Calf muscle hemoglobin oxygen saturation in patients with peripheral artery disease who have different types of exertional leg pain

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Background: This study compared calf muscle hemoglobin oxygen saturation (StO2) and exercise performance during standardized treadmill exercise in patients with peripheral artery disease (PAD) who describe different types of exertional leg pain and compared secondary outcomes consisting of daily ambulatory activity and exercise performance during a 6-minute walk test (6MWT).

Methods: Leg pain symptoms were evaluated in 114 patients with PAD using the San Diego Claudication Questionnaire, by which atypical exertional leg pain was defined in 31, claudication in 37, and leg pain on exertion and rest in 46. Patients were evaluated on a standardized, graded treadmill test during which calf muscle StO2 was continuously monitored. The 6MWT distance, Walking Impairment Questionnaire (WIQ), and ambulatory activity were monitored during 1 week.

Results: All patients experienced symptoms during the treadmill test consistent with claudication. The groups were not significantly different on the primary outcomes of time to reach the minimum calf muscle StO2 (P = .350) or peak walking time (P = .238) during treadmill exercise. Patients with atypical leg pain had the highest daily ambulatory activity for total strides per day (P = .032), average daily cadence (P = .010), maximum cadences for durations between 5 minutes (P = .035) and 60 minutes (P = .029), speed score on the WIQ (P = .006), and lowest rating of perceived exertion at the end of the 6MWT (P = .017).

Conclusions: PAD patients with atypical leg pain have vascular-mediated limitations in exercise performance during standardized treadmill testing similar to patients with claudication and patients with leg pain on exertion and rest but have higher levels of daily ambulatory activity in the community setting and higher perceived ambulatory function.


Peripheral artery disease (PAD) is prevalent in >12% of the United States population aged ≥65 years1 and is associated with increased prevalence of cardiovascular disease risk factors1,2 and increased comorbidity of disease in the coronary, cerebral, and renal arteries.1,2 More than 60% of those with PAD have concomitant cardiovascular or cerebrovascular disease, or both,2 thereby contributing to their elevated risk of mortality.3,4 In addition to having high cardiovascular risk, many of those with PAD are physically limited by ambulatory leg pain that results in impaired ambulation,5,6 reduced physical function,7,8 and lower daily physical activity.9,10 On initial clinical presentation, 10% to 35% of patients with PAD report claudication symptoms, and 30% to 50% report other leg pain that is atypical of the classic description of claudication.1,2 When PAD patients with different types of exertional leg pain are compared, patients with claudication have worse functional status, self-reported ambulatory function, and health-related quality of life than patients with atypical pain11 but have better values than those reporting leg pain on exertion and rest.7,11 We recently found that regardless of the type of leg pain reported, all patients experienced symptoms during a standardized treadmill test consistent with classic claudication,12 indicating the limitations associated with descriptions of leg pain during the initial clinical presentation. Furthermore, patients with different types of exertional leg pain were remarkably similar on claudication onset time (COT) and peak walking time (PWT) during treadmill exercise, and on the ankle-brachial index (ABI) and ischemic window.12 Calf muscle hemoglobin oxygen saturation (StO2), a measure of the microcirculation in the musculature during exercise, is highly associated with COT and PWT,13,14 and this association persists even after adjusting for ABI.14 As such, differences in the microcirculation may partially ex-
plain the different descriptions of leg pain. However, calf muscle \( \text{StO}_2 \) in PAD patients with different types of exertional leg pain has not been examined.

The primary purpose of this study was to compare calf muscle \( \text{StO}_2 \) and exercise performance during standardized treadmill exercise in patients with PAD who describe different types of exertional leg pain. An additional aim was to compare secondary outcomes, consisting of daily ambulatory activity and exercise performance during a 6-minute walk test (6MWT), among the groups with exertional leg pain. We hypothesized that the group with leg pain on exertion and rest would have the most impaired calf muscle \( \text{StO}_2 \) during treadmill exercise, and the lowest 6MWT distance and daily ambulatory activity.

**METHODS**

**Patients**

The procedures used in this study were approved by the Institutional Review Board at the University of Oklahoma Health Sciences Center (HSC) and by the Research and Development committee at the Oklahoma City VA Medical Center. Written informed consent was obtained from each patient before investigation.

**Recruitment.** Patients were recruited by referrals from vascular and primary care clinics from the University of Oklahoma HSC and the Oklahoma City VA Medical Center, and by newspaper advertisements for possible enrollment into a randomized controlled exercise rehabilitation study for the treatment of leg pain secondary to PAD. The data and analyses for this study were part of the baseline assessments obtained for the exercise study. A consecutive series of 174 individuals were evaluated for study eligibility in the General Clinical Research Center (GCRC) at the University of Oklahoma HSC.

**Medical screening.** Patients arrived at the GCRC in the morning fasted, but were permitted to take their usual morning medication regimen. Demographic information, height, weight, cardiovascular risk factors, comorbid conditions, claudication history, blood samples, and a list of current medications were obtained from a medical history and physical examination at the beginning of the study. During the physical examination, arterial oxygen saturation was measured from the index finger using a standard pulse oximeter. Subcutaneous fat over the medial gastrocnemius muscle was measured from a skinfold using a Lange skinfold tape.16 and waist circumference was recorded using a plastic measuring tape.16

**Inclusion and exclusion criteria.** Patients with PAD were included in this study if they met the following criteria: (1) a history of any type of exertional leg pain, (2) ambulatory leg pain confirmed during a graded treadmill test, and (3) an ABI \( \leq 0.90 \) at rest or an ABI \( \leq 0.73 \) after exercise, because some PAD patients have normal values at rest that only become abnormal after an exercise test.17

Exclusion criteria were (1) absence of PAD (ABI >0.90 at rest and ABI >0.73 after exercise), (2) inability to obtain an ABI measure due to noncompressible vessels, (3) asymptomatic PAD determined from the medical history and verified during the graded treadmill test, (4) use of medications indicated for the treatment of intermittent claudication (cilostazol and pentoxifylline) initiated \( \leq 3 \) months before the investigation, (5) exercise tolerance limited by any disease process other than PAD, (6) active cancer, (7) kidney failure defined as stage 5 chronic kidney disease, (8) abnormal liver function, (9) calf skinfold >50 mm because of potential interference with the light path of the near infrared spectrometer probe from penetrating the subcutaneous tissue, and (10) pulse arterial oxygen saturation of the index finger <95% because of the potential deleterious effect on calf muscle \( \text{StO}_2 \) from poor pulmonary gas exchange. A total of 174 patients were evaluated for this study, and 114 were deemed eligible.

**Groups with exertional leg symptoms.** Leg symptoms were evaluated by administering the San Diego Claudication Questionnaire (SDCQ), a standardized and validated 11-item questionnaire based on the Rose questionnaire for intermittent claudication. According to the responses from the SDCQ, PAD patients were placed into one of the following exertional leg symptom groups:

1. Atypical exertional leg pain group (n = 31), defined as leg pain on exertion that does not cause the patient to stop or slow down (9 of the 31 patients) or pain that does cause the patient to stop or slow down but does not fulfill the remaining criteria for claudication (22 of the 31 patients),
2. Claudication group (n = 37), defined as leg pain on exertion that causes the patient to stop or slow down, is located in the calves, does not resolve while walking, and goes away within 10 minutes of rest, and
3. Leg pain on exertion and rest group (n = 46), defined as leg pain on exertion that sometimes begins at rest.7,11,20-22

**Primary outcome measures**

Calf muscle \( \text{StO}_2 \), COT, PWT, and ischemic window obtained during the graded treadmill test. Patients performed a progressive, graded treadmill protocol to determine study eligibility as well as to obtain outcome measures related to peak exercise performance.6 The COT, measured as the walking time at which the patient first experienced pain, and the PWT, measured as the walking time at which ambulation could not continue due to maximal pain, were recorded to quantify the severity of claudication.

Peak oxygen uptake was measured by oxygen uptake obtained during the peak exercise workload with a Medical Graphics VO2000 metabolic system (Medical Graphics Inc, St. Paul, Minn). The test–retest intraclass reliability coefficient with these procedures is \( R = .89 \) for COT, \( R = .93 \) for PWT, and \( R = .88 \) for peak oxygen uptake.23 Calf muscle \( \text{StO}_2 \) was measured before, during, and after the treadmill test using a continuous-wave, near infrared spectrometer unit (InSpectra model 325; Hutchinson
Technology Inc, Hutchinson, Minn), an optical cable attached to a 25-mm probe, InSpectra 2.0 software, and a dedicated laptop computer as previously described.13 The probe was attached to the skin over the medial gastrocnemius muscle of the more severely affected leg using a double-sided adhesive light-excluding patch.24 A baseline measure of calf muscle StO2 was obtained at rest as patients stood on the treadmill for 2 minutes to allow for equilibration. From the start of treadmill exercise, the minimum StO2 value, the time taken to reach the minimum value, the absolute and percentage drops in calf muscle StO2 from rest to the minimum exercise value, the average rate of decline from rest to the minimum exercise value, and the calf muscle StO2 at PWT were obtained. The recovery times for StO2 to reach one-half of the resting StO2 value (recovery half-time), to reach the full resting StO2 value (recovery time), and to reach the maximum StO2 value were calculated by subtracting the time of exercise from the time the recovery StO2 values were observed.

As in our previous investigations,13,14 we attempted to calculate tau using exponential models for StO2 data.25 However, the individual graphs of the time course of StO2 during exercise did not fit this kinetic model for calculating tau. As such, we calculated the parameters described above because they are easily obtained metrics that do not require prior assumptions. In addition to their clinical utility, particularly the strong association between the time to minimum calf muscle StO2 with COT and PWT,13,14 we also have found that calf muscle StO2 measures can be reliably obtained during and after exercise. Reliability of these measures was assessed in 110 patients who performed the progressive, graded treadmill protocol twice in our laboratory. The test–retest intraclass reliability coefficient was R = .85 for calf muscle StO2 obtained at rest, R = .91 for the minimum value obtained during exercise, R = .86 for the time to reach the minimum calf muscle StO2 value during exercise, and between R = .81 and R = .91 for the remaining calf muscle StO2 measures obtained during and after exercise.

ABI measures were obtained from the more severely diseased lower extremity before and at 1, 3, 5, and 7 minutes after the treadmill test.5,23 The reduction in ankle systolic blood pressure after treadmill exercise from the resting baseline value was quantified by calculating the area under the curve, referred to as the ischemic window.26 Because the ischemic window is a function of PAD severity and also the amount of exercise performed, the ischemic window was normalized per meter walked.

Secondary outcome measures

Walking Impairment Questionnaire. Self-reported ambulatory ability was assessed using the Walking Impairment Questionnaire (WIQ), a validated questionnaire for PAD patients that assesses ability to walk at various speeds and distances and to climb stairs.27

6-Minute walk test. Patients performed an over-the-ground 6MWT supervised by trained exercise technicians.28 The pain-free and total distance walked during the test was recorded. The test–retest intraclass reliability coefficient is R = .75 for distance to onset of claudication pain, and R = .94 for total 6MWT distance.28

Ambulatory activity monitoring. Daily ambulatory activity was assessed using the StepWatch3 step activity monitor (Orthoinnovations Inc, Oklahoma City, Okla), as previously described.29 Ambulatory activity was measured for 7 consecutive days in which patients were instructed to wear the monitor during waking hours and to remove it before retiring to bed and while showering. The step activity monitor was attached to the right ankle above the lateral malleolus using an elastic Velcro strap and continuously recorded the number of strides taken each day and the number of minutes spent ambulating each day. The daily ambulatory strides and time were further analyzed by the software program and quantified into the following variables:

- Maximum cadence for 60, 30, 20, and 5 continuous minutes of ambulation each day,
- Maximum cadence for 1 minute of ambulation each day (ie, the minute with the highest cadence value each day), and
- Peak activity index obtained by ranking all minutes of the day according to cadence and then taking the highest 30 values.

These outcome measures were recorded and averaged for each day, and then the daily averages were averaged over the 7-day monitoring period. The accuracy of the step activity monitor exceeds 99% ± 1% in patients with claudication,29 and the test–retest intraclass reliability coefficient for the daily ambulatory activity measures ranges from R = .83 to R = .94.29

Statistical analyses

Means of all measurement variables were compared among the three groups using a one-way analysis of variance, and where significance (P < .05) was observed, a Tukey-Kramer multicomparison test among the three means was conducted. For the primary outcome variables, 95% confidence intervals (95% CI) were calculated for the difference from the claudication group mean and the mean of each of other two groups. For these sample sizes, the power was approximately 95% for effect size of .37 and 80% for effect size of .29, indicating that this study was more than adequately powered to detect rather small effect size differences among groups for the time to minimum calf muscle StO2. The proportions for the dichotomous variables were tested for differences using two-degree of freedom χ2 test. All calculations and power analysis were made using NCSS 2000 software (NCSS, Kaysville, Utah).

RESULTS

Clinical characteristics. Patients with PAD were classified into three groups according to their type of exertional leg pain. The clinical characteristics of these groups are reported in Table I. Groups were significantly different on body mass index (P = .018), ABI (P = .002), prevalence of
obesity \( (P = .009) \), and prevalence of abdominal obesity \( (P = .030) \). The group with leg pain on exertion and rest had the highest values, and the claudication group had the lowest values. The groups were not significantly different \( (P > .05) \) on all remaining variables.

**Primary outcome measures.** The exercise measures of each group during the treadmill test are reported in Table II. All patients experienced symptoms during the treadmill test consistent with claudication. The groups were not significantly different \( (P > .05) \) on any of the exercise performance measures or on any of the calf muscle \( \text{StO}_2 \) measures. Of particular importance, the time to reach the minimum calf muscle \( \text{StO}_2 \) value during exercise was remarkably similar among the groups \( (P = .350) \). The 95% CI comparing the time to minimum calf muscle \( \text{StO}_2 \) between those with atypical exertional leg pain and those with claudication was \(-34\) to 200 seconds, indicating that the group difference for the populations of inference is within \~4 minutes during the treadmill test (equivalent to two exercise stages). An even smaller 95% CI of \(-120\) to 77 seconds was noted for the comparison between those with claudication and those with leg pain on exertion and rest, indicating that the group difference for the population of inference is within \~3 minutes.

**Secondary outcome measures.** The 6MWT performance, daily ambulatory activity, and walking impairment questionnaire measures are reported in Table III. Patients with atypical exertional leg pain reported the lowest rating of perceived exertion at the end of the 6MWT \( (P = .017) \). Patients with atypical exertional leg pain also had the highest daily ambulatory activity measures for total strides per day \( (P = .032) \), peak activity index \( (P = .040) \), average daily cadence \( (P = .010) \), and maximum cadences for durations of 5 \( (P = .035) \), 20 \( (P = .007) \), 30 \( (P = .020) \), and 60 minutes \( (P = .029) \). Patients with atypical exertional leg pain also reported the highest speed score on the WIQ \( (P = .006) \).

**DISCUSSION**

**Novel findings: calf muscle \( \text{StO}_2 \)**

The novel finding of this investigation is that calf muscle \( \text{StO}_2 \) variables were not significantly different among the groups with exertional leg pain during standardized treadmill exercise. A key measure of calf muscle \( \text{StO}_2 \) during exercise is the observed time to reach the minimum \( \text{StO}_2 \) value because this measure is positively associated with \( \text{COT} \) and \( \text{PWT} \);\(^ {13,14} \) and this association persists even after
adjusting for ABI. No group differences in the time to minimum calf muscle StO2 or in the minimum value of calf muscle StO2 indicates that the microcirculation in the calf musculature during exercise is impaired to a similar extent among groups and is unlikely to be a reason for different descriptions of exertional leg pain obtained from the SDCQ.

Atypical leg pain is defined as pain located in the buttocks or thighs or pain that does not force the patient to slow down or stop exercising. Furthermore, atypical leg pain is characterized by not resolving within 10 minutes after exercise. As such, it might be anticipated that the atypical group would have prolonged time to minimum calf muscle StO2 or in the minimum value of calf muscle StO2, particularly while at rest. This was not the case: the calf muscle StO2 of the two groups was similar throughout testing.

Exercise performance comparisons

Leg symptoms. All patients experienced symptoms during the treadmill test consistent with claudication. Each patient reported pain in the calf musculature that gradually progressed to maximal tolerable pain to end the test, and each patient reported pain relief ≤10 minutes of rest after the treadmill test. Thus, claudication secondary to vascular insufficiency should be suspected in patients who complain of any type of leg pain, until proven otherwise, regardless of whether the pain description exactly matches that of classic claudication. If high-risk patients with atypical leg pain are not further evaluated, many may go undertreated.

In the current study, only 37 of 114 patients (32%) with confirmed PAD described exertional leg pain consistent with classic claudication according to the SDCQ. This percentage is at the upper end of the reported range of 10%
to 35% of patients with PAD describing their symptoms consistent with classic claudication.\textsuperscript{1,2} It may be surmised that the percentage of patients with classic claudication seen in vascular clinics, but who were not referred to the study for evaluation, was even lower than 32%.

Treadmill exercise. The groups did not have significantly different results for COT, PWT, peak oxygen uptake, and ischemic window. This finding is in agreement with our earlier results that exercise performance is not different in patients with claudication, atypical leg pain, and leg pain on exertion and rest.\textsuperscript{12} Collectively, these results suggest that PAD symptom subtype has little effect on exercise performance during a standardized treadmill test. Thus, patients with varying symptoms have similar pain-mediated exercise limitations and vascular compromise. From an exercise rehabilitation standpoint, all symptomatic patients should be considered for an exercise program to treat symptoms, regardless of leg pain subtype.

6MWT, WIQ, and daily ambulatory activity. Despite no differences among the groups on calf muscle StO\textsubscript{2} and exercise performance during standardized exercise, significant group differences were found for subjective and self-paced exercise tasks and for monitored daily ambulatory activity. In general, the patients with atypical exertional leg pain had the most favorable measures for the 6MWT, self-reported ambulatory function, and daily ambulatory activity. Patients with atypical leg pain reported the lowest rating of perceived exertion at completion of the 6MWT and the highest walking speed score on the WIQ. This latter result supports previous studies that found those with atypical leg pain have higher WIQ scores than those with claudication.\textsuperscript{7,11}

Patients with atypical leg pain also had the highest measures of daily ambulatory activity, supporting our previous observation that they had higher levels of monitored daily physical activity than those with leg pain on exertion and rest.\textsuperscript{12} The unique aspect of the current activity data is that they provide information regarding daily ambulatory cadences and, thereby, the intensity of ambulation. The average daily cadence, the maximum cadences, ranging from 5 continuous minutes to 60 continuous minutes, and the peak activity index were higher in the patients with atypical claudication pain. These data indicate that the total daily activity of patients with atypical claudication pain is higher than that of the other groups, primarily due to ambulating at faster paces throughout the day. It is possible that atypical leg pain is less uncomfortable, enabling patients to ambulate faster.

The findings in the group with leg pain on exertion and rest are also worth noting. Even though this group had the highest ABI, indicating less severe PAD than the other two groups, they also had the highest prevalence of obesity and the highest BMI values. Their calf muscle StO\textsubscript{2} and treadmill exercise performance measures were similar to the other groups, but not better, which suggests that obesity exerts a negative influence on the microcirculation and exercise performance that counteracts the potential advantage of having milder PAD. This supports previous

### Table III. 6-Minute walk performance, daily ambulatory activity recorded during a 7-day monitoring period, and Walking Impairment Questionnaire measures in patients with peripheral artery disease (PAD) placed in three exertional leg symptom groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-Minute walk test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain-free distance, meters</td>
<td>202 (117)</td>
<td>148 (79)</td>
<td>151 (118)</td>
<td>.072</td>
</tr>
<tr>
<td>Total distance, meters</td>
<td>370 (102)</td>
<td>317 (104)</td>
<td>333 (102)</td>
<td>.100</td>
</tr>
<tr>
<td>Rating of perceived exertion, score</td>
<td>12.5 (2.8)</td>
<td>13.5 (2.0)</td>
<td>14.1 (2.4)*</td>
<td>.017</td>
</tr>
<tr>
<td>Walked continuously for 6 min, % of subjects</td>
<td>68 (48)</td>
<td>42 (50)</td>
<td>59 (50)</td>
<td>.087</td>
</tr>
<tr>
<td>Daily ambulatory activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum cadence, strides/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 minute</td>
<td>47.7 (6.0)</td>
<td>44.5 (6.1)</td>
<td>44.8 (5.8)</td>
<td>.061</td>
</tr>
<tr>
<td>5 minutes</td>
<td>32.4 (8.8)</td>
<td>27.4 (6.7)*</td>
<td>28.9 (7.9)</td>
<td>.035</td>
</tr>
<tr>
<td>20 minutes</td>
<td>23.4 (16.8)</td>
<td>15.7 (5.3)*</td>
<td>17.4 (6.9)*</td>
<td>.007</td>
</tr>
<tr>
<td>30 minutes</td>
<td>17.5 (7.4)</td>
<td>13.3 (4.8)*</td>
<td>14.6 (6.1)</td>
<td>.020</td>
</tr>
<tr>
<td>60 minutes</td>
<td>13.0 (5.8)</td>
<td>9.9 (3.6)*</td>
<td>10.9 (4.7)</td>
<td>.029</td>
</tr>
<tr>
<td>Peak activity index, strides/min</td>
<td>32.2 (8.0)</td>
<td>27.9 (6.3)*</td>
<td>28.9 (7.1)</td>
<td>.040</td>
</tr>
<tr>
<td>Average cadence, strides/min</td>
<td>13.0 (3.1)</td>
<td>11.1 (2.2)*</td>
<td>11.6 (2.3)</td>
<td>.010</td>
</tr>
<tr>
<td>Total strides, strides/d</td>
<td>4051 (2109)</td>
<td>2901 (1380)*</td>
<td>3386 (1767)</td>
<td>.032</td>
</tr>
<tr>
<td>Total activity time, min/d</td>
<td>309 (124)</td>
<td>254 (92)</td>
<td>283 (110)</td>
<td>.128</td>
</tr>
<tr>
<td>Walking Impairment Questionnaire, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distance score</td>
<td>42 (28)</td>
<td>26 (27)</td>
<td>37 (35)</td>
<td>.083</td>
</tr>
<tr>
<td>Speed score</td>
<td>45 (20)</td>
<td>30 (23)*</td>
<td>29 (25)*</td>
<td>.006</td>
</tr>
<tr>
<td>Stair climbing score</td>
<td>48 (28)</td>
<td>34 (27)</td>
<td>33 (30)</td>
<td>.056</td>
</tr>
</tbody>
</table>

*Different than atypical leg pain group (P < .05).
studies reporting a negative effect of obesity on COT and PWT\textsuperscript{20,33} and a negative effect of obesity on reactive hyperemia and transcutaneous oxygen tension\textsuperscript{12,34} through elevated fasting glucose.\textsuperscript{25} Finally, no group differences in treadmill exercise performance in the current study corresponded better with the calf muscle StO\textsubscript{2} findings (ie, no differences among groups) than with the ABI findings (ie, significant difference among groups), which supports our previous work that COT and PWT are more strongly associated with the time to minimum calf muscle StO\textsubscript{2} than with ABI.\textsuperscript{13,14}

Limitations

Patients who participated in this trial were volunteers and may therefore represent those who were more interested in exercise, who had better access to transportation to the program, and who had relatively better health than PAD patients who did not volunteer. The cross-sectional design comparing patients with different types of exertional leg pain does not allow causality to be established, as it is possible that patients in each group were different in daily ambulatory activity and perceived ambulatory function before the development of symptoms.

The present findings are also limited to PAD patients with a history of leg pain who are limited by their pain during a standardized treadmill test, regardless of whether the leg pain is typical or atypical of claudication. Thus, the current findings cannot be generalized to patients with less severe PAD (ie, asymptomatic PAD), or more severe symptoms (ie, critical leg ischemia), or to those who are limited in their exercise performance by other significant comorbid conditions.

There are limitations associated with the measurement of calf muscle StO\textsubscript{2} as previously described.\textsuperscript{13} Although calf muscle StO\textsubscript{2} reflects a balance between oxygen delivery and utilization, other factors may also contribute to the StO\textsubscript{2} measurement. First, venous blood, which has low oxygen saturation, may mix with capillary blood in the local tissue. Second, myoglobin may partially contribute to the calf muscle StO\textsubscript{2} measurement. Finally, the subcutaneous fat thickness directly under the probe may interfere with the measure of calf muscle StO\textsubscript{2}. However, we believe these limitations have minimal influence on calf muscle StO\textsubscript{2}, as discussed earlier.\textsuperscript{13}

There are limitations associated with the step activity monitor. It is possible that the patients did not wear the step activity monitor during portions of their waking hours, thereby resulting in an underestimate of daily ambulation. We believe this possibility is unlikely because long durations in which no active minutes were recorded during daytime hours were rarely evident from the software graphs. Another limitation is that the step activity monitor does not quantify nonambulatory physical activity and therefore underestimates to some extent the total amount of daily physical activity accomplished.

CONCLUSIONS

All patients experienced symptoms consistent with classic claudication during a standardized treadmill test, regardless of their pain description. Each group with exertional leg pain demonstrated similar impairments in calf muscle StO\textsubscript{2} and exercise performance during standardized treadmill exercise, but those with atypical exertional leg pain were most active in the community setting and viewed their ambulatory function most favorably.

PAD patients with atypical leg pain have vascular-mediated limitations in exercise performance during standardized treadmill testing similar to patients with claudication and patients with leg pain on exertion and rest but have higher levels of daily ambulatory activity in the community setting and higher perceived ambulatory function. From an exercise standpoint, the clinical significance is that PAD symptom subtype obtained at the initial clinical presentation has little correlation with exercise performance during standardized treadmill exercise. Thus, claudication secondary to vascular insufficiency should be suspected in patients who complain of any type of leg pain, until proven otherwise.

AUTHOR CONTRIBUTIONS

Conception and design: AG, PM, RR
Analysis and interpretation: AG, DP
Data collection: PM, AK, SB
Writing the article: AG, DP
Critical revision of the article: AG, DP
Statistical analysis: DP
Obtained funding: AG
Overall responsibility: AG

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Submitted Oct 6, 2011; accepted Dec 22, 2011.