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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 for early interventions 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 among 1,029 community-living adults. We measured superficial (SFA) and common femoral artery (CFA) IMT and atherosclerotic plaque presence by ultrasound. Estimated glomerular filtration rate (eGFR; continuous) and eGFR < 60 ml/min/1.73m^2 (binary) were evaluated as outcomes.

Results—Mean age was 70 ± 10 years, mean eGFR was 78 ± 17 ml/min/1.73m^2 and 156 (15%) individuals had eGFR <60. Two-hundred sixty (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% CI −5.3, −0.08) ml/min/1.73m^2 lower than those without plaque (P <0.01). The presence of plaque was also associated with a 1.7 fold higher odds of eGFR

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< 60 (95% CI 1.1, 2.8; P <0.02). Associations were similar in persons with normal ankle brachial index (ABI). The directions of associations were similar evaluating associations of femoral IMT measures with eGFR and CKD, but were rendered no longer statistically significant with adjustment for demographic variables and CVD risk factors.

Conclusions—Femoral artery plaque is significantly associated with CKD prevalence in community-living individuals, even among those with normal ABI. Femoral artery ultrasound may allow evaluation of relationships and risk factors linking PAD and kidney disease earlier in its course.

INTRODUCTION

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 (ESRD) 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 over four decades.[8] However, it may be insensitive to “pre-clinical” 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] Multiples 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 pre-clinical PAD would allow for preventative measures to delay renal function decline and associated morbidity. Moreover, early detection may allow new opportunities to understand mechanisms linking CKD and PAD at an earlier stage of both diseases.

Ultrasonography of the peripheral arteries provides a non-invasive 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, ultrasonographic detection of plaque in the femoral artery has been linked to higher coronary calcium scores and CVD events.[16–21]

Little is known regarding 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 examine the relationship between plaque and IMT with CKD in the general population. This is important, as early detection of femoral atherosclerosis and CKD may prove important for prevention interventions. Thus, we examine the association between femoral artery plaque and IMT by ultrasound with 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.

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, and is described in detail elsewhere.[23] Briefly, a multi-ethnic group of individuals who were current and former employees of the University of California San Diego were invited to participate. Between 1994 and 1998, 6,115 individuals were randomly selected and 2,404 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 2,205 persons contacted, 1,103 returned for the follow-up exam. 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, CA) was used to image 10 mm segments of two femoral artery sites on the left and right legs: 1) 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 2) 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 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- and intra-reader intraclass correlations were >80% for common femoral IMT, and >75% for superficial femoral IMT. Spearman correlations for both inter- and intra-reader were >0.89 for common femoral IMT and >0.70 for superficial femoral 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 encroaching into the arterial lumen at least 0.50 mm or 50% greater thickness relative to the surrounding IMT, or 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 due to 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, IA).

ABI Measurement

With the subject resting in the supine position, continuous-wave Doppler ultrasound (LifeDop, Wallach Surgical Inc, Trumbull, CT) was utilized to measure the SBP twice at the same setting in both brachial arteries, and twice in both the dorsalis pedis and the posterior tibial arteries of each leg. The ABI for each side was calculated as the higher average SBP of the posterior tibial or dorsalis pedis divided by the highest average arm SBP. The higher arm SBP was used in these calculations due to previous studies showing a strong association between PAD and subclavian stenosis.[26] The lower of the two leg ABIs was used as the index ABI for that participant.

We defined three ABI categories: low (<0.9), normal (0.90 – 1.30) and high (>1.30). Low ABI was defined as <0.90 on the basis of studies showing high sensitivity and specificity for angiographic PAD at this cut point and an association with CVD morbidity and mortality.[5,27] Although the optimal cut point for high ABI is unknown, prior studies have defined a high ABI as >1.30, and shown its association with poorly compressible arteries and presence of medial arterial calcinosis.[28–31]

Kidney Function

Non-fasting blood specimens were collected, stored at −80° Celsius, transferred to a laboratory and analyzed within 24 hours. Serum creatinine levels were measured using a Roche Cobas 6000 analyzer (Roche Diagnostics Corporation, Indianapolis, IN) and calibrated to the isotope dilution mass spectrometry standard. The eGFR was calculated using the CKD-EPI equation.[32] CKD was defined by an eGFR < 60 ml/min/1.73m^2.[33] Urine albumin to creatinine ratio was not available in this study.

Other Measures

Age, sex, race/ethnicity, cigarette smoking history and medical co-morbidities were determined by self-report. Medication use was determined from bottles or medication lists provided by the participants. We defined use of anti-hypertensive medications to include beta-blockers, calcium-channel blockers, diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers and other medications used specifically to control hypertension. Diabetes was defined by self-report or use of glucose lowering medications including insulin. Hypertension was defined by a seated systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or treatment for hypertension. Height and weight obtained in light clothing and without shoes were used to calculate body mass index (BMI) as kg/m^2. The Roche Cobas 6000 analyzer (Roche Diagnostics Corporation, Indianapolis, IN) was used to determine total and high density lipoprotein (HDL) cholesterol concentrations measured via direct enzymatic assay.[34,35] Low density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation.[36]

Statistical Analysis

In the main analysis, we combined persons with probable or definite plaque and compared to others with no evidence of plaque. We compared the distribution of demographic data and clinical characteristics using t-tests for continuous variables and the Chi-squared test for categorical variables. Similarly, we divided participants into three mutually exclusive ABI categories and compared their eGFR and vascular measures using analysis of variance (ANOVA) or Chi-squared tests. Unless the specific femoral artery segment was noted, plaque presence was defined as evidence of at least 1 plaque in any of the left or right CFA or SFA.

We then used linear regression to evaluate the associations between the femoral ultrasound measurements with eGFR. Logistic regression was used to evaluate the association of the femoral ultrasound measurements with CKD. In both cases, we used the identical series of models. The initial model was unadjusted; a subsequent model adjusts for age, sex and race/ethnicity, and a final model also including total cholesterol, HDL, BMI, systolic blood pressure, diabetes, smoking, and anti-hypertensive and statin medication use. For all models, participants without any femoral artery plaque served as a reference to compare the difference in eGFR or odds of CKD in those with plaque. Similarly, participants with a normal ABI were used as a reference to compare differences seen with low and high ABI measurements. All statistical analyses were conducted using Stata version 14.1 (StataCorp LP, College Station, TX), and two sided p-values < 0.05 were considered statistically significant.

RESULTS

The 1,307 study participants seen at the follow-up visit from which this data was derived were of similar age, gender and race distribution compared to those who did not attend the follow-up exam, but had lower rates of CVD likely driven by those who died in the interim (5.9% vs. 10.9%; data not shown). Of the 1,103 study participants, 37 were missing femoral ultrasound imaging, 13 were missing ABI measurements and 24 were missing serum creatinine measurements, leaving 1,029 participants as the analytic sample for this study. The mean age was 70 ± 10 years, 67% were female, 59% were Caucasian, 12% were African American, 14% were Hispanic, and 14% were Asian or other race/ethnicities. The mean eGFR was 78 ± 17 ml/min/1.73m^2 and 15% (n=156) had CKD. Overall, 256 (25%) participants had femoral artery plaque, whereas plaque prevalence was much higher (n=71, 46%) among those with CKD. The mean CFA and SFA IMT measurements were 0.99 ± 0.61 mm, and 0.63 ± 0.16 mm, respectively.

Individuals with femoral artery plaque were older, and more likely to be male and Caucasian (Table I). They also had a higher prevalence of hypertension, diabetes and PAD, higher systolic blood pressure, lower diastolic blood pressure, and lower eGFR.

Persons with low ABI had the highest prevalence of femoral artery plaque (76%), followed by those with high ABI measurements (42%), and prevalence was lowest in those with a normal ABI (23%). Results were similar when examining the CFA and SFA plaque separately (Figure 1). Results were also similar when evaluating the CFA and SFA IMT,

where persons with low ABI had the highest mean IMT (CFA = 1.72 mm; SFA = 0.79 mm), those with high ABI had intermediate IMT (CFA = 1.42 mm; SFA = 0.69 mm), and those with normal ABIs had the lowest mean IMT (CFA = 0.95 mm; SFA = 0.62 mm) (Table II).

When compared to individuals without femoral artery plaque, the presence of plaque in any of the four femoral arteries was associated with a 9.2 ml/min/1.73m^2 lower eGFR in the unadjusted model (Table III). When adjusted for age, sex and race/ethnicity, the association of any plaque remained significantly associated with lower eGFR. Results remained similar in the fully adjusted models, such that individuals with any plaque had mean eGFR approximately 3.0 ml/min/1.73m^2 lower (95% CI −5.3, −0.8), on average, than those without plaque. Importantly, results were similar in analyses limited to persons with ABI between 0.90–1.30 (Supplemental Table I).

Results were similar when evaluating the CFA plaque, whereas the association of SFA plaque presence was attenuated and no longer statistically significant when adjusted for age, sex, and race/ethnicity. Age was the major confounding factor in attenuating the relationship between femoral artery plaque presence and eGFR (Figure 2).

In sensitivity analyses, we evaluated associations of the number of femoral artery plaques with the severity of eGFR lowering, but did not find a clear monotonic relationship (Supplemental Table II). We also evaluated probable and definite plaques as separate categories and found similar results to our main analysis combining both probable and definite plaques together (data not shown).

Thicker CFA and SFA IMT were also associated with a lower eGFR in an unadjusted model, where each SD higher CFA or SFA was associated with approximately 2 ml/min/1.73m^2 lower eGFR. However, when adjusted for age, sex, and race/ethnicity these associations were attenuated and no longer statistically significant.

Last, we evaluated associations between the same vascular measures with odds of CKD (Table IV). Similar to the models described above, plaque prevalence and IMT were associated with greater odds of CKD in unadjusted models. In the fully adjusted model, the association of the IMT with CKD was attenuated. In contrast, any plaque prevalence and common femoral plaque prevalence remained statistically significantly associated with 1.7 to 1.8 fold greater odds of CKD in fully adjusted models.

DISCUSSION

The principal findings of this study are that the presence of femoral artery plaque determined by duplex ultrasound is associated with significantly lower eGFR and higher odds of CKD prevalence in community-living, older adults. These associations remained evident even among persons with normal ABI measurements. Conversely, while femoral artery IMT had similar associations with eGFR and CKD prevalence in unadjusted models, the associations were attenuated and rendered no longer statistically significant in fully adjusted models.

Multiple prior studies show that clinical PAD, the progressive arterial obstruction of the lower extremity arteries by atherosclerosis, is associated with lower eGFR.[1,7] However, our

finding that subclinical femoral artery plaque is associated with greater odds of CKD in a community-living population with predominantly normal kidney function suggests that the processes that link lower extremity artery disease and kidney disease may start early, prior to symptom onset or an abnormally low ABI. Furthermore, we show that this association at an earlier time point is readily detectable with femoral ultrasound. PAD and CKD are highly prevalent in the community, each is an independent risk factor for CVD and mortality, and those with both diseases concurrently are at a higher risk of mortality than those affected by one condition alone.[37,38] Our data opens the possibility that early detection of subclinical PAD may provide new insights to factors linking CKD and PAD, and suggests that femoral ultrasound might ultimately allow early and targeted preventive measures to prevent or delay development of clinically apparent PAD in persons with CKD.

We also found a higher prevalence of femoral plaque in individuals with either a low or a high ABI measurement relative to those with normal ABI. This finding supports the hypothesis that high ABI measurements are not “normal”. Many such individuals may have underlying atherosclerotic PAD that may be missed by a normal or high ABI measurement.[39–41] Existing data suggest that the etiology of peripheral artery stiffening known as medial artery calcification (MAC) may be a distinct pathophysiologic process separate from atherosclerosis, as MAC is not associated with traditional CVD risk factors or inflammation, and is not flow limiting.[42–44] This does not mean, however, that these two disease processes cannot exist concomitantly.[45] We and others have used the toe brachial index (TBI) as a method to determine the underlying flow limiting PAD in individuals with high ABIs in prior studies.[46] However, TBI measurements show greater intra-individual variability, as they can be influenced by vasospasm in toe arteries, and a low TBI may reflect either small vessel disease in toe arteries, or larger vessel PAD in the proximal leg arteries.[47] The findings of this study suggest that femoral artery plaque measurements may provide an alternative method to determine whether persons with normal or high ABI measurements may have underlying PAD nonetheless, and whether CKD may be a contributor in its pathogenesis.

Several lines of evidence support the notions that subclinical atherosclerosis is most likely identified in the femoral arteries[17,48] and that femoral artery plaque is independently associated with CVD events and coronary heart disease death.[18,20,21,49] In a cohort of 1,423 healthy middle-aged men, Laclaustra et al. showed that femoral plaques were more common than carotid artery plaques (54% vs. 34%), and had a stronger association than carotid plaques with known CVD risk factors and with coronary artery calcification.[17] Notably, this study investigated asymptomatic community-living individuals, and found plaque prevalence much higher than expected in individuals otherwise considered to be at low risk for atherosclerosis. Evidence also suggests femoral ultrasound may provide a sensitive test for subclinical PAD. In our study, we found that 23% of participants with a normal ABI had evidence of femoral artery plaque by ultrasound. Flanigan et al showed the sensitivity of the ABI in detecting lower extremity atherosclerosis was only 17% when using femoral ultrasound as the standard for screening, but the sensitivity of femoral ultrasound was 100% when using ABI as the screening standard.[12] They suggest ultrasound is a superior screening tool for the detection of early lower extremity vascular disease.[17,48] Recently, Gracia et al. evaluated 1,553 persons with CKD who underwent carotid and femoral ultrasound at

baseline and after 24 months. Participants in this study were enrolled from CKD clinics, thus whether results are generalizable to other populations, particularly community-living individuals as studied here, was uncertain. Nonetheless, similar to our findings, they noted a high prevalence of atherosclerotic plaque among persons with CKD (68.7%) and found that plaque progression was associated with concurrent CKD progression.[22]

In sum, our findings, and the findings in these prior studies suggest that femoral artery ultrasound measurements may provide a sensitive marker of atherosclerotic disease burden and a method to determine the vascular consequences in early stages of CKD. Although we lack long-term outcomes data, we believe femoral artery ultrasound has promise and may be used for subclinical PAD screening in the future. We would likely advocate for using it in patients with normal or high ABI. Those with low ABI are very likely to have flow limited atherosclerotic PAD, and the added value of the femoral ultrasound is uncertain. Similarly, given the association between femoral plaque and kidney disease found in this study and the minimally invasive nature of a blood test, it seems reasonable to check a serum creatinine if this is discovered.

Strengths of this study include the relatively large study sample and good representation of women and minorities all in a community-living population. This is the first study to examine the relationship of femoral artery ultrasound measures with eGFR in a community-living population, and not sampled based on prevalent CKD. By comparison, prior studies that examine associations between femoral plaque and CVD events have been small and/or limited to Caucasian men.[17,18,20] To our knowledge, this is the first study to examine relationships of femoral artery ultrasound measures with CKD prevalence in a community-living population. The concurrent availability of ABI measurements and traditional CVD risk factors are additional strengths.

This study also has important limitations. The cross-sectional design precludes determination of whether femoral artery measures of PAD precede CKD or vice versa. The point estimate for the association of superficial femoral IMT with eGFR was −0.4 (−1.4, 0.6), which suggests a possible association but is not statistically significant. One likely explanation is that the study was underpowered. Alternatively, the femoral IMT measurements are technically challenging and some measurement error may have accounted for weaker associations. Lastly, factors leading to plaque formation may not be identical to those leading to femoral IMT, so biological pathways may be different. Although we did not find a statistically significant association between femoral IMT and kidney function in fully adjusted models, it remains possible that such an association may exist in those with more severe kidney disease. Future studies should assess for associations between femoral ultrasound vascular measures and change in eGFR over time, and whether femoral artery ultrasound might identify prevalent PAD in persons on dialysis with high ABI measurements. Such studies may ultimately allow improved monitoring of PAD, preventative interventions, and may hold promise to prevent lower limb infections and amputations.

In conclusion, among community-living individuals, femoral artery plaques identified by ultrasound are independently associated with lower eGFR and higher odds of CKD. This

association was evident even in persons with normal ABI measurements. Although persons with low ABI had the highest prevalence of femoral artery plaque, many persons with normal or high ABI also had femoral artery plaque. Femoral ultrasound may provide a non-invasive method to detect PAD earlier in its course where closer surveillance and or life-style or medication management may prevent progression of CKD. Moreover, femoral artery ultrasound may hold promise to identify atherosclerotic PAD in populations characterized by stiff peripheral arteries, where the ABI may lack sensitivity for detection of atherosclerotic PAD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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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 those asymptomatic patients at risk of chronic kidney disease.

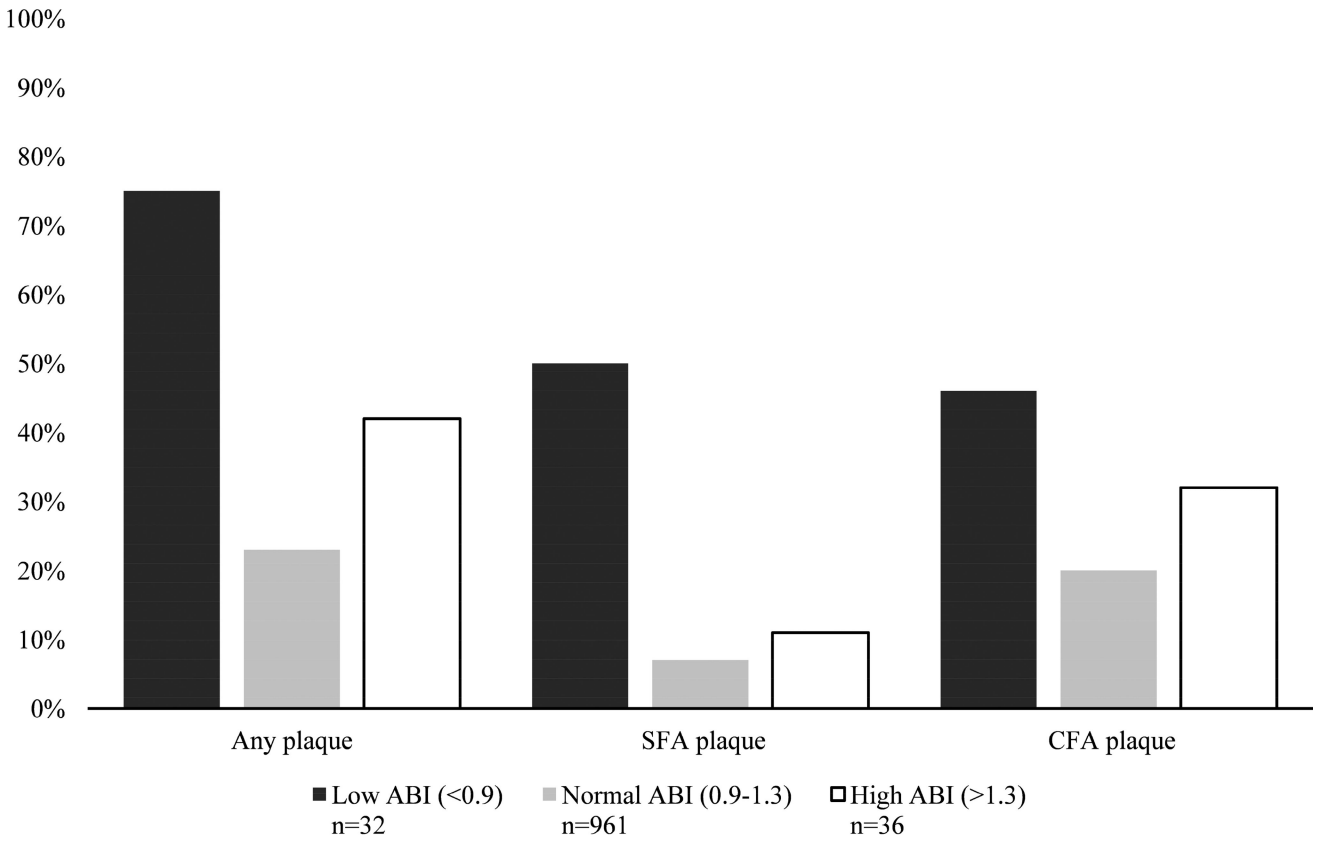

Figure 1. Femoral Artery Plaque Prevalence by ABI Categories

ABI = ankle-brachial index; SFA = superficial femoral artery; CFA = common femoral artery Any plaque defined as detection of plaque by ultrasound in any of the left or right common femoral or superficial femoral arteries; P <0.001 for all

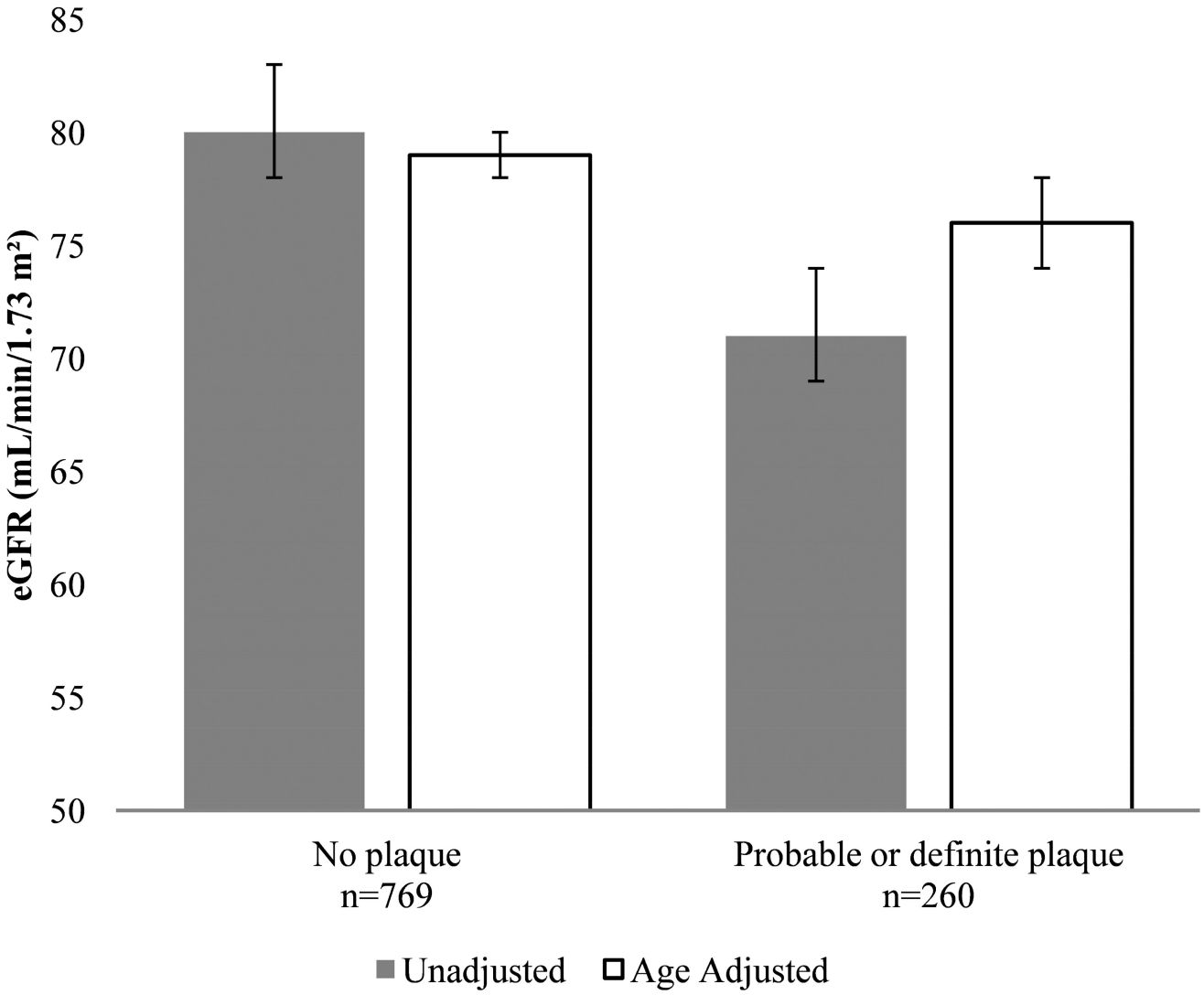

Figure 2. Estimated glomerular filtration rate (eGFR) by femoral artery plaque presence

Plaque presence defined as detection by ultrasound in any of the left or right common femoral or superficial femoral arteries; Error bars show 95% confidence intervals

Table I

Baseline Characteristics by Femoral Artery Plaque Presence

	Plaque Presence[a]		
	None (n = 769, 75%)	Probable or Definite (n = 260, 25%)	p-value
Age (years)	68 ± 9	75 ± 9	<0.001
Female	528 (69%)	160 (62%)	0.035
Race			<0.001
White	423 (55%)	186 (72%)	
Black	103 (13%)	22 (8%)	
Hispanic	126 (16%)	21 (8%)	
Other	117 (15%)	31 (12%)	
Smoking, current or ever	240 (31%)	105 (41%)	0.017
BMI (kg/m^2)	27 ± 5	26 ± 5	0.003
Hypertension	445 (58%)	196 (75%)	<0.001
Diabetes	66 (9%)	37 (14%)	0.009
Systolic BP (mmHg)	130 ± 18	135 ± 19	<0.001
Diastolic BP (mmHg)	76 ± 10	73 ± 10	<0.001
eGFR (mL/min/1.73 m^2)	81 ± 16	71 ± 19	<0.001
CKD[b]	85 (11%)	71 (27%)	<0.001
Total Cholesterol (mg/dL)	199 ± 40	191 ± 40	0.006
HDL (mg/dL)	61 ± 21	59 ± 21	0.34
PAD[c]	10 (1%)	25 (10%)	<0.001
ABI			
Mean	1.15 ± 0.13	1.11 ± 0.23	0.002
Normal (0.9–1.3)	740 (96%)	221 (85%)	<0.001
Low (<0.90)	8 (1%)	24 (9%)	<0.001
High (>1.3)	21 (3%)	15 (6%)	<0.001

Continuous data are presented as mean ± standard deviation, categorical data as number (%)

BMI = body mass index; PAD = peripheral artery disease; BP = blood pressure eGFR = estimated glomerular filtration rate; HDL = high density lipoprotein; LDL = low density lipoprotein; ABI = arterial-brachial index

[a] Evidence of plaque as detected by ultrasound in any of the left or right common femoral or superficial femoral arteries

[b] eGFR <60 mL/min/1.73 m^2

[c] Clinically diagnosed PAD

Table II

eGFR, Femoral Intima-Media Thickness and Plaque Presence by ABI Categories

		ABI Categories[a]			
		Low (<0.9) (n = 32)	**Normal (0.9 – 1.3) (n = 961)**	**High (> 1.3) (n = 36)**	**p-value**
eGFR (mL/min/1.73 m^2)		67 ± 23	79 ± 17	74 ± 16	<0.001
Superficial Femoral IMT (mm)[b]		0.79 ± 0.40	0.62 ± 0.15	0.69 ± 0.17	<0.001
Common Femoral IMT (mm)[b]		1.72 ± 1.22	0.95 ± 0.51	1.42 ± 1.23	<0.001
Plaque present[c]					<0.001
	Probable or Definite (n=260)	24 (76%)	221 (23%)	15 (42%)	
	None (n=769)	8 (25%)	740 (77%)	21 (58%)	

Continuous data are presented as mean ± standard deviation; categorical data as number (%)

eGFR = estimated glomerular filtration rate; IMT = intima-media thickness; ABI = ankle-brachial index

[a] Defined as the lower of the left and right ABI measurements

[b] Defined as the thicker of the left and right femoral IMT measurements

[c] Evidence of plaque as detected by ultrasound in any of the left or right common femoral or superficial femoral arteries

Table III

Adjusted Associations of Femoral Ultrasound Vascular Measures with eGFR

Variable	Models		
	Unadjusted	Model 1[a]	Model 2[b]
	Difference in eGFR[c] (CI)	Difference in eGFR[c] (CI)	Difference in eGFR[c] (CI)
Probable or Definite Plaque vs. None			
Any Plaque[d]	−9.2 (−11.6, −6.8)	−2.6 (−4.8, −0.4)	−3.0 (−5.3, −0.8)
Superficial Femoral Plaque[e]	−8.3 (−12.1, −4.6)	−1.9 (−5.2, 1.3)	−2.3 (−5.6, 1.1)
Common Femoral Plaque[e]	−8.9 (−11.3, −6.4)	−2.7 (−4.9, −0.5)	−3.1 (−5.4, −0.8)
Superficial Femoral IMT per SD[f]	−2.2 (−3.2, −1.1)	−0.6 (−1.5, 0.3)	−0.4 (−1.4, 0.6)
Common Femoral IMT per SD[g]	−2.4 (−3.4, −1.3)	0.1 (−0.9, 1.0)	0.1 (−0.9, 1.0)
ABI			
Low (<0.9), n=32	−11.6 (−17.6, −5.5)	−1.3 (−6.5, 3.9)	−1.1 (−6.5, 4.3)
Normal (0.9–1.3), n=961	Reference	Reference	Reference
High (>1.3), n=36	−4.9 (−10.6, 0.8)	1.3 (−3.7, 6.3)	1.4 (−3.6, 6.6)

eGFR = estimated glomerular filtration rate; IMT = intima-media thickness; ABI = ankle-brachial index PAD = peripheral artery disease; CI = 95% confidence interval; SD = standard deviation

[a] Adjusted for age, sex, ethnicity (non-Hispanic white, African American, Hispanic)

[b] Adjusted for variables in Model 1, as well as total cholesterol, high density lipoprotein, body mass index, systolic blood pressure, diabetes, anti-hypertensive and statin use and smoking history

[c] Per ml/min/1.73m^2

[d] Evidence of plaque as detected by ultrasound in any of the left or right common femoral or superficial femoral arteries

[e] Evidence of plaque as detected by ultrasound in either the left or right femoral arteries

[f] SD = 0.16 mm

[g] SD = 0.61 mm

Table IV

Association of Femoral Ultrasound Measures of Vascular Disease with Odds of CKD

	Models		
	Unadjusted	**Model 1[a]**	**Model 2[b]**
Variable	**OR (CI)**	**OR (CI)**	**OR (CI)**
Probable or Definite Plaque vs. None			
Any Plaque[c]	3.0 (2.1, 4.3)	1.6 (1.1, 2.4)	1.7 (1.1, 2.8)
Superficial Femoral Plaque[d]	2.3 (1.4, 3.9)	1.3 (0.7, 2.3)	1.6 (0.8, 2.9)
Common Femoral Plaque[d]	2.9 (2.1, 4.3)	1.7 (1.1, 2.5)	1.8 (1.1, 2.8)
Superficial Femoral IMT per SD[e]	1.3 (1.1, 1.5)	1.2 (1.0, 1.4)	1.2 (1.0, 1.4)
Common Femoral IMT per SD[f]	1.3 (1.1, 1.5)	1.0 (0.9, 1.2)	1.1 (0.9, 1.3)
ABI			
Low (<0.9), n=32	4.2 (2.0, 8.7)	1.7 (0.7, 3.7)	2.0 (0.8, 5.0)
Normal (0.9–1.3), n=961	Reference	Reference	Reference
High (>1.3), n=36	1.7 (0.8, 3.9)	1.1 (0.4, 2.8)	1.3 (0.5, 3.7)

eGFR = estimated glomerular filtration rate; IMT = intima-media thickness; ABI = ankle-brachial index CKD = chronic kidney disease; PAD = peripheral artery disease; CI = 95% confidence interval Std Dev = standard deviation; OR = odds ratio

[a] Adjusted for age, sex, ethnicity (non-Hispanic white, African American, Hispanic)

[b] Adjusted for variables in Model 1, as well as total cholesterol, high density lipoprotein, body mass index, systolic blood pressure, diabetes, anti-hypertensive and statin use and history of smoking

[c] Evidence of plaque as detected by ultrasound in any of the left or right common femoral or superficial femoral arteries

[d] Evidence of plaque as detected by ultrasound in either the left or right femoral arteries

[e] SD = 0.16 mm

[f] SD = 0.61 mm