Leg Symptoms in Peripheral Arterial Disease
Associated Clinical Characteristics and Functional Impairment

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Intermittent claudication (IC) has long been considered the most classic manifestation of peripheral arterial disease (PAD). However, when noninvasive testing with the ankle-brachial index (ABI) is used to diagnose PAD objectively, many people with PAD have latent disease or are asymptomatic (ie, have no exertional leg symptoms), while others have symptoms other than classic IC. Noninvasive testing with the ABI is the clinical standard for diagnosing PAD. The low sensitivity of IC for PAD may contribute to underrecognition of PAD in general medicine practices.

With its associated functional limitations, IC is appreciated as a serious clinical symptom of PAD. However, it is unclear whether other forms of PAD, with and without leg symptoms, cause functional limitations. Comorbidities such as hip and knee arthritis, back disease, or neuropathy might alter the nature of leg symptoms experienced in PAD. Characteristics such as depression might affect PAD patients' awareness or description of leg pain.

The purposes of this study were to document the spectrum of leg symptoms reported by men and women with PAD. The following values are for patients without IC vs those with IC. Participants in the group with leg pain on exertion and rest (n = 88) had a higher (poorer) score for neuropathy (5.6 vs 3.5; P < .001), prevalence of diabetes mellitus (48.9% vs 26.7%; P < .001), and spinal stenosis (20.8% vs 7.2%; P = .002). The atypical exertional leg pain/carry on group (exertional leg pain other than IC associated with walking through leg pain [n = 41]) and the atypical exertional leg pain/stop group (exertional leg pain other than IC that causes one to stop walking [n = 90]) had better functioning than the IC group.

Conclusions There is a wide range of leg symptoms in persons with PAD beyond that of classic IC. Comorbid disease may contribute to these symptoms in PAD. Functional impairments are found in every PAD symptom group, and the degree of functional limitation varies depending on the type of leg symptom.
LEG SYMPTOMS IN PERIPHERAL ARTERIAL DISEASE

Figure 1. Leg Symptoms Commonly Present in Peripheral Arterial Disease

PAD and to identify clinical characteristics and functional limitations associated with leg symptom categories identified among patients with PAD. Our results should sensitize clinicians to the common occurrence of leg symptoms other than IC in patients with PAD and highlight that the type of symptoms reported determines the degree of associated lower-extremity impairment. Our findings underscore that PAD-associated leg pain may be blurred by the contribution of symptoms produced by comorbid conditions.

METHODS

Participant Identification

The protocol was approved by the Northwestern University Medical School and Catholic Health Partners Hospital institutional review boards. Participants gave informed consent. PAD participants were identified consecutively from patients diagnosed with PAD in 3 Chicago-area noninvasive vascular laboratories. Non-PAD participants were identified consecutively from patients with appointments in a large general medicine practice. In addition, individuals with PAD identified in the general medicine practice (n=13) were included in the PAD group. Individuals were contacted and invited to return to the medical center for a study visit between October 1998 and January 2000.

Exclusion Criteria

Presence of PAD was established using objective, noninvasive testing.7-11 The current standard for diagnosing PAD is defined as an ABI of less than 0.90. Absence of PAD was defined as an ABI of 0.90 or higher and of 1.50 or less.10 An ABI of less than 0.90 is 95% sensitive and 99% specific for angiographically diagnosed PAD.11 At present, angiography is reserved for PAD patients under consideration for revascularization. Individuals with an ABI greater than 1.50 were excluded (n=136) because this indicates poorly compressible leg arteries and inability to gauge arterial perfusion accurately.7,9

Individuals with PAD who were diagnosed in the noninvasive vascular laboratory were excluded if their study visit ABI result indicated absence of PAD. This occasionally occurred when PAD participants were revascularized between vascular laboratory testing and their study visit. It also occurred in individuals with borderline ABI values of approximately 0.90, due to measurement variation. Patients with dementia were excluded because of their inability to answer questions accurately (n=7). Nursing home residents (n=59), wheelchair-bound patients (n=27), and patients with foot or leg amputations (n=77) were also excluded because they have severely impaired functioning. Non–English-speaking patients were excluded because investigators were not fluent in non-English languages (n=47). Patients with recent major surgery were excluded (n=5).

ABI Measurement

The ABI was measured using established methods.7-10,12 After participants rested supine for 5 minutes, a handheld Doppler probe (Nicolet Vascular Pocket Dop II, Golden, Colo) was used to measure systolic blood pressures in the right brachial artery, right dorsalis pedis and posterior tibial arteries, left dorsalis pedis and posterior tibial arteries, and left brachial artery. Each pressure was measured twice: in the order listed and then in reverse order. The ABI was calculated in each leg by dividing average pressures in each leg by the average of the 4 brachial pressures.12,13 Average brachial pressures in the arm with highest pressure were used when 1 brachial pressure was higher than the opposite brachial pressure in both measurement sets, and the 2 brachial pressures differed by 10 mm Hg or more in at least 1 measurement set, since in such cases subclavian stenosis was possible.12,13 The lowest leg ABI measurement was used in our analyses.

Leg Symptom Groups

Leg symptoms were characterized into 1 of 6 mutually exclusive groups using the San Diego claudication questionnaire.7 We used symptom groups previously developed by Criqui et al7 as a starting point for our group definitions and made 2 changes a priori for the present study (FIGURE 1). The San Diego
LEG SYMPTOMS IN PERIPHERAL ARTERIAL DISEASE

Claudication questionnaire is a standardized questionnaire based on the Rose claudication questionnaire and was administered by certified health interviewers.

Four groups have exertional leg symptoms. Individuals in the IC group experience exertional calf pain that does not begin at rest, causes the participant to stop walking, and resolves within 10 minutes of rest. Individuals in the leg pain on exertion and rest group sometimes experience exertional leg pain at rest. Two groups experience atypical exertional leg pain. Individuals in the atypical exertional leg pain/carry on group experience exertional leg symptoms that do not begin at rest and do not stop the individual from walking. Similarly, individuals in the atypical exertional leg pain/stop group experience exertional leg symptoms that do not begin at rest, but that do stop the individual from walking, and do not involve the calves or do not resolve within 10 minutes of rest. Two groups do not have exertional leg pain. Individuals in the no exertional leg pain/active group do not experience exertional leg pain symptoms and are considered active because they had walked more than 6 blocks during the previous week. Similarly, individuals in the no exertional leg pain/inactive group do not experience exertional leg pain, but are considered inactive because they had only walked 6 or fewer blocks during the previous week.

Rationale for Leg Symptom Group Definitions

Our leg symptom groups differ in 2 ways from those previously defined by Criqui et al. First, for exertional symptoms other than IC or leg pain on exertion and rest, we defined symptoms according to whether participants walked through exertional pain (atypical leg pain/carry on vs atypical leg pain/stop). We reasoned that functioning levels might be substantially different between these 2 groups. Second, we divided the asymptomatic category of Criqui et al into 2 groups based on physical activity. In some instances insufficient physical activity may prevent exertional leg pain symptoms. Alternatively, absence of leg pain symptoms might indicate a more mild form of PAD. Of PAD participants without exertional leg pain symptoms, 31% walked 6 or fewer blocks during the previous week. We chose this criterion a priori to define asymptomatic PAD participants who were inactive.

Comorbidities

Algorithms developed for the Women’s Health and Aging Study and the Cardiovascular Health Study were used to document comorbidities. These algorithms combine data from patient report, physical examination, medical record review, medications, laboratory values, and a primary care physician questionnaire. Criteria developed by the American College of Rheumatology were used to diagnose knee and hip osteoarthritis. Comorbidities assessed were angina, diabetes mellitus, myocardial infarction, stroke, heart failure, pulmonary disease, knee and hip arthritis, spinal stenosis, disk disease, Parkinson disease, and hip fracture.

Functional Measures

Six-Minute Walk. Six-minute walk data correlate with treadmill performance, physical activity, and the ABI. Following a standardized protocol, participants walked up and down a 100-foot (30-m) hallway for 6 minutes after being instructed to cover as much distance as possible.

Accelerometer-Measured Physical Activity. Physical activity levels were measured over 7 days using a vertical accelerometer (Caltrac). To directly compare activity among participants, we programmed each accelerometer identically for height, weight, age, and sex using previously reported methods. Because we had a limited number of accelerometers, they were distributed to participants whenever available in a nonrandom fashion. There were no significant differences in age, race, sex, or average ABI of participants based on accelerometer use.

Repeated Chair Raises. This test measured leg strength and balance. Participants sat in a straight-backed chair with arms folded across their chest and stood 5 times consecutively as quickly as possible. Time for 5 chair raises was measured.

Standing Balance. Participants were asked to stand with 1 foot directly in front of the other for 10 seconds (full tandem stand).

Four-Meter Walking Velocity. Walking velocity was measured with a 4-m walk performed at usual and fastest pace. Each walk was performed twice. The faster walk in each pair was used in our analyses.

Other Assessments

The Geriatric Depression Score Short-Form measures depressive symptoms. Depression was defined as 6 or more depressive symptoms. A monofilament assessed sensation on the dorsal and ventral surface of each foot in specific locations. We used an ordinal neuropathy score to represent the number of items missed (range, 0-22, a lower score equaled a better score). Using the Walking Impairment Questionnaire, participants recorded the degree to which specific symptoms (including joint symptoms and chest pain) impaired walking during the past week on a Likert scale ranging from 0 to 4.

Statistical Analyses

For continuous variables, differences among PAD participants with IC, PAD participants without IC, and non-PAD participants were evaluated using analysis of covariance adjusted for age, sex, and race. Among PAD participants, differences in continuous variables between IC and the remaining leg symptom categories were evaluated using analysis of variance. Rates for dichotomous variables were estimated using linear regression models with dummy variables for leg symptom categories; however, the test of significance was based on logistic regression analyses. Differences in continuous variables between IC and the remaining leg symptom categories were evalu-
ated using analysis of covariance adjusted for age, race, sex, ABI, and comorbidities likely to confound the association between leg symptom group and functioning (neuropathy, depression, disk disease, spinal stenosis, hip or knee osteoarthritis, and diabetes mellitus).

Each symptom group was ranked from 1 to 6 for the 9 functional measures, in which 1 represented best performance and 6 represented worst performance. These rank scores were summed, resulting in a score in which the minimum possible score was 9 (best) and the maximum possible score was 54 (worst). This summary score allowed for numerical comparison of composite functional performance across all 6 groups.

The significance of between-group comparisons in dichotomous variable rates was based on logistic regression using dummy variables for leg symptom groups. When comparing differences between IC and other groups, a significance level of .01 was used for each comparison so that the overall level of significance was less than .05 (Bonferroni inequality). Analyses were performed using SAS statistical software (version 8.0, SAS Institute Inc, Cary, NC).

RESULTS

Figure 2 depicts reasons for nonparticipation among individuals identified for the study. Participants included 460 men and women with PAD and 130 without PAD. For participants, the mean (SD) age was 70.9 (8.4) years and 56.2% were male vs 72.6 (9.8) years for nonparticipants (49.8% were male). In pairwise comparisons, the 310 PAD participants without IC performed significantly more poorly on each functional measure than non-PAD participants (data available from authors).

Of the 460 PAD participants, 150 (32%) had IC, 88 (19%) had leg pain on exertion and rest, 41 (9%) had atypical exertional leg pain/carry on, 90 (20%) had atypical exertional leg pain/stop, and 91 (20%) had no exertional leg pain (63 active and 28 inactive).

Table 1 compares characteristics among the symptom groups. All results are presented in reference to IC.

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### Table 1. Characteristics Associated With Intermittent Claudication vs Other Leg Symptom Categories Among Men and Women Aged 55 Years or Older With Peripheral Arterial Disease (N = 460)*

<table>
<thead>
<tr>
<th></th>
<th>Intermittent Claudication (n = 150)†</th>
<th>Atypical Exertional Leg Pain</th>
<th>No Exertional Leg Pain</th>
<th>Leg Pain on Exertion and Rest (n = 88)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Carry On (n = 41)</td>
<td>Stop (n = 90)</td>
<td>Active (n = 63)§</td>
<td>Inactive (n = 28)§</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>70.7 (8.4)</td>
<td>72.0 (7.6)</td>
<td>71.3 (8.6)</td>
<td>74.7 (7.8)</td>
</tr>
<tr>
<td>Men</td>
<td>64.0</td>
<td>73.2</td>
<td>56.7</td>
<td>74.7</td>
</tr>
<tr>
<td>Black</td>
<td>13.3</td>
<td>7.3</td>
<td>12.4</td>
<td>12.7</td>
</tr>
<tr>
<td>Ankle-brachial index, mean (SD)</td>
<td>0.61 (0.14)</td>
<td>0.70 (0.12)</td>
<td>0.64 (0.14)</td>
<td>0.70 (0.12)</td>
</tr>
<tr>
<td>Neuropathy, mean (SD)</td>
<td>3.5 (3.7)</td>
<td>4.3 (4.3)</td>
<td>3.1 (3.6)</td>
<td>4.2 (4.3)</td>
</tr>
<tr>
<td>Obesity¶</td>
<td>44.7</td>
<td>39.0</td>
<td>40.0</td>
<td>34.9</td>
</tr>
<tr>
<td>Current and past smoking</td>
<td>86.7</td>
<td>80.5</td>
<td>85.6</td>
<td>78.0</td>
</tr>
<tr>
<td>Diabetes</td>
<td>26.7</td>
<td>24.4</td>
<td>26.7</td>
<td>30.2</td>
</tr>
<tr>
<td>Disk disease</td>
<td>29.3</td>
<td>29.3</td>
<td>31.1</td>
<td>19.0</td>
</tr>
<tr>
<td>Spinal stenosis</td>
<td>7.2</td>
<td>9.7</td>
<td>13.6</td>
<td>1.8</td>
</tr>
<tr>
<td>Hip or knee arthritis</td>
<td>16.0</td>
<td>9.4</td>
<td>11.1</td>
<td>4.8</td>
</tr>
<tr>
<td>Lower-extremity revascularization</td>
<td>45.3</td>
<td>22.0</td>
<td>40.0</td>
<td>42.9</td>
</tr>
<tr>
<td>Depression#</td>
<td>25.9</td>
<td>5.1</td>
<td>18.8</td>
<td>19.3</td>
</tr>
<tr>
<td>≥3 Comorbidities</td>
<td>43.3</td>
<td>29.3</td>
<td>38.9</td>
<td>36.5</td>
</tr>
<tr>
<td>Report leg pain during the 6-min walk</td>
<td>88.6</td>
<td>72.5</td>
<td>83.1</td>
<td>33.3</td>
</tr>
</tbody>
</table>

*Values are expressed as percentages unless otherwise indicated.
†Reference group for the other 5 leg pain categories.
‡Walked more than 6 blocks during the previous week.
§Walked 6 or fewer blocks during the previous week.
¶Defined as body mass index of greater than 27 kg/m².
#Defined as a Geriatric Depression Scale score of 6 or greater.

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The atypical exertional leg pain/carry on group had a higher ABI measurement (0.70 vs 0.61; \( P = .004 \)) and lower prevalences of lower-extremity revascularization (22.0% vs 45.3%; \( P = .008 \)) and depression (5.1% vs 25.9%; \( P = .01 \)). Participants in the leg pain on exertion and rest group had a higher prevalence of comorbidities associated with leg pain than those with IC (Table 1). They also had a higher (worse) neuropathy score (5.6 vs 3.5; \( P < .001 \)) and higher prevalences of diabetes mellitus (48.9% vs 26.7%; \( P < .001 \)), spinal stenosis (20.8% vs 7.2%; \( P = .002 \)), and 3 or more comorbidities (68.2% vs 43.3%; \( P = .003 \)).

A substantial proportion in the 2 no exertional leg pain groups developed leg pain during the 6-minute walk. However, these groups were less likely to develop leg pain than the IC group (33.3% vs 88.6% \( P < .001 \)) for the no exertional leg pain/active group; and 53.6% vs 60.0% \( P = .01 \) for the no exertional leg pain/inactive group \( \langle P < .001 \rangle \).

Table 2 shows functioning levels by symptom group among PAD participants adjusted for age, sex, race, and comorbidities. Overall, participants with atypical leg pain/carry on and atypical exertional leg pain/stop had better functioning than those with IC. The no exertional leg pain/inactive group and the pain on exertion and rest group performed more poorly than those with IC. The no exertional leg pain/active group performed comparably with those who had IC. In the 6-minute walk, participants in the atypical exertional leg pain/carry on group were less likely to stop (6.8% vs 36.0%; \( P = .002 \)) and achieved a greater distance (404.3 vs 328.5 m; \( P < .001 \)) compared with the IC group. Participants in the atypical exertional leg pain/stop group were less likely to stop (19.8% vs 36.0%; \( P < .01 \)) and achieved a greater distance in the 6-minute walk (378.8 vs 328.5 m; \( P < .01 \)) than IC.

The no exertional leg pain/inactive group had a slower walking velocity (0.78 vs 0.90 m/s for usual pace 4-m walk \( P < .01 \); 1.03 vs 1.24 m/s for the fast 4-m walk \( P < .01 \)) compared with the IC group. The pain on exertion and rest group had a slower time for 5 chair raises (13.5 vs 11.9 seconds; \( P < .01 \)), slower walking velocities (0.80 vs 0.90 m/s \( P < .01 \) for usual pace; and 1.05 vs 1.24 m/s \( P < .01 \) for fast-pace 4-m walk), and held the full tandem stand less often (37.5% vs 60.0%; \( P < .01 \)) compared with the IC group.

Table 3 compares the degree to which walking was impaired by specific symptoms in each group. Compared with IC, the atypical exertional leg pain/carry on group reported less walking impairment from the following: pain, aching, or cramps in the calves/buttocks \( P < .001 \), pain or aching in the thighs \( P = .004 \), pain, stiffness, and aching in lower-extremity joints (knee/ankle/hip) \( P = .007 \), and weakness in 1 or both legs \( P < .001 \). Compared with the IC group, the leg pain on exertion and rest group reported greater impairment from pain or aching in the thighs \( P < .01 \), pain, stiffness, or aching in lower-extremity joints \( P < .001 \), pain or discomfort in the chest \( P = .01 \), shortness of breath.

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COMMENT

This study shows that patients with PAD, confirmed with noninvasive ABI testing, have a broad range of symptoms other than classic IC. Additionally, a substantial proportion of patients with PAD are asymptomatic or have exertional leg symptoms other than IC. Our findings suggest that comorbid disease and activity levels contribute to the diversity of leg symptoms in PAD. In particular, PAD participants with leg pain on exertion and rest have higher prevalences of comorbid diseases such as diabetes mellitus, neuropathy, and spinal stenosis that may blur PAD-associated leg symptoms.

Although IC is considered indicative of functional impairment, our data show functional impairment occurs in PAD patients without IC. Furthermore, the type of leg symptoms reported is an important correlate of the degree of functional impairment in PAD.

Participants in the atypical exertional leg pain/carry on group achieved significantly greater distance in the 6-minute walk than the IC group, which may indicate greater pain tolerance and/or greater willingness to “walk through” exertional leg pain. These same atypical exertional leg pain/carry on participants had a low prevalence of depression, suggesting they may be more motivated and more likely to “push through” leg symptoms.

Compared with IC, subjects with leg pain on exertion and rest had more comorbid diseases, greater walking impairment from comorbidity-related symptoms, and worse functioning. Leg pain on exertion and rest in PAD may result in part from comorbid diseases, particularly neurogenic and degenerative arthritis problems affecting the legs. Our data suggest that clinicians should seriously consider the possibility that comorbid diseases such as diabetes mellitus, neuropathy, intervertebral disk disease, and spinal stenosis are contributing to walking impairment in PAD patients with leg pain on exertion and rest. Since our data show that the leg pain on exertion and rest group often report walking impairment from symptoms such as shortness of breath and lower-extremity joint pain, diagnostic assessment might be pursued based on patients’ symptoms.

More than half of the no exertional leg pain/inactive group developed leg pain during the 6-minute walk, suggesting some participants were limiting their activity to avoid leg pain symptoms. Possibly some had previously experienced exertional leg symptoms and limited their activity to avoid the pain. Although we did not ascertain reasons for referral to the noninvasive vascular laboratory, this could explain why 20% of persons with PAD reported no exertional leg pain symptoms, despite prior referral to the vascular laboratory. Other potential explanations follow. First, some may have previously had leg pain symptoms that resolved after revascularization, despite their lower-extremity arterial perfusion remaining abnormal. Others may have been referred to the vascular laboratory for testing prior to coronary artery bypass grafting or because of a nonhealing leg ulcer. Some patients may have minimized symptoms to the study interviewer.

We did not find clinically meaningful differences in ABI values between groups. Measurement error for ABI is ±0.15.8 Thus, while the ABI is highly sensitive and specific for diagnosing PAD, it cannot be used to classify patients into symptom groups.

Table 3. Severity of Walking Impairment by Cause Associated With Intermittent Claudication vs Other Leg Symptom Categories Among Men and Women Aged 55 Years or Older With Peripheral Arterial Disease (n = 427)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Intermittent Claudication (n = 140)</th>
<th>Atypical Exertional Leg Pain (n = 39)</th>
<th>Stop (n = 86)</th>
<th>No Exertional Active (n = 107)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD) Median (IQR)</td>
<td>Mean (SD) Median (IQR)</td>
<td>Mean (SD) Median (IQR)</td>
<td>Mean (SD) Median (IQR)</td>
</tr>
<tr>
<td>Pain, aching, or cramps in calves/buttocks</td>
<td>2.46 (0.93) 3.0 (2.0-3.0)</td>
<td>1.61 (0.97) 1.0 (1.0-2.0)</td>
<td>1.81 (1.03) 2.0 (1.0-2.0)</td>
<td>0.84 (1.05)</td>
</tr>
<tr>
<td>Pain or aching in thighs</td>
<td>1.25 (1.24) 1.0 (0-2.0)</td>
<td>0.64 (0.96) 0 (0-1.0)</td>
<td>0.92 (1.11) 0 (0-2.0)</td>
<td>0.42 (0.75)</td>
</tr>
<tr>
<td>Pain, stiffness, aching in joints (knee/ankle/hip)</td>
<td>1.64 (1.16) 2.0 (1.0-2.0)</td>
<td>0.92 (1.01) 0 (1.0-2.0)</td>
<td>1.36 (1.11) 1.0 (0-2.0)</td>
<td>0.95 (1.14)</td>
</tr>
<tr>
<td>Weakness in 1 or both legs</td>
<td>1.84 (1.26) 2.0 (1.0-3.0)</td>
<td>1.08 (0.93) 1.0 (0-2.0)</td>
<td>1.26 (1.15) 1.0 (0-2.0)</td>
<td>0.81 (1.14)</td>
</tr>
<tr>
<td>Pain or discomfort in chest</td>
<td>0.46 (0.83) 0 (0-1.0)</td>
<td>0.26 (0.55) 0 (0-0)</td>
<td>0.36 (0.73) 0 (0-0)</td>
<td>0.28 (0.59)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>0.94 (1.03) 1.0 (0-2.0)</td>
<td>0.72 (0.92) 0 (0-1.0)</td>
<td>0.85 (0.91) 1.0 (0-1.0)</td>
<td>0.72 (0.82)</td>
</tr>
<tr>
<td>Heart palpitations</td>
<td>0.34 (0.67) 0 (0-0)</td>
<td>0.15 (0.37) 0 (0-0)</td>
<td>0.42 (0.71) 0 (0-1.0)</td>
<td>0.09 (0.20)</td>
</tr>
</tbody>
</table>

*Participants ranked each symptom on a 0 to 4 Likert scale, in which 0 indicated no impairment and 4 indicated greatest walking impairment for each symptom. Thirty-three participants did not complete the questionnaire that provided the data for this table. IQR indicates interquartile range.
†Walked more than 6 blocks during the previous week.
‡Walked 6 or fewer blocks during the previous week.
§Reference group for the other 5 leg pain categories.
¶Medians are statistically significantly different between intermittent claudication and leg pain category. Five pairwise comparisons between intermittent claudication and leg pain categories were made using the Wilcoxon rank sum test, with Bonferroni adjustments to control the overall type I error. A P value of .01 was used as the level of statistical significance for individual pairwise comparisons.
This study has several study limitations. First, our findings may not be generalizable to persons with PAD identified from a community-dwelling setting. Because participants were required to return for the study, the most ill or disabled may be underrepresented. We did not systematically collect data allowing us to compare participants from the 3 vascular laboratories from where participants were recruited. However, participants in this study are comparable with individuals with established PAD from other medical centers. We did not perform power calculations a priori for this study. Data are from a large, observational study with the primary purpose of identifying predictors of poorer functioning in PAD. Although our study cohort included 460 participants with PAD, sample sizes were small for some symptom groups, limiting power to detect significant differences. We did not collect data on the duration or severity of comorbidity. Further study is needed to determine whether treatment of associated comorbid illnesses and other factors influencing leg symptoms improve functioning in patients who have PAD associated with symptoms other than IC.

In conclusion, our findings show that patients with PAD, as determined by noninvasive ABI testing, have a range of leg symptoms beyond IC. Our data suggest that clinicians can use leg symptoms to gauge the degree of functional impairment associated with PAD. Clinicians should consider the possibility that comorbid disease and physical activity may alter PAD-associated leg symptoms. Further study is needed to determine whether treatment of associated comorbid illnesses and other factors influencing leg symptoms improve functioning in patients who have PAD associated with symptoms other than IC.

Author Contributions: Study concept and design: McDermott, Greenland, Guralnik, Criqui, Dolan, Celic, Schneider, Martin. Acquisition of data: McDermott, Celic, Pearce, Schneider, Clark, Gibson. Analysis and interpretation of data: Greenland, Liu, Guralnik, Criqui, Dolan, Chan, Schneider, Sharma. Drafting of the manuscript: McDermott, Greenland, Liu, Dolan, Celic, Gibson. Critical revision of the manuscript for important intellectual content: McDermott, Greenland, Guralnik, Criqui, Dolan, Celic, Pearce, Schneider, Sharma, Clark, Martin. Statistical expertise: Liu, Guralnik, Criqui, Chan, Schneider. Obtained funding: McDermott, Greenland, Criqui. Administrative, technical, or material support: Greenland, Crici, Celic, Clark, Gibson, Martin. Study supervision: McDermott, Greenland, Guralnik, Criqui, Clark.

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REFERENCES
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To be surprised, to wonder, is to begin to understand. This is the sport, the luxury, special to the intellectual man.
—José Ortega y Gasset (1883-1955)