Exertional Leg Pain in Patients With and Without Peripheral Arterial Disease

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**Background**—Although exertional leg pain is a hallmark of peripheral arterial disease (PAD) and can occur in persons without PAD, symptom variation has received inadequate attention.

**Methods and Results**—Three cohort studies were combined for cross-sectional analysis. The San Diego Claudication Questionnaire assessed exertional leg pain. PAD was defined as ankle brachial index (ABI) ≤0.90 or history of lower-extremity revascularization. Of 3658 subjects, 3629 were analyzed after exclusions. Of these, 24.1% had PAD in 1 or both legs. There was a stepwise decrease in average ABI, from no pain to pain on exertion and rest, noncalf pain, atypical calf pain, and classic claudication (P=0.002). When stratified by PAD, this trend was no longer significant. Legs with ABIs >0.90 and revascularization had pain distributions intermediate between that of normal legs (ABI, 1.00 to 1.39) and legs with ABIs ≤0.90. Compared with normal legs, legs with low-normal (0.91 to 0.99) and high-normal (≥1.40) ABIs had higher pain rates, suggesting borderline disease and vascular stiffness, respectively. Multivariable logistic regression models showed that ABI was a strong correlate of pain category throughout the ABI range. Independently of ABI, age, male sex, diabetes, smoking history, high body mass index, myocardial infarction, and previous revascularization were all significant correlates of exertional leg pain.

**Conclusions**—No category of exertional leg pain was sufficiently sensitive or specific for routine PAD diagnosis. Legs with low-normal and high-normal ABIs appeared to have ischemic leg pain; thus, a “normal ABI” is likely to range from 1.00 to 1.39. In addition to ABI, several risk variables were independent correlates of exertional leg pain. (Circulation. 2005;112:3501-3508.)

**Key Words:** claudication ■ epidemiology ■ exercise ■ peripheral vascular disease

Peripheral arterial disease (PAD) is a highly prevalent condition in middle-aged and older persons that frequently goes undiagnosed. PAD is often undertreated when diagnosed relative to other manifestations of cardiovascular disease.1-5 PAD affects ≈8 million people in the United States and portends an increased risk of myocardial infarction (MI) and stroke, critical leg ischemia and amputation, and overall mortality, as well as a compromised quality of life.2-6 PAD classically presents as intermittent claudication.7 Reduced perfusion of leg muscles (mainly calf, occasionally thigh or buttock) secondary to atherosclerotic narrowing of peripheral arteries, aggravated by exercise, leads to pain that typically subsides within 10 minutes of rest. However, up to 90% of persons with PAD in the general population do not have classic symptoms of intermittent claudication.1 For example, in the multicenter PARTNERS study, 29% of the 6417 patients had PAD, but only 11% of PAD patients had classic claudication.1 Fully one third of PAD patients reported no leg pain at all, whereas the remaining 55% had atypical symptoms.

Patients with PAD span the spectrum from asymptomatic to ischemic rest pain and threatened limb loss. Pain secondary to PAD may become misconstrued as an unrelated condition such as arthritis or sciatica. Elderly patients may also disregard leg pain as a normal condition that accompanies old age. Alternately, physical inactivity or comorbid diseases limiting ambulation may prevent even patients with severe PAD from reaching an ischemic threshold.8 It is important to better understand the pain symptomatology in PAD to improve diagnosis and initiation of measures to mitigate symptoms, progression, and its associated risk for ischemic events.

To evaluate exertional leg pain in patients with and without PAD, we combined data from 3 studies and used the San Diego Claudication Questionnaire (SDCQ)9 to systematically group exertional leg pain into 5 categories (no pain, pain on exertion and rest, noncalf pain, atypical calf pain, and classic claudication). We used the ankle brachial index (ABI) and history of revascularization to define PAD. Finally, we assessed whether comorbidities such as diabetes, stroke, MI,
a high body mass index (BMI) and a history of smoking were independently related to exertional leg pain in either PAD or non-PAD patients. We hypothesized that patients with PAD would report proportionately more classic claudication symptoms than patients without PAD.

Methods

Study Populations
This was a cross-sectional study combining subjects from 3 prior studies. Two were clinical cohorts enriched with vascular patients, and 1 was a free-living population. All 3 studies were approved by their respective institutional review committees, and all subjects involved gave informed consent.

San Diego Veterans Administration Study
Data from the San Diego Veterans Administration (SD-VA) study were collected between 1990 and 1994 at the San Diego Veterans Administration Medical Center and the University of California, San Diego Medical Center vascular laboratories. Subjects who had visited the vascular laboratories in these 2 hospitals in the prior 10 years were invited to return for a noninvasive vascular examination involving the lower extremities. Detailed methods have been published.

Chicago Study
Subjects from this study were recruited from 3 noninvasive vascular laboratories and from a large general medicine practice in the Chicago area between 1998 and 2000. Detailed methods have been published.

San Diego Population Study
The San Diego Population Study (SDPS) consisted of subjects for whom data were collected between 1995 and 1999. This cohort consisted of current, former, and retired employees of the University of California, San Diego and their respective spouses or significant others who were randomly selected from a database by a computer. Selection occurred within each category of age, ethnicity, and gender for the purposes of oversampling minorities and women to increase the underrepresented populations. Detailed methods have been published.

Questionnaires
The SDCQ, which uniquely allows ipsilateral determination of pain symptoms, was used in all 3 studies to assess leg pain. The laterality of the pain (right, left, or both legs) and location (calf, thigh, or buttock) were noted. Symptoms (or no ambulatory pain) were classified separately for each leg into 5 categories: No pain, pain on exertion and rest, noncalf pain, atypical calf pain, and classic claudication. The details of classification are given in Table 1. Note that “pain on exertion and rest” is any exercise leg or buttock pain that at least sometimes occurs at rest, as distinguished from “pain on exertion and rest,” which usually refers to severe resting ischemic pain in severe PAD.

Each of the 3 studies had questionnaires that asked about catheter-based or surgical interventions for PAD, as well as a history of MI or stroke. Age, gender, ethnicity, diabetes, cigarette smoking, and statin use history were determined with standard questionnaires. BMI was calculated as weight in kilograms divided by height in meters squared.

ABI Measurement
ABI was measured with accurate, validated methods that were comparable across the 3 studies.

SD-VA Study
Trained vascular laboratory personnel administered noninvasive vascular examinations, which included segmental systolic blood pressure measurements at 5 segments of the lower extremities, including the ankle, with a photoplethysmographic sensor. Bilateral brachial systolic pressures also were measured with a photoplethysmographic sensor.

Chicago Study
Bilateral systolic blood pressure measurements at the brachial arteries, posterior tibial (PT) arteries, and dorsalis pedis (DP) arteries with a hand-held continuous-wave Doppler were performed twice for each artery.

SDPS
The noninvasive vascular examinations included systolic blood pressure measurements of the brachial arteries and PT arteries bilaterally with a hand-held continuous-wave Doppler. If a pressure in a PT artery could not be obtained, the DP artery was used. Each ankle artery was assessed twice.

PAD Definition
For these analyses, the ABI for each leg was defined as the highest (or highest average if measured twice) ankle pressure (DP or PT) of each leg divided by the highest (or highest average if measured twice) brachial pressure. Support for averaging the DP and PT pressure in calculating ABI has been published. However, DP and PT pressures were not measured for every subject in the SD-VA and SDPS cohorts; therefore, the highest leg pressures were used for equivalence among the 3 cohorts. Legs with ABI ≤0.90 or with higher ABIs but previous intervention (surgery or angioplasty) for PAD in that leg were defined as PAD.

Exclusion Criteria
Initially, a total of 3658 subjects were examined before exclusion. Because ABI measurements were central to the purposes of this study, subjects with absent or incomplete ABI measurements in 1 or both legs were excluded (n=29), leaving 3629 subjects for analysis pertaining to the whole person. Amputation in the lower extremities, inability of the technician to obtain a reliable systolic pressure reading from the upper extremities (brachial artery) or the lower extremities (PT or DP arteries), or patient refusal typically accounted for the missing or incomplete ABIs.

Analysis pertaining to individual legs used slightly different exclusion criteria. Only legs without ABI data were excluded from leg-specific analysis, regardless of whether ABI data were available on the contralateral leg. Of a possible 7316 legs (3658×2), 37 had missing ABIs, leaving 7279 legs available for leg-specific analyses.
Statistical Analyses

All statistical analyses were performed on Microsoft Excel 2000 and SAS version 8.1 software for the personal computer. Leg-specific, age- and sex-adjusted frequency distributions of pain categories were initially performed for each cohort individually and then for all subjects combined. Leg-specific logistic regression models, adjusted by the generalized estimating equation technique to account for the intraindividual leg correlation, were computed to assess independent relationships of selected risk factors to the 5 pain categories. Each of the 4 leg pain categories was separately compared with the reference category of no pain. Potential risk factors analyzed were age, sex, ethnicity, ABI, diabetes, smoking history, statin use, BMI, MI, stroke, and intervention for PAD (revascularization). Age and BMI were modeled as continuous variables; all other variables were defined categorically. ABI was defined as a 4-category variable: ≤0.70, 0.71 to 0.99, 1.00 to 1.39, and ≥1.40, with the normal category, 1.00 to 1.39, as the reference group. Male was the reference variable for sex, and non-Hispanic white was the reference variable for ethnicity.

Pain concordance was defined in the following manner: (1) Concordance for no pain meant that subjects had no exercise pain in either leg, (2) pain category concordance meant that the same pain category was evident in both legs, (3) unilateral pain was pain in only 1 leg, and (4) pain category discordance indicated different pain categories in the 2 legs.

Results

Table 2 describes the demographic and clinical characteristics of the participants in the 3 cohorts. Before exclusion, the 508 subjects from the SD-VA clinical study comprised 448 men and 60 women, with a mean age of 68.6 years. The ethnic distribution was 87.2% non-Hispanic white, 5.5% Hispanic, 4.5% black, and 2.8% other. In this study, 65.9% had PAD. In the Chicago clinical study, there were a total of 740 subjects; 416 were male and 324 were female, with a mean age of 70.9 years. This group was 78.1% non-Hispanic white, 1.5% Hispanic, 17.2% black, and 3.1% other. In this group, 62.4% had PAD. Of the 2410 subjects in the SD population study, 9 subjects had missing ABIs in both legs and were excluded from demographic data, leaving 2401 subjects for analysis. Of these, 824 were male and 1577 were female, with an overall mean age of 59.7 years. This population consisted of 67.2% non-Hispanic white, 10.7% Hispanic, 13.0% black, and 9.0% other (primarily Asian). In this study, 3.5% had PAD.

A total of 3629 subjects remained after exclusions; 1671 (46.0%) were male, and 1958 (54.0%) were female. Their mean age was 62.9 years, and the ethnic distribution was as follows: 67.2% non-Hispanic white, 10.7% Hispanic, 13.0% black, and 9.0% other (primarily Asian). Of these subjects, 24.1% had definable PAD in 1 or both legs; 18.9% of the 7279 total legs used for leg-specific analysis had PAD. Note that in the clinical cohorts, most subjects had PAD and, as expected, had much higher rates of cigarette smoking, diabetes, prior MI, and prior stroke. The low rates of statin use in the SD-VA study reflect the fact that the data were collected in 1990 to 1994, when lipid therapy was less common than in current clinical practice.

Table 3 shows leg-specific, age- and sex-adjusted pain distributions in the SD-VA, Chicago, and SDPS cohorts individually and combined stratified by PAD. As expected,
the SD-VA and Chicago studies had a much higher proportion of legs with pain symptoms. In subjects with PAD, the SD-VA and Chicago studies are similar in the distribution of the 4 pain categories, with classic claudication being the most common, followed by pain on exertion and rest. In contrast, subjects with PAD in the SDPS were more likely to complain of pain on exertion and rest or atypical calf pain than classic claudication.

Compared with the pain distribution in the PAD group, the non-PAD group had a greater proportion of no pain and a smaller proportion of pain symptoms. However, exertional leg pain was reported in 56%, 35%, and 12% of the non-PAD legs in the SD-VA, Chicago, and SDPS studies, respectively. Pain (also occurring) at rest was the most common pain symptom in legs without PAD in all 3 studies. The similarity of pain distributions in the SD-VA and Chicago studies and the lower pain rates in the free-living population are apparent.

Table 4 shows person-specific pain concordance in subjects with unilateral PAD, bilateral PAD, and no PAD. As expected, subjects without PAD were most likely to report concordance for no pain (79%), and subjects with bilateral PAD were most likely to report concordant pain (59%). However, subjects with unilateral PAD were more likely to report bilateral (42%) than unilateral (29%) pain. In addition, in these 29% (n=80) of subjects with unilateral PAD and unilateral pain, PAD and pain were in the same leg in 69 subjects but in different legs in 11 subjects. Pain category discordance was reported in only 12.5% of subjects with either unilateral or bilateral PAD.

Figure 1 shows the leg-specific age- and sex-adjusted mean ABI for each pain category for all legs and stratified by PAD presence. For all legs, there was a statistically significant stepwise decrease in the mean ABI from no pain to pain on exertion and rest, noncalf pain, atypical calf pain, and classic claudication (P<0.002) by simple linear regression models for monotonicity. When stratified by PAD presence, the tendency to trend was weak. Simple linear models did not support a trend for PAD legs only (P=0.09) and non-PAD legs only (P=0.71).

Table 5 shows leg-specific pain category distribution by PAD presence and severity with 0.1 ABI increments. As the ABI increased, the proportion of legs reporting no pain increased, from 17% for ABIs ≤0.40 to 87% for ABIs in the 1.20 to 1.29 interval. However, as the ABI increased further above 1.30, the proportion with no pain progressively decreased to 61% with an ABI ≥1.50. The proportion of subjects with classic claudication followed a similar pattern. More than 40% of subjects with ABIs <0.60 had classic claudication compared with 22% to 36% in those with an ABI between 0.60 and 0.89. The lowest rate of

| TABLE 4. Person-Specific Age- and Sex-Adjusted Pain Concordance Stratified by PAD |
|----------------------------------|--------------|--------------|---------------|----------------|
| SD-VA Study | Chicago Study | SDPS | Combined |
| Unilateral PAD | |
| Total subjects, n | 109 | 140 | 39 | 288 |
| Concordance for no pain, % | 30.2 | 20.1 | 52.8 | 28.2 |
| Pain category concordance, % | 50.0 | 42.1 | 18.0 | 41.4 |
| Unilateral pain, % | 18.9 | 35.0 | 27.3 | 28.4 |
| Pain category discordance, % | 0.7 | 2.9 | 2.0 | 2.0 |
| Bilateral PAD | |
| Total subjects, n | 216 | 321 | 832 | 553 |
| Concordance for no pain, % | 13.0 | 18.7 | 44.6 | 19.0 |
| Pain category concordance, % | 73.9 | 53.1 | 34.0 | 58.3 |
| Unilateral pain, % | 12.5 | 24.9 | 21.8 | 20.6 |
| Pain category discordance, % | 0.6 | 3.3 | 0.0 | 2.1 |
| No PAD | |
| Total subjects | 168 | 278 | 2312 | 2758 |
| Concordance for no pain, % | 39.0 | 62.5 | 84.6 | 78.9 |
| Pain category concordance, % | 49.8 | 23.4 | 6.4 | 11.4 |
| Unilateral pain, % | 10.0 | 13.3 | 8.6 | 9.2 |
| Pain category discordance, % | 1.1 | 0.8 | 0.3 | 0.4 |

Figure 1. Leg-specific age- and sex-adjusted mean ABI by leg pain category.
classic claudication was in the 1.00 to 1.39 ABI range (1.0% to 2.7%). However, normal ABIs (≥0.90) that were either higher or lower than the 1.00 to 1.39 range showed higher levels of classic claudication.

Figure 2 shows leg-specific pain categories in 5 ABI groups: ≤0.90, >0.90 but with prior PAD intervention, 0.90 to 0.99, 1.00 to 1.39, and ≥1.40. More than half the group with prior intervention and a normal ABI had exertional leg pain, and 15% had classic claudication. The 0.90 to 0.99 and ≥1.40 ABI groups had strikingly similar pain category distributions. Compared with subjects with ABIs of 1.00 to 1.39, these 2 “borderline” groups had fewer subjects with no pain and higher rates in each of the 4 pain categories, the most marked difference being in the classic claudication category.

A leg-specific logistic multivariable regression model adjusted by the generalized estimating equation technique for intrindividual leg correlation was constructed to assess the independent contributions of a number of selected risk factors to the different categories of pain. Preliminary models showed similar results in the 3 cohorts, so they were combined for analysis. Table 6 shows odds ratios (ORs) and probability values.

Age was associated with all pain types except exercise and rest. Women were less likely to report pain except for noncalf pain. Compared with non-Hispanic whites, other ethnic groups reported less atypical calf pain and classic claudication.

As expected, both lower ABI categories, ≤0.7 and 0.71 to 0.99, were independently related to all pain groups, with the strongest associations for atypical calf pain and classic claudication. A high ABI (≥1.40) was independently related to classic claudication, with positive nonsignificant ORs for the other pain categories, suggesting that arterial stiffness masked many PAD cases. Diabetes independently contributed to all pain categories except noncalf pain, in which it was inversely associated. Current smoking was a strong correlate of all pain groups, and ex-smoking was correlated with classic claudication. Statin use was inversely associated with pain on exertion and rest but positively correlated with atypical calf pain, possibly related to myalgia. Higher BMI was independently associated with 2 of the 4 pain categories. A history of MI was related to both exercise/rest pain and classic claudication. Finally, previous intervention for PAD was positively related to all pain types except atypical calf pain. Note that this result was independent of the ABI level after intervention and the other variables in Table 6.

Discussion

Our results indicate that leg pain is common in PAD patients and can present in atypical ways. In addition, leg pain is not uncommon in patients without definitive PAD, particularly in those with borderline ABI values. These data show that in patients with normal ABIs, pain is still inversely related to the

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**TABLE 5. Leg-Specific Age- and Sex-Adjusted Pain Distributions for Combined Studies by 0.1 ABI Increments**

<table>
<thead>
<tr>
<th>Pain Category</th>
<th>ABI Group</th>
<th>Legs, n</th>
<th>No pain, %</th>
<th>Pain on exertion/rest, %</th>
<th>Noncalf pain, %</th>
<th>Atypical pain, %</th>
<th>Classic claudication, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤0.40</td>
<td>47</td>
<td>17.2</td>
<td>29.6</td>
<td>12.0</td>
<td>41.5</td>
<td></td>
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<tr>
<td></td>
<td>0.40–0.49</td>
<td>120</td>
<td>16.7</td>
<td>16.7</td>
<td>4.7</td>
<td>45.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.50–0.59</td>
<td>244</td>
<td>23.7</td>
<td>16.4</td>
<td>2.2</td>
<td>41.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.60–0.69</td>
<td>265</td>
<td>21.8</td>
<td>19.8</td>
<td>5.0</td>
<td>35.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.70–0.79</td>
<td>327</td>
<td>33.4</td>
<td>20.9</td>
<td>2.7</td>
<td>28.1</td>
<td></td>
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<tr>
<td></td>
<td>0.80–0.89</td>
<td>312</td>
<td>38.7</td>
<td>16.1</td>
<td>3.2</td>
<td>21.9</td>
<td></td>
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<tr>
<td></td>
<td>0.90–0.99</td>
<td>699</td>
<td>67.0</td>
<td>12.4</td>
<td>1.6</td>
<td>7.0</td>
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<td></td>
<td>1.00–1.09</td>
<td>1762</td>
<td>81.6</td>
<td>10.7</td>
<td>0.9</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.10–1.19</td>
<td>2122</td>
<td>84.4</td>
<td>8.7</td>
<td>1.2</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.20–1.29</td>
<td>956</td>
<td>87.1</td>
<td>14.1</td>
<td>1.2</td>
<td>1.0</td>
<td></td>
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<tr>
<td></td>
<td>1.30–1.39</td>
<td>193</td>
<td>79.7</td>
<td>16.1</td>
<td>4.1</td>
<td>6.1</td>
<td></td>
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<tr>
<td></td>
<td>1.40–1.49</td>
<td>48</td>
<td>67.8</td>
<td>21.5</td>
<td>0.0</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥1.50</td>
<td>33</td>
<td>61.2</td>
<td>924</td>
<td>0.10</td>
<td>2.7</td>
<td></td>
</tr>
</tbody>
</table>

*Legs with intervention and an ABI >0.90 were excluded.

**Figure 2.** Leg-specific age- and sex-adjusted pain distributions for 5 distinct subgroups by ABI and intervention history.
ABI level, at least to an ABI level of 1.40, where arterial stiffness may result in a false-negative ABI.

These data suggest that patients who complain of bilateral leg pain, whether or not it is PAD related, have a very strong tendency to report the same type of pain in both legs. Interestingly, in the 80 patients with unilateral PAD and unilateral pain, the pain was not in the leg with PAD 13.8% of the time. This finding underscores the limitation of claudication questionnaires that do not assess symptoms separately for each leg or limitations in our own understanding of pain-processing pathways.

Taking all patients combined, there was a stepwise decrease in average ABI from no pain, pain on exertion and rest, noncalf pain, atypical calf pain, and classic claudication (Figure 1). This corresponds with the clinical concepts that the pain on exertion and rest groups have a significant number of cases of nonvascular pain, that the noncalf pain group has proximal ischemia with some reconstitution distally, and that the atypical calf pain group has on average less severe disease than the classic claudication group, because the most common difference between the former and latter groups is walk-through pain in the former.

In a recent study of PAD patients who had previously come to clinical attention, there was little correlation between the ABI and leg pain category. Similarly, in our data for either PAD patients or non-PAD patients separately, there was only a weak correlation between ABI and leg pain category. However, when these 2 groups were combined, there was a statistically significant stepwise decrease in ABI between pain groups. This finding can be explained by the effects of range restriction, whereby a larger ABI gradient exists between pain categories when considering all patients versus the non-PAD only or PAD only groups that are inherently defined by ABI and restricted to ABI $\geq 0.90$ and ABI $\leq 0.90$ or history of prior revascularization, respectively.

We found that 63.6% of all legs had ABIs in the 1.10 to 1.30 range. The average ABI in non-PAD persons has been reported to be $\approx 1.15$, near the middle of this range. The 1.10 to 1.19 and 1.20 to 1.29 ABI categories had similar high rates of no pain (85.3% and 87.4%) and identical low classic claudication rates (0.8%). As one moves above and below these categories in 0.1 ABI increments, the no pain rates decrease and classic claudication rates increase, although the immediately adjacent categories, 1.00 to 1.09 and 1.30 to 1.39, maintain high no pain rates ($\approx 80\%$) and low classic claudication rates ($\approx 2\%$).

From the 5 ABI categories created (Figure 2), it is striking that high and low ABIs outside the 1.00 to 1.39 range show more pain and more classic claudication. Patients with PAD and ABIs $>0.90$ after intervention had pain intermediate
between the groups outside the 1.00 to 1.39 range and those with ABIs ≤0.90, suggesting on average benefit from intervention but short of restoration to normal. The pain distributions in the low-normal (0.90 to 0.99) and high-normal (≥1.40) ABI categories were strikingly similar. This finding could suggest early or borderline ischemia in the low-normal group, with a further ABI drop perhaps inductive with exercise, and possibly false-negative ABIs resulting from stiff or incompressible arteries in the high-normal group. A recent article from a large population study reported that in men, compared with an ABI group of 1.10 to 1.29, there were significantly higher carotid intimal medial thickness and coronary calcium scores in the 0.90 to 0.99 ABI group and significantly higher coronary calcium scores in the ≥1.30 ABI group.14 The Strong Heart Study by Resnick et al15 demonstrated that in a population-based setting, individuals in the high ABI groups (ABI ≥1.40) had associated mortality rates similar to those of low ABI groups (ABI <0.90), whereas mortality rates were uniformly low in the 1.00 to 1.39 ABI range. Our data, taken in conjunction with the Strong Heart Study data, suggest that the definition of a normal ABI should be revised from >0.90 to the range of 1.00 to 1.39.

The relationship between low ABI and leg pain persisted in multivariable analysis for all pain groups, and high ABI showed an independent relationship with classic claudication. Multiple other conditions were associated with leg pain symptoms even after consideration of the ABI. Age, gender, ethnicity, diabetes, cigarette smoking, and previous intervention for PAD each were significantly and independently associated with at least 3 of the 4 pain categories. Such variables should be considered when the patient presenting with leg pain is evaluated.

Diabetics are less likely to report pain symptoms in acute MI but are more likely to report nonpain symptoms, including dyspnea, cough, weakness, and nausea.16 Conversely, in our study, diabetes was associated with more leg pain for 3 of the 4 pain categories after adjustment for ABI level, including high ABI, but diabetes showed an inverse association with noncalf pain. This latter result was highly significant and consistent with previous observations showing a greater degree of infrageniculate PAD in diabetes17,18 and the lack of an independent association between diabetes and aorto-iliac disease.18 The increased risk of diabetes for the other 3 pain categories could in part reflect peripheral neuropathy.

This study has several limitations. First, we pooled data from 3 cohort studies with different demographic profiles and from different time periods. The SD-VA study had a higher proportion of male subjects than the Chicago study, but these 2 studies had similar demographic profiles and drew subjects primarily from patient populations with leg pain. SDPS involved somewhat younger and healthier subjects with a higher proportion of women. However, all comparisons were adjusted for the age and sex differences; all 3 cohort studies were evaluated with the same questionnaire (SDQC); and ABI calculations were consistent between the 3 cohorts. In addition, had exercise ABI been routinely performed, particularly in subjects with borderline ABIs, many persons with normal ABIs undoubtedly would have shown an ankle pressure decrease with exercise, which would help explain exercise leg pain in patients with normal ABIs.

In conclusion, exertional leg pain is a common finding in adult populations, and although it is more common in PAD patients, no category of exertional leg pain is sufficiently sensitive or specific to be reliable for PAD diagnosis. When patients report exertional leg pain bilaterally, they nearly always report the same pain category in both legs. In the population, there is a stepwise decrease in the ABI as one moves from reports of no pain to pain on exertion and rest, non-calf pain, atypical calf pain, and classic claudication. The ABI predicts the probability of pain throughout the ABI range, and age, sex, ethnicity, diabetes, cigarette smoking, BMI, previous MI, and previous lower-extremity intervention for PAD are all independently associated with exertional leg pain. Finally, a normal ABI is probably best defined as between 1.00 to 1.39.

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References


12. McDermott MM, Criqui MH, Liu K, Guralnik JM, Greenland P, Martin GI, Pearce W. Lower ankle/brachial index, as calculated by averaging the dorsalis pedis and posterior tibial arterial pressures, and association with...
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