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Abnormal Joint Powers Before And After The Onset Of Claudication Symptoms

Panagiotis Koutakis
University of Nebraska at Omaha

Jason Johanning
University of Nebraska Medical Center

Sara A. Myers
University of Nebraska at Omaha, samyers@unomaha.edu

Nicholas Stergiou
University of Nebraska at Omaha, nstergiou@unomaha.edu

G. Matthew Longo
University of Nebraska Medical Center

See next page for additional authors

Authors
Panagiotis Koutakis, Jason Johanning, Sara A. Myers, Nicholas Stergiou, G. Matthew Longo, and Iraklis Pipinos

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Corresponding Author: Dr Iraklis I. Pipinos, M.D., Ph.D.

Corresponding Author's Institution: University of Nebraska Medical Center

First Author: Panagiotis Koutakis, BS

Order of Authors: Panagiotis Koutakis, BS; Jason M Johanning, MD; Sara A Myers, MS; Nicholas Stergiou, PhD; G.Matthew Longo, MD; Iraklis I. Pipinos, M.D., Ph.D.

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Panagiotis Koutakis,BS[1], Jason M. Johanning,MD[2], Sara A. Myers,MS[1], Nicholas Stergiou,PhD[1], G. Matthew Longo,MD[2], Iraklis I. Pipinos, MD[2]

[1] Nebraska Biomechanics Core Facility, University of Nebraska at Omaha, Omaha, NE

[2]Departments of Surgery, University of Nebraska Medical Center and Veterans Affairs Medical Center, Omaha, NE

Iraklis I. Pipinos, MD

983280 UNMC Surgery

Omaha, NE 68198-3280

Work Phone: (402) 559-4395

Work FAX: (402) 559-6749

Email: ipipinos@unmc.edu

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ABSTRACT

Objective: Claudication is the most common manifestation of peripheral arterial disease, producing significant ambulatory compromise.The purpose of our study was to evaluate patients with bilateral lower limb claudication and characterize their gait abnormality based on advanced biomechanical analysis using joint torques and powers.

Methods: Twenty patients with bilateral claudication (40 limbs) and eleven healthy matched controls (22 limbs) ambulated on a walkway while three dimensional biomechanical data were collected. Patients walked before and after onset of claudication pain. Joint torques and powers at early-, mid-, and late-stance for the hip, knee and ankle joints were calculated for claudicating patients before and after the onset of claudication pain, and were compared to healthy controls.

Results: Claudicating patients exhibited significantly reduced hip and knee power at early-stance due to decreased torques produced by the hip and knee extensors. In mid-stance, patients had significantly reduced knee power due to the decreased torques produced by the knee extensors. In late-stance, reduced propulsion was noted with significant reduction in ankle plantar flexor torques and power. All differences were present before the onset of pain with worsening of specific parameters after the onset of pain.

Conclusions: Advanced biomechanical analysis demonstrates that the gait of claudicating patients is abnormal at baseline in the absence of pain and worsens after onset of pain. Gait of claudication is characterized by failure of specific and identifiable muscle groups needed to perform normal walking (weight acceptance, transfer and propulsion).

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INTRODUCTION

Intermittent claudication is the most common clinical manifestation of peripheral arterial disease (PAD) presenting as exercise induced leg muscle pain and gait dysfunction. Claudication and its associated ambulatory impairment produce impaired quality of life[1-3], physical dependence and poor health outcomes[4]. Previous work suggests that PAD patients walk slower with decreased cadence, increased stance time, shorter stride length and a narrower step width as compared with healthy controls[4, 5]. However, these changes alone are unable to describe in sufficient detail the locomotor impairments of claudicating patients and aid in our understanding of its underlying pathophysiology.

A more detailed quantitative evaluation of gait can be obtained using advanced biomechanical analysis including joint torques and powers[6]. Although muscles produce linear forces, motions at joints are all rotary. The rotary torque is a measure of the tendency of a force to rotate the limb around a joint and is calculated as the product of the muscle force and the distance from the joint center that the force is being applied. The net muscle torque does not represent any one particular muscle but rather describes the net activity of all the muscles acting across a joint. Joint power can be defined as the rate of work produced by muscles contracting to move a joint and is determined as the product of the net torque (moment) of the muscles acting across a joint and the resulting angular velocity of the joint. Joint powers have been used extensively to identify the mechanisms responsible for pathological gait (in populations such as elderly, patients with knee and hip arthritis and arthroplasty, anterior cruciate ligament reconstruction and below knee amputees) and to assess and guide successful rehabilitation strategies[6-8]. Similar insights can be gained from patients with PAD utilizing this approach.

Previous studies of claudicating PAD patients from our laboratory utilizing basic biomechanical analysis[9-11] suggested a potential weakness of the posterior compartment muscles of the hip and calf as key components of PAD gait impairment. The purpose of the current study is to utilize joint torques and powers to isolate and identify the individual muscle compartments responsible for the gait impairment of claudicating patients.

METHODS

Key events during gait stance

The gait cycle (from heel touchdown to heel touchdown) consists of a stance and a swing period. The stance phase is the most important segment of the gait cycle because during it the ambulating limb accepts, supports and propels the weight of the body. Furthermore, it is the only portion of the gait cycle that can be accurately evaluated for joint moments and powers. The stance segment can be divided in three distinct phases including the weight acceptance, the single limb support and the propulsion phases (**Figure 1**).

INSERT FIGURE 1 ABOUT HERE

Subject inclusion and exclusion criteria

Twenty patients (age: 64.25±9.01 years, body mass: 79.52±13.83 kg; body height: 1.72±0.04 m) diagnosed with moderate arterial occlusive disease and bilateral claudication were recruited from the vascular surgery clinics of the VA Nebraska and Western Iowa and University of Nebraska Medical Centers and signed an inform consent prior their participation to the study that was approved by the institutional review boards of each respective institution. In addition, eleven gender, age, body-mass, height matched healthy controls (age: 66.27±9.22 years, body mass: 77.89±10.65 kg, body height: 1.74±0.08 m) were recruited. Patients and controls were screened and evaluated by two board certified vascular surgeons. Those PAD patients with

ambulation limiting cardiac, pulmonary, neuromuscular or musculoskeletal disease or those who experienced pain or discomfort during walking for any reason other than claudication (i.e. arthritis, low back pain, musculoskeletal problems, and neuropathy) were excluded. Patient evaluation included resting ankle brachial index (ABI; a measurement below 0.90 was present in all subjects with claudication), detailed history, physical exam and direct assessment/observation of the patient's walking impairment. A vascular surgeon observed the patient walking and recorded all symptoms and signs affecting ambulation to insure limitation was secondary to claudication pain. Control subjects had a resting ABI greater than 0.90 and no subjective or objective ambulatory dysfunction. Controls were screened in a similar fashion as PAD patients and were excluded for the same ambulation limiting problems or if pain was experienced during walking. Informed consent was obtained from all subjects prior to data collection according to the guidelines of the Institutional Review Boards of the two medical centers. The gait of all recruited participants was tested in the Biomechanics Laboratory of the University of Nebraska at Omaha.

Experimental Procedure* and *Data Collection

Prior to data collection, reflective markers were placed at specific anatomical locations of each subject's lower limb utilizing the modified Helen Hayes marker set[10]. Each subject was directed to walk using their self-selected pace over a ten meters pathway, while three-dimensional marker trajectories (kinematics) and ground reaction forces (kinetics) were simultaneously collected. The marker trajectories were captured with an eight high-speed real-time camera system (EvaRT 5.0, Motion Analysis Corp., Santa Rosa, CA) sampling at 60Hz. The ground reaction force data were acquired with a Kistler force platform sampling at 600 Hz.

Each patient was tested before ("Pain Free" condition) and after ("Pain" condition) the onset of claudication pain. During "Pain Free" testing, mandatory rest occurred between the walking trials to insure that all trials were in a "Pain Free" condition. Once patients completed all "Pain Free" trials, "Pain" trials were performed. In order to accomplish this, each patient was asked to walk on an inclined treadmill with 10% grade at a speed of $0.67 m/s^{-1}$[12] until claudication pain was established. The patients were then immediately removed from the treadmill and returned to the collection walk-way to acquire the data for the "Pain" condition without the mandatory resting periods. Controls completed only the "Pain Free" condition trials. A total of five walking trials were collected from each leg of the subjects for each condition.

Data Analysis

Joint kinetics and kinematics were calculated for the sagittal plane during the stance phase of walking. An inverse dynamic solution was performed to calculate joint muscle torques and powers from the joint kinetics and kinematics[6]. Joint muscle power (P_j) is calculated as the product of the net torque of force at a joint (M_j) and the relative joint angular velocity (ω_j) or $P_j = M_j \times \omega_j$ (Joules*sec^{-1} or Watts). Power combines both kinetic (forces) and kinematic (angles and velocities) information and can be expressed positively or negatively. Positive power indicates that energy is being generated and negative power that energy is being absorbed by the muscle group under study. Thus, positive joint muscle power is associated with concentric muscular contractions, while negative power is associated with eccentric muscular contractions [6]. Joint torques and joint muscle powers were normalized with respect to the subject's body mass and expressed as a percentage of the stance phase. All normalizations occurred after the discrete points were determined to ensure that the normalization did not distort these values. The peak values for extensor and flexor torques were identified for the ankle, knee and hip joints (Figure

2) [6]. The variables identified for the ankle were the ankle dorsiflexor torque (ADT) in early stance and the ankle plantar flexor torque (APT) in late stance; for the knee were the knee extensor torque (KET) in early stance and the knee flexor torque (KFT) in late stance; for the hip were the hip extensor torque (HET) in early stance and the hip flexor torque (HFT) in late stance. In addition, the peak values for power absorption (eccentric contraction) and generation (concentric contraction) were identified for the ankle, knee and hip joints (Figure 3) [6]. The power variables indentified for the ankle were the power absorption in early (A1) and mid (A2) stance (correspond to eccentric contraction of the ankle dorsiflexor group) and the power generation in late stance (A3); for the knee were the power absorption in early stance (K1), the power generation in the early part of mid-stance (K2), and the knee power absorption in late stance (K3); for the hip joint were the power generation in early stance (H1), the power absorption in mid-stance (H2) and the power generation in late stance (H3) [6]. Custom made Matlab (Matlab 2007, Mathworks, Inc., Concord, MA) software was used to calculate the joint torques and powers.

Statistical Analysis

Group means of the peak joint torques and powers were calculated for each testing condition ("Pain Free" and "Pain" conditions) by combining all legs of each group. Thus, an N of 40 limbs was generated for the claudicating group and an N of 22 limbs for the control healthy group. Paired t-tests were used to detect the effects of induced claudication pain, and independent t-tests were used to examine group effects for each dependent variable using SPSS (Base 12.0, SPSS Inc., Chicago, IL) software package and parametric statistics[13].

RESULTS

Time – distance gait measurements

The baseline clinical characteristics of patients and healthy controls are presented in **Table 1**. No significant differences were found between groups regarding age, body mass and body height. When compared to controls, patients had significantly decreased gait velocity, stride length, cadence and step length in the "Pain Free" condition (**Table 2**). The differences for these parameters were further amplified when the patients walked experiencing muscle pain in the "Pain" condition, with the addition of a significant difference for the duration of the double support phase (**Table 2**). Comparing gait time – distance gait measurements before and after onset of claudication, there was a significant decrease in gait velocity, stride length and step length and a significant increase in double support phase (**Table 2**).

INSERT TABLE 1 AND TABLE 2 ABOUT HERE

Weight Acceptance Phase

In comparison to the controls (**Tables 3, 4;Figures 2, 3**), patients in the "Pain Free" condition generated significantly decreased torque by the hip extensors (HET) and by the knee extensors (KET) which translated to significantly decreased power at the hip (H1, reduced concentric contraction of the hip extensors) and at the knee (K1, reduced eccentric contraction of the knee extensors). Decreased (although not significant) torque was also produced by the ankle dorsiflexors (ADT) leading to decreased power absorption at the ankle (A1, reduced eccentric contraction of the ankle dorsiflexors). In the "Pain" condition, the results for the same parameters remained significantly different compared to healthy controls (**Table 3;Figure 2**) while they became significantly augmented at the knee and ankle level compared to the "Pain Free" condition.

INSERT TABLE 3 AND TABLE 4 ABOUT HERE

Single Limb Support or Mid-Stance Phase (all the body weight on one limb)

In comparison to the controls (**Table 3;Figure 2**), patients in both conditions generated significantly decreased knee torque by the knee extensors (KET) which then translated to significantly decreased knee joint power generation in the early part of mid-stance phase (K2, reduced concentric contraction of the knee extensors).

Propulsion or Late-Stance Phase

In comparison to the controls (**Table 3;Figure 2**), patients in the "Pain Free" condition produced significantly less power at the ankle (A3, reduced concentric contraction of the ankle plantarflexors). Once in the "Pain" condition, patients generated significantly decreased ankle plantarflexor torque (APT) compared to controls and the "Pain Free" condition. This significant decrease in torque (reduced concentric contraction of the ankle plantar flexors) translated into further decrease of power generation at the ankle (A3).

INSERT FIGURE 2 AND FIGURE 3 ABOUT HERE

DISCUSSION

The purpose of this study was to utilize joint torques and powers in order to characterize and provide an in depth understanding of the gait impairment of claudicating patients. Joint torques and powers were measured while patients walked both with and without claudication pain and were compared to those of gender-, height-, mass-, and age-matched healthy controls. Our results from the time-distance gait parameters demonstrate that the character of the PAD gait appears overall ‘‘sluggish and tired’’. Patients with claudication have decreased gait velocity, stride length, cadence and step length and spend more time in the double stance (both limbs on the ground). These findings are in agreement with previous studies and unequivocally document the abnormal temporal and spatial gait parameters of claudicating PAD patients[4, 5]. Utilizing advanced biomechanical analysis in the form of joint torques and powers, we were able to isolate

and describe the specific muscle group impairments that operate to produce the gait deficit in claudicating patients. Our data demonstrate a decreased ability of the knee and hip extensors to control weight acceptance and ankle dorsiflexors to eccentrically control the lowering of the foot to the ground after heel strike in early stance. In mid stance we found a decreased ability of the knee extensors to concentrically extend the knee in preparation for the single support phase. Finally, in late stance we demonstrated a decreased ability of the ankle plantarflexors to concentrically propel the body forward.

Decreased weight acceptance

Trunk support in early stance is provided by the hip extensors concentrically contracting to extend the hip (H1), the knee extensors eccentrically contracting to allow the knee to flex (K1) and the ankle dorsiflexors which eccentrically control the movement of the foot towards full contact with the ground (A1)[14]. Our findings in PAD patients demonstrate that all three muscle groups involved in the weight acceptance phase produce less power than in controls both in the "Pain Free" and the "Pain" conditions. Specifically PAD patients have decreased power generation by the hip extensors (Gluteus muscles, H1;**Figure 2**) and the knee extensors (quadriceps) in early stance (K1;**Figure 2**) which appear unable to optimally support the body weight. These power results are supported by our joint torque findings which showed significantly decreased torque development by the hip (HET) and knee (KET) extensors[10]. The demonstrated weakness of the hip and knee extensors in early stance is present before and becomes worse after the onset of claudication symptoms resulting in diminished ability for weight acceptance and control of forward momentum when a claudicating patient walks. The demonstrated weakness of the ankle dorsiflexors in early stance is in agreement with findings our group has previously published showing that PAD patients have a "foot drop" upon heel strike[9].

Decreased weight support during the mid-stance phase

In the early part of the mid-stance phase the knee extensors concentrically contract to extend the knee joint in preparation for single leg support. To maintain the energy required for walking[15], it is necessary to "straighten" the leg and maximize the ability to generate potential energy at its highest point of the gait cycle. Our work shows that PAD patients have significantly decreased knee joint power generation (K2) due to the reduced concentric contraction of the knee extensors.

Decreased forward propulsion

In late stance the body is propelled forward mainly by the action of the ankle plantarflexors. Functionally, these muscles contract concentrically and accelerate the leg and the trunk forward to initiate swing, while decelerating the downward motion of the trunk (i.e., providing forward progression and support)[16]. Our results in the PAD patients, demonstrate that power generation via concentric contractions of the ankle plantarflexor muscles in late stance (A2;**Figure 2**) is decreased in the "Pain Free" condition and worsens in the "Pain" condition. This hypothesis is supported by previous findings from our and other laboratories demonstrating that PAD patients have significantly decreased ankle plantarflexor torques[10] and strength[11, 17, 18].

Potential Clinical Implications for the Observed Gait Abnormalities: Our findings for the time-distance gait parameters provide definitive evidence of abnormal temporal and spatial parameters in patients with PAD and confirm the generally accepted thought that claudicating patients have an abnormal gait[5, 10, 19]. More importantly, our advanced analysis with joint torques and powers provides a much more detailed delineation of the gait disturbance than that documented with spatial and temporal parameters and clearly documents the inability of the

PAD patient to walk efficiently, which by definition leads to increased energy cost and earlier fatigue[20, 21].

When comparing the abnormalities of joint torques and powers in PAD to other conditions, our values are in line with those of healthy elderly and elderly patients with osteoarthritis[8, 22, 23]. In contrast to these two groups however, the gait biomechanics of PAD patients appear to be significantly worse than healthy elderly subjects and those patients with severe arthritis. Specifically our data demonstrate that from the first few steps they take and before they experience any muscle pain claudicants walk with 29% decrease (versus controls) of their ankle plantarflexor power compared to a 13% for elderly osteoarthritis patients. Arthritis patients compensate for the 13% decrease in the power of their ankle plantarflexors by increasing the power of their knee and hip extensors (by 13% and 28% respectively). In marked contrast to the arthritic patients, claudicants demonstrate a drop of compensatory power in these muscle groups by 38 and 21% respectively[23]. It is clear from a biomechanical standpoint that claudication produces a worse functional limitation than osteoarthritis. Our data support the findings that claudicating patients typically gather around the extreme low end of the physical activity spectrum[24] and experience a severe decline in all domains of physical function[17, 25].

Potential Mechanisms for the Observed Gait Abnormalities The present data demonstrate significant abnormalities in the gait of claudicants that are present at the initiation of ambulation and prior to onset of pain. These baseline biomechanical impairments likely reflect a muscle metabolic myopathy and an axonal polyneuropathy in the lower extremities of patients with PAD[26-28]. Specifically, a number of reports have documented a metabolic myopathy in the PAD muscle that is related to defective mitochondrial bioenergetics and oxidative damage to skeletal muscle structures and components[28-32]. Furthermore, there is accumulating evidence suggesting

that chronic ischemia in patients with PAD results in a consistent pattern of electrodiagnostic abnormalities indicating axonal nerve loss[28, 33]. Our data further demonstrate that the baseline impairments worsen after the onset of claudication. This likely reflects exercise induced ischemia producing progressively worsening ischemic muscle pain and restriction of the lower extremity bioenergetics. The end result is a baseline metabolic neuromyopathy exacerbated by increased workload and ischemia. **Figure 4** illustrates a proposed pathway linking these basic pathophysiologic mechanisms with the specific biomechanic deficits identified in this work. The role played by each one of these mechanisms (blood flow, myopathy, neuropathy) and the way they are related to the clinical biomechanical findings of leg dysfunction should be the focus of intense future investigation and may hold the key to understanding PAD pathophysiology.

INSERT FIGURE 4 ABOUT HERE

On a clinical level, only recently have studies with large sample sizes (N= 700-2000) been able to demonstrate the long held assumption that claudicating patients have significantly reduced muscle strength [17, 34]. Our study utilizing advanced biomechanical analysis has allowed us to confirm these large scale studies with a limited number of patients and to implicate the site of the muscular deficit. Advanced biomechanical techniques thus provide a new avenue for evaluation, treatment, and rehabilitation of the PAD patient.

Conclusions

Biomechanical analysis using joint torques and powers demonstrates significant abnormalities in the gait of claudicating patients with bilateral PAD. These abnormalities are present at the onset of ambulation and worsen with the pain of claudication. Our work points to a failure of major muscle groups to optimally perform the sequence of functions (weight acceptance, transfer and propulsion) that characterize normal gait. The muscle groups most

affected by the chronic ischemia are the hip extensors, knee extensors and ankle dorsi- and plantar flexors. These findings introduce new insights into the pathophysiology of claudicating gait. In the future these advanced biomechanical techniques will provide for detailed objective and quantitative evaluation of the gait deficit of the claudicating patient, allowing for evaluation of new treatment and rehabilitation strategies.

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Figure1
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Figure 1.

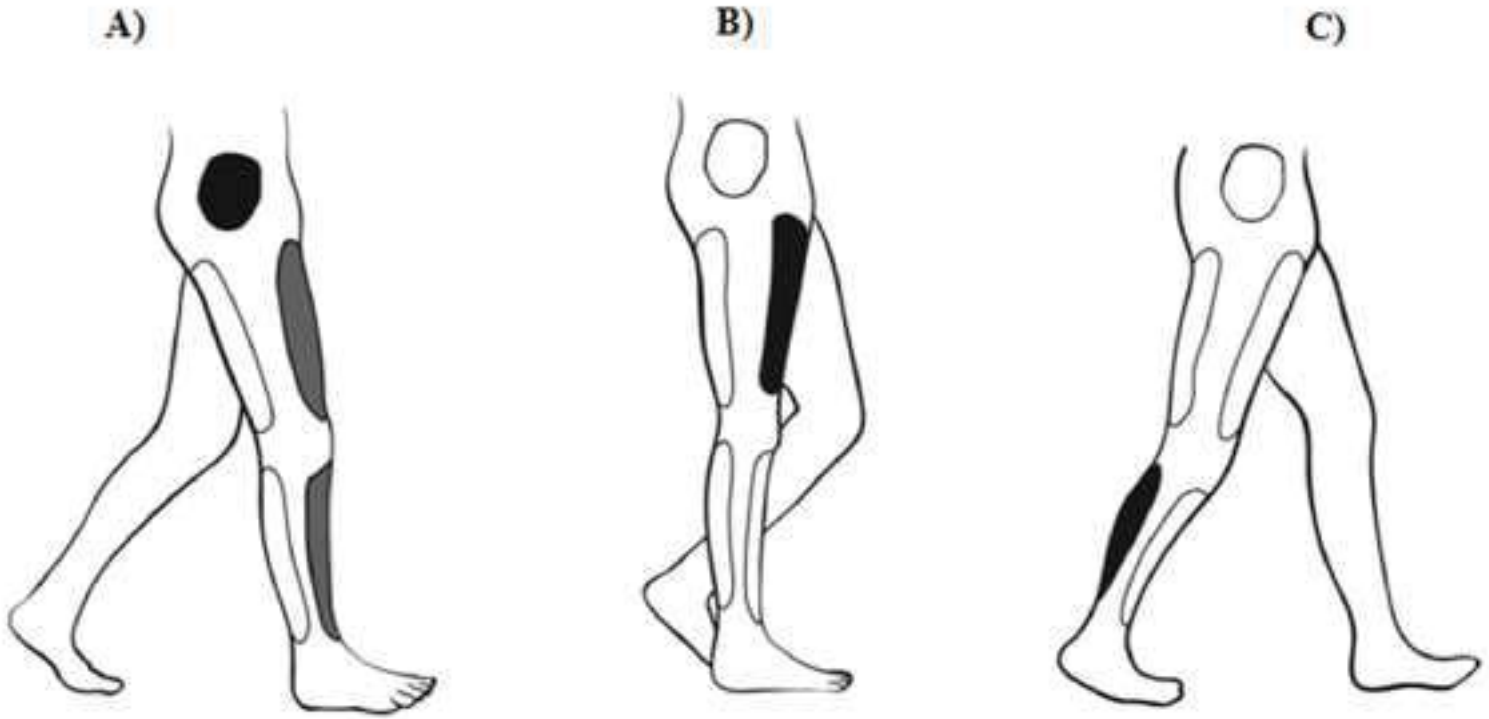

Figure2a
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Figure 2.

a)

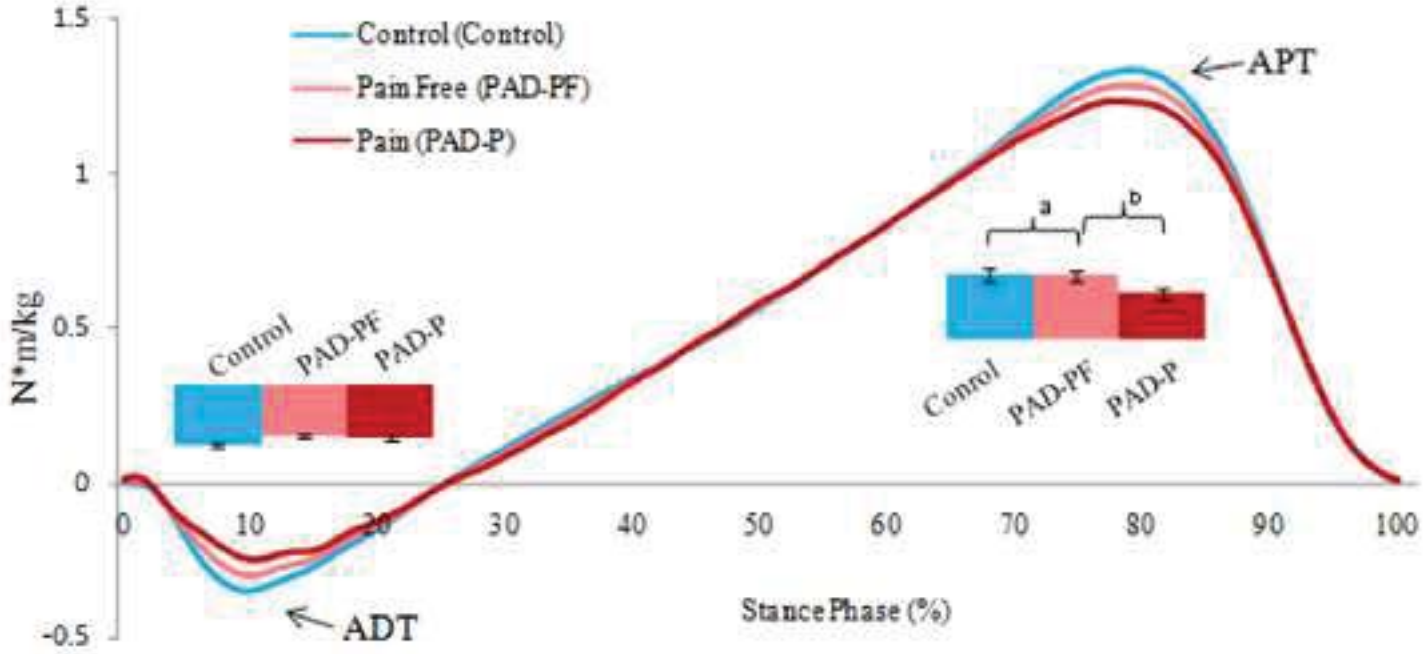

Figure2b

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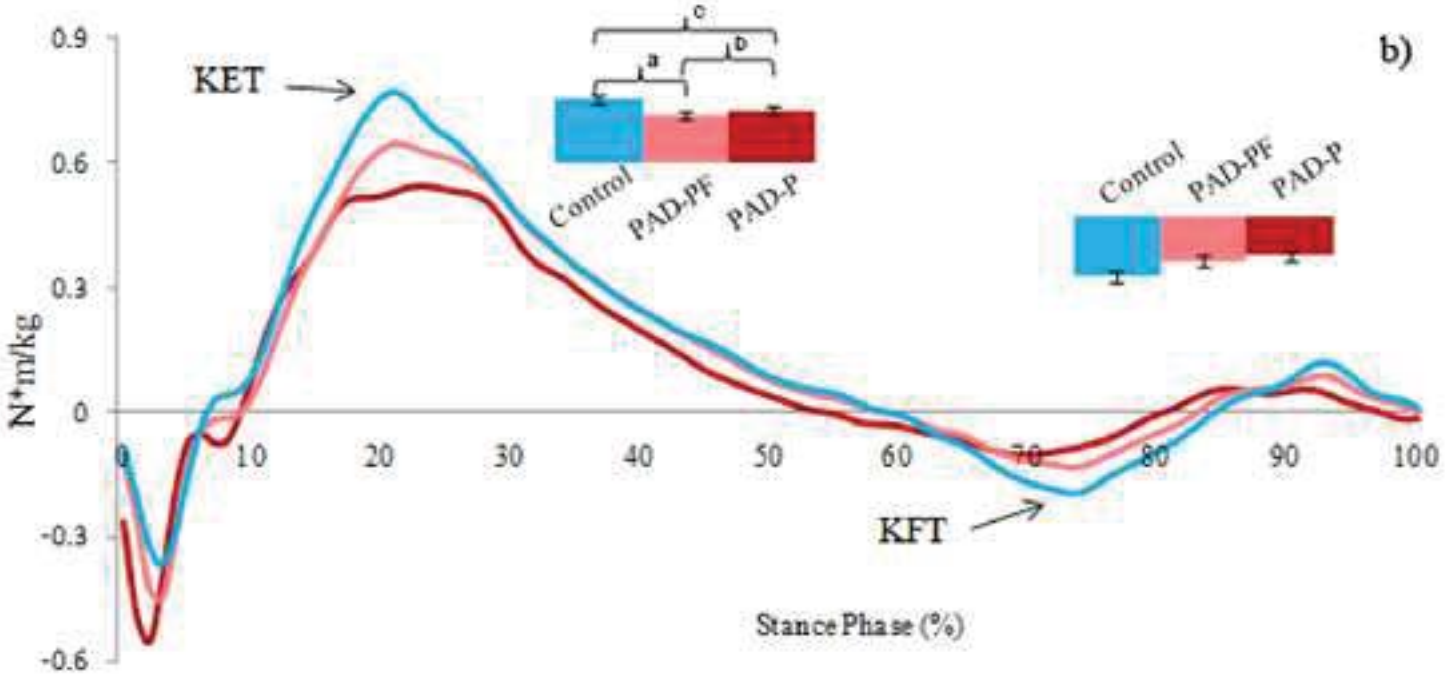

Figure2c

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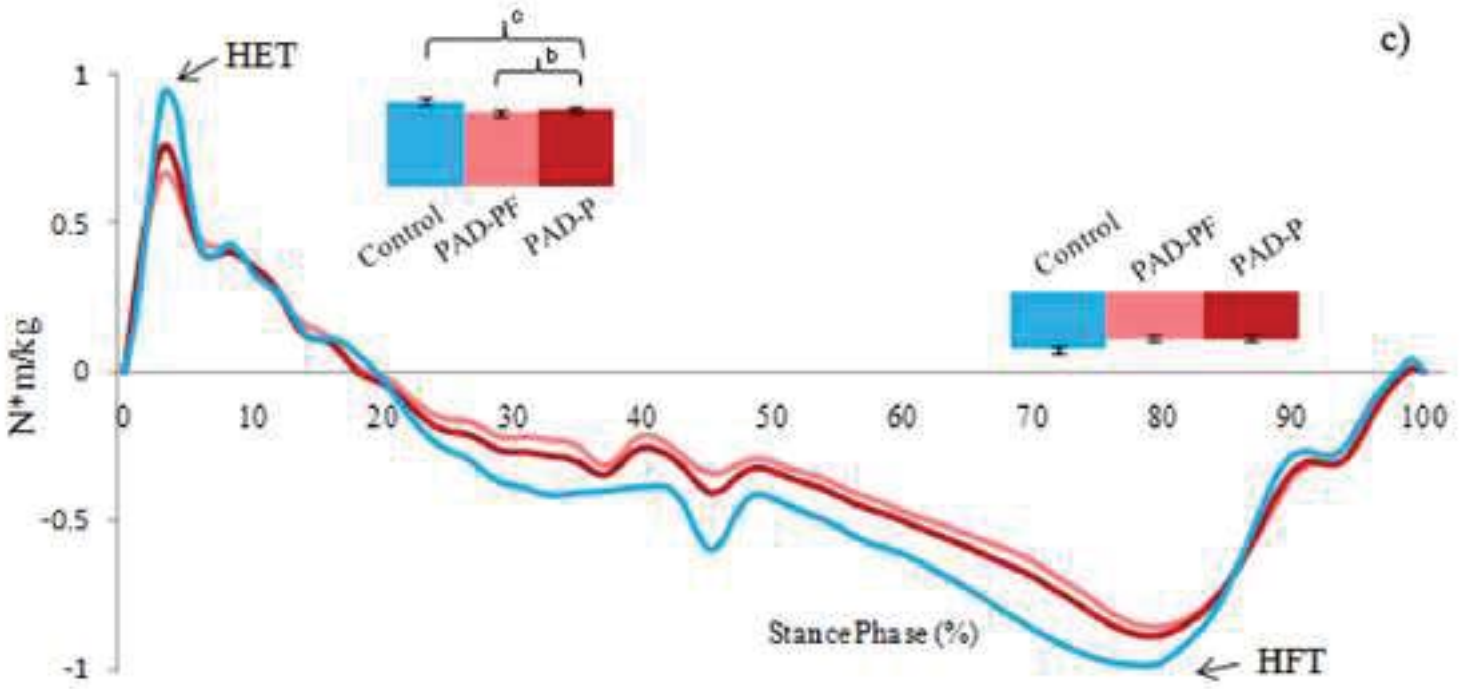

Figure3a
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Figure 3.

a)

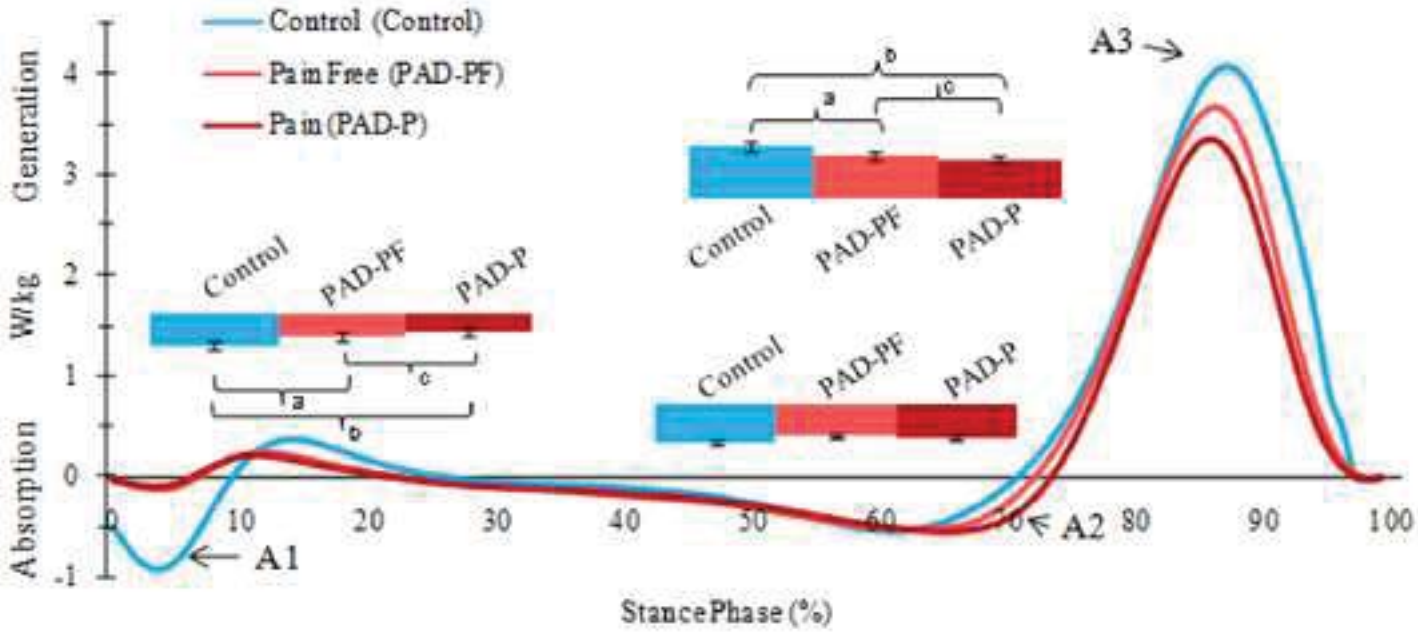

Figure3b

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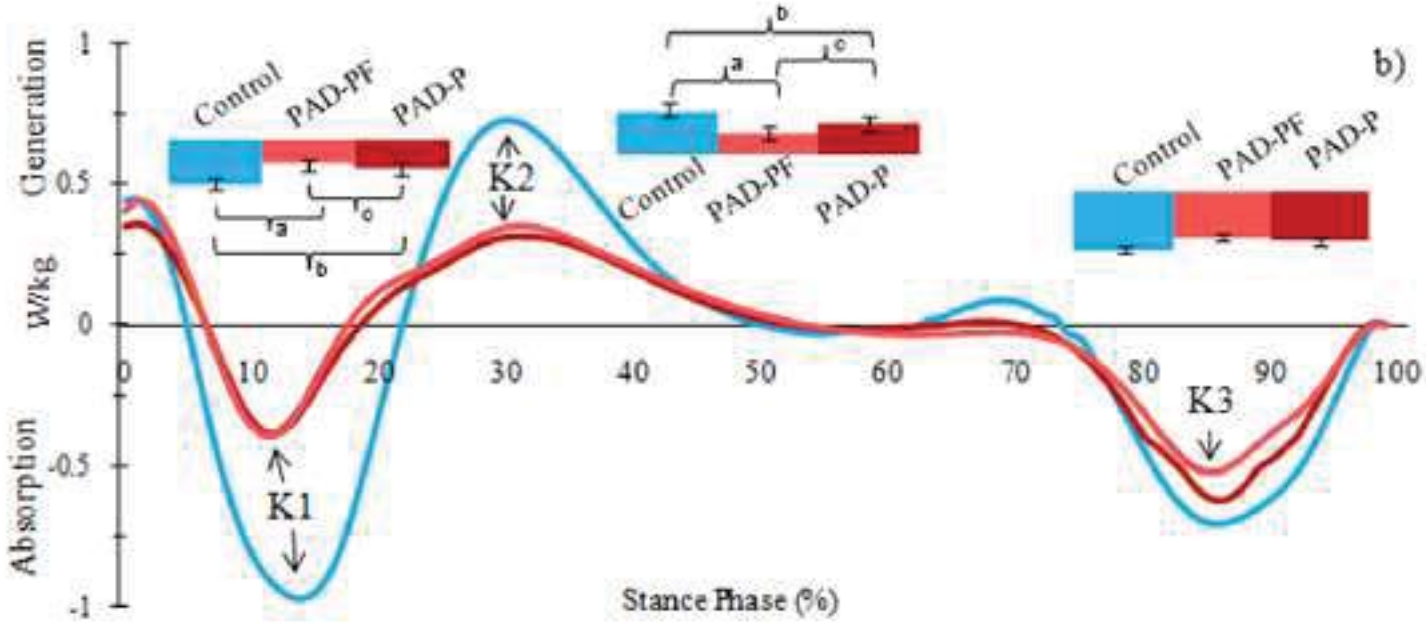

Figure3c

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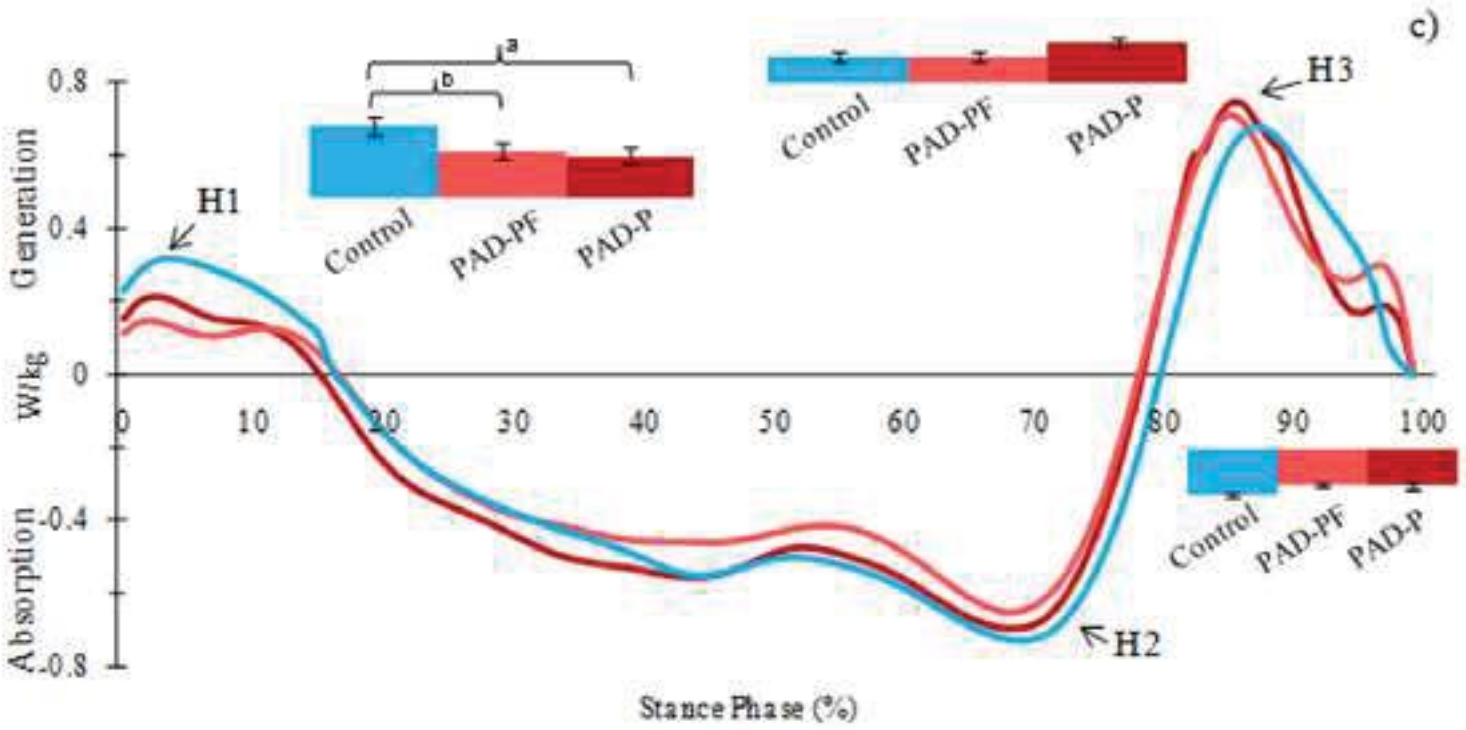

Figure4
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Figure 4.

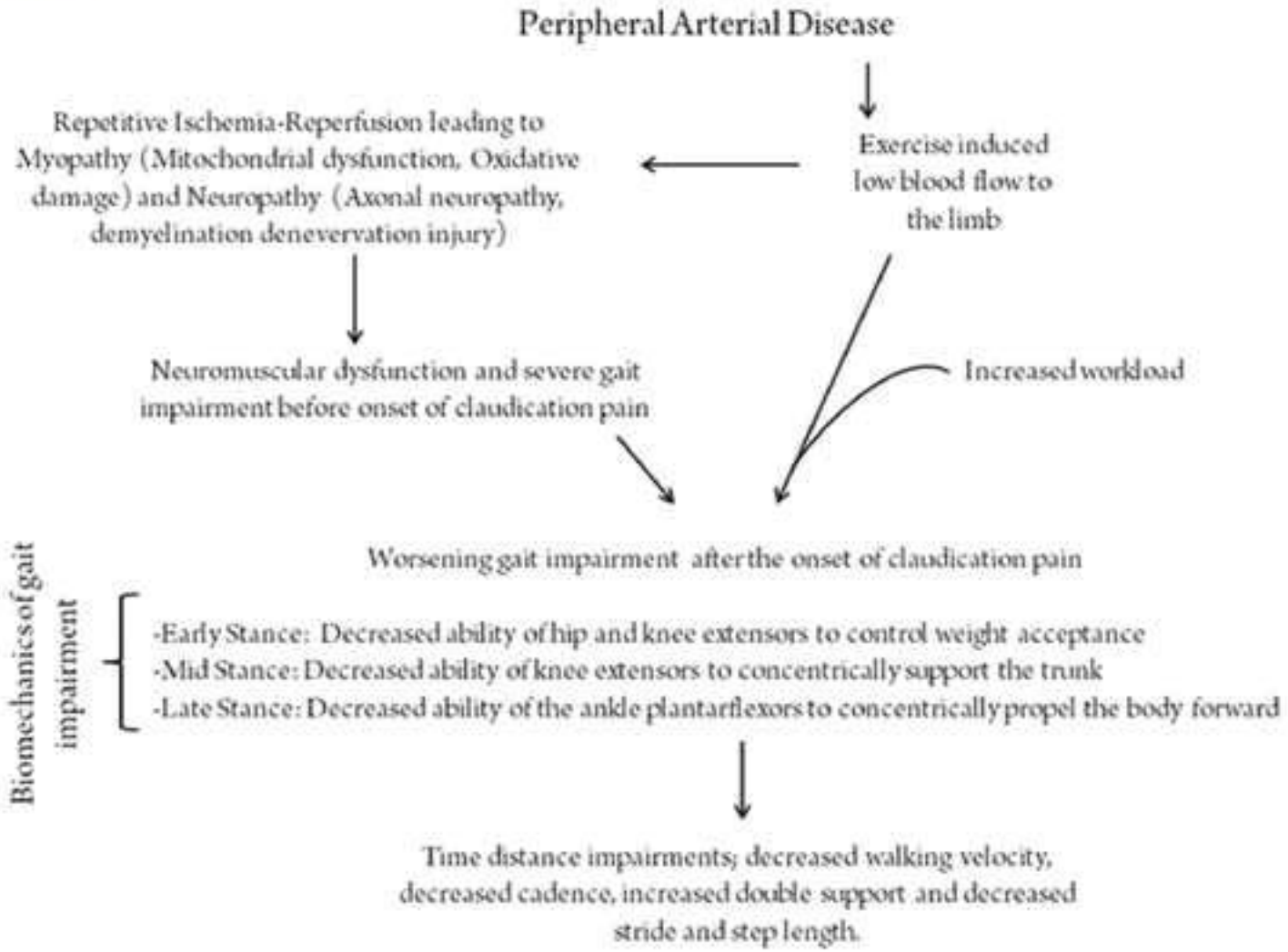

Table 1

Baseline characteristics of Peripheral Arterial Disease (PAD) patients and healthy controls.

Clinical characteristics	PAD (N=40 Limbs)	Control (N=22 Limbs)
Gender (male/female)	19/1	10/1
Age (years)	64.25±9.01	66.27±9.22
Body mass (kg)	79.52±13.83	77.89±10.65
Body height (m)	1.72±0.04	1.74±0.08
Disease duration (years)	6.05±3.84	0
ABI	<0.9	>0.9
Right limb	0.55±0.22	1.1±0.11
Left limb	0.50±0.23	1.1±0.09
Smokers, n (%)	14 (70)	0 (0)
Hypertension, n (%)	19 (95)	1 (9.09)
Diabetes mellitus, n (%)	4 (20)	0 (0)
Hyperlipidemia, n (%)	16 (80)	0 (0)
BMI	26.82±4.66	25.60±2.94

Note: ABI = ankle brachial index; BMI = body mass index

Table 2

Group means and standard deviations for the time–distance gait measurements for Peripheral Arterial Disease (PAD) and control groups. PAD-PF= "Pain Free" and PAD-P= "Pain" conditions

	Control (*N=22 limbs*)	PAD (*N= 40 limbs*)	
		PAD-PF	PAD-P
Gait velocity (m/s)	1.37±0.15	1.04±0.14[a,c]	1.02±0.13[b]
Stride length (m)	1.51±0.10	1.27±0.11[a,c]	1.22±0.09[b]
Cadence (Steps/min)	110.09±9.09	99.15±8.51[c]	100.68±8.79[b]
Step length (m)	0.68±0.05	0.62±0.07[a,c]	0.58±0.05[b]
Step width (m)	0.13±0.03	0.14±0.03	0.15±0.05
Stance phase (% of gait cycle)	62.75±2.11	63.38±3.70	63.42±4.60
Swing phase (% of gait cycle)	37.25±2.11	36.62±3.70	36.58±3.83
Double support (% of gait cycle)	12.41±1.75	13.20±1.76[a]	15.14±4.23[b]

Note: [a]$p<0.05$, significant differences between PAD-PF and control.

[b]$p<0.05$, significant differences between PAD-P and control.

[c]$p<0.05$, significant differences between PAD-PF and PAD-P

Table 3

Group means and standard deviations for joint torques of the ankle, knee and hip joint for Peripheral Arterial Disease (PAD) and control groups. PAD-PF= "Pain Free" and PAD-P= "Pain" conditions. The units for all values are N*m/kg.

	Control (*N=22 limbs*)	PAD (*N=40 limbs*)	
		PAD-PF	PAD-P
ADT	-0.317±0.087	-0.279±0.086	-0.287±0.094
APT	1.432±0.106	1.339±0.116[a]	1.246±0.199[b]
KET	0.858±0.161	0.654±0.281[a,c]	0.704±0.219[b]
KFT	-0.154±0.082	-0.115±0.149	-0.102±0.161
HET	0.841±0.159	0.738±0.148[c]	0.759±0.120[b]
HFT	-0.979±0.213	-0.893±0.147	-0.897±0.200

ADT ankle dorsi flexor torque in early stance, APT ankle plantar flexor torque in late stance, KET knee extensor torque in early stance, KFT knee flexor torque in late stance, HET hip extensor torque in early stance, HFT hip flexor torque in late stance.

Note: [a]$p<0.05$, significant differences between PAD-PF and control.

[b]$p<0.05$, significant differences between PAD-P and control.

[c]$p<0.05$, significant differences between PAD-PF and PAD-P

Table 4

Group means and standard deviations for joint powers of the ankle, knee and hip joint for Peripheral Arterial Disease (PAD) and control groups. PAD-PF = "Pain free" and PAD-P = "Pain" conditions. The units for all values are Watts/kg.

	Control (*N=22 limbs*)	PAD (*N=40 limbs*)	
		PAD-PF	PAD-P
A1	-0.344±0.063	-0.226±0.103[a,b]	-0.182±0.107[b]
A2	-0.484±0.223	-0.550±0.181	-0.539±0.326
A3	3.944±0.959	3.240±1.068[a,b]	2.810±0.705[b]
K1	-0.698±0.220	-0.433±0.263[a,b]	-0.508±0.240[b]
K2	0.587±0.250	0.323±0.257[a,c]	0.404±0.211[b]
K3	-0.726±0.230	-0.692±0.336	-0.698±0.295
H1	0.416±0.196	0.327±0.120[c]	0.314±0.132[b]
H2	-0.776±0.235	-0.584±0.253	-0.605±0.249
H3	0.759±0.293	0.735±0.272	0.745±0.268

A1 ankle power absorption in early stance, A2 ankle power absorption in mid stance A3 ankle power generation in late stance, K1 knee power absorption in early stance, K2 knee power generation in early mid-stance, K3 knee power absorption in late stance, H1 hip power generation in early stance, H2 hip power absorption in mid-stance, H3 hip power generation in late stance

Note: [a]$p<0.05$, significant differences between PAD-PF and control.

[b]$p<0.05$, significant differences between PAD-P and control.

[c]$p<0.05$, significant differences between PAD-PF and PAD-P

FIGURE LEGENDS

Figure 1. An illustration of the three phases of walking with the dominant flexor and extensor muscle groups that are involved in each phase based on the joint torques generated. The dominant muscle groups are identified in black if they contract concentrically (muscle shortens as it contracts) and in grey if they contract eccentrically (muscle lengthens as it contracts).

A) Weight acceptance phase. It is also known as early stance, initial contact and heel strike phase and lasts from ipsilateral heel strike to contralateral toe off thus covering the first double support phase (initial 20% of stance). The right leg is accepting most of the weight of the body as it descents from previously being in single support on the left leg. In this phase the right hip extensors concentrically contract to extend the hip (reflected in the HET torque and H1 power in **Figures 2** and **3**), the knee extensors eccentrically contract to allow the knee to bend (reflected in the KET torque and K1 power in **Figures 2** and **3**) and the ankle dorsiflexors eccentrically contract to maintain the ankle dorsi-flexed (reflected in the ADT torque and A1 power in **Figures 2** and **3**).

B) Single limb support phase. It is also known as the mid-stance phase and lasts from contralateral (here left) toe off until contralateral heel strike. During single support the body is at its highest point and over the extended ipsilateral leg. The body has maximum potential energy getting ready to fall forward for the next double support. Limited muscular contractions are needed during this phase except its early part where the knee extensors contract concentrically to extend the knee and straighten the leg (reflected in the KET torque and K2 power in **Figures 2** and **3**).

C) Propulsion phase. It is also known as the late stance or toe-off phase and lasts from contralateral heel strike to ipsilateral toe off. It is the last 20% of stance and it is the second

double support phase. In this phase the body is propelled forward onto the extended left leg mainly by the action of the right ankle plantarflexors (posterior calf compartments muscles, the most important of which are the gastrocnemius and soleus). Functionally, these muscles contract concentrically (reflected in the APT torque and A3 power in **Figures 2** and **3**) and accelerate the leg and the trunk forward and upward over the left leg (i.e., providing forward progression and weight support.

Figure 2. The ensemble-average joint torque curves for the Peripheral Arterial Disease (PAD) patients ("Pain Free" PAD-PF and "Pain" conditions PAD-P; N=40 limbs) and the healthy controls (N=22 limbs) during the stance phase for the (a) ankle, (b) knee, and (c) hip joints. *Note:* ADT=ankle dorsiflexor torque in early stance, APT=ankle plantarflexor torque in late stance, KET=knee extensor torque in early stance, KFT=knee flexor torque in late stance, HET=hip extensor torque in early stance, and HFT=hip flexor torque in late stance. Torques are normalized to body mass. A positive (+) value indicates extensor torque, and a negative (-) value indicates flexor torque.

[a]$p<0.05$, significant differences between PAD-PF and control.

[b]$p<0.05$, significant differences between PAD-P and control.

[c]$p<0.05$, significant differences between PAD-PF and PAD-P.

Figure 3. The ensemble-average joint power curves for the Peripheral Arterial Disease (PAD) patients ("Pain free" PAD-PF and "Pain" conditions PAD-P; N = 40 limbs) and the healthy controls (N = 22 limbs) during the stance phase for the (a) ankle, (b) knee, and (c) hip joints. *Note:* A1 is the ankle power absorption in early stance, A2 is the ankle power absorption in mid stance, A3 is the ankle power generation in late stance, K1 is the knee power absorption in early stance, K2 is the knee power generation in mid-stance, K3 is the knee power absorption in late

stance, H1 is the hip power generation in early stance, H2 is the hip power absorption in mid-stance, H3 is the hip power generation in late stance.

A positive (+) value indicates power generation (concentric contraction), and a negative (-) value indicates power absorption (eccentric contraction). Powers are normalized to body mass.

[a]$p<0.05$, significant differences between PAD-PF and control.

[b]$p<0.05$, significant differences between PAD-P and control.

[c]$p<0.05$, significant differences between PAD-PF and PAD-P.

Figure 4. Proposed pathway for the pathogenesis of gait impairment in patients with Peripheral Arterial Disease (PAD). The fundamental problem in claudicating patients is the presence of atherosclerotic blockages in the arteries supplying their legs. At rest, claudicating patients have adequate leg perfusion and experience no symptoms. During walking, however, the increased metabolic needs of the limb cannot be met and as the exercise continues the limb becomes progressively ischemic and painful, eventually forcing the patient to stop and rest. During rest, the metabolic demands of the limb return to baseline and the leg is reperfused. Repeated cycles of ischemia/reperfusion, occurring with basic daily activities, as simple as walking, initiate a combination of oxidative damage and inflammation which eventually produces a myopathy and axonal polyneuropathy in the claudicating limbs. We propose that the gait impairments we have identified at baseline (in the first few steps taken and prior to the onset of muscle pain) reflect the effects of this myopathy and neuropathy in the function of the PAD limbs. Several of these biomechanic impairments get worse after onset of claudication symptoms when exercise induced ischemia and increasing workload produce progressively worsening ischemic muscle pain and restriction of the lower extremity bioenergetics.