CKD and PAD remain poorly understood.[1,6,7]

The ankle-brachial index (ABI) has been the standard screening test for PAD for more than four decades.[8] However, it may be insensitive to "preclinical" PAD, that is, evidence of atherosclerosis and vascular dysfunction in the femoral artery that develops earlier in the course of the disease than an abnormally low ABI, as it requires occlusive plaque that is sufficient to decrease distal blood pressure. Using the ABI is particularly problematic in persons with CKD as they have high prevalence of stiff peripheral arteries, which decreases the ABI's sensitivity.[8-12] Multiple studies have shown that both asymptomatic PAD and borderline normal ABI values (0.90-1.00) are associated with decreased functional status and loss of mobility.[8-10] Earlier detection of preclinical PAD would allow preventive measures to delay renal function decline and associated morbidity. Moreover,

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early detection may allow new opportunities to understand mechanisms linking CKD and PAD at an earlier stage of both diseases.

Ultrasound of the peripheral arteries provides a noninvasive method to detect early atherosclerotic changes.[11] Ultrasound of the femoral artery may allow early detection of subclinical PAD even in persons with normal ABIs and in populations with stiff arteries as seen in CKD.[12] Greater femoral intima-media thickness (IMT) has been associated with both traditional and novel CVD risk factors in asymptomatic adults.[13-15] Similarly, ultrasound detection of plaque in the femoral artery has been linked to higher coronary calcium scores and CVD events.[16-21]

Little is known about the relationship of femoral artery ultrasound measures of PAD with kidney function. One study found that longitudinal plaque progression was associated with CKD progression in a population with prevalent CKD.[22] However, these individuals were enrolled from CKD clinics. No studies, to our knowledge, have examined the relationship of plaque and IMT with CKD in the general population. This is important, as early detection of femoral atherosclerosis and CKD may prove significant for prevention interventions. Thus, we examined the association of femoral artery plaque and IMT by ultrasound with estimated glomerular filtration rate (eGFR) and CKD in a community-living older population. We hypothesized that femoral artery plaque presence and greater femoral artery IMT would be associated with lower eGFR and greater prevalence of CKD.

ARTICLE HIGHLIGHTS

- **Type of Research:** Cross-sectional observational study
- **Take Home Message:** In 1029 community-living adults with a mean age of 70 ± 10 years, femoral artery plaque, found on ultrasound, was associated with chronic kidney disease, even in patients with normal ankle-brachial indices.
- **Recommendation:** This study suggests that femoral artery ultrasound can be used as an early test to identify peripheral artery disease in those with chronic kidney disease.

METHODS

Participants. The San Diego Population Study is a prospective population-based cohort designed to assess the prevalence and incidence of both chronic venous disease and PAD; it is described in detail elsewhere.[23] Briefly, a multiethnic group of individuals who were current and former employees of the University of California San Diego were invited to participate. Between 1994 and 1998, 6115 individuals were randomly selected and 2404 persons presented for the baseline visit. Persons of African American, Asian, and Hispanic descent and women were oversampled to increase the statistical power for contrasts by race/ethnicity and gender. Between 2007 and 2011, we conducted a follow-up clinical examination. Using the Social Security Death Index, we determined that 199 had died since the baseline visit. Of the remaining 2205 persons contacted, 1103 returned for the follow-up examination. Blood samples and ultrasound imaging of the femoral arteries were obtained at the second visit and used for this study. The Institutional Review Board at the University of California San Diego approved the study. All subjects gave informed consent.

Ultrasound protocol and vascular measurements. An Acuson Aspen ultrasound device (Siemens Corporation, Mountain View, Calif) was used to image 10-mm segments of two femoral artery sites on the left and right legs: at the common femoral artery (CFA) as it emerged from under the inguinal ligament proximal to its bifurcation into the deep femoral and superficial femoral branches; and at the superficial femoral artery (SFA) distal to the bifurcation. Five-second image clips were obtained at an angle of insonation of 90 degrees.

Four trained ultrasound technicians used software to measure the femoral IMT and to determine femoral plaque presence. Quality control monitoring was performed at regular intervals throughout the study using the ultrasound images from 10 to 20 participants repeatedly by different readers. Both inter-reader and intra-reader intraclass correlations were >80% for CFA IMT and >75% for SFA IMT. Spearman correlations for both inter-reader and intra-reader were >0.89 for CFA IMT and >0.70 for SFA IMT.

The femoral IMT was defined, as in prior studies, as the combined thickness of the intima and media layers, from the leading edge of the intima-lumen border to the leading edge of the media-adventitia border.[13,24] As it provided the best images with the least amount of noise, the IMT measurement was taken from the far (posterior) arterial wall. The higher of the two leg IMTs was used for the statistical analysis.

Plaque presence was defined by the Mannheim consensus criteria as a focal structure that encroaches into the arterial lumen at least 0.50 mm or 50% greater thickness relative to the surrounding IMT or demonstrates a thickness >1.5 mm as measured from the media-adventitia border to the intima-lumen border.[18,25] For some arterial segments, clear visualization of plaques was limited because of the presence of artifact. These were classified as probable plaques. The software used to analyze the ultrasound images was Carotid Analyzer from the software suite Vascular Research Tools 5 (Medical Imaging Applications LLC, Coralville, Iowa).

ABI measurement. With the subject resting in the supine position, continuous-wave Doppler ultrasound (LifeDop; Wallach Surgical Inc, Trumbull, Conn) was used