Lower Extremity Peripheral Artery Disease and Quality of Life Among Older Individuals in the Community

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Background—Evidence regarding the association of lower extremity peripheral arterial disease with quality of life (QOL) is mainly from selected clinical populations or relatively small clinical cohorts. Thus, we investigated this association in community-derived populations.

Methods and Results—Using data of 5115 participants aged 66 to 90 years from visit 5 (2011-2013) of the Atherosclerosis Risk in Communities Study, we quantified the associations of ankle-brachial index (ABI) with several QOL parameters, including 12-item Short-Form Health Survey (SF-12), after accounting for potential confounders using linear and logistic regression models. Peripheral arterial disease defined by an ABI <0.90 (n=402), was independently associated with a low SF-12 Physical Component Summary score (−3.26 [95% CI −5.60 to −0.92]), compared to the ABI reference 1.10 to 1.19 (n=1900) but not with the Mental Component Summary score (−0.07 [−2.21 to 2.06]). A low ABI was significantly associated with poorer status of all SF-12 physical domains (physical functioning, role-physical, bodily pain, and general health) but only vitality out of 4 mental domains. Similarly, low ABI values were more consistently associated with other physically related QOL parameters (leisure-time exercise/activity/walking) than mentally related parameters (significant depressive symptoms and hopeless feeling). Lower physical QOL was observed even in individuals with borderline low ABI (0.90 to 0.99; n=426).

Conclusions—Low ABI (even borderline) was independently associated with poor QOL, especially for physical components, in community-dwelling older adults. QOL is a critical element for older adults, and thus, further studies are warranted to assess whether peripheral arterial disease-specific management can improve QOL in older populations. (***J Am Heart Assoc***. 2017;6: e004519. DOI: 10.1161/JAHA.116.004519.)

Key Words: aging • atherosclerosis • epidemiology • peripheral vascular disease • quality of life

Peripheral arterial disease (PAD), commonly identified by an ankle-brachial index (ABI) less than 0.9, is a growing problem.[1] In the United States, PAD affects over 8 million individuals,[2] with particularly high prevalence among people aged over 70 years.[3,4] Persons with PAD have 3- to 5-fold higher mortality risk compared with those without PAD.

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Accompanying Tables S1 through S10 are available at http://jaha.ahajournals.org/content/6/1/e004519/DC1/embed/inline-supplementary-material-1.pdf

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Increased mortality is mainly driven by a higher cardiovascular disease (CVD) risk[5,6] and reflects the underlying systemic atherosclerosis process in PAD patients.[7]

PAD can also impact quality of life (QOL). As the disease progresses, patients with PAD may develop intermittent claudication and critical limb ischemia (a condition including ischemic rest pain, ulcers, or gangrene, with up to 25% risk of amputation within 1 year of diagnosis),[8] leading to the reduction of health-related QOL. Indeed, several studies have evaluated the impact of PAD on QOL measures,[9-18] but most of these studies have been conducted in small clinic-based populations with symptomatic PAD[9-14] or in selected populations with specific cardiovascular disease risk profiles.[16,17] The impact of clinical and subclinical PAD on QOL in the general population is thus yet to be characterized.

The aim of this study was to comprehensively investigate the association of PAD—across a spectrum of ABI values—with health-related QOL among older adults in the community using data from the Atherosclerosis Risk in Communities (ARIC) Study. We hypothesized that lower ABI value, including borderline low ABI (ABI <1.00),[19] would be comprehensively

associated with reduced health-related QOL in community-dwelling older adults. Some people (particularly as they age) may value QOL relatively more than merely survival, and PAD-specific management (eg, supervised exercise, pharmacotherapy, and revascularization) has been shown to improve QOL in some patients.[20,21] Thus, our findings may have clinical and public health implications.

Methods

Study Population

The ARIC Study is an ongoing prospective cohort originally designed to investigate the natural history of atherosclerosis and related cardiovascular events. The cohort consisted of 15 792 participants aged 45 to 64 at baseline visit in 1987-1989 from 4 US communities: Forsyth County, North Carolina; Jackson, Mississippi; suburbs of Minneapolis, Minnesota; and Washington County, Maryland. The ARIC Study conducted the fifth examination (visit 5) between June 1, 2011 and August 30, 2013, which 6538 participants aged 66 to 90 years attended. Among these visit attendees, we excluded 18 nonwhite/nonblack participants, 868 participants without ABI measurement, and 537 participants with missing information for QOL data and covariates, leaving the final population of 5115 participants for this study. A main reason for missing ABI measurement was home visit provided to participants who were unable to come to the field centers. As anticipated from this aspect, 5115 participants in this study had healthier profiles as compared to those who were excluded from this analysis (Table S1). All participants gave informed consent, and the study was approved by the institutional review board at each study site.

ABI Measurement

ABI was defined as the ratio of systolic blood pressure in the ankle to the systolic pressure in the arm. An oscillometric device, OMRON VP-1000 plus (Kyoto, Japan), allowed blood pressure to be automatically and simultaneously measured in both ankles and arms by trained and certified technicians after at least 5 minutes of rest.[22] The higher value of the right or left arm blood pressure was used as the denominator, and the ABI was calculated for both the right and left legs. The measurement was repeated after 5 minutes, and the mean ABI was recorded for each leg. The lower value of right and left ABI was used for this analysis in general.[9,23] One exception was when both ABIs were greater than 1.0 and at least 1 ABI was higher than 1.3. In this situation, to capture pathophysiological information of high ABI (indicating arterial noncompressibility),[2,24-26] we used the higher ABI value for our analysis.

Health-Related Quality of Life

Our primary measure of health-related QOL relied on the 12-item Short-Form Health Survey (SF-12), which captures both physical and mental elements of health-related QOL. To assess the robustness of our findings, we also evaluated physical activity and hopeless feeling by self-report and significant depressive symptoms by use of the Epidemiologic Studies Depression Scale (CES-D) Short Form.

The 12-Item Short-Form Health Survey

The SF-12v2 questionnaire, adopted in the ARIC study, is designed to assess health-related QOL, which has been validated across populations[27] and is comparable to the original full form of SF-36.[27,28] It reports 2 summary measurements for physical and mental health-related QOL, the Physical Component Summary and Mental Component Summary scores. Each summary component was based on 4 domains: Physical Component Summary—physical functioning (the ability to do moderate activities or climb stairs), role-physical (impaired working ability or daily activities due to physical issue), bodily pain (extent to which pain interferes with daily work), and general health (self-graded health status); Mental Component Summary—mental health (whether feeling peaceful or depressed), role-emotional (impaired working ability or daily activities due to emotional issue), social functioning (frequency of social activities interfered by physical or emotional issues), and vitality (whether feeling energetic). All information was based on the respondents' experience during the previous 4 weeks. The method that defines the calculation of these QOL scores was published elsewhere.[29] Briefly, the answer for each question was scaled based on the frequency and intensity of a certain QOL condition using a point between 1 and 5. A higher score indicates better QOL status. A raw QOL score for each domain was calculated by summing the points for relevant questions. Then, the final score for each domain ranging from 0 to 100 was calculated based on the following formula: ([actual raw score—lowest possible raw score]/possible raw score range)×100. The QOL scores used in this study were further standardized to the general US population in 1998, with a mean of 50 and a standard deviation of 10. Thus, scores above and below 50 are above and below the average in the general US population.[30]

Other Health-Related QOL Variables

Leisure-time exercise frequency, activity level compared to peers, and walking frequency were collected by questionnaire during an interview. Participants selected their leisure-time exercise and walking frequency from 5 categories of "Never," "Seldom," "Sometimes," "Often," and "Very Often." "Never"

and "Seldom" were defined as "low" for leisure-time exercise and walking frequency. Similarly, among the 5 categories of "Much less," "Less," "The same," "More," and "Much more" for the question on leisure-time activity compared to their peers, "Much less" and "Less" were considered "low" leisure-time activity.

The CES-D Short Form is a measurement instrument of depression symptoms, with 11 items selected from 20 items that define the full CES-D Form. This short-form CES-D demonstrates good validity[31] and high correlation with the full CES-D Form (Pearson r=0.95).[32] With a scale between 0 and 2 (0=hardly ever or never; 1=some of the time; 2=much or most of the time) for each item, the total CES-D score ranges between 0 and 22. The score was treated as missing if more than 1 item was missing. Significant depressive symptoms were defined as any CES-D score ≥9.[33] Information about the frequency of feeling hopeless in the past week (none, 1-2 days, 3-7 days) was gathered via a simple question asked during the interview. "Hopeless feeling" was defined by any self-report of feeling hopeless at least 1 day in the previous week.

Covariates

Age, sex, and race were self-reported. Information regarding each participant's education level (high school or lower vs college or above) was collected during the ARIC visit 1 interview. Subjective economic status was measured based on the MacArthur scale,[34] a self-estimated rank of the family financial status compared to the whole US population and ranked into 10 categories (rank score 1 [lowest] to 10 [highest]), and lower economic status was defined as having a rank score <6 (median score among study participants). The subjective economic status has demonstrated a good predictability for health status.[35] Smoking and drinking status were classified as current or not. Body mass index was calculated as weight (kg) divided by the square of height (m). Total cholesterol was assessed via enzymatic methods.[36] Glucose level was measured by glucose-6-phosphate dehydrogenase methods.[37] Diabetes mellitus was defined as fasting glucose level ≥126 mg/dL (≥7 mmol/L), nonfasting glucose level ≥200 mg/dL (≥11.1 mmol/L), medication use for diabetes mellitus, or self-reported physician diagnosis. Hypertension was defined as a systolic blood pressure (mean of the second and third measurements in sitting position) ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg or use of antihypertensive medication. History of coronary heart disease (CHD) or stroke was identified by the clinical history acquired at visit 1 and study-adjudicated CHD and stroke events between visit 1 and visit 5, respectively. History of heart failure was defined as cases adjudicated by the ARIC physician panel from 2005 onward,

hospitalizations with ICD code 428.x prior to 2005, or heart failure diagnosis confirmed with the participant's physician. Lung disease was based on the self-reported physician diagnosis of emphysema/chronic obstructive pulmonary disease, chronic bronchitis, or asthma. Estimated glomerular filtration rate was derived using the CKD-EPI equation incorporating serum creatinine level, sex, race, and age.[38] Reduced kidney function was defined as estimated glomerular filtration rate <60 mL/min per 1.73 m^2.[38]

Statistical Analysis

According to previous literature,[19,23,26,39] ABI was a priori categorized into 6 groups: <0.90, 0.90 to 0.99 (≥0.9 to <1), 1.00 to 1.09 (≥1 to <1.1), 1.10 to 1.19 (≥1.1 to <1.2), 1.20 to 1.29 (≥1.2 to <1.3), and ≥1.30. The category of 1.10 to 1.19 was used as reference because it was the most prevalent category in our study and was used as a reference in a previous meta-analysis.[23] Participants' baseline characteristics were compared across these 6 ABI groups based on chi-squared tests and analysis of variance (ANOVA) tests, as appropriate. We used linear regression models to evaluate continuous QOL parameters from the SF-12 (2 summary components and 8 health-related domains) and logistic regression models for the other QOL variables (ie, "low" leisure-time exercise, activity, and walking, significant depressive symptoms, and hopeless feeling). To evaluate the influence of potential confounders, 3 types of models were constructed for each QOL parameter. Model 1 adjusted for demographic variables, age, sex, ethnicity, education level, and economic status. Model 2 further adjusted for CVD risk factors (current smoking/drinking status, body mass index, total cholesterol level, diabetes mellitus, and hypertension) and history of CVD (history of CHD, heart failure, and stroke). Model 3 additionally included the presence of noncardiovascular comorbidities (lung disease and reduced kidney function). Because we are particularly interested in the independent association of ABI with health-related QOL, we primarily present results derived from Model 3. We repeated the analysis in subgroups according to sex, race, and the status of CVD history, diabetes mellitus, and reduced kidney function. In this subgroup analysis we maintained our analytic frame of 6 ABI categories for continuous QOL parameters. However, to obtain reliable estimates, we dichotomized ABI (<1.00 [low and borderline low][19] and ≥1.00 [as reference]) for dichotomous QOL parameters. Residual normality and equal variance assumptions were confirmed for the major outcome variables, the Physical/Mental Component Summary scores. Due to the ordinal nature of the measurements for each SF-12 subdomain, the normality assumption did not necessarily hold for every subdomain. Nonetheless, given the sample size and the Central Limit Theorem, the comparison of

average subdomain scores across ABI categories would be still valid.[40] *P*<0.05 was considered statistically significant.

Results

Participant Characteristics

The mean age of the 5115 participants was 75.4 (SD 5.0) years, and 21.8% (n=1113) were black. There were 402 participants (7.9%) with a low ABI <0.90, a category considered as PAD, and 426 (8.3%) with a borderline low ABI of 0.90 to 0.99.[41] As compared to participants with ABI in the reference range (1.10-1.19), those with lower ABI values (ABI <1.10) tended to have a worse cardiovascular risk factor profile, namely increased age, lower socioeconomic status, higher prevalence of current smoking, diabetes mellitus, hypertension, history of CVD and chronic lung disease, and reduced kidney function (Table 1). Those with high ABI (≥1.30) also demonstrated a worse risk factor profile and more adverse clinical comorbidity profile with increased age, higher adiposity, higher prevalence of diabetes mellitus, and prior history of CVD compared to those with ABI in the reference range (1.10-1.19).

The 12-Item Short-Form Health Survey

In the study population the mean scores for the Physical and Mental Component Summary were 46.8 (SD 9.9) and 55.5 (SD 7.5), respectively. Compared to the reference of ABI 1.10 to 1.19, individuals with ABI <1.00 demonstrated a significantly lower Physical Component Summary score (−3.26 [95% CI −5.60 to −0.92] for ABI <0.90 and −2.23 [95% CI −4.07 to −0.39] for ABI 0.90-0.99) in Model 3 (Figure). This decrement by lower ABI was not significant for the Mental Component Summary score.

When we looked at each domain separately, ABI <0.90 was significantly associated with lower scores in all physical component domains, compared to the reference, in Model 3. This was most apparent for the physical functioning score (−3.42 [95% CI −5.50 to −1.35]), followed by the role physical, general health, and bodily pain scores (Table 2 and Table S2). Individuals with ABI 0.90 to 0.99 had lower scores for all physical domains compared to the reference group as well, but the difference reached significance only for the "role-physical" domain (−1.87 [95% CI −3.58 to −0.16]) and bodily pain domain (−1.59 [95% CI −3.13 to −0.05]). As

Table 1. Characteristics of the Study Population According to Categories of ABI, the ARIC Study (2011-2013)

Characteristics	ABI Categories (n)							
	All (5115)	<0.9 (402)	0.90 to 0.99 (426)	1.00 to 1.09 (1234)	1.10 to 1.19 (1900)	1.20 to 1.29 (694)	≥1.3 (459)	P Value*
Age (y), mean (SD)	75.4 (5.0)	77.3 (5.5)	76.0 (5.6)	75.3 (5.1)	75.0 (4.8)	74.8 (4.9)	75.5 (4.8)	<0.001
Sex (Females)	2948 (57.6%)	214 (53.2%)	298 (70.0%)	878 (71.2%)	1138 (59.9%)	289 (41.6%)	131 (28.5%)	<0.001
Blacks	1113 (21.8%)	164 (40.8%)	133 (31.2%)	352 (28.5%)	352 (18.5%)	66 (9.5%)	46 (10.0%)	<0.001
Education†	2819 (55.1%)	258 (64.2%)	264 (62.0%)	732 (59.3%)	1029 (54.2%)	339 (48.8%)	197 (42.9%)	<0.001
Economic status†	2367 (46.3%)	232 (57.7%)	229 (53.8%)	642 (52.0%)	828 (43.6%)	267 (38.5%)	169 (36.8%)	<0.001
Current smoker	297 (5.8%)	56 (13.9%)	53 (12.4%)	77 (6.2%)	80 (4.2%)	16 (2.3%)	15 (3.3%)	<0.001
Current drinker	2559 (50.8%)	147 (36.6%)	179 (42.0%)	561 (45.5%)	1040 (54.7%)	410 (59.1%)	262 (57.1%)	<0.001
Body mass index (kg/m²), mean (SD)	28.6 (5.5)	28.9 (5.9)	29.5 (6.6)	29.0 (5.7)	28.2 (5.1)	28.0 (4.7)	29.1 (5.6)	<0.001
Total cholesterol (mmol/L), mean (SD)	4.7 (1.1)	4.6 (1.1)	4.8 (1.1)	4.8 (1.1)	4.7 (1.1)	4.6 (1.0)	4.4 (1.0)	<0.001
Diabetes mellitus	1606 (31.4%)	173 (43.0%)	142 (33.3%)	388 (31.4%)	546 (28.7%)	205 (29.5%)	152 (33.1%)	<0.001
Hypertension	3774 (73.8%)	347 (86.3%)	338 (79.3%)	953 (77.2%)	1343 (70.7%)	481 (69.3%)	312 (68.0%)	<0.001
CHD history	734 (14.3%)	115 (28.6%)	72 (16.9%)	153 (12.4%)	229 (12.1%)	88 (12.7%)	77 (16.8%)	<0.001
Heart failure history	239 (4.7%)	58 (14.4%)	28 (6.6%)	56 (4.5%)	59 (3.1%)	16 (2.3%)	22 (4.8%)	<0.001
Stroke history	174 (3.4%)	29 (7.2%)	26 (6.1%)	36 (2.9%)	50 (2.6%)	18 (2.6%)	15 (3.3%)	<0.001
Lung disease	566 (11.1%)	72 (17.9%)	64 (15.0%)	155 (12.6%)	185 (9.7%)	54 (7.8%)	36 (7.8%)	<0.001
Kidney function†	1424 (27.8%)	176 (43.8%)	160 (37.6%)	351 (28.4%)	463 (24.4%)	156 (22.5%)	118 (25.7%)	<0.001

ABI indicates ankle-brachial index; CHD, coronary heart disease.
*P-value calculated by analysis of variance (ANOVA) test for continuous variables and by chi-squared test for categorical variables.
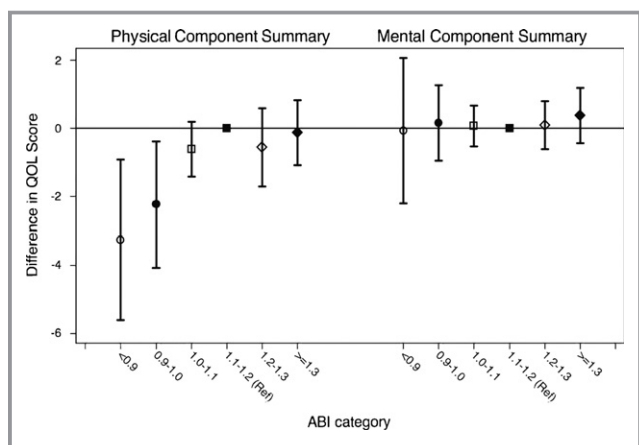†Showing the prevalence of lower level, ie, lower education level, lower economic status, and reduced kidney function.

Figure. The adjusted difference and 95% CI in quality of life (QOL) scores according to ankle-brachial index (ABI) categories (Physical/Mental Component Summary from SF-12). Physical Component Summary and Mental Component Summary scores were adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol level, diabetes mellitus, hypertension, history of coronary heart disease, heart failure, and stroke, lung disease, and reduced kidney function.

anticipated, a stronger association was observed between lower ABI values and reduced physical domains in Models 1 and 2 (Tables S3 and S4).

Compared to physical components, the association with mental domains was weaker (Table 2). One exception was vitality score, which was significantly lower in ABI categories <1.00 compared to the reference (−1.54 [95% CI −2.25 to −0.83] for ABI <0.9 and −1.38 [95% CI −1.98 to −0.78] for ABI 0.90-0.99). Similar results were observed in Models 1 and 2 except for the presence of a significant association between lower ABI and lower role emotional score as well as a more pronounced ABI-vitality association (Tables S3 and S4). High ABI ≥1.30 did not demonstrate significantly lower score in any of the physical and mental domains.

The Other QOL Parameters

We observed dose-response relationships between ABI and the other physical activity QOL parameters (Table 3). In line with the results for physical components in SF-12, low ABI <0.90 was significantly associated with these 3 other physical activity parameters (OR 1.34 [95% CI 1.09-1.64] for "low" leisure-time exercise, 1.35 [95% CI 1.21-1.50] for "low" leisure-time activity, and 1.43 [95% CI 1.25-1.63] for "low" leisure-time walk) compared to the reference ABI group. The significantly lower leisure-time activity level and walking frequency were also observed in borderline low ABI 0.90 to 0.99. Of note, low normal ABI 1.00 to 1.09 was also significantly associated with these 3 parameters of physical activity (OR 1.21 [95% CI 1.09-1.35] for "low" leisure-time

exercise, 1.15 [95% CI 1.04-1.26] for "low" leisure-time activity, and 1.24 [95% CI 1.11-1.39] for "low" leisure-time walk). Again, stronger associations were observed in Models 1 and 2 (Tables S5 and S6).

The other mental parameters, significant depressive symptoms and hopeless feeling, demonstrated weaker independent associations with lower ABI compared to the other physical activity parameters (Table 3). Although significant depressive symptoms tended to associate with lower ABI, none of the odds ratios was significant. The odds of hopeless feeling were significantly higher only in borderline low ABI 0.90 to 0.99 compared to the reference ABI group. However, these mental parameters were consistently associated with low ABI categories in demographically adjusted Model 1 (Table S5).

Subgroup Analysis

The associations between ABI and physical components of QOL were also observed in most subgroups tested (Table S7 for SF-12 physical summary score and Table S8 for the other physical QOL parameters). Notably, the associations between lower ABI and poor physical QOL components were consistently stronger in participants without a history of CVD than in those with history of CVD (Tables S7 and S8).

Reflecting overall weak association, we did not observe consistently lower mental QOL components in any subgroups for SF-12 mental summary score (Table S9). However, of interest, for the other mental QOL parameters, lower ABI (<1.00), compared to ABI ≥1.00, was significantly associated with higher odds of significant depressive symptoms and hopeless feeling in whites, whereas lower ABI was significantly related to lower odds of those mental conditions in blacks (Table S10).

Discussion

This study quantified the association between ABI and several domains of QOL among community-dwelling older adults from 4 US communities. With ABI 1.10 to 1.19 as reference group, low ABI (<0.90) and borderline low ABI (0.90-0.99) were associated with poorer QOL status, as defined by a number of subdomains. The association with lower ABI was more evident for physical components of QOL than for mental components in SF-12. The association of ABI with physical components of QOL was confirmed by analyses of leisure-time exercise, activity, and walking. A lower ABI was also significantly associated with a mental domain in SF-12, ie, vitality, which may be a psychological basis to be engaged in physical activity. Poor QOL status for physical health components was observed even among those participants who were without any other clinically recognized CVD

Table 2. Fully Adjusted* Difference in Quality of Life Scores According to ABI Categories

| QOL Domains | ABI Categories (n) | | | | |
| | <0.90 (402) | 0.90 to 0.99 (426) | 1.00 to 1.09 (1234) | 1.10 to 1.19 (1900) | 1.20 to 1.29 (694) | ≥1.30 (459) |
	Coefficient† (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Reference	Coefficient (95% CI)	Coefficient (95% CI)
Physical components	−3.26 (−5.60 to −0.92)‡	−2.23 (−4.07 to −0.39)‡	−0.62 (−1.42 to 0.19)	0	−0.56 (−1.71 to 0.59)	−0.13 (−1.09 to 0.82)
Physical functioning	−3.42 (−5.50 to −1.35)‡	−1.71 (−3.94 to 0.52)	−0.68 (−1.58 to 0.22)	0	−0.21 (−1.61 to 1.18)	−0.43 (−1.58 to 0.71)
Role physical	−2.76 (−4.98 to −0.55)‡	−1.87 (−3.58 to −0.16)‡	−0.90 (−2.25 to 0.45)	0	−0.45 (−1.48 to 0.58)	−0.01 (−1.64 to 1.62)
Bodily pain	−1.99 (−3.77 to −0.22)‡	−1.59 (−3.13 to −0.05)‡	−0.15 (−0.81 to 0.52)	0	−1.01 (−2.48 to 0.45)	−0.03 (−1.42 to 1.35)
General health	−2.31 (−3.52 to −1.09)‡	−1.55 (−3.30 to 0.20)	−0.16 (−1.36 to 1.04)	0	0.00 (−1.16 to 1.16)	0.50 (−0.63 to 1.63)
Mental components	−0.07 (−2.21 to 2.06)	0.15 (−0.96 to 1.26)	0.06 (−0.54 to 0.66)	0	0.09 (−0.62 to 0.79)	0.37 (−0.44 to 1.19)
Mental health	−0.62 (−2.47 to 1.23)	0.01 (−0.51 to 0.53)	0.29 (−0.59 to 1.17)	0	0.04 (−1.15 to 1.23)	0.47 (−0.64 to 1.57)
Role emotional	−1.41 (−2.98 to 0.16)	−0.42 (−1.49 to 0.64)	−0.74 (−1.49 to 0.00)	0	−0.13 (−0.91 to 0.65)	−0.17 (−0.97 to 0.64)
Social functioning	−0.58 (−2.07 to 0.92)	−0.54 (−1.99 to 0.92)	0.02 (−0.42 to 0.46)	0	−0.02 (−1.23 to 1.19)	0.09 (−1.27 to 1.45)
Vitality	−1.54 (−2.25 to −0.83)‡	−1.38 (−1.98 to −0.78)‡	−0.18 (−0.49 to 0.13)	0	−0.31 (−0.88 to 0.26)	0.42 (−0.03 to 0.88)

ABI indicates ankle-brachial index; QOL, quality of life.

*Adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol, diabetes mellitus, hypertension, history of coronary heart disease (CHD), heart failure, and stroke, lung disease, and reduced kidney function.

†Linear regression coefficient. It represents the difference in QOL score between a given ABI category and the reference category (1.10-1.19).

‡Indicates significant results.

Table 3. Fully Adjusted* Odds Ratio of Other Quality of Life Aspects According to ABI Categories

Other QOL Aspects	ABI Categories (n)					
	<0.90	0.90 to 0.99 (426)	1.00 to 1.09 (1234)	1.10 to 1.19 (1900)	1.20 to 1.29 (694)	≥1.30 (459)
	No. Low QOL/Total OR† (95% CI)	No. Low QOL/Total OR (95% CI)	No. Low QOL/Total OR (95% CI)	Reference	No. Low QOL/Total OR (95% CI)	No. Low QOL/Total OR (95% CI)
Physical activity						
"Low" leisure-time exercise	230/402 1.34 (1.09-1.64)‡	248/426 1.38 (0.98-1.93)	656/1234 1.21 (1.09-1.35)‡	859/1900 1	299/694 1.01 (0.79-1.30)	191/459 0.95 (0.68-1.32)
"Low" leisure-time activity	101/402 1.35 (1.21-1.50)‡	103/426 1.26 (1.13-1.40)‡	253/1234 1.15 (1.04-1.26)‡	304/1900 1	80/694 0.74 (0.62-0.88)‡	59/459 0.76 (0.60-0.98)‡
"Low" leisure-time walk	158/402 1.43 (1.25-1.63)‡	162/426 1.38 (1.08-1.76)‡	413/1234 1.24 (1.11-1.39)‡	501/1900 1	163/694 0.94 (0.77-1.14)	110/459 0.93 (0.80-1.08)
Mental health						
Significant depressive symptoms	46/402 1.51 (0.87-2.62)	35/426 1.19 (0.79-1.81)	91/1234 1.22 (0.98-1.52)	95/1900 1	24/694 0.79 (0.46-1.34)	19/459 0.91 (0.62-1.32)
Feel hopeless	55/402 1.13 (0.97-1.31)	56/426 1.20 (1.07-1.33)‡	159/1234 1.32 (0.96-1.80)	165/1900 1	50/694 0.91 (0.63-1.32)	35/459 0.94 (0.53-1.66)

ABI indicates ankle-brachial index; QOL, quality of life.

*Adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol, diabetes mellitus, hypertension, history of coronary heart disease (CHD), heart failure, and stroke, lung disease, and reduced kidney function.

†Logistic regression models were applied to assess the 5 binary other QOL aspects.

‡Indicates significant results.

(ie, CHD, stroke, and heart failure) or clinical conditions tightly related to PAD (eg, reduced kidney function).

The more evident association of low ABI with physical components of QOL status compared to mental components of QOL is consistent with previous studies performed in clinical populations.[11,16,17,42] Of note, our study is the first to test the full spectrum of ABI in this context among community-dwelling older adults not selected for clinical conditions. It is of importance that even borderline low ABI was associated with reduced physical QOL. There are several potential mechanisms linking PAD to the impairments for physical components of QOL. Individuals with low ABI often have other manifestations of CVD and comorbidities, which may lead to poor physical condition and reduce QOL. However, the association of ABI with physical domains of QOL was independent of major comorbidities. These relationships could certainly be hypothesized to have potential PAD-specific mechanisms, such as decreased blood flow to the legs, which can induce clinically significant skeletal muscle atrophy and denervation through ongoing ischemia.[43] Exertional leg pain or discomfort (whether due to classic claudication or atypical leg pain) may additionally contribute to these lower physical ability QOL scores. Importantly, fear of falling was reported among those with intermittent claudication[44] and could further impact and limit their physical activity.

Low ABI was significantly associated with lower vitality, a mental measure of QOL. The data from this ARIC analysis are concordant with those of a previous study that demonstrated a stronger association of low ABI values with diminished vitality than with other mental domains.[17] We also observed significant associations with significant depressive symptoms and hopeless feeling in some low-ABI categories, particularly in Models 1 and 2. Although the exact mechanisms for the association between PAD and mental elements of QOL represented by vitality are not clear, limited physical activity as well as impaired working ability due to PAD may impact mental QOL domains. In addition, resting or exertional leg symptoms or fear of falling due to PAD, mentioned above, may further contribute to reduced mental elements of QOL.

Although a weaker association was seen among individuals with a history of CVD than those without, the contribution of low ABI to physical QOL parameters was qualitatively consistent across all subgroups tested in our study. The weaker association among those with a history of CVD may be due to the fact that many participants with prior CVD had already reduced QOL, especially for physical components, and low ABI may not considerably contribute to further discrimination beyond other CVDs. Indeed, the mean Physical Component Summary score was lower among participants with a history of CVD compared to those without CVD (43.6 versus 47.5). Regarding mental elements, we observed a significant qualitative racial interaction for low ABI and significant depressive symptoms/hopeless feeling, with positive associations in whites but negative associations in blacks. The potential background for this interaction is not

clear. Nonetheless, this subgroup analysis should be considered hypothesis generating, as we tested multiple subgroups without an a priori hypothesis of biological interaction.

Our findings of the association of low ABI and impaired QOL among community-dwelling older adults may have some clinical and public health implications. Staying physically active is an important goal for older adults as a determinant of the ability to sustain independent living. Because several lifestyle (eg, smoking cessation or supervised exercise) or medical (eg, cilostazol or revascularization) interventions have demonstrated improvement in physical function among patients with PAD,[45-47] it seems important to identify the contribution of PAD to the reduction of physical components of QOL in older adults. It is important to keep in mind that reduced QOL was also observed in those with borderline low ABI (<1.00) in our study. Further studies might assess whether PAD-specific interventions would comprehensively improve physical components of QOL and vitality in community-dwelling older adults with a low ABI but otherwise not diagnosed as PAD.

Our study has several limitations. First, for any cross-sectional analysis, it is not possible to establish the temporality or causality of our observed associations of low ABI with poor QOL status.[48] Second, the ARIC Study did not collect specific information on leg pain at visit 5. Third, our results may not be entirely generalizable to racial/ethnic groups other than whites and blacks. Fourth, it is possible that those individuals with a very low ABI and/or severely reduced QOL were less likely to attend ARIC visit 5, raising the possibility that our results may underestimate the relationship between low ABI <0.9 and QOL. Finally, as any observational study, we cannot deny the possibility of residual confounding.

In conclusion, among older adults in the community, those with ABI <1.0 were independently associated with reduced QOL status. The association was particularly evident for physical components of QOL but was also observed for a mental domain, vitality. Because QOL is a critical element in addition to survival, especially in older adults, further studies are warranted to assess the causality of ABI in the development of poor QOL and, if so, to explore whether the management of PAD can improve QOL among older adults afflicted by this disease.

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Disclosures

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SUPPLEMENTAL MATERIAL

Table S1. Baseline characteristics in participants included and those excluded in the analysis

Characteristics	Participants Included	Participants Excluded
Number of participants	5115	1405
Age (year), mean (SD)	75.4 (5.0)	77.5 (5.7)
Sex(Females)	2948 (57.6%)	887 (63.1%)
African Americans	1113 (21.8%)	431 (30.7%)
Education[†‡]	2819 (55.1%)	876 (62.8%)
Economic Status[†‡]	2367 (46.3%)	625 (54.6%)
Body Mass Index[‡] (kg/m^2), Mean (SD)	28.6 (5.5)	29.5 (7.0)
Total Cholesterol[‡] (mmol/L), Mean (SD)	4.7 (1.1)	4.7 (1.1)
Diabetes[‡]	1606 (31.4%)	515 (45.0%)
Hypertension[‡]	3774 (73.8%)	1040 (79.3%)
CVD History[‡§]	973 (19.0%)	357 (27.5%)

* P-value calculated by analysis of variance (ANOVA) test for continuous variables and by chi-squared test for categorical variables.

† Using lower level as reference, i.e. lower education level and lower economic status.

‡ Covariates with missingness but is less than 5% of the total 6520 participants for the study population.

§ Cardiovascular disease (CVD) history was defined as having any history of coronary heart disease, heart failure or stroke.

Table S2. Description of participant's SF-12 quality of life (QOL) parameters according to ankle brachial index (ABI) categories

Characteristics	ABI categories (n)							
	All (5,115)	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)	P-value*
Physical Component[†]	46.8 (9.9)	41.9 (10.5)	43.6 (10.8)	46.3 (10.0)	48.1 (9.2)	48.2 (9.5)	48.1 (9.0)	<0.001
Physical Functioning[†]	47.9 (10.4)	43.0 (11.5)	45.1 (11.6)	47.2 (10.6)	49.0 (9.7)	49.7 (9.7)	49.0 (9.5)	<0.001
Role Physical[†]	48.5 (9.1)	44.5 (9.7)	46.1 (9.6)	47.9 (9.3)	49.6 (8.8)	49.6 (8.5)	49.5 (8.5)	<0.001
Bodily Pain[†]	48.7 (10.1)	46.1 (10.9)	46.5 (11.6)	48.5 (10.1)	49.5 (9.7)	49.0 (9.7)	49.8 (9.3)	<0.001
General Health[†]	50.1 (9.7)	44.8 (10.8)	47.1 (10.2)	49.5 (9.4)	51.2 (9.3)	52.1 (8.9)	52.2 (8.8)	<0.001
Mental Component [†]	55.5 (7.5)	54.6 (9.0)	55.1 (8.4)	55.2 (7.9)	55.5 (7.0)	56.0 (6.8)	56.4 (6.4)	0.002
Mental Health[†]	54.9 (7.9)	53.3 (9.1)	54.0 (8.8)	54.7 (8.0)	55.1 (7.6)	55.7 (7.1)	56.2 (7.0)	<0.001
Role Emotional[†]	51.9 (7.5)	49.7 (9.4)	51.1 (7.9)	51.1 (8.2)	52.5 (6.9)	52.7 (6.4)	52.6 (6.8)	<0.001
Social Functioning[†]	52.7 (7.9)	51.0 (9.5)	51.6 (8.7)	52.5 (8.0)	53.1 (7.8)	53.4 (7.0)	53.4 (6.9)	<0.001
Vitality[†]	53.1 (9.1)	50.4 (9.6)	50.9 (9.3)	52.8 (9.1)	53.8 (8.9)	53.9 (8.7)	54.3 (8.6)	<0.001

* P-value calculated by analysis of variance (ANOVA) tests.

† Mean (SD) was reported.

Table S3. Partially adjusted[†] difference in quality of life (QOL) scores according to ankle brachial index (ABI) categories (Model 1)

QOL Domains	ABI categories (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	Coefficient[‡] (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)
Physical Components	-5.28 (-8.32 to -2.24)*	-3.72 (-5.03 to -2.41)*	-1.29 (-1.82 to -0.75)*	0	-0.39 (-1.98 to 1.20)	-0.72 (-1.90 to 0.47)
Physical Functioning	-5.41 (-8.11 to -2.71)*	-3.17 (-5.02 to -1.33)*	-1.33 (-2.12 to -0.55)*	0	-0.03 (-2.05 to 2.00)	-1.01 (-2.78 to 0.76)
Role Physical	-4.33 (-7.14 to -1.52)*	-3.03 (-4.01 to -2.04)*	-1.41 (-2.34 to -0.48)*	0	-0.32 (-1.21 to 0.58)	-0.44 (-2.02 to 1.14)
Bodily Pain	-3.21 (-5.24 to -1.19)*	-2.60 (-4.34 to -0.85)*	-0.61 (-0.94 to -0.29)*	0	-0.91 (-2.59 to 0.77)	-0.47 (-2.29 to 1.34)
General Health	-4.12 (-5.97 to -2.26)*	-2.71 (-4.26 to -1.17)*	-0.69 (-2.05 to 0.68)	0	0.14 (-1.26 to 1.54)	0.16 (-0.35 to 0.68)
Mental Components	-0.34 (-2.25 to 1.57)	-0.01 (-1.04 to 1.03)	0.00 (-0.60 to 0.61)	0	0.11 (-0.54 to 0.76)	0.37 (-0.51 to 1.26)
Mental Health	-1.24 (-2.84 to 0.36)	-0.42 (-0.77 to -0.06)*	0.11 (-0.73 to 0.96)	0	0.11 (-1.00 to 1.21)	0.39 (-0.82 to 1.60)
Role Emotional	-2.00 (-3.60 to -0.39)*	-0.83 (-2.10 to 0.43)	-0.93 (-1.70 to -0.16)*	0	-0.09 (-0.93 to 0.75)	-0.32 (-1.44 to 0.79)
Social Functioning	-1.28 (-2.88 to 0.32)	-1.01 (-2.61 to 0.59)	-0.19 (-0.51 to 0.13)	0	0.05 (-1.23 to 1.34)	-0.07 (-1.52 to 1.39)
Vitality	-2.89 (-4.54 to -1.25)*	-2.41 (-3.11 to -1.71)*	-0.62 (-1.25 to 0.02)	0	-0.20 (-0.90 to 0.50)	0.05-0.83 to 0.94)

* Indicates significant results.

† Adjusted for age, sex, ethnicity, education level, economic status.

‡ Linear regression coefficient: It represents the difference in QOL score between a given ABI category to the reference category (1.10-1.19).

Table S4. Partially adjusted[†] difference in quality of life (QOL) scores according to ankle brachial index (ABI) categories (Model 2)

QOL Domains	ABI categories (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	Coefficient[‡] (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)
Physical Components	-4.40 (-6.88 to -1.92)*	-2.82 (-4.28 to -1.36)*	-0.84 (-1.46 to -0.23)*	0	-0.38 (-1.62 to 0.86)	-0.07 (-0.80 to 0.66)
Physical Functioning	-4.62 (-6.83 to -2.42)*	-2.32 (-4.19 to -0.46)*	-0.92 (-1.71 to -0.14)*	0	-0.03 (-1.59 to 1.54)	-0.37 (-1.71 to 0.96)
Role Physical	-3.65 (-6.01 to -1.28)*	-2.34 (-3.76 to -0.91)*	-1.08 (-2.30 to 0.14)	0	-0.31 (-1.28 to 0.65)	0.03 (-1.36 to 1.42)
Bodily Pain	-2.59 (-4.23 to -0.94)*	-1.91 (-3.69 to -0.14)*	-0.27 (-0.92 to 0.37)	0	-0.91 (-2.36 to 0.54)	0.01 (-1.40 to 1.42)
General Health	-3.27 (-4.76 to -1.79)*	-2.06 (-3.54 to -0.57)*	-0.35 (-1.59 to 0.89)	0	0.16 (-1.07 to 1.39)	0.56 (-0.25 to 1.38)
Mental Components	-0.17 (-2.32 to 1.98)	0.09 (-1.07 to 1.24)	0.03 (-0.57 to 0.63)	0	0.11 (-0.62 to 0.84)	0.38 (-0.46 to 1.23)
Mental Health	-0.92 (-2.75 to 0.91)	-0.15 (-0.72 to 0.42)	0.22 (-0.62 to 1.06)	0	0.09 (-1.06 to 1.25)	0.49 (-0.63 to 1.60)
Role Emotional	-1.73 (-3.33 to -0.14)*	-0.61 (-1.84 to 0.63)	-0.82 (-1.59 to -0.05)*	0	-0.08 (-0.85 to 0.69)	-0.15 (-1.04 to 0.75)
Social Functioning	-1.03 (-2.55 to 0.49)	-0.76 (-2.40 to 0.88)	-0.08 (-0.48 to 0.33)	0	0.06 (-1.20 to 1.31)	0.12 (-1.27 to 1.50)
Vitality	-2.17 (-3.41 to -0.93)*	-1.75 (-2.25 to -1.25)*	-0.32 (-0.73 to 0.10)	0	-0.21 (-0.77 to 0.36)	0.46 (-0.12 to 1.05)

* Indicates significant results.

† Adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol, diabetes, hypertension, history of coronary heart disease, history of heart failure and history of stroke

‡ Linear regression coefficient: It represents the difference in QOL score between a given ABI category to the reference category (1.10-1.19).

Table S5. Partially adjusted[†] odds-ratio of other quality of life (QOL) aspects according to ankle brachial index (ABI) categories

(Model 1)

Other QOL Aspects	ABI categories (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	OR[‡] (95% CI)	OR (95% CI)	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)
Physical Activity						
"Low" leisure time exercise	1.51 (1.20 to 1.90)*	1.54 (1.06 to 2.23)*	1.28 (1.13 to 1.45)*	1	1.01 (0.80 to 1.28)	1.01 (0.71 to 1.42)
"Low" leisure time activity	1.74 (1.51 to 2.01)*	1.58 (1.36 to 1.83)*	1.26 (1.11 to 1.42)*	1	0.74 (0.59 to 0.92)*	0.90 (0.67 to 1.20)
"Low" leisure time walk	1.62 (1.42 to 1.85)*	1.56 (1.17 to 2.09)*	1.31 (1.16 to 1.49)*	1	0.93 (0.76 to 1.13)	0.99 (0.84 to 1.16)
Mental Health						
Significant depressive symptoms	1.97 (1.14 to 3.41)*	1.46 (1.00 to 2.14)*	1.32 (1.10 to 1.59)*	1	0.78 (0.48 to 1.27)	1.02 (0.65 to 1.61)
Feel Hopeless	1.33 (1.10 to 1.61)*	1.37 (1.26 to 1.50)*	1.39 (1.03 to 1.88)*	1	0.91 (0.64 to 1.30)	1.02 (0.56 to 1.84)

* Indicates significant results.

† Adjusted for age, sex, ethnicity, education level, economic status.

‡ Logistic regression models were applied to assess the 5 binary other QOL aspects.

Table S6. Partially adjusted† odds-ratio of other quality of life (QOL) aspects according to ankle brachial index (ABI) categories

(Model 2)

Other QOL Aspects	ABI categories (n)					
	<0.90 (402)	0.90-0.99 (426)	1.00-1.09 (1,234)	1.10-1.19 (1,900)	1.20-1.29 (694)	≥1.30 (459)
	OR‡ (95% CI)	OR (95% CI)	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)
Physical Activity						
"Low" leisure time exercise	1.38 (1.12 to 1.71)*	1.41 (1.00 to 1.99)	1.22 (1.10 to 1.36)*	1	1.01 (0.79 to 1.29)	0.95 (0.68 to 1.33)
"Low" leisure time activity	1.51 (1.38 to 1.66)*	1.36 (1.18 to 1.57)*	1.17 (1.09 to 1.27)*	1	0.73 (0.60 to 0.90)*	0.78 (0.58 to 1.04)
"Low" leisure time walk	1.50 (1.33 to 1.69)*	1.44 (1.14 to 1.82)*	1.26 (1.13 to 1.42)*	1	0.93 (0.77 to 1.12)	0.92 (0.79 to 1.07)
Mental Health						
Significant depressive symptoms	1.76 (0.99 to 3.13)	1.32 (0.85 to 2.03)	1.27 (1.04 to 1.56)*	1	0.78 (0.47 to 1.28)	0.92 (0.60 to 1.42)
Feel Hopeless	1.21 (1.01 to 1.45)*	1.27 (1.12 to 1.44)*	1.35 (0.99 to 1.83)	1	0.91 (0.63 to 1.30)	0.95 (0.53 to 1.71)

* Indicates significant results.

† Adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol, diabetes, hypertension, history of coronary heart disease, history of heart failure and history of stroke.

‡ Logistic regression models were applied to assess the 5 binary other QOL aspects.

Table S7. Adjusted† difference in Physical Component Summary scores across ankle brachial index (ABI) categories in different

subgroups

Subgroups	ABI categories (n)						P value for interaction
	<0.90	0.90-0.99	1.00-1.09	1.10-1.19	1.20-1.29	≥1.30	
	Coefficient‡ (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)	
Sex							
Males	-3.84 (-8.25 to 0.57)	-1.72 (-3.68 to 0.24)	-0.46 (-1.90 to 0.98)	0	0.57 (-0.30 to 1.45)	0.28 (-1.01 to 1.56)	0.014*
Females	-2.56 (-5.39 to 0.27)	-2.44 (-4.41 to -0.48)*	-0.74 (-2.20 to 0.73)	0	-1.88 (-4.33 to 0.58)	-0.45 (-2.73 to 1.83)	
Ethnicity							
Caucasians	-3.68 (-7.13 to -0.23) *	-2.00 (-4.53 to 0.53)	-0.48 (-1.40 to 0.45)	0	-0.37 (-0.87 to 0.12)	0.05 (-0.90 to 1.00)	0.051
African Americans	-3.05 (-3.78 to -2.31) *	-2.73 (-3.79 to -1.68)*	-0.88 (-1.49 to -0.27)*	0	-2.47 (-6.31 to 1.36)	-1.54 (-3.01 to -0.07)*	
CVD History							
No CVD history	-4.54 (-7.70 to -1.38) *	-2.56 (-5.23 to 0.10)	-0.67 (-1.73 to 0.39)	0	-0.96 (-2.29 to 0.38)	-0.42 (-2.20 to 1.36)	0.001*
CVD history	-1.10 (-2.82 to 0.62)	-1.01 (-3.62 to 1.60)	-0.22 (-1.15 to 0.71)	0	1.58 (-0.64 to 3.80)	1.20 (-2.02 to 4.41)	
Diabetes							
No Diabetes	-3.60 (-7.10 to -0.09)*	-2.56 (-4.81 to -0.31)*	-0.95 (-2.64 to 0.74)	0	-1.05 (-2.43 to 0.33)	-0.39 (-1.76 to 0.98)	0.388
Diabetes	-2.37 (-3.20 to -1.53)*	-1.32 (-5.83 to 3.18)	0.19 (-1.25 to 1.64)	0	0.63 (-0.88 to 2.14)	0.71 (-1.52 to 2.94)	
Reduced Kidney Function							
Not Reduced	-3.33 (-5.59 to -1.06)*	-2.78 (-4.79 to -0.77)*	-1.26 (-2.46 to -0.07)*	0	-1.00 (-2.16 to 0.17)	-0.04 (-1.64 to 1.56)	0.096
Reduced	-2.86 (-5.40 to -0.31)*	-0.87 (-2.94 to 1.20)	1.14 (-0.14 to 2.43)	0	0.84 (-2.85 to 4.52)	-0.26 (-1.66 to 1.13)	

* Indicates significant results.

† Adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol, diabetes, hypertension, cardiovascular disease (CVD) history, lung disease and reduced kidney function (excluding corresponding covariate indicating each subgroup).

‡ Linear regression coefficient: It represents the difference in Physical Component Summary score between ABI category <1.00 and the reference category (≥1.00).

Table S8. Adjusted[†] odds-ratio of other physical activity aspects for lower ankle brachial index (ABI) (<1.00) in different subgroups.

Subgroups	Physical Activity Aspects					
	"Low" leisure time exercise		"Low" leisure time activity		"Low" leisure time walk	
	Case/N[‡]	OR[§] (95% CI)	Case/N	OR (95% CI)	Case/N	OR (95% CI)
Sex						
Males	162/316	1.30 (0.91 to 1.87)	56/316	1.10 (0.81 to 1.48)	104/316	1.34 (1.05 to 1.71)*
Females	316/512	1.25 (1.04 to 1.50)*	148/512	1.41 (1.18 to 1.69)*	216/512	1.30 (1.18 to 1.43)*
P value for interaction		0.854		0.661		0.629
Ethnicity						
Caucasians	314/531	1.38 (1.01 to 1.88)*	122/531	1.29 (1.14 to 1.47)*	206/531	1.38 (1.14 to 1.66)*
African Americans	164/297	1.10 (0.98 to 1.23)	82/297	1.27 (1.24 to 1.30)*	114/297	1.18 (1.07 to 1.30)*
P value for interaction		0.150		0.686		0.278
CVD History						
No CVD history	329/565	1.31 (1.01 to 1.70)*	149/565	1.50 (1.34 to 1.69)*	226/565	1.41 (1.24 to 1.61)*
CVD history	149/263	1.17 (0.91 to 1.51)	55/263	0.96 (0.69 to 1.32)	94/263	1.08 (0.84 to 1.39)
P value for interaction		0.185		0.007*		< 0.001*
Diabetes						
No Diabetes	276/513	1.14 (0.83 to 1.56)	111/513	1.47 (1.04 to 2.07)*	192/513	1.40 (1.04 to 1.88)*
Diabetes	202/315	1.57 (1.21 to 2.03)*	93/315	1.08 (0.79 to 1.48)	128/315	1.18 (0.88 to 1.57)
P value for interaction		0.315		0.262		0.352
Reduced Kidney Function						
Not Reduced	283/492	1.35 (1.06 to 1.71)*	117/492	1.42 (1.24 to 1.62)*	176/492	1.35 (1.17 to 1.56)*
Reduced	195/336	1.15 (0.86 to 1.53)	87/336	1.15 (0.88 to 1.50)	144/336	1.26 (1.04 to 1.53)
P value for interaction		0.383		0.069		0.662

* Indicates significant results.

† Adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol, diabetes, hypertension, cardiovascular disease (CVD) history, lung disease and reduced kidney function (excluding corresponding covariate indicating each

subgroup).

‡ Number of individuals having outcome with ABI < 1.00 for each subgroup/ Total number of individuals with ABI < 1.00 for each subgroup.

§ Logistic regressions were applied to assess the odds ratio for 3 binary physical activity aspects between ABI <1.00 and the reference category (≥1.00).

Table S9. Adjusted[†] difference in Mental Component Summary scores across ankle brachial index (ABI) categories in different

subgroups

Subgroups	ABI categories (n)						P value for interaction
	<0.90	0.90-0.99	1.00-1.09	1.10-1.19	1.20-1.29	≥1.30	
	Coefficient[‡] (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Ref	Coefficient (95% CI)	Coefficient (95% CI)	
Sex							
Males	0.27 (-2.23 to 2.78)	-0.71 (-2.16 to 0.75)	0.62 (-0.20 to 1.44)	0	0.19 (-1.01 to 1.40)	0.19 (-0.74 to 1.12)	0.280
Females	-0.36 (-2.21 to 1.48)	0.47 (-1.46 to 2.40)	-0.20 (-0.88 to 0.49)	0	0.06 (-1.90 to 2.02)	0.95 (-0.74 to 2.64)	
Ethnicity							
Caucasians	-0.39 (-2.85 to 2.07)	0.09 (-1.37 to 1.55)	0.20 (-0.41 to 0.81)	0	0.26 (-0.27 to 0.80)	0.58 (-0.15 to 1.31)	0.152
African Americans	0.24 (-1.55 to 2.04)	0.14 (-0.55 to 0.83)	-0.41 (-2.08 to 1.25)	0	-0.73 (-1.89 to 0.43)	-0.50 (-1.00 to -0.01)*	
CVD History							
No CVD history	-0.39 (-2.87 to 2.10)	0.39 (-0.84 to 1.61)	0.04 (-0.63 to 0.71)	0	0.24 (-0.42 to 0.91)	0.35 (-0.58 to 1.28)	0.011*
CVD history	0.29 (-1.57 to 2.16)	-0.53 (-1.68 to 0.63)	0.20 (-1.39 to 1.79)	0	-0.81 (-2.39 to 0.77)	0.31 (-0.14 to 0.76)	
Diabetes							
No Diabetes	-0.37 (-1.73 to 1.00)	0.09 (-1.25 to 1.44)	-0.05 (-1.21 to 1.11)	0	0.30 (-0.08 to 0.67)	0.47 (-1.14 to 2.09)	0.976
Diabetes	0.36 (-2.86 to 3.57)	0.61 (-2.23 to 3.45)	0.33 (-1.87 to 2.53)	0	-0.27 (-2.17 to 1.63)	0.31 (-1.13 to 1.76)	
Reduced Kidney Function[§]							
Not Reduced	0.31 (-2.78 to 3.41)	0.59 (0.09 to 1.08)*	0.44 (-0.22 to 1.10)	0	0.22 (-0.19 to 0.64)	0.37 (-1.09 to 1.83)	0.031*
Reduced	-0.96 (-3.85 to 1.93)	-0.85 (-2.84 to 1.14)	-0.99 (-2.60 to 0.61)	0	-0.35 (-3.59 to 2.89)	0.19 (-0.84 to 1.21)	

* Indicates significant results.

† Adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol, diabetes, hypertension, cardiovascular disease (CVD) history, lung disease and reduced kidney function (excluding corresponding covariate indicating each subgroup).

‡ Linear regression coefficient: It represents the difference in Mental Component Summary score between ABI category <1.00 and the reference category (≥1.00).

Table S10. Adjusted[†] odds-ratio of other mental health aspects for lower ankle brachial index (ABI) (<1.00) in different subgroups.

Subgroups	Mental Health Aspects			
	Significant depressive symptoms		Hopeless feeling	
	Case/N[‡]	OR[§] (95% CI)	Case/N	OR (95% CI)
Sex				
Males	24/316	1.22 (0.62 to 2.39)	37/316	1.09 (0.84 to 1.42)
Females	57/512	1.29 (0.68 to 2.43)	74/512	1.04 (0.78 to 1.40)
P value for interaction		0.809		0.289
Ethnicity				
Caucasians	51/531	1.65 (1.05 to 2.59)*	70/531	1.23 (1.10 to 1.36)*
African Americans	30/297	0.84 (0.74 to 0.96)*	41/297	0.83 (0.78 to 0.88)*
P value for interaction		0.001*		< 0.001*
CVD History				
No CVD history	52/565	1.20 (0.69 to 2.09)	77/565	1.06 (0.70 to 1.59)
CVD history	29/263	1.50 (0.88 to 2.58)	34/263	1.11 (0.79 to 1.57)
P value for interaction		0.036*		0.936
Diabetes				
No Diabetes	40/513	1.23 (0.51 to 2.94)	64/513	1.15 (0.89 to 1.50)
Diabetes	41/315	1.28 (0.81 to 2.02)	47/315	0.91 (0.61 to 1.37)
P value for interaction		0.975		0.070
Reduced Kidney Function				
Not Reduced	41/492	1.11 (0.70 to 1.75)	61/492	1.05 (0.73 to 1.51)
Reduced	40/336	1.63 (0.73 to 3.62)	50/336	1.07 (0.81 to 1.40)
P value for interaction		0.271		0.809

* Indicates significant results.

† Adjusted for age, sex, ethnicity, education level, economic status, current smoking/drinking status, body mass index, total cholesterol, diabetes, hypertension, cardiovascular disease (CVD) history, lung disease and reduced kidney function (excluding corresponding covariate indicating each

subgroup).

‡ Number of individuals having outcome with ABI < 1.00 for each subgroup / Total number of individuals with ABI < 1.00 for each subgroup.

§ Logistic regressions were applied to assess the odds ratio for 2 binary mental health aspects between ABI <1.00 and the reference category (≥1.00).