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ASSOCIATION BETWEEN DAILY AMBULATORY ACTIVITY PATTERNS AND EXERCISE PERFORMANCE IN PATIENTS WITH INTERMITTENT CLAUDICATION

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Abstract

Purpose—To determine the association between daily ambulatory activity patterns and exercise performance in patients with intermittent claudication.

Methods—One hundred thirty-three patients limited by intermittent claudication participated in this study. Patients were assessed on their ambulatory activity patterns for one week with a small, lightweight step activity monitor attached to the ankle using elastic velcro straps above the lateral malleolus of the right leg. The step activity monitor recorded the number of strides taken on a minute-to-minute basis, and the time spent ambulating. Patients also were characterized on ankle/brachial index (ABI), ischemic window (IW) after a treadmill test, as well as initial claudication distance (ICD), and absolute claudication distance (ACD) during treadmill exercise.

Results—The patient characteristics (mean ± SD) were as follows: ABI = 0.71 ± 0.23, IW = 0.54 ± 0.72 mmHg·min·meter^{-1}, ICD = 236 ± 198 meters, and ACD = 424 ± 285 meters. The patients took 3366 ± 1694 strides/day, and were active for 272 ± 103 minutes/day. The cadence for the 30 highest, consecutive minutes of each day (15.1 ± 7.2 strides/minute) was correlated with ICD ($r = 0.316$, $p < 0.001$) and ACD ($r = 0.471$, $p < 0.001$), and the cadence for the 60 highest, consecutive minutes of each day (11.1 ± 5.4 strides/minute) was correlated with ICD ($r = 0.290$, $p < 0.01$) and ACD ($r = 0.453$, $p < 0.001$). Similarly, the cadences for the highest 1, 5, and 20 consecutive minutes, and the cadence for the 30 highest, non-consecutive minutes all were correlated with ICD and ACD ($p < 0.05$). None of the ambulatory cadences were correlated with ABI ($p > 0.05$) or with ischemic window ($p > 0.05$).

Conclusion—Daily ambulatory cadences are associated with severity of intermittent claudication, as measured by ACD and ICD, but not with peripheral hemodynamic measures.

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INTRODUCTION

Peripheral arterial disease (PAD) is prevalent in 16 percent of the US population older than 55 years of age, and the symptom of intermittent claudication is prevalent in 5 percent.[1] Intermittent claudication is ischemic muscular leg pain that occurs during ambulation when the peripheral circulation is inadequate to meet the metabolic requirement of the active leg musculature. Consequently, intermittent claudication leads to ambulatory dysfunction,[2–5] a decline in daily physical activities,[6] and lower health-related quality of life.[7] The lifestyle limitations imposed by intermittent claudication further compounds poor long-term survival,[8–12] as the mortality risk of sedentary patients with intermittent claudication is higher than their more active counterparts.[13]

Few studies have objectively quantified physical activity in patients with PAD[6,14–16] Daily physical activity is lower in PAD patients than in age-matched controls, and is associated with the absolute claudication distance (ACD) during a standardized treadmill test,[15] and with 6-minute walk distance[15] in patients limited by intermittent claudication. However, it is not clear whether patients with worse exercise performance have lower daily physical activity because of spending less time in physical activity, because of engaging in less intense physical activity, or a combination of both. Decline in physical activity of moderate and high intensity are particularly noteworthy because this may reflect greater difficulty in performing activities of daily living, and because this increases the risk of mortality in patients with intermittent claudication.[13]

The purpose of this study was to determine the association between daily ambulatory activity patterns and exercise performance in patients with intermittent claudication.

METHODS

SUBJECTS

Recruitment—Patients between the ages of 50 and 90 years were evaluated in the General Clinical Research Center at the University of Oklahoma Health Sciences Center (HSC). Patients were recruited by referrals from the HSC vascular clinics and laboratories, as well as by newspaper advertisements for a free evaluation to assess peripheral vascular function in those who experience ambulatory leg pain. The procedures used in this study were approved by the Institutional Review Boards at the University of Oklahoma HSC. Written informed consent was obtained from each subject prior to investigation.

Patient Screening—Patients with intermittent claudication secondary to vascular insufficiency were included in this study if they met the following criteria: (a) positive test on the San Diego claudication questionnaire,[17] (b) ambulation during a graded treadmill test limited by intermittent claudication,[18] and (b) an ABI ≤ 0.90.[1] Patients were excluded from this study for the following conditions: (a) absence of PAD (ABI > 0.90), (b) inability to obtain an ABI measure due to non-compressible vessels, (c) asymptomatic PAD, (d) rest pain PAD, (e) use of medications indicated for the treatment of intermittent claudication (cilostazol and pentoxifylline) initiated within three months prior to investigation, (f) exercise tolerance limited by factors other than leg pain (e.g., severe coronary artery disease, dyspnea, poorly controlled blood pressure), and (g) active cancer, renal disease, or liver disease. A total of 133 patients with intermittent claudication were deemed eligible for this investigation, whereas 17 subjects were ineligible.

MEASUREMENTS

Medical History—Demographic information, height, weight, waist and hip circumferences,[19] cardiovascular risk factors, co-morbid conditions, claudication history, and a list of current medications were obtained during a medical history and physical examination to begin the evaluation.

Gardner Treadmill Test—Patients performed a progressive, graded treadmill protocol (2 mph, 0% grade with 2% increase every 2 minutes) until maximal claudication pain as previously described.[18] The initial claudication distance (ICD), defined as the walking distance at which the patient first experienced pain, and the absolute claudication distance (ACD), defined as the walking distance at which ambulation could not continue due to maximal pain, were both recorded to quantify the severity of claudication. Exercise capacity was measured by oxygen uptake at peak exercise with a Medical Graphics VO2000 metabolic system. Using these procedures, the test-retest intraclass reliability coefficient is R = 0.89 for ICD,[18] R = 0.93 for ACD[18], and R = 0.88 for peak oxygen uptake.[20] Additionally, ABI measures were obtained from the more severely diseased lower extremity before and 1, 3, 5, and 7 minutes after each treadmill test as previously described.[18,21] Ankle systolic blood pressure was measured from the posterior tibial and dorsalis pedis arteries in both legs, and the higher of the two arterial pressures from the more severely diseased leg was recorded as the ankle pressure at rest.[15,22] Ankle systolic pressure was taken from the same arterial location during measurements following the treadmill test. The reduction in ankle systolic blood pressure from the resting baseline value, and its recovery over time following treadmill exercise was quantified by calculating the area over the curve using the trapezoidal rule, referred to as the ischemic window.[23] The ischemic window is a measure of the severity of the ischemic deficit of exercise.[23] Because the ischemic deficit is a function of both PAD severity as well as the amount of exercise performed, the ischemic window was divided by ACD to normalize the ischemic window per meter walked.

Ambulatory Activity Monitoring—Daily ambulatory activity was assessed using a small (75 × 50 × 20 mm), lightweight (38 g) step activity monitor (Step Watch 3^{TM}, Cyma Inc., Mountlake Terrace, WA) containing a sensor, electronics, and a battery inside a completely sealed and durable polycarbonate case.[16] The monitor is a stride counter that utilizes a microprocessor linked accelerometer with filtering thresholds for cadence and motion parameters.[24] The step activity monitor was programmed by placing the unit on a USB docking station connected to a computer with StepWatch3^{TM} Analysis Software. Ambulatory activity was measured during seven consecutive days in which subjects were instructed to wear the monitor during waking hours and to remove it before retiring to bed. The step activity monitor was attached to the right ankle above the lateral malleolus using elastic Velcro straps, and continuously recorded the number of steps taken on a minute-to-minute basis. Subjects returned the monitor at the end of the seven-day period, and the data were downloaded into a subject file stored in the software program. The accuracy of the step activity monitor exceeds 99% ± 1% compared to hand-tallied step counts during a 6-minute walk test performed by a subset of subjects with intermittent claudication (n = 15) and controls (n = 15).[16] This accuracy is similar to previous studies which have reported step count accuracies ranging from 96% to 99.9% in various clinical populations.[24–28]

Variables Obtained from the Step Activity Monitor—The step activity monitor records the number of ambulatory strides taken per minute for each minute throughout a 24-hour period. After data from the step activity monitor is downloaded to a computer, the software program displays the number of strides taken each day and the number of minutes spent ambulating each day. The daily ambulatory strides and time are further analyzed by the software program, and are quantified into the following variables: (a) daily strides taken

and time spent ambulating at low cadence (between 1 and 15 strides/min), medium cadence (between 16 and 30 strides/min), and high cadence (more than 30 strides/min), (b) daily sedentary time in which no ambulation occurs (0 strides/min), (c) maximum cadence for 60, 30, 20, and 5 continuous minutes of ambulation each day, (d) maximum cadence for 1 minute of ambulation each day (i.e., the minute having the single highest cadence value each day), and (e) peak activity index obtained by ranking all minutes of the day according to cadence, and then taking the highest 30 values.

These outcome measures are recorded and averaged for each day, and then the daily averages are averaged over the seven-day monitoring period. The maximum 60-minute, maximum 30-minute, and maximum 20-minute cadences calculated from the software program are intended to provide information on whether individuals meet the traditional recommended guidelines to improve cardiopulmonary fitness by exercising between 20 to 60 minutes at moderate-to-high endurance exercise three or more times per week.[29] The average cadence obtained for the maximum 60-minute, maximum 30-minute, and maximum 20-minute measures gives an indication of whether individuals ambulate at a sufficient rate over these durations to elicit a potential training stimulus to improve cardiopulmonary fitness. The peak activity index cadence is intended to provide information on whether individuals meet the newer recommended guidelines to attain health benefits by accumulating 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week.[29] The newer guidelines emphasize that physical activity does not need to be done continuously, but rather can be accumulated throughout the day in an intermittent manner. The average cadence obtained for the peak activity index indicates whether individuals intermittently ambulate at a sufficient rate for 30 minutes during the day to elicit potential health benefits. In contrast to these endurance-related measures, the maximum 5-minute and maximum 1-minute cadences calculated from the software program are more characteristic of short-duration activity, and may reflect the ability of individuals to ambulate quickly. The cadences attained during these short ambulatory durations are not a reflection of cardiopulmonary function, but rather they may be indicators of functioning of the lower extremities. In subjects with intermittent claudication, the test-retest intraclass reliability coefficient for the measurement of total daily strides and total daily minutes of activity over the 7-day period are $R = 0.87$ and $R = 0.85$, respectively.[16] The intraclass reliability coefficients for the remaining variables pertaining to daily ambulatory strides, daily ambulatory durations, and daily ambulatory cadences range from $R = 0.83$ to $R = 0.94$.

STATISTICAL ANALYSES

Partial correlation coefficients were calculated to determine the association between daily ambulatory activity patterns and exercise performance in patients with intermittent claudication, adjusting for age, weight, BMI, sex, race, current smoking, diabetes, hypertension, dyslipidemia, abdominal obesity, obesity, coronary artery disease, chronic obstructive pulmonary disease, and congestive heart failure. It was noted that the distributions of some variables were asymmetric. To minimize the possible distorting effect of extreme values, both Pearson and Spearman partial correlation coefficients were computed for each pair of variables of interest, with Spearman used only if the two estimates differed by more than 0.1. Reported p values are for individual tests. All analyses were performed using the SPSS-PC statistical package. Statistical significance was set at $p < 0.05$. Measurements are presented as means ± standard deviations.

RESULTS

The clinical characteristics of the patients with intermittent claudication are shown in Table 1. The group consisted of a similar proportion of men and women, as well as Caucasians and

African-Americans. The ABI, ICD, ACD, and cardiovascular risk factors are typical for those with intermittent claudication.

The ambulatory strides recorded during the one-week monitoring period, and their association with exercise performance in patients with intermittent claudication is shown in Table II. On average, the patients took 3366 daily strides in which 35% were at low cadence, 44% were at medium cadence, and 21% were at high cadence. The total daily strides were positively correlated with ACD ($p < 0.001$) and negatively correlated with ischemic window ($p < 0.05$). The daily strides at low cadence were negatively correlated with ischemic window ($p < 0.05$), and the percentage of strides at low cadence was negatively associated with ICD ($p < 0.05$) and ACD ($p < 0.001$). The daily strides at medium cadence, high cadence, and the percentage of strides at high cadence were all positively associated with ACD ($p < 0.001$). None of the stride variables were correlated with ABI ($p > 0.05$).

The ambulatory durations and their associations with exercise performance in patients with intermittent claudication are shown in Table III. On average, the patients were active for 272 minutes each day, in which 69% of the time was spent at low cadence, 25% was at medium cadence, and 6% was at high cadence. Total activity time was positively correlated with ACD ($p < 0.05$) and negatively correlated with ischemic window ($p < 0.05$). The percentage of activity time at low cadence was negatively correlated with ICD ($p < 0.05$) and ACD ($p < 0.001$). The activity time at medium cadence was positively correlated with ischemic window ($p < 0.05$) and ACD ($p < 0.01$), and the percentage of activity time at medium cadence was positively correlated with ICD ($p < 0.05$) and ACD ($p < 0.01$). The activity time at high cadence and the percentage of activity at high cadence were positively associated with ACD ($p < 0.001$). None of the activity durations were correlated with ABI ($p > 0.05$).

The ambulatory cadences and their associations with exercise performance in patients with intermittent claudication are shown in Table IV. The average daily cadence was 12.2 strides per minute, ranging between 11.1 strides per minute for the most active 60 consecutive minutes of each day to 46.1 strides per minute for the most active single minute of each day. The cadence for the 30 highest, non-consecutive minutes of each day (peak activity index) was 28.3 strides per minute. All of the cadence variables were positively associated with ICD ($p < 0.05$) and ACD ($p < 0.001$). None of the ambulatory cadences were correlated with ABI ($p > 0.05$) or with ischemic window ($p > 0.05$).

DISCUSSION

The major findings of this investigation are that (1) daily ambulatory strides, durations, and cadences are associated with ACD, (2) ambulatory cadences are more closely correlated with ACD and ICD than are ambulatory strides or ambulatory duration, and (3) daily ambulatory strides, durations, and cadences are not associated with ABI or with ischemic window.

The patients in this investigation ambulated for an average of 272 minutes each day and took an average of 3,366 strides, which are 13% and 20% lower than in controls of similar age.[16] Both the total time and total strides during ambulation were positively associated with ACD, indicating that patients with milder intermittent claudication ambulate more in a community-based setting than patients with more severe symptoms. This observation is supported by previous investigations in our laboratory which found that ACD was correlated with the daily number of steps objectively recorded by a pedometer,[6] and with total leisure-time physical activity subjectively measured with a questionnaire.[6,30] Collectively, these results

indicate that the total daily physical activity is associated with ACD in patients with intermittent claudication.

A novel finding in the present investigation is that the cadence of ambulation is a stronger correlate of ICD and ACD than are measures of total physical activity (e.g., total daily strides and total daily activity time). This suggests that ambulatory cadence in a community-based setting is the aspect of ambulation that is most associated with the severity of intermittent claudication. In particular, ambulatory cadence was more closely related to ACD than to ICD, suggesting that the ability or willingness to walk to maximal claudication pain (i.e., ACD) is partially explained by activity level as well as by the severity of vascular insufficiency, whereas ICD may be more related to the latter. On closer examination of the cadence data, the maximum cadence for 30-minute and 60-minute durations throughout the day were the highest correlates of ACD. Continuous ambulation for 30 minutes to one hour reflects endurance-related activities, and suggests that patients with lower ACD values must slow their cadence to complete ambulatory activities of prolonged durations compared to patients with higher ACD values.

The slower rate of continuous ambulation in patients with lower ACD compared to those with higher ACD may be an adopted strategy to delay the onset and development of intermittent claudication during prolonged, continuous ambulation. For example, patients with severe intermittent claudication may select a slow ambulatory pace while walking in the community setting as a strategy to avoid experiencing the onset of claudication. This is also evident for discontinuous ambulation, as peak activity index was directly correlated with ACD. Peak activity index represents the average stride rate for the highest 30 minutes of each day, regardless of whether they occurred continuously or discontinuously. Thus, patients with severe intermittent claudication may try to avoid experiencing claudication by ambulating slowly even during prolonged, intermittent ambulation.

Patients with shorter ACD also had patterns of slower ambulation for relatively short durations, as the maximum cadence attained for one-minute and five-minute durations throughout the day were associated with ACD. These slower ambulatory cadences, especially for the maximum one-minute duration, suggests that ambulatory pattern is altered even at the initiation of ambulation in those with shorter ACD. This agrees with our previous report that gait is altered in patients with intermittent claudication that favors stability over speed of ambulation even during pain-free ambulation.[31] Another plausible explanation for the association between ACD and ambulatory cadence of short duration is that greater muscle weakness is associated with a progression of intermittent claudication. Isokinetic and isometric strength of the gastrocnemius, tibialis anterior, and dorsiflexor muscle groups are lower in patients with intermittent claudication than in controls, and are lower in the more symptomatic leg.[32–34] Thus, impaired strength of the lower extremities as well as altered gait may account for the decline in community-based, short-duration ambulation in patients with severe intermittent claudication.

Although ambulatory cadences are associated with ACD, they are not associated with either ABI or ischemic window. These results suggest that community-based ambulatory cadences are primarily a function of the severity of intermittent claudication. Although poor ABI and ischemic window values are characteristic of patients with PAD and intermittent claudication, the lack of association between vascular measures and ambulatory cadences indicates that the severity of intermittent claudication is a better correlate of the paces performed during daily ambulation. ABI is not a strong predictor of ICD and ACD,[4] suggesting that factors other than vascular insufficiency also are related to claudication distance and ambulation. These factors may include cardiopulmonary function,[35] walking

economy,[36] muscle mass,[37] muscle strength,[32] ability of muscle to extract oxygen,[38] obesity,[4] and metabolic syndrome.[39]

The lack of association between ABI and ambulatory cadence is in disagreement with previous reports showing that ABI is related to self-reported leisure-time physical activity,[30] monitored physical activity using an accelerometer,[6,14,40] and energy expenditure of physical activity with the doubly-labeled water technique.[15] The physical activity measures obtained with the accelerometer and with the doubly-labeled water technique are characteristic of the total amount of physical activity performed (i.e., ambulatory and non-ambulatory), which is distinct from the cadence (i.e., intensity) at which ambulation is performed. One of the advantages of the step activity monitor is that is can distinguish between the two, and the results from this trial suggest that ambulatory cadence throughout daily activities is more associated with symptoms than with ABI.

There are several limitations to this study. The correlations calculated from this cross-sectional design does not allow causality be established, as it is possible that daily ambulation influences ACD or vice versa. A longitudinal follow-up study is necessary to better understand the causality of this relationship in patients with intermittent claudication. A second limitation is that it is possible patients did not wear the step activity monitor during portions of their waking hours, thereby resulting in an underestimate of daily ambulation. We believe that this possibility is unlikely because long durations in which no active minutes were recorded during daytime hours were rarely evident from the software graphs depicting the number of strides taken on a minute-to-minute basis. Even during several hours of being sedentary, a few minutes in which some strides occurred were typically evident, indicating that the step activity monitor had not been removed. Another limitation is that the type of sedentary activity which took place during non-active minutes cannot be determined by the step activity monitor. Consequently, it is not possible to quantify the time spent in various sedentary activities such as watching television, taking naps, and sitting while eating. Furthermore, the step activity monitor does not quantify non-ambulatory physical activity, and therefore it underestimates the total amount of daily physical activity accomplished to some extent. The present findings are also limited to PAD patients with intermittent claudication, and may not be generalized to patients with less severe and more severe symptoms. However, subjects with intermittent claudication had a good proportion of women and African-Americans, and they had typical risk factors for PAD, including smoking, diabetes, hypertension, dyslipidemia, and obesity. Thus, the findings of the present study are generalizable to the majority of subjects with intermittent claudication who typically have numerous co-morbid conditions.

We conclude that daily ambulatory cadences are associated with the severity of intermittent claudication, as measured by ACD and ICD, but not with peripheral hemodynamic measures. Future trials should examine whether daily ambulatory cadences of patients with intermittent claudication change during long-term follow-up, and in response to interventions designed to improve symptoms.

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Table I

Clinical characteristics of 133 peripheral arterial disease patients with intermittent claudication. Values are means (SD) or percentages.

Variables	Values
Age (years)	67 (10)
Weight (kg)	82.5 (18.9)
Body Mass Index	29.2 (6.6)
Ankle/Brachial Index	0.71 (0.23)
Ischemic Window ($mmHg \cdot min \cdot meter^{-1}$)	0.54 (0.72)
ICD (meters)	236 (198)
ACD (meters)	424 (285)
Peak Oxygen Uptake ($ml \cdot kg^{-1} \cdot min^{-1}$)	12.6 (4.0)
Sex (% Men)	50
Race (% Caucasian)	49
Coronary Artery Disease (% yes)	42
Chronic Obstructive Pulmonary Disease (% yes)	26
Congestive Heart Failure (% yes)	11
Current Smoking (% yes)	32
Diabetes (% yes)	29
Hypertension (% yes)	79
Dyslipidemia (% yes)	79
Abdominal Obesity (% yes)	65
Obesity (% yes)	39

ACD = absolute claudication distance, ICD = initial claudication distance,. Obesity was defined as having a body mass index ≥ 30 kg / m^2. Abdominal obesity was defined as having a waist circumference > 102 cm for men and > 88 cm for women.

Table II

Ambulatory strides recorded during a one-week monitoring period and their associations with exercise performance measures in patients with intermittent claudication.

Variables	Mean (SD)	ABI (r)	IW (r)	ICD (r)	ACD (r)
Strides at Low Cadence (strides/day)	1177 (461)	*.172*	*−.218**	−.067	.071
Strides at Medium Cadence (strides/day)	1477 (940)	.112	*−.169*	.135	*.255***
Strides at High Cadence (strides/day)	712 (779)	−.049	−.076	.143	.336***
Total Strides (strides/day)	3366 (1694)	.089	−.213*	.121	.314***
Percentage of Strides at Low Cadence (%)	35 (11)	.062	.049	*−.242**	−.345***
Percentage of Strides at Medium Cadence (%)	44 (10)	.063	*−.134*	.111	.077
Percentage of Strides at High Cadence (%)	21 (13)	−.105	.061	.130	.248**

r = Pearson partial correlation coefficients or Spearman partial correlation coefficients (indicated in italicized print), adjusting for age, weight, BMI, sex, race, current smoking, diabetes, hypertension, dyslipidemia, abdominal obesity, obesity, coronary artery disease, chronic obstructive pulmonary disease, and congestive heart failure.

* $p < 0.05$,

** $p < 0.01$,

*** $p < 0.001$.

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Table III

Ambulatory durations recorded during a one-week monitoring period and their associations with exercise performance measures in patients with intermittent claudication.

Variables	Mean (SD)	ABI (r)	IW (r)	ICD (r)	ACD (r)
Time at Low Cadence (min/day)	188 (73)	*.152*	*−.149*	−.076	.029
Time at Medium Cadence (min/day)	67 (38)	.109	*−.222**	.128	.277**
Time at High Cadence (min/day)	17 (18)	−.0173	−.069	.108	.310***
Total Activity Time (min/day)	272 (103)	.139	−.202*	.011	.211*
Percentage of Activity Time at Low Cadence (%)	69 (10)	*−.066*	.096	*−.227**	−.345***
Percentage of Activity Time at Medium Cadence (%)	25 (8)	−.002	*−.136*	.211*	.268**
Percentage of Activity Time at High Cadence (%)	6 (6)	−.122	.013	.125	.268**

r = Pearson partial correlation coefficients or Spearman partial correlation coefficients (indicated in italicized print), adjusting for age, weight, BMI, sex, race, current smoking, diabetes, hypertension, dyslipidemia, abdominal obesity, obesity, coronary artery disease, chronic obstructive pulmonary disease, and congestive heart failure.

* $p < 0.05$,

** $p < 0.01$,

*** $p < 0.001$.

Table IV

Ambulatory cadences recorded during a one-week monitoring period and their associations with exercise performance measures in patients with intermittent claudication.

Variables	Mean (SD)	ABI	IW	ICD	ACD
Maximum 1-minute cadence (strides/min)	46.1 (5.4)	.064	−.046	.194*	.338***
Maximum 5-minute cadence (strides/min)	29.5 (8.1)	.053	−.050	*.351***	.456***
Maximum 20-minute cadence (strides/min)	18.6 (10.9)	−.034	−.115	*.233**	.324***
Maximum 30-minute cadence (strides/min)	15.1 (7.2)	.069	−.158	.316***	.471***
Maximum 60-minute cadence (strides/min)	11.1 (5.4)	.058	−.174	.290**	.453***
Peak Activity Index (strides/min)	28.3 (7.3)	.027	−.191	.310***	.473***
Average Cadence (strides/min)	12.2 (3.2)	−.027	−.089	.194*	.311***

r = Pearson partial correlation coefficients or Spearman partial correlation coefficients (indicated in italicized print), adjusting for age, weight, BMI, sex, race, current smoking, diabetes, hypertension, dyslipidemia, abdominal obesity, obesity, coronary artery disease, chronic obstructive pulmonary disease, and congestive heart failure.

* $p < 0.05$,

** $p < 0.01$,

*** $p < 0.001$.