The Associations Between Peripheral Artery Disease (PAD) and Physical Outcome Measures in Men and Women with Chronic Kidney Disease (CKD)

Grace J. Wang, MD[1], **Pamela A. Shaw, PhD**[2], **Raymond R. Townsend, MD**[3], **Amanda H. Anderson, PhD, MPH**[2], **Dawei Xie, PhD**[2], **Xue Wang, MS**[2], **Lisa C. Nessel, MSS**[2], **Emile R. Mohler, MD**[3], **Stephen M. Sozio, MD**[4], **Bernard G. Jaar, MD**[4], **Jing Chen, MD**[5], **Jackson Wright, MD, PhD**[6], **Jonathan J. Taliercio, DO**[7], **Akinlolu Ojo, MD, PhD**[8], **Ana C. Ricardo, MD, MPH, MS**[9], **Eva Lustigova, MD**[10], **Ronald M. Fairman, MD**[1], **Harold I. Feldman, MD, MSCE**[2], **Bonnie Ky, MD, MSCE**[3], and **the CRIC Study Investigators**[11]

[1]Department of Surgery, 3400 Spruce Street, Hospital of the University of Pennsylvania, Philadelphia, PA, 19104, USA

[2]Department of Biostatistics and Epidemiology, 423 Guardian Drive, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA 19104, USA

[3]Department of Medicine, 3400 Civic Center Boulevard, Hospital of the University of Pennsylvania, Philadelphia, PA 19104, USA

[4]Department of Medicine, 4940 Eastern Ave, Johns Hopkins Medical Center, Baltimore, MD 21224, USA

[5]Department of Medicine, 1415 Tulane Ave, Tulane University School of Medicine, New Orleans, LA 70112, USA

[6]Department of Medicine, 11100 Euclid Ave, Case Western Reserve University, Cleveland, OH 44106, USA

[7]Department of Nephrology and Hypertension, 9500 Euclid Ave, Cleveland Clinic, Cleveland, OH 44195, USA

[8]Department of Medicine, 1500 E. Medical Center Drive, University of Michigan School of Medicine, Ann Arbor, MI 48109-5364, USA

[9]Department of Medicine, 1740 W Taylor Street, University of Illinois College of Medicine, Chicago, IL 60612, USA

[10]Tulane University Health Science Center, 1440 Canal Street, New Orleans, LA 70112, USA

Abstract

[*]Correspondence to: Dr. Grace J. Wang, Department of Surgery, 4 Silverstein, Hospital of the University of Pennsylvania, Philadelphia, PA 19104, Grace.Wang@uphs.upenn.edu, Phone: 215-662-2069, Fax: 215-614-0463.

[11]The CRIC Study Investigators include: Lawrence J. Appel, Alan S. Go, Jiang He, John W. Kusek, James P. Lash, and Mahboob Rahman

Background—Peripheral artery disease (PAD) is highly prevalent and associated with significant morbidity and mortality, but sex-based differences are incompletely understood. We sought to define the associations between PAD and physical outcome measures, and to determine if these associations differed by sex in the Chronic Renal Insufficiency Cohort (CRIC).

Methods—Among 3,543 participants, we assessed the cross-sectional relationship between PAD severity defined by ankle brachial index (ABI) and 1) physical activity (MET-hours/week) 2) walking pace (slow vs medium/fast) and 3) physical function (12-item Short Form Health Survey [SF-12]).

Results—In a multivariable linear regression model, PAD severity was not associated with physical activity defined by total MET-hours/week in men or women (P=0.432). However, PAD severity was significantly associated with walking activity (P=0.037), although this relationship did not differ by sex (P=0.130). Similarly, PAD severity was significantly associated with walking pace (P<0.001), although this relationship did not differ by sex (P=0.086). In contrast, there was an independent association between PAD severity and SF-12 (P=0.018), with a significant interaction by sex (P<0.001).

Conclusions—These data suggest that tools used to evaluate the functional consequences of PAD should focus on walking activity and walking pace, as well as physical function, where sex-specific associations should be accounted for.

INTRODUCTION

Peripheral artery disease affects an estimated 8 million adults in the United States, a number which will continue to rise as the population ages.[1,2] PAD remains a significant source of morbidity and mortality resulting in functional impairment, limb loss, as well as death.[3] The burden of PAD is particularly relevant to the chronic kidney disease (CKD) population. Data from the National Health and Nutrition Examination Survey (NHANES) demonstrated that 24% of persons with CKD stage 3 or greater had PAD as defined by an ankle brachial index (ABI) < 0.9, which was significantly greater than the 4% prevalence in the group with normal renal function.[4] Indeed, the National Kidney Foundation Task Force issued a statement suggesting that patients with CKD were in the highest risk category for subsequent cardiovascular events.[5]

Several survey instruments have been developed for the detection of PAD.[6–8] While these survey instruments have been widely used for the diagnosis of PAD, the diagnosis can be mired by a lack of sensitivity and specificity. Prior literature has suggested that PAD is associated with a decline in physical function as well as physical activity.[9,10] In the Women's Health and Aging Study, asymptomatic women with an ABI<0.9 had a slower walking rate, poorer standing balance score, slower time to arise from a seated position, and fewer blocks walked per week after adjusting for age, smoking and other comorbidities. In the Walking and Leg Circulation Study (WALCS), an ABI<0.50 was associated with a shorter 6-minute walk distance, less physical activity, slower 4-m walking rate, and an

inability to maintain a tandem stand for 10 seconds after adjusting for confounders.[10] These data suggest that physical activity and function measures may be more sensitive than conventional questionnaires designed to detect circulatory insufficiency. Yet, the data on the utility and validity of these tests to measure degree of circulatory impairment is lacking.

Compounding the difficulty of identification of patients with PAD, prior epidemiologic studies suggest that the presentation of PAD differs in men and women. For example, data from cohort studies[11,12] and large population studies suggest that women are typically older, have more atypical symptoms, and present with more advanced disease compared to men.[13] Furthermore, collective data from large cohort studies have suggested worse outcomes in terms of rates of limb salvage, morbidity and mortality in women undergoing lower extremity revascularization.

Together, these data indicate a need to develop more robust strategies to evaluate PAD that will also account for sex differences in presentation. We leverage the strengths of a uniquely phenotyped cohort of individuals with CKD, the CRIC Study population, to determine if there is an association between PAD and physical activity, walking pace and physical function, and whether these associations differ between men and women. We hypothesized that circulatory impairment would be reflected in a corresponding decrease in these measures of physical outcome, and that their relationships with PAD severity would differ in men and women.

METHODS

Study design

The CRIC study design and methods have been described in detail previously.[14] Briefly, CRIC is a prospective cohort study of 3,939 participants enrolled from June 2003 to August 2008 through 7 clinical centers in the United States (Ann Arbor and Detroit, Michigan; Baltimore, Maryland; Chicago, Illinois; Cleveland, Ohio; New Orleans, Louisiana; Philadelphia, Pennsylvania; and Oakland, California). Participants included men and women 21 to 74 years of age with mild to moderate CKD as defined by estimated glomerular filtration rate (eGFR). Age-based eGFR was used as an inclusion criterion for the study. Exclusion criteria included New York Heart Association class 3 and 4 heart failure, cancer and immunosuppressive therapies during the previous 6 months. Participants underwent detailed examinations including measurement of ankle-brachial index, undergoing the Multiethnic Study of Atherosclerosis (MESA) Typical Week Physical Activity Survey, ascertainment of walking pace and Short Form 12-item Health Survey (SF-12) scores (detailed below) at baseline and during annual in-person follow-up exams. The study was approved by the Institutional Review Board of each participating clinical center and the Scientific and Data Coordinating Center. Written informed consent was obtained from all participants.

For the purposes of this study, participants were excluded if they had a history of an amputation or a prior revascularization procedure (angioplasty or surgical bypass) because of uncertainty of how these procedures would affect physical activity and function. In this way, we limited the evaluation to those patients where their circulatory impairment could be

directly compared to measures of physical outcome. Therefore, we focused on a subset of 3,543 participants for this analysis.

Primary outcome measures

Physical activity—Physical activity as measured by total MET (metabolic equivalent) - hours per week was derived from the MESA questionnaire. In brief, the MESA Typical Week Physical Activity Survey[15] was based on the Cross-Cultural Activity Participation Study[16] which quantitated the type, amount and intensity of physical activity experienced in a typical week in women of varying ethnicities. Activities captured in the survey included household chores, walking, conditioning exercises, leisure and occupational activities, which were further differentiated by light, moderate and heavy-intensity levels. These data were used to calculate total MET-hours/week spent on physical activity. Because prior studies have shown that certain summaries of physical activity (eg, time spent in moderate or heavy activity) are better associated with cardiorespiratory fitness[17], we also considered the time (hours/week) spent in light, moderate, moderate/heavy, and heavy intentional exercise, as well as walking activity separately, as sub-categories of physical activity potentially associated with ABI.

Walking pace—Because the 6-minute walking distance has previously been reported to be associated with daily physical activity level[18] and cardiorespiratory fitness[19], walking pace (slow vs medium/fast) was also considered as a physical outcome measure.

Physical function—Physical function was measured via the physical component of SF-12, an abbreviated version of the SF-36 questionnaire which has been validated for assessing functional status, well-being and one's overall perception of their health.[20,21]

PAD severity—The ankle brachial index (ABI) is the standard test utilized to diagnose PAD.[22] After lying supine for 5 minutes, systolic blood pressure was measured in both arms using appropriately-sized cuffs. The systolic blood pressure for the dorsalis pedis artery and posterior tibial artery was measured for each leg using a Doppler probe. The ABI was determined by dividing the systolic blood pressure for each pedal artery by the higher systolic blood pressure of the brachial artery. In participants with functioning fistulae or arteriovenous grafts, the available contralateral brachial artery blood pressure was used. The lower ABI of the two limbs was used for each participant. We divided ABI into 4 categories and defined the degree of PAD as the following: (ABI<0.6-moderate-severe; 0.6 ABI<0.9-mild; 0.9 ABI<1.3-normal, ABI 1.3-noncompressible). These categories are in accordance with previously published guidelines.[23]

Statistical analysis

Baseline demographic and clinical characteristics were summarized using mean and standard deviation for continuous variables and frequencies for categorical data, by sex. T-tests were used for between sex comparisons of continuous variables and chi-square tests were used for between sex comparisons of categorical variable frequencies. We assessed the association between PAD severity and measures of physical outcome as detailed below.

or intentional exercise, walking activity, all $P<0.020$). However, there was no independent association between ABI and physical activity defined as light, moderate, heavy, moderate/heavy activity, or intentional exercise. After adjusting for hypertension, smoking, age, race, eGFR, and BMI, there was an independent association between ABI and walking activity ($P=0.037$), but no effect modification by sex ($P=0.130$). The results of the univariable and multivariable analyses for walking activity are summarized in Table 4.

Association between ABI and walking pace

ABI was associated with walking pace ($P<0.001$). As PAD worsened, the odds of having a slower walking pace increased (Table 5). After adjusting for hypercholesterolemia, congestive heart failure, coronary artery disease, diabetes, smoking status, age, race, eGFR, BMI, sex and clinical center, there remained an association between ABI and walking pace ($P<0.001$), although there was no significant interaction by sex, ($P=0.086$). The results of the univariable and multivariable analysis are summarized in Table 5.

Association between ABI and physical function

There was a significant univariate association between ABI and SF-12 score ($P<0.001$, Table 6). With worsening circulatory impairment, there was a decrement in median physical function score in men and women (Table 2; Figure 2). This remained significant after adjusting for congestive heart failure, coronary artery disease, diabetes, age, smoking status, race, sex, clinical center and eGFR, ($P=0.018$). Furthermore, the adjusted association between ABI and physical function differed by sex, ($P<0.001$). For men, ABI was significantly associated with SF-12 such that with mild circulatory impairment, there was a decrease in SF-12 score by a mean of 1.05 points (SE, 0.79) compared to those with normal ABI. In the presence of moderate-severe disease, there was a greater decrease in SF-12, by a mean of 6.03 points (SE, 1.66). For women, ABI was associated with SF-12 such that mild PAD was associated with a decrease in SF-12 score by a mean of 2.09 points (SE,0.78). Moderate-severe disease in women, paradoxically, was associated with a mean 2.80 point higher SF-12 score (SE,1.60). The results from the univariable and multivariable regression analyses are summarized in Table 6.

DISCUSSION

In this study, we demonstrate that ABI was not significantly associated with physical activity as measured by total MET-hours/week after adjustment for other sociodemographic and clinical factors. ABI was also not associated with other physical activity outcomes defined by MET-hours/week (light, moderate, heavy, moderate-heavy, intentional, exercise) in the multivariable models. PAD severity was associated with walking activity (MET-hours/week) and walking pace (slow-<2mph, or medium/fast - 2 mph), but this relationship did not differ by sex.

PAD severity was independently associated with physical function, and this association differed by sex. In men, as PAD worsened, there was a corresponding decrease in SF-12 score. In women, on the other hand, those with mild PAD had a pronounced decrement of their SF-12 score, whereas those with moderate-severe PAD and a paradoxical increase in

SF-12 score, reflecting the nonlinear association between ABI and SF-12 in women. The effect of PAD on SF-12 scores in men and women is clinically relevant, given that a 2–3 point difference has been shown to be clinically important.[21] In a study of adults older than 45 years with chronic kidney disease, a decline in the eGFR from   90 mL/min/1.73 m^2 to 15–29 mL/min/1.73 m^2 was associated with a 3.6 point decrease in SF-12 score (from a score of 40.9 to a score of 37.3) in the adjusted model.[25] Using data from the Medical Expenditure Panel Survey, the physical SF-12 score was 4.6 points lower in those with coronary heart disease compared to those without coronary heart disease.[26]

The results of this study have implications for improved strategies in evaluating for PAD. Specifically, walking activity (MET-hours/week) may be more appropriate to include in questionnaires than the total number of MET-hours expended per week. Indeed, prior studies have shown that general physical activity surveys lack sensitivity and specificity.[27,28] Further, more specific measures of physical activity such as the 6-minute walk test have been performed with better validity and reliability, consistent with the findings from this study.[9] The results from our study also suggest that incorporating walking pace would enhance the ability to detect PAD. Physical function via the SF-12 could also be incorporated in questionnaires evaluating for PAD, and would need to take into account the differing relationship between PAD severity and the decrement in functioning in men compared to women. Men experienced a decline in physical function with worsening categories of circulatory impairment, while women had a greater decline with mild disease, but paradoxically reported better function in the worst category of PAD. This could be interpreted in a few ways. Women could be more sensitive to circulatory impairment and experience a greater reduction in function at milder stages of PAD. In addition, the relatively greater functioning reported in women with moderate-severe PAD could be a result of social desirability bias, where there is a tendency of survey respondents to answer questions in a manner that will be viewed favorably by others.[29] Further, women with severe PAD may have adapted to the reduction in circulation by avoidance of activities that exacerbate their symptoms.[9] Lastly, there may be a biological explanation for why women may be less affected by moderate-severe PAD, compared to men. PAD is characterized histopathologically by an ischemic myopathy with calf muscle atrophy and fatty infiltration, or abnormal mitochondrial dysfunction.[30] If women had less muscle atrophy in the moderate-severe stage of PAD, it could be reflected in relatively preserved function in severe stages of circulatory impairment. Overall, these nonlinear patterns suggest a more complex relationship between physical function and circulation in women, and deserve to be an area of future research.

The findings from this study are congruent with those found in the literature. One study compared the physical performance of patients with PAD to those without PAD via accelerometers as well as two general physical activity questionnaires, LTPAQ (Leisure Time Physical Activity Questionnaire) and PARQ (Stanford 7-day Physical Activity Recall Questionnaire).[27] Neither physical activity questionnaire detected a statistically significant difference between groups, despite a difference in accelerometer measurements between groups. These findings reaffirm the insensitivity of general physical activity surveys, and their lack of correlation with objective data. The significant relationship between ABI and walking activity and walking pace also parallels prior findings in the general population. The

Walking and Leg Circulation Study (WALCS)[10] showed that participants with an ABI<0.50 had a shorter 6-minute walking distance compared to those with an ABI of 1.10–1.50, as well as a slower 4-m walking velocity. Further, less than 40% of participants with an ABI<0.40 could walk continuously for 6 minutes compared to more than 95% of those with an ABI between 1.00 and 1.50. Thus, circulatory impairment is reflected in less walking activity as well as a slower walking pace, results that were also found in this cohort of patients with CKD, a finding that has not been reported previously.

The SF-12 Survey is a well-validated, general health questionnaire[21] designed to monitor the impact of disease states over time[31], or to assess the impact of different diseases on health status.[32] The questions detect how one's health may limit particular activities, such as climbing flights of stairs or work-related activities. PAD severity in this study was closely related to a decrease in functioning, analogous to prior studies. In the Women's Health and Aging Study (WHAS)[33], amongst community-dwelling women of 65 years of age, women with low ABI values were more likely to report an inability to walk ¼ of a mile or climb a flight of stairs without assistance, compared to women with normal ABI values. In the WALCS cohort, people with PAD had higher rates of mobility loss, compared to those without PAD.[34] These studies reflect that ABI decrement is associated with a decrease in physical function, congruent with the results from our study. We additionally discovered that physical function was affected by circulation impairment in a more linear pattern in men, whereas in women, there was a nonlinear pattern.

There are some limitations to our study. Patients with CKD can have calcific, noncompressible vessels, which can lead to an overestimation of the ABI and misclassification. However, there was a low prevalence of ABI>1.3 (6.74% in men and 4.11% in women), suggesting that our main findings would not be different. This is a cross-sectional study, thus cause and effect cannot be determined, although it is more plausible to hypothesize that impaired circulation caused the decrease in walking activity, walking pace and physical function, rather than the converse. Additionally, the physical outcomes of physical activity, walking pace, and physical function were ascertained via self-report, which is subject to measurement error and social desirability bias and thus could alter associations between PAD and physical outcome. However, these questionnaires are well-validated surveys for the study of physical activity and physical function. Finally, the cohort is designed to study participants with CKD, and may not generalizable to the population at large. However, this is a rich dataset which lends important insight into a highly relevant population commonly afflicted by PAD.

We also note important strengths of this study. The near equal representation of the sexes, the rigorous determination of ABI, along with consistent administration of physical activity and function surveys represent key strengths in this study exploring the associations between PAD and decline in physical function and activity. These circumvent the pitfalls of earlier trials for PAD which reflected an underrepresentation of women[35] and a general reluctance on the part of women to report leg symptoms to their medical providers. [36]

In summary, in our cohort of 3,543 participants with CKD, a decrement in ABI was associated with a decline in walking activity and walking pace, as well as physical function,

as defined by the SF-12. Furthermore, the decline in physical function differed in men versus women. Future studies should be devoted to developing tools to detect PAD that incorporate walking variables as well as physical function items, where sex-based differences should be accounted for.

Acknowledgments

Abbreviations

ABI	ankle-brachial index
BMI	body mass index
CAD	coronary artery disease
CRIC	Chronic Renal Insufficiency Cohort
eGFR	estimated glomerular filtration rate
MESA	Multi-Ethnic Study of Atherosclerosis
PAD	peripheral artery disease
SF-12	short-form health survey

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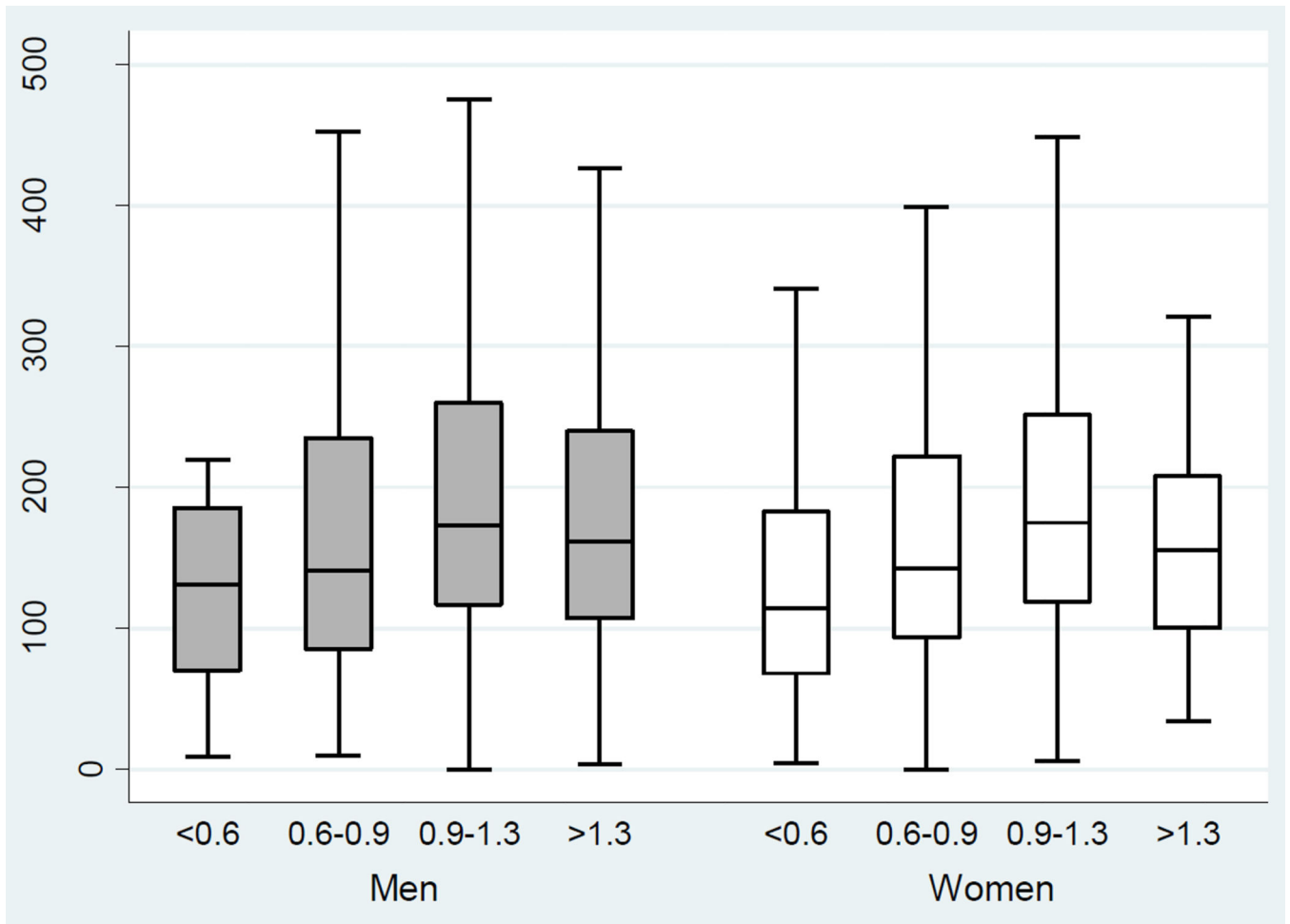
Figure 1.
Physical Activity versus ABI in Men versus Women in the Unadjusted Model, CRIC, United
States, 2003–2008
MET-metabolic equivalent
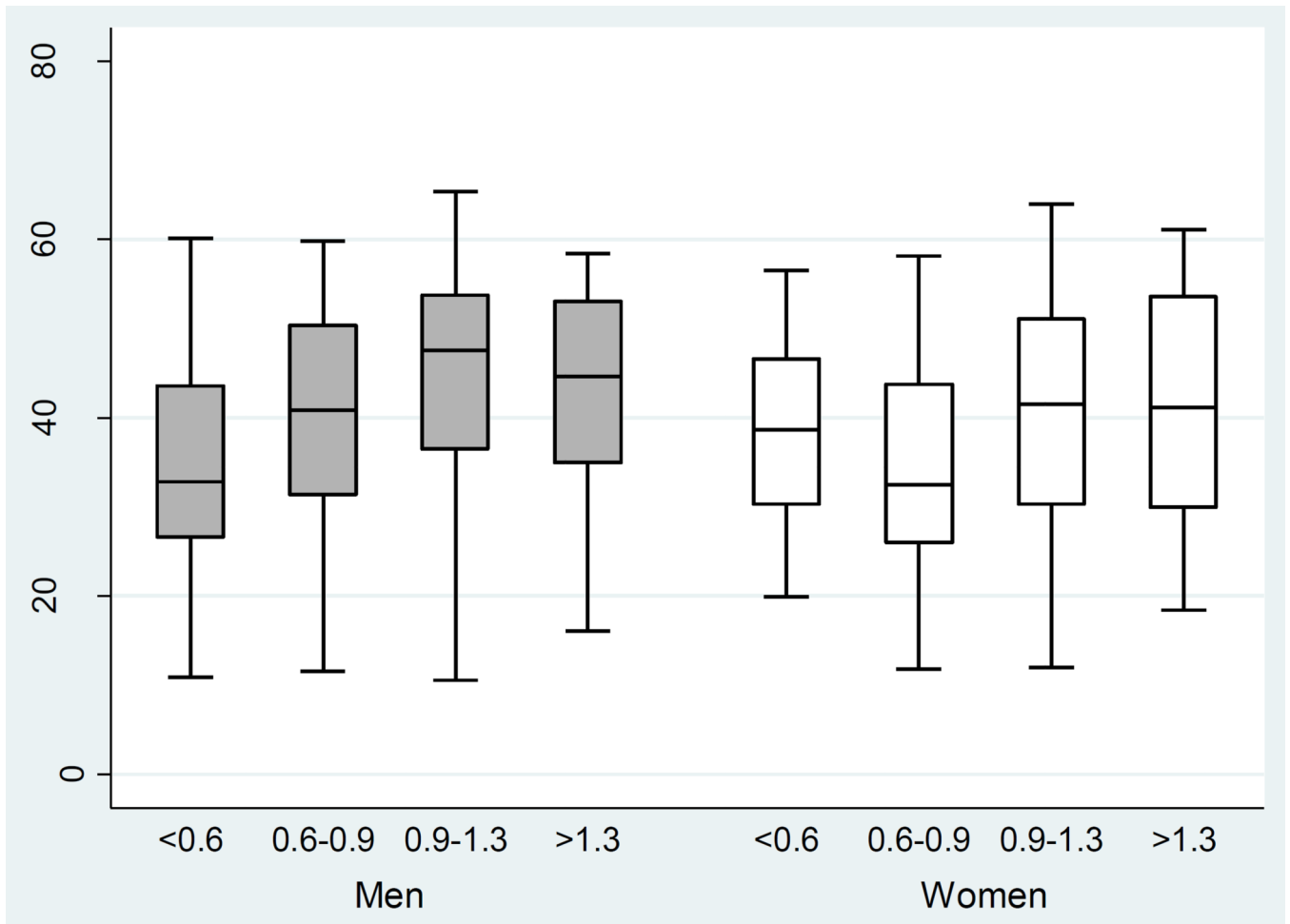
Figure 2.
Physical Function versus ABI in Men versus Women in the Unadjusted Model, CRIC, United States, 2003–2008
SF-12-Short Form Health Survey

Table 1

Baseline Characteristics of CRIC Participants by Sex, CRIC, United States, 2003- 2008

Clinical Characteristic	Women N=1630	Men N=1913	*P*-value
Age mean (SD)	57.3 (11.2)	57.5 (11.0)	0.555
Race (overall)			<0.001
White (%)	42.1	49.8	
Black (%)	47.4	37.5	
Other (%)	10.5	12.7	
CHF (%)	7.7	8.9	0.196
Diabetes (%)	45.1	45.5	0.818
eGFR mL/min/1.73 m^2, mean(SD)	44.7(17.5)	46.7(16.5)	<0.001
Hypertension (%)	83.4	86.9	0.003
CAD (%)	15.7	22.3	<0.001
Cigarette Smoking (overall)			<0.001
Never (%)	54.2	40.2	
Former (%)	33.4	46.8	
Current (%)	12.4	13.0	
Hypercholesterolemia (%)	74.9	86.3	<0.001
BMI mean(SD)	33.0(8.9)	31.0(6.3)	<0.001
Clinical center			<0.001
ABI mean (SD)	1.0(0.2)	1.1(0.2)	<0.001
ABI category (overall)			<0.001
ABI<0.6 (%)	2.8	2.0	
ABI 0.6<0.9 (%)	12.8	10.2	
ABI 0.9<1.3 (%)	80.3	81.0	
ABI 1.3 (%)	4.1	6.7	

[*] ABI-Ankle Brachial Index; BMI-Body Mass Index; CAD-coronary artery disease; CHF-congestive heart failure; eGFR-estimated glomerular filtration rate

Table 2

Summary of Physical Activity and Physical Function by ABI Category, Stratified by Sex, CRIC, United States, 2003–2008

Physical Activity or Physical Function Variable	Women	Men	*P*-value
Total MET-hours/week (median, IQR)	167.5 (113.2, 246.5)	167.4 (110.6, 256.1)	0.546
ABI <0.6	114.4 (67.4, 182.6)	131.03 (70.0, 185.6)	0.536
ABI 0.6<0.9	142.7 (93.8, 222.1)	140.6 (85.4, 234.7)	0.995
ABI 0.9<1.3	175.0 (118.4, 251.4)	173.5 (116.5, 260.1)	0.819
ABI 1.3	155.2 (99.9, 208.0)	161.5 (106.5, 240.0)	0.801
SF-12 (median, IQR)	39.9 (29.8, 50.6)	46.5 (35.6, 53.5)	<0.001
ABI <0.6	38.7 (30.3, 46.6)	32.8 (26.7, 43.5)	0.128
ABI 0.6<0.9	32.4 (25.9, 43.8)	40.8 (31.3, 50.4)	<0.001
ABI 0.9<1.3	41.5 (30.3, 51.1)	47.6 (36.4, 53.7)	<0.001
ABI 1.3	41.2 (30.0, 53.6)	44.6 (34.9, 53.1)	0.245

[*] ABI-Ankle Brachial Index; MET-metabolic equivalent; SF-12-Short form health study

[†] Wilcoxon rank sum used for statistical comparison

[‡] *P*-value comparing women and men within a given ABI category

Table 3

Summary of Unadjusted and Adjusted association between Physical Activity (total MET hours/week) and Demographic variables, CRIC, United States, 2003–2008

Clinical characteristic	Univariable			Multivariable		
	β	SE	P-value	β	SE	P-value
Intercept				402.09	20.22	<0.001
HTN	−30.19	7.03	<0.001			
Hypercholesterolemia	−24.09	6.36	<0.001			
Smoking (overall)			<0.001			0.190
Smoke (former)	−26.44	5.34	<0.001	−9.43	5.31	0.076
Smoke (current)	−1.47	7.87	0.852	−1.33	7.69	0.862
Diabetes	−33.19	4.99	<0.001	−13.84	5.03	0.006
Age	−3.64	0.22	<0.001	−3.24	0.23	<0.001
CHF	−46.08	9.00	<0.001	−23.39	9.12	0.010
CAD	−40.79	6.30	<0.001	−8.73	6.57	0.184
Race (overall)			0.070			0.615
Black	−2.03	5.32	0.702	4.07	5.27	0.440
Other	−18.75	8.20	0.022	−3.16	8.60	0.713
BMI	−0.70	0.32	0.031			
eGFR	1.38	0.14	<0.001	0.63	0.16	<0.001
Sex (women)	−11.13	5.01	0.026	−14.78	4.97	0.003
ABI (overall)			<0.001			0.432
ABI<0.6	−48.98	16.37	0.003	−5.99	15.94	0.707
ABI 0.6<0.9	−35.40	7.87	<0.001	−5.62	7.77	0.469
ABI 1.3	−23.11	10.92	0.034	−16.15	10.57	0.127
Clinical center (overall)			<0.001			<0.001

*ABI-Ankle Brachial Index; BMI-Body Mass Index; CAD-coronary artery disease; CHF-congestive heart failure; eGFR-estimated glomerular filtration rate; SE-standard error

†Covariates were added using forward selection method

‡0.9 ABI <1.3 used as the referent category

Table 4

Summary of Unadjusted and Adjusted association between Walking Activity (walk-MET hours/week) and Demographic variables, CRIC, United States, 2003–2008

Clinical characteristic	Univariable			Multivariable		
	β	SE	*P*-value	β	SE	*P*-value
Intercept				53.33	5.80	<0.001
HTN	−1.10	1.72	0.522	2.05	1.84	0.266
Hypercholesterolemia	−3.04	1.55	0.050			
Smoking (overall)			<0.001			0.012
Former	−4.60	1.30	<0.001	−3.54	1.34	0.008
Current	2.03	1.92	0.290	0.89	1.97	0.649
Diabetes	−4.00	1.22	0.001			
Age	−0.36	0.05	<0.001	−0.31	0.06	<0.001
CHF	−2.43	2.20	0.269			
CAD	−4.59	1.54	0.003			
Race (overall)			<0.001			<0.001
Black	3.99	1.29	0.002	4.66	1.36	0.001
Other	−3.48	2.00	0.081	−2.55	2.17	0.240
BMI	−0.20	0.08	0.012	−0.18	0.08	0.025
eGFR	0.18	0.04	<0.001	0.09	0.04	0.024
Sex (women)	−3.93	1.22	0.001	−4.18	1.27	0.001
ABI (overall)			<0.001			0.037
ABI<0.6	−7.08	3.99	0.076	−4.36	4.02	0.278
ABI 0.6<0.9	−7.75	1.92	<0.001	−5.22	1.95	0.008
ABI 1.3	−3.83	2.66	0.150	−2.86	2.68	0.286
Clinical center (overall)			0.005			0.166

*
ABI-Ankle Brachial Index; BMI-Body Mass Index; CAD-coronary artery disease; CHF-congestive heart failure; eGFR-estimated glomerular filtration rate; SE-standard error

†
Covariates were added using forward selection method

‡
0.9 ABI <1.3 used as the referent category

Table 5

Summary of Unadjusted and Adjusted Association Between Slow Walking Pace and Demographic variables, CRIC, United States, 2003–2008

	Univariable		Multivariable	
Clinical characteristic	**OR**	**95% CI**	**OR**	**95% CI**
HTN	2.11	1.73, 2.58		
Hypercholesterolemia	1.60	1.34, 1.90	1.15	0.94, 1.40
Smoke (never)	1.00	Referent	1.00	Referent
Smoke (former)	1.21	1.05, 1.39	1.09	0.93, 1.28
Smoke (current)	1.59	1.29, 1.96	1.53	1.21, 1.93
Diabetes	1.82	1.59, 2.08	1.16	0.99, 1.35
Age	1.02	1.02, 1.03	1.02	1.01, 1.03
CHF	2.33	1.81, 2.99	1.33	1.01, 1.76
CAD	1.90	1.60, 2.25	1.41	1.16, 1.72
Race (White)	1.00	Referent	1.00	Referent
Race (Black)	2.31	2.00, 2.67	1.80	1.53, 2.11
Race (Other)	1.20	0.96, 1.50	1.25	0.96, 1.63
BMI	1.08	1.07, 1.09	1.06	1.05, 1.07
eGFR	0.98	0.97, 0.98	0.99	0.98, 0.99
Sex (Women)	1.62	1.42, 1.85	1.55	1.33, 1.81
ABI 0.9<1.3	1.00	Referent	1.00	Referent
ABI<0.6	3.98	2.41, 6.55	2.44	1.44, 4.15
ABI 0.6<0.9	2.26	1.82, 2.80	1.49	1.18, 1.89
ABI 1.3	1.22	0.91, 1.63	1.16	0.84, 1.59

[*] ABI-Ankle Brachial Index; BMI-Body Mass Index; CAD-coronary artery disease; CHF-congestive heart failure; eGFR-estimated glomerular filtration rate

[†] Covariates were added using forward selection method

[‡] Also adjusted for clinical center

Table 6

Summary of Unadjusted and Adjusted Association Between Physical Function (SF-12) and Demographic variables, CRIC, United States, 2003–2008

Clinical characteristic		Univariable			Multivariable		
		β	SE	P-value	β	SE	P-value
Intercept					58.59	1.58	<0.001
HTN		−4.42	0.55	<0.001			
Hypercholesterolemia		−2.93	0.50	<0.001			
Smoking (overall)				<0.001			<0.001
	Former	−2.06	0.42	<0.001	−1.32	0.38	0.001
	Current	−3.65	0.62	<0.001	−3.38	0.56	<0.001
Diabetes		−5.01	0.38	<0.001	−1.86	0.37	<0.001
Age		−0.14	0.02	<0.001	−0.07	0.02	<0.001
CHF		−8.42	0.69	<0.001	−4.20	0.66	<0.001
CAD		−5.82	0.49	<0.001	−3.35	0.48	<0.001
Race (overall)				<0.001			<0.001
	Black	−3.92	0.41	<0.001	−1.49	0.38	<0.001
	Other	−2.40	0.63	<0.001	−1.62	0.62	0.009
BMI		−0.44	0.02	<0.001	−0.32	0.02	<0.001
eGFR		0.18	0.01	<0.001	0.08	0.01	<0.001
Sex (Women)		−4.15	0.39	<0.001	−4.00	0.40	<0.001
ABI (overall)				<0.001			0.002
	ABI<0.6	−5.80	1.29	<0.001	−6.03	1.66	<0.001
	ABI 0.6<0.9	−5.17	0.61	<0.001	−1.05	0.79	0.184
	ABI 1.3	−0.44	0.84	0.603	0.10	0.94	0.916
Sex(Women)*ABI overall							<0.001
Sex*ABI<0.6					8.82	2.29	<0.001
Sex*ABI 0.6<0.9					−1.03	1.09	0.345
Sex*ABI 1.3					1.37	1.57	0.381

Clinical characteristic	Univariable			Multivariable		
	β	SE	*P*-value	β	SE	*P*-value
Clinical center (overall)			<0.001			<0.001

*
ABI-Ankle Brachial Index; BMI-Body Mass Index; CAD-coronary artery disease; CHF-congestive heart failure; eGFR-estimated glomerular filtration rate; SE-standard error

†
Covariates were added using forward selection method

‡
0.9 ABI <1.3 used as the referent category