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# Clinically Recognized Varicose Veins and Physical Function in Older Individuals: The ARIC Study

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## Abstract

**Background:** Although a few studies reported an association between varicose veins and physical function, this potentially bidirectional association has not been systematically evaluated in the general population.
**Method:** In 5 580 participants (aged 71–90 years) from the Atherosclerosis Risk in Communities study, varicose veins were identified in outpatient and inpatient administrative data prior to (prevalent cases) and after (incident cases) visit 5 (2011–2013). Physical function was evaluated by the Short Physical Performance Battery (SPPB, score ranging from 0 to 12). We evaluated (i) cross-sectional association between prevalent varicose veins and physical function, (ii) association of prevalent varicose veins with subsequent changes in physical function from visit 5 to visits 6 (2016–2017) and 7 (2018–2019), and (iii) association of physical function at visit 5 with incident varicose veins during a median follow-up of 3.6 years (105 incident varicose veins among 5 350 participants without prevalent cases at baseline).
**Results:** At baseline, varicose veins were recognized in 230 (4.1%) participants and cross-sectionally associated with reduced physical function. Longitudinally, prevalent varicose veins were not significantly associated with a decline in SPPB over time. In contrast, a low SPPB ≤6 was associated with a greater incidence of varicose veins compared to SPPB ≥10 (adjusted hazard ratio 2.13 [95% confidence interval = 1.19, 3.81]).
**Conclusion:** In community-dwelling older adults, varicose veins and low physical function were associated cross-sectionally. Longitudinally, low physical function was a risk factor for incident varicose veins, but not vice versa. Our findings suggest an etiological contribution of low physical function to incident varicose veins.

**Keywords:** Epidemiology, Physical function, Varicose veins

Lower extremity varicose veins, a manifestation of chronic venous insufficiency, affect approximately 23% of adults in the United States, including 22 million women and 11 million men aged 40–80 years (1). Varicose veins can progress to serious morbidities such as leg ulcers (2) or deep venous thrombosis (3–5). The medical costs of chronic venous disease in the United States have been reported to total $3 billion per year, mostly due to advanced cases with leg ulcers (2,6).

Impaired leg function (ie, decreased lower extremity strength and limited mobility) is another potential consequence of varicose veins due to feelings of leg heaviness or tightness from varicosities (7). Conversely, impaired leg function may cause varicose veins through reduced leg muscle contraction which is important for venous return (8). However, this potentially bidirectional association has not been systematically evaluated in the general population. A few cross-sectional studies have reported an association between chronic venous insufficiency and reduced physical function (9–13), but cross-sectional study designs cannot clarify the temporality of these 2 conditions. In contrast, longitudinal data can establish the temporal sequence of events, such as whether varicose veins contribute to a decline in physical function and/or whether poor physical function increases the risk of varicose veins. This distinction will have crucial implications for contemplating preventive strategies of these conditions.

Therefore, to comprehensively evaluate the potentially bidirectional association between varicose veins and physical function, we conducted cross-sectional and prospective analyses of these 2 conditions using data from the Atherosclerosis Risk in Communities (ARIC) study.

## Method

### Study Population

The ARIC study enrolled 15 792 middle-aged (45–64 years of age) in 1987–1989, predominantly Black and White men and women recruited from 4 U.S. communities: Forsyth County, North Carolina; Jackson, Mississippi; suburbs of Minneapolis, Minnesota; and Washington County, Maryland (14). Follow-up study visits were conducted in 1990–1992 (visit 2), 1993–1995 (visit 3), 1996–1998 (visit 4), 2011–2013 (visit 5), 2016–2017 (visit 6), and 2018–2019 (visit 7). This study assessed the relationship between varicose veins and physical function in 3 ways: (i) the cross-sectional association between prevalent varicose veins and low physical function at visit 5, (ii) the association of prevalent varicose veins at visit 5 with subsequent changes in physical function from visit 5 to visits 6 and 7, and (iii) the association of physical function at visit 5 with incident varicose veins (Supplementary Figure S1). Of 6 538 participants at visit 5, we excluded individuals who were neither White nor Black ($n$ = 18), who were Black participants from Minnesota and Washington County centers ($n$ = 25) due to small numbers (15,16), and who had missing data for physical function ($n$ = 726) or covariates of interest ($n$ = 189), leaving a final study sample of 5 580 participants in analyses 1 and 2 (Supplementary Figure S2). Of these participants, 5 350 did not have prevalent varicose veins at visit 5 and were included in the analysis 3.

### Varicose Veins

We captured diagnoses of varicose veins among ARIC participants as 1 hospitalization or 2 outpatient visits for varicose veins based on the International Classification of Diseases (ICD)-9 codes (454.xx) and ICD-10 codes (I84.xx) from baseline visit through December 31, 2015. Hospitalizations in ARIC were identified through annual telephone interviews with participants (semi-annual since 2012), ascertaining discharge lists from the local hospital, or linkage to Centers for Medicare and Medicaid Services (CMS) Medicare claims. Outpatient diagnosis relied solely on the CMS Medicare data. ICD codes for any hospital discharge were recorded, and varicose veins in any diagnostic position were identified. Varicose veins cases occurring before visit 5 were considered prevalent while cases occurring after visit 5, among those without prevalent varicose veins at visit 5, were considered an incident.

### Physical Function

Physical function was assessed at visits 5, 6, and 7 using the Short Physical Performance Battery (SPPB) (17,18), which includes 3 components of physical function: chair stands, standing balance, and gait speed. Chair stands were assessed by the time to complete standing from and sitting on a chair 5 times within 60 seconds, with participant's arms crossed on their chest. Those who could not complete 5 stands within 60 seconds, we allocated 60 seconds. Standing balance was evaluated by the ability to maintain the standing posture for 10 seconds with 3 different foot positions, side-by-side, semi-tandem, and tandem. The balance was examined first in the semi-tandem position; those unable to hold semi-tandem next attempted to stand with feet in a parallel position. If the semi-tandem was held for 10 seconds, the test of side-by-side was omitted (considered as completion) and the tandem position was assessed with 2 attempts allowed. Those who were unable to hold a position for at least one second were allocated 0 seconds. Gait speed was measured at the participant's self-selected usual pace over 4 m; the faster result out of 2 trials was used for the analysis. A score of zero was assigned to any task a participant was physically unable or unsafe to complete. Each subcomponent was scored from 0 to 4 based on established cutpoints then summed to create the SPPB summary score ranging from 0 (poorest) to 12 (best) (17,18).

### Other Covariates

Covariates were assessed at visit 5 unless otherwise specified. Information on demographic (age, sex, and race) and education level were assessed at visit 1 based on a self-reported questionnaire. Behavioral variables (smoking and alcohol intake) and medical history were collected by a trained interviewer. Physical assessment and blood sample collection were performed according to standardized procedures. Education levels were categorized into basic (less than high school), intermediate (high school or vocational school), or advanced (any college). Smoking status and alcohol intake were classified as current versus former/never. Seated blood pressure was measured by certified technicians after 5-minute rest using a validated automatic sphygmomanometer, and the average of the last 2 of 3 readings was recorded. Participants were asked to bring to the clinic all of their medications, including antihypertensive, antidyslipidemic, and antidiabetic drugs, which were coded by trained personnel. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or antihypertensive medication use. Diabetes mellitus was defined as a fasting blood glucose ≥7.0 mmol/L, non-fasting blood glucose ≥11.1 mmol/L, self-reported physician diagnosis of diabetes, or use of glucose-lowering medications. Total cholesterol and high-density lipoprotein (HDL)-cholesterol were determined using enzymatic methods meeting the National Cholesterol Education Program's accuracy performance criteria. Body mass index (BMI) was defined as the weight (kg) divided by the square of height ($m^2$). History of cardiovascular disease (CVD) was defined as prevalent coronary heart disease (CHD), stroke, or heart failure. Prevalent CHD and stroke were defined as self-reported history at visit 1 or adjudicated clinical events between visit 1 and visit 5. Hospitalization for heart failure, physician diagnosis of heart failure, or self-reported treatment for heart failure between visit 1 and 5 were considered prevalent heart failure. History of deep vein thrombosis was defined as clinical events between visit 1 and visit 5 adjudicated by a physician panel (19).

### Statistical Analysis

Descriptive statistics (mean [*SD*] and proportion) of baseline characteristics were summarized according to the presence and absence of prevalent varicose veins at visit 5. Among those without prevalent varicose veins at visit 5, we also summarized baseline characteristics across an SPPB score—low (0–6), fair (7–9), and good (10–12) (20).

We used linear regression models to conduct analysis 1 (cross-sectional association) and mixed-effects models to conduct analysis 2 (longitudinal association of prevalent varicose veins at visit 5 with changes in SPPB or its subcomponents at visit 6 and 7 as continuous variables). We used years since visit 5 as the time scale in these mixed-effects models. For analysis 1, we also performed logistic regression with SPPB and its subcomponents at visit 5 as a dichotomous outcome variable (≤6 [poor] vs >6 for SPPB and ≤2 [poor] vs >2 for subcomponents).

For analysis 3 (physical function at visit 5 and incident varicose veins), we examined the associations of categories of SPPB (0–6, 7–9, and 10–12 [reference]) and its subcomponents (0–2, 3, and 4 [reference]) with incident varicose veins among those without prevalent varicose veins at visit 5 using Cox proportional hazards models. *p* values for trend were based on Cox models with categories of SPPB and its components as discrete variables. We also modeled the SPPB score, the time required for 5 chair stands, and gait speed as continuous variables using linear splines and 2 knots (their interquartile values), and plotted their hazard ratios. Their median values were selected as references (score of 10 for SPPB, 13.5 seconds for chair stands, and 0.94 m/s for gait speed). We did not include standing balance in this continuous analysis because it did not show a positive association in a linear model likely due to its unique distribution with majority of participants able to stand for the max of 10 seconds (eg, 78% with tandem feet standing).

For all analyses, we implemented the following 2 models to evaluate the impact of potential confounders: model 1 was unadjusted and model 2 was adjusted for demographic and socioeconomic status variables (age, sex, race-ARIC field center, and education levels) and potential risk factors for low physical function and varicose veins as shown in previous literature (BMI with linear spline terms and knots at 25 and 30 kg/m$^2$, systolic blood pressure, antihypertensive medication, diabetes, total cholesterol, HDL-cholesterol, lipid-lowering therapy, history of CVD, history of deep vein thrombosis, smoking status, and alcohol intake) (3–5,20,21).

We conducted several sensitivity analyses. We repeated our analyses in demographic subgroups by age (<75 vs ≥75 years), sex (male vs female), and race (White vs Black). Interaction by these factors was assessed with the likelihood ratio test. Since we could not capture outpatient visits for varicose veins outside of Medicare fee-for-service plan (Medicare parts A and B), we restricted to participants who enrolled in the Medicare fee-for-service within a year prior to visit 5. For analysis 2, attending subsequent visits (visits 6 and 7) was highly likely to be influenced by demographic and clinical factors. To account for potential bias due to attrition (namely those who attended visit 6 or visit 7 may have different characteristics compared to those who did not), we applied inverse probability weighting using the estimated probability of attending subsequent visits conditioned on the covariates in model 2 (22,23). All analyses were performed with Stata version 16 (StataCorp LLC, College Station, TX), and a *p* value <.05 was considered statistically significant.

## Results

### Baseline Characteristics

The mean age of the 5 580 participants at ARIC visit 5 was 75.9 (*SD* 5.1) years. There were 230 participants with prevalent varicose veins (48 inpatient and 182 outpatient diagnoses). As compared to participants without prevalent varicose veins, those with prevalent varicose veins were more likely to be older, White, female, and have higher BMI, and less likely to have diabetes and dyslipidemia, and enrolled in Medicare fee-for-service plan within a year prior to visit 5 (Table 1).

### Prevalent Varicose Veins and Physical Function at Baseline

The cross-sectional analysis showed that prevalent varicose veins were consistently associated with a lower SPPB score at visits 5, compared with no varicose veins, regardless of the adjustment for potential confounders (eg, SPPB score 8.1 [95% confidence interval {CI} = 7.8, 8.5] vs 9.4 [9.2, 9.7] in Model 2) (Table 2). We confirmed similar cross-sectional associations when we modeled poor SPPB and subcomponents using logistic regression (Supplementary Table S1). Also, we observed similar cross-sectional associations within demographic subgroups (Supplementary Figure S3).

### Prevalent Varicose Veins and Change in Physical Function

Although there was a consistent inverse association of prevalent varicose veins with SPPB at visit 6 and at visit 7, prevalent varicose veins at visit 5 were not significantly associated with the decline in SPPB between visits 5 and 7 (median follow-up 5.0 [Interquartile interval (IQI) 0–6.4]) (Table 2). We observed consistent results within demographic subgroups (Supplementary Table S2). When we restricted to those who enrolled in the Medicare fee-for-service plan within a year prior to visit 5, results were generally consistent (Supplementary Table S3, Sensitivity analysis A). When we repeated our mixed-effect models with inverse probability weighting to account for attrition, results were generally similar (Supplementary Table S3, Sensitivity analysis B).

### Baseline Physical Function and Incident Varicose Veins

Of 5 350 participants without prevalent varicose veins at visit 5, those with lower SPPB scores were more likely to be older, Black, female, and less educated, and have higher BMI, hypertension, diabetes, and history of CVD (Supplementary Table S4).

During a median follow-up of 3.6 (IQI 3.2–4.1) years, 105 participants developed varicose veins (98 outpatient diagnoses). An SPPB score ≤6 was positively associated with the incidence of varicose veins in an unadjusted model (Table 3). Results were robust to adjustment for potential confounding factors (adjusted hazard ratio 2.13 [95% CI = 1.19, 3.81] for SPPB ≤6 vs ≥10). The association was strongest for gait speed (eg, *p* for trend < .05 in both Models 1 and 2). When we restricted to those who enrolled in the Medicare fee-for-service plan within a year prior to visit 5, results were generally consistent

**Table 1.** Baseline Characteristics by Varicose Veins Prevalence at ARIC Visit 5 (*n* = 5 580)

| | Varicose Veins | |
|---|---|---|
| | No (*n* = 5 350) | Yes (*n* = 230) |
| Age, y | 75.3 (5.1) | 77.5 (5.0) |
| Black | 21.7% | 12.6% |
| Female | 56.9% | 77.8% |
| Education levels | | |
| Basic | 13.3% | 13.0% |
| Intermediate | 42.0% | 45.7% |
| Advanced | 44.7% | 41.3% |
| Body mass index, kg/m$^2$ | 28.6 (5.5) | 29.8 (7.1) |
| Systolic blood pressure, mm Hg | 130.1 (17.9) | 129.3 (19.6) |
| Diastolic blood pressure, mm Hg | 66.3 (10.6) | 64.0 (10.6) |
| Antihypertensive medication | 74.6% | 79.6% |
| Hypertension | 74.0% | 75.1% |
| Antidiabetic medication | 19.5% | 15.7% |
| Diabetes | 36.9% | 30.0% |
| Total cholesterol, mmol/L | 4.7 (1.1) | 4.7 (1.0) |
| HDL-cholesterol, mmol/L | 1.3 (0.4) | 1.3 (0.3) |
| Lipid-lowering therapy | 56.5% | 48.3% |
| History of cardiovascular disease | 21.4% | 25.2% |
| History of deep vein thrombosis | 1.8% | 3.9% |
| Current smoker | 5.9% | 4.4% |
| Current drinker | 50.4% | 45.7% |
| Medicare parts A and B (fee-for-service plan) within 1 y prior to visit 5 | 54.9% | 77.0% |

*Notes*: ARIC = Atherosclerosis Risk in Communities; HDL = high-density lipoprotein. Values for continuous variables are given as mean (*SD*) and values for categorical variables are given as percentage.

**Table 2.** Association of Prevalent Varicose Veins at ARIC Visit 5 With Changes in Physical Function From Visit 5 to Visit 7 (*N* = 5 580)

| Measured Elements of Physical Function | Visit 5 | | Visit 6 | | Visit 7 | | Visits 5–7 |
|---|---|---|---|---|---|---|---|
| Varicose Veins at Visit 5 | No (*n* = 5 350) | Yes (*n* = 230) | No (*n* = 3 017) | Yes (*n* = 114) | No (*n* = 2 510) | Yes (*n* = 84) | Coefficient (95% CI) |
| SPPB | | | | | | | |
| Model 1 | 9.4 (9.3, 9.5) | 8.1 (7.8, 8.5)* | 8.8 (8.7, 8.9) | 7.5 (7.0, 8.1)* | 8.8 (8.7, 8.9) | 7.5 (6.9, 8.1)* | −0.054 (−0.120, 0.013) |
| Model 2 | 9.4 (9.2, 9.7) | 8.1 (7.8, 8.5)* | 8.5 (8.1, 8.9) | 7.1 (6.6, 7.7)* | 8.4 (8.0, 8.9) | 7.0 (6.4, 7.7)* | −0.052 (−0.115, 0.012) |
| Time required for 5 chair stands (s) | | | | | | | |
| Model 1 | 17.3 (16.9, 17.6) | 23.5 (21.8, 25.2)* | 20.7 (20.1, 21.3) | 26.2 (23.2, 29.3)* | 21.8 (21.1, 22.5) | 28.4 (24.5, 32.3)* | 0.216 (−0.255, 0.688) |
| Model 2 | 17.3 (15.8, 18.7) | 23.5 (21.4, 25.7)* | 22.0 (19.6, 24.5) | 28.1 (24.5, 31.8)* | 23.4 (20.5, 26.3) | 30.7 (26.2, 35.3)* | 0.215 (−0.242, 0.671) |
| Time held side-by-side stance (s) | | | | | | | |
| Model 1 | 9.9 (9.8, 9.9) | 9.4 (9.2, 9.5)* | 9.7 (9.6, 9.7) | 9.5 (9.1, 9.8) | 9.7 (9.6, 9.8) | 9.0 (8.7, 9.4)* | −0.000 (−0.057, 0.057) |
| Model 2 | 9.9 (9.7, 10.0) | 9.4 (9.2, 9.6)* | 9.6 (9.3, 9.9) | 9.3 (8.9, 9.8) | 9.6 (9.3, 9.9) | 8.9 (8.5, 9.4)* | 0.001 (−0.055, 0.056) |
| Time held semi-tandem stance (s) | | | | | | | |
| Model 1 | 9.3 (9.2, 9.4) | 8.5 (8.2, 8.8)* | 9.1 (9.0, 9.2) | 8.4 (7.9, 8.9)* | 9.0 (8.9, 9.1) | 8.2 (7.6, 8.7)* | −0.020 (−0.105, 0.064) |
| Model 2 | 9.3 (9.0, 9.6) | 8.5 (8.1, 8.9)* | 8.9 (8.4, 9.3) | 8.1 (7.4, 8.7) | 8.8 (8.3, 9.2) | 7.8 (7.1, 8.5)* | −0.026 (−0.108, 0.056) |
| Time held tandem stance (s) | | | | | | | |
| Model 1 | 8.3 (8.2, 8.4) | 7.5 (6.9, 8.0)* | 7.8 (7.7, 8.0) | 6.6 (5.8, 7.4)* | 7.4 (7.3, 7.6) | 6.8 (5.8, 7.8) | −0.079 (−0.220, 0.062) |
| Model 2 | 8.2 (7.8, 8.6) | 7.3 (6.6, 8.0) | 7.4 (6.7, 8.1) | 6.0 (5.0, 7.1) | 6.9 (6.1, 7.7) | 5.8 (4.6, 7.1) | −0.092 (−0.230, 0.046) |
| Gait speed (m/s) | | | | | | | |
| Model 1 | 0.94 (0.94, 0.95) | 0.84 (0.82, 0.87)* | 0.94 (0.93, 0.95) | 0.83 (0.79, 0.87)* | 0.93 (0.92, 0.94) | 0.80 (0.76, 0.84)* | −0.003 (−0.008, 0.003) |
| Model 2 | 0.94 (0.92, 0.96) | 0.84 (0.81, 0.88)* | 0.92 (0.89, 0.95) | 0.80 (0.75, 0.85)* | 0.90 (0.87, 0.93) | 0.76 (0.71, 0.81)* | −0.004 (−0.009, 0.002) |

*Notes*: ARIC = Atherosclerosis Risk in Communities; CI = confidence interval; SPPB = Short Physical Performance Battery. Model 1: crude. Model 2: adjusted for age (y), sex, race-ARIC field center, education levels (advanced vs intermediate vs basic), body mass index with spline terms and knots with 25 and 30 kg/m$^2$, systolic blood pressure (mm Hg), antihypertensive medication, diabetes, total cholesterol (mmol/L), high-density lipoprotein-cholesterol (mmol/L), lipid-lowering therapy, history of cardiovascular disease, history of deep vein thrombosis, current smoker, and current drinker.

*Statistical significance ($p < .05$) with no varicose veins as the reference.

**Table 3.** Hazard Ratios (95% CI) of Incident Varicose Veins by SPPB and Individual Component Scores at ARIC Visit 5 ($n$ = 5 350)

| SPPB | 0–6 ($n$ = 655) | 7–9 ($n$ = 1 587) | 10–12 ($n$ = 3 108) | $p$ for Trend |
|---|---|---|---|---|
| Cases | 21 | 35 | 49 | |
| Model 1 | 2.25 (1.35, 3.76) | 1.46 (0.94, 2.25) | Ref. | 0.002 |
| Model 2 | 2.13 (1.19, 3.81) | 1.45 (0.92, 2.28) | Ref. | 0.01 |
| Chair Stands Score | 0–2 ($n$ = 2 566) | 3 ($n$ = 1 376) | 4 ($n$ = 1 408) | $p$ for Trend |
| Cases | 58 | 26 | 21 | |
| Model 1 | 1.61 (0.97, 2.65) | 1.31 (0.74, 2.33) | Ref. | 0.06 |
| Model 2 | 1.63 (0.96, 2.76) | 1.34 (0.75, 2.39) | Ref. | 0.07 |
| Standing Balance Score | 0–2 ($n$ = 1 205) | 3 ($n$ = 382) | 4 ($n$ = 3 763) | $p$ for Trend |
| Cases | 29 | 7 | 69 | |
| Model 1 | 1.40 (0.91, 2.16) | 1.01 (0.46, 2.20) | Ref. | 0.14 |
| Model 2 | 1.19 (0.74, 1.90) | 0.91 (0.42, 1.99) | Ref. | 0.52 |
| Gait Speed Score | 0–2 ($n$ = 480) | 3 ($n$ = 1 135) | 4 ($n$ = 3 735) | $p$ for Trend |
| Cases | 13 | 31 | 61 | |
| Model 1 | 1.79 (0.98, 3.26) | 1.75 (1.13, 2.69) | Ref. | 0.01 |
| Model 2 | 1.69 (0.87, 3.28) | 1.75 (1.09, 2.79) | Ref. | 0.03 |

*Notes*: ARIC = Atherosclerosis Risk in Communities; CI = confidence interval; SPPB = Short Physical Performance Battery.

Model 1: crude. Model 2: adjusted for age (y), sex, race-ARIC field center, education levels (advanced vs intermediate vs basic), body mass index with spline terms and knots with 25 and 30 kg/m², systolic blood pressure (mm Hg), antihypertensive medication, diabetes, total cholesterol (mmol/L), high-density lipoprotein-cholesterol (mmol/L), lipid-lowering therapy, history of cardiovascular disease, history of deep vein thrombosis, current smoker, and current drinker.

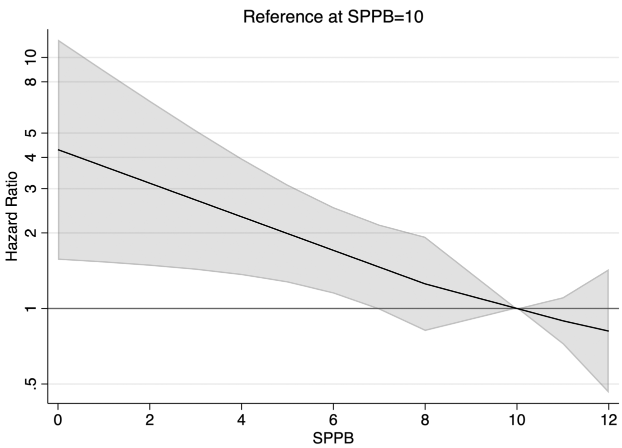


**Figure 1.** Adjusted hazard ratios (95% CI) of incident varicose veins by linear splines of SPPB with 2 knots (scores of 8 and 11). The results were adjusted for age (y), sex, race-ARIC field center, education levels (advanced vs intermediate vs basic), body mass index with spline terms and knots with 25 and 30 kg/m², systolic blood pressure (mm Hg), antihypertensive medication, diabetes, total cholesterol (mmol/L), HDL-cholesterol (mmol/L), lipid-lowering therapy, history of cardiovascular disease, history of deep vein thrombosis, current smoker, and current drinker. ARIC = Atherosclerosis Risk in Communities; CI = confidence interval; HDL = high-density lipoprotein; SPPB = Short Physical Performance Battery.

(Supplementary Table S5). When the SPPB score was modeled continuously, we observed that a lower SPPB score remained linearly and positively associated with the incidence of varicose veins (Figure 1).

With SPPB of 10 as a reference, the adjusted hazard ratio exceeded 1.5 and 2.0 at a reduced SPPB score of around 7 and 5, respectively. This pattern was confirmed for subcomponents for SPPB (Supplementary Figures S4 and S5). We observed similar associations of poor physical function with incident varicose veins in most demographic subgroups (Figure 2). Blacks and Whites showed

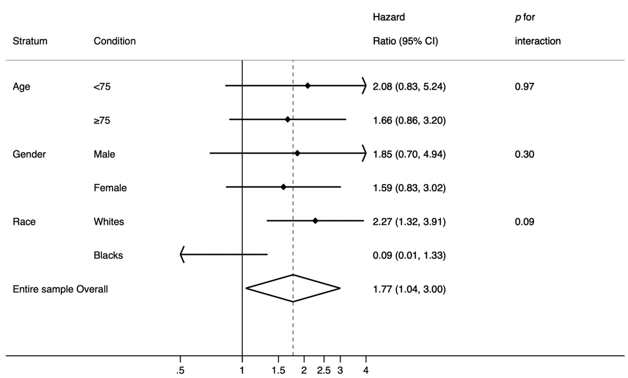


**Figure 2.** Adjusted hazard ratios (95% CI) of incident varicose veins for poor physical function (SPPB ≤6 vs >6) by subgroups. The results were adjusted for age (y), sex, race-ARIC field center, education levels (advanced vs basic), body mass index with spline terms and knots with 25 and 30 kg/m², systolic blood pressure (mm Hg), antihypertensive medication, diabetes, total cholesterol (mmol/L), HDL-cholesterol (mmol/L), lipid-lowering therapy, history of cardiovascular disease, history of deep vein thrombosis, current smoker, and current drinker. ARIC = Atherosclerosis Risk in Communities; CI = confidence interval; HDL = high-density lipoprotein; SPPB = Short Physical Performance Battery.

qualitatively different results, but there were small number of incident varicose veins in the reference group of Blacks (9/1 161), and the interaction term did not reach statistical significance.

## Discussion

Among community-dwelling older adults, we observed a robust cross-sectional association between clinically recognized varicose veins and reduced physical function, represented by the SPPB. The association was consistent across SPPB subcomponents (ie, chair stands, standing balance, and gait speed). However, prevalent varicose veins were not associated with declines in SPPB over approximately 6.5 years, whereas lower physical function was significantly associated with greater subsequent risk of varicose veins. As compared to SPPB of 10, SPPB of 5 was associated with ~2 times greater risk of developing varicose veins after accounting for potential confounders. We confirmed largely consistent results across subgroups stratified by demographic variables and after a few other sensitivity analyses.

Our findings from cross-sectional analyses are generally consistent with extant studies (9–13). However, there are a few unique aspects of our study. First, in contrast to somewhat limited measures of physical function in previously studies (eg, only walking, (9,12), range of ankle motion (10), lower extremity muscle strength (11), or those relying on self-report (13)), we used validated objective measures of overall physical function, SPPB, as well as its subcomponents—chair stands, standing balance, and gait speed. Second, we confirmed robust associations despite rigorous adjustment for many potential confounders (eg, age, diabetes, history of CVD). Third, a large sample size allowed us to evaluate this association within demographic subgroups, although some subgroups (eg, Black adults) were relatively small.

A recent study reported that low physical function was associated with incident multimorbidity, including varicose veins as one of 16 clinical conditions in older adults (24). However, this recent study did not report results specific for varicose veins. Thus, to our knowledge, our study is the first to comprehensively and specifically evaluate a bidirectional prospective association between varicose veins and physical function. Our study suggests that low physical function may contribute to incident varicose veins, but not vice versa. Our observation is in line with the fact that reduced calf muscle strength, impaired mobility, and limited physical activity increase venous pressure in the legs (25). Sustained high venous pressure is associated with structural and functional changes in vein walls, leading to varicose veins (26). Indeed, a body of literature has reported physical inactivity as a major risk factor of varicose veins (27–32).

Our results suggest several clinical implications. Varicose veins are a common manifestation of chronic venous disease (1), which may result in severe conditions such as leg ulceration (2,6). Therefore, health care providers should pay attention to varicose veins among older adults, especially among those with reduced lower extremity physical function. Although indicative, our observational study cannot prove whether interventions to improve leg physical function can prevent varicose veins. Nonetheless, a previous systematic review of randomized clinical trials demonstrated that an exercise program to rehabilitate the muscle-pumping function in patients with varicose veins has a beneficial effect on blood flow (33). Therefore, physical exercise may contribute to the improvement of physical function, leading to the prevention of varicose veins.

Several limitations of this study should be acknowledged. We identified varicose veins based on clinical diagnosis and thus missed some undiagnosed or unrecorded cases of varicose veins. On the other hand, our case definition should be regarded highly specific. Indeed, a previous study showed that the positive predictive value of varicose vein based on ICD codes was 98% with a duplex ultrasound examination report as a gold standard (3). Since the number of participants with prevalent varicose veins at baseline was low, we should cautiously interpret our results of no significant association between varicose veins as an exposure and subsequent declines in SPPB. Our study included White and Black adults aged 66–90 years. Thus, the extrapolation of our results to other racial groups or other age ranges should be done carefully. Finally, although we did our best to control for potential confounders, we cannot rule out the possibility of residual confounding, as is true in any observational study.

In community-dwelling older adults, clinically recognized varicose veins and lower physical function were robustly associated with each other in a cross-sectional design among older adults. However, our prospective analysis revealed that lower physical function predates incident varicose veins, but not vice versa. Since varicose veins are common and their complications can be costly, clinical attention to varicose veins among older adults, especially those with reduced physical function, should be warranted before severe manifestation of chronic venous disease.

## Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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## Conflict of Interest

None declared.

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## Author Contributions

Y.M. and K.M. designed the study and analytic plan. J.C. and A.R.F. oversaw data acquisition. Y.M. and Y.S. performed the statistical analysis. Y.M. and K.M. drafted the manuscript. All authors contributed to data interpretation and edited the manuscript for content; all authors reviewed the manuscript and approved the final version.

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