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Coactivation Pattern in Leg Muscles During Treadmill Walking in Patients Suffering From Intermittent Claudication

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Abstract

Background: In patients with peripheral arterial disease and presenting intermittent claudication (PAD-IC), the pain due to ischemia impacts gait parameters, particularly in cases of unilateral disease. Deterioration of gait parameters in a pathological context is frequently associated with increased coactivation (simultaneous activation of agonist and antagonist muscles around a joint).

Research question: Does unilateral PAD-IC affect the coactivation pattern during walking? Does the coactivation pattern change with increasing pain intensity?

Method: We evaluated symptomatic and asymptomatic legs in 17 subjects with unilateral PAD-IC and 16 without PAD-IC (control group), during walking. *Tibialis anterior* (TA) and *gastrocnemius medialis* (GM) electromyographic activity, and peaks of vertical ground reaction force were recorded in this prospective study. We analyzed the coactivation index ($CI_{(GM/TA)}$) during three periods (pain-free, pain and maximum pain) and phases of the gait cycle. Statistical analysis was carried out using the ANOVA procedure.

Results: During single support, $CI_{(GM/TA)}$ increases in the symptomatic leg during the pain period (+28%) and in the asymptomatic leg during the maximum pain period (+29%). During second double support, $CI_{(GM/TA)}$ increases in the symptomatic leg only (+49%). In these gait phases, pain elicits differences in $CI_{(GM/TA)}$ between legs ($p < 0.05$). Second peak force decreases in the symptomatic leg only (-9%) and is negatively correlated with $CI_{(GM/TA)}$ during the three periods ($r = -0.57$; -0.76 and -0.78 respectively, $p < 0.05$). No difference is found in the control group.

Significance: The appearance and development of pain in the lower limbs is associated with a higher level of $CI_{(GM/TA)}$, revealing a compensatory gait pattern in PAD-IC patients. Optimal prevention, rehabilitation and re-training strategies for PAD-IC patients should take into consideration neuromuscular compensatory mechanisms between asymptomatic and symptomatic legs.

Keywords: leg muscle coactivation, electromyographic activity, gait, peripheral arterial disease

1. Introduction

Peripheral arterial disease can induce pain when walking, leading to intermittent claudication (PAD-IC). This affects gait parameters and is associated with a reduced walking performance [1] that, in the long term, may affect muscular capacity and increase the risk of falling [2]. Understanding gait control in patients suffering from PAD-IC is important for optimizing rehabilitation and training strategies. It implies a consideration for the pain-adaptation theory proposed by Lund et al. (1991), suggesting that painful muscles exhibit reduced activity during voluntary efforts whereas activity in antagonist muscles increases [3]. However, they did not express any point of view concerning coactivation strategies. Coactivation is the simultaneous activation of agonist and antagonist muscles around a joint [4], designed to optimize the output of the agonist during refined motor performance [5]. This neurophysiological phenomenon can be observed during typical gait at the ankle level, with *gastrocnemius medialis* (GM) and *tibialis anterior* (TA) [6,7]. Interestingly, a relation between the level of coactivation and the deterioration of gait parameters, such as stance phase duration or of vertical ground reaction force, has been reported [8].

Discrepancies appear in the literature concerning this pain adaptation theory, in particular in PAD-IC patients. Calf muscles, especially GM, are strongly involved in the propulsive phase of the gait and the calf is frequently reported by PAD-IC patients when describing pain location. Despite this, Gommans et al. (2016) observed no change in GM muscle activity during a pain-free and a pain period in a population of PAD-IC patients, while TA muscle activity increased [9].

Gait alterations in PAD-IC patients also include a decreased peak of vertical ground reaction force responsible for propulsion (Peak 2) and thus a reduced ability to swing their leg forward [10]. It can be seen that local ischemia, as observed in PAD-IC patients, can induce neuromuscular alterations leading to partial denervation of calf muscles and a loss in nerve

conduction velocity [11] could affect the level of coactivation strategy, partly explaining the reduced propulsion force observed in these patients. These factors question the impact of pain on GM and TA coactivation during walking in PAD-IC patients, which, to the best of our knowledge, has never been investigated.

Thus, the aim of this study is to describe whether pain affects the GM/TA coactivation pattern in PAD-IC patients during walking and its relationship with gait parameters. We hypothesized that coactivation in ankle muscles increases with the increase of pain in the calf, especially during the propulsive phase.

2. Method

2.1. Participants

33 volunteers recruited from the functional vascular investigations department in Angers University Hospital (France) were divided into two groups according PAD diagnostic examination. A control group (controls) included patients without symptoms of PAD (with an ankle brachial index (ABI) ≥ 0.90) but with similar cardiovascular risk factors (smoking status, diabetes, hypercholesterolemia, etc.). A group with PAD-IC included patients diagnosed with an ABI ≤ 0.90 , exhibited claudication and suffered unilateral (one leg) ischemia. The presence of ischemia was investigated using a transcutaneous oxygen pressure recording with an index indicating ischemia (delta from rest oxygen pressure (DROP) < -15 mmHg, maximal absolute value was reported) [12] during a treadmill-walking test. The PAD-IC group was also asked to perform a tomography examination in order to identify stenosis location of the ischemic leg. Smoking status, presence of treated hypertension, diabetes, hypercholesterolemia, distance for onset of pain and maximal walking distance were recorded (Table 1). For the two groups, patients were excluded if they presented a comorbid condition that might influence gait pattern, such as previous vascular surgery on the lower extremities (bypass, percutaneous angioplasty), lower extremity amputation, severe osteoarthritis, knee or hip prosthesis, severe cardiopulmonary problems (e.g. chronic obstructive pulmonary disease), neurological diseases (e.g. diabetes neuropathy), Parkinson's disease, stroke, or use of walking aids. Each participant provided written informed consent before protocol. The study was conducted according to the declaration of Helsinki and was approved by the local ethics committee of human research (Committee for Protection of Persons Ouest II). It was promoted by Angers University Hospital and registered in Clinicaltrials.gov website (under reference: NCT02754804, April 28, 2016).

2.2. Gait analysis

2.2.1. Procedure

The two groups were instructed to walk on an instrumented gait analysis treadmill (Zebris; FDM-T, sampling rate: 100 Hz; Zebris medical GmbH, Isny, Germany) during a standard constant load procedure with a 10% slope, at a speed of 3.2 km/h [13]. The PAD-IC was asked to describe pain development in the lower limbs (intensity). Exercise was definitely stopped at the patient's request (pain or other difficulties in maintaining the effort). Controls walked 15 minutes without stopping.

2.2.2. Data recording

Data from ten successive gait cycles at three different periods were collected and averaged: in the 1st, 7th and 14th minutes for controls, and in the 10th second (pain-free), at the moment of pain onset (pain) and before stopping the test (max-pain) for the PAD-IC. The two peaks of the vertical ground reaction force during gait for symptomatic (i.e., ischemic and painful) and asymptomatic legs were sampled from treadmill force plates at 100 Hz by the treadmill software (Zebris, Suite FDM-T): the first peak force during early stance (Peak 1: loading phase) and the second peak force evident through push-off (Peak 2: propulsive phase). Peak forces were normalized by the body weight.

2.3. Electromyography recording

2.3.1. Procedure

Electromyographic (EMG) data of the ankle joint muscles were recorded while walking on the treadmill (Zebris EMG measuring system, Isny, Germany). Two unipodal surface electrodes (Uni-gel Single Electrode-T3425, Thought Technology Ltd, Montreal, Canada) were placed on the GM and TA of the two legs during walking. Before attaching the electrodes, to reduce impedance, the skin was carefully shaved and cleaned using an abrasive

cleaner and alcohol swabs. The placement and location of the surface electrodes conformed to the recommendations of SENIAM (Surface EMG for Noninvasive Assessment of Muscles) [14]. Electrodes were carefully positioned on the belly of each muscle parallel to the orientation of the muscle fibers at inter-electrode intervals of 20 mm.

2.3.2. Data analysis

The EMG recording was time synchronized with the treadmill data. The EMG analysis was post-processed using Matlab (Matlab R2013a, MathWorks, Natick, USA), and raw EMG signals were band-pass filtered at 15–500 Hz through a second-order Butterworth digital filter to remove noise or movement interference [15]. The data corresponding to ten successive gait cycles of each period (previously defined) were rectified and smoothed using root mean square analysis (RMS) with a 20-ms window. All RMS EMG data were normalized to respect to the RMS peak values of ten gait cycles of the first period of each group [16]. The normalized RMS of the GM and TA of each cycle, divided into four phases corresponding to gait cycle phases (first double support, single support, second double support and swing phase), were used in the study to evaluate the coactivation levels of the GM/TA. The coactivation index (CI) was calculated using the following equation [17]:

$$CI = \frac{2 \times I_{antagonist}}{I_{total}} \times 100,$$

where $I_{antagonist}$ is the area of the total antagonistic activity and I_{total} is the integral of the sum of (TA + GM) during the task, which were calculated using the following equations:

$$(1) I_{antagonist} = \int_{T_1}^{T_2} TA(t)dt + \int_{T_2}^{T_3} GM(t)dt,$$

$$(2) I_{total} = \int_{T_1}^{T_3} [agonist + antagonist](t)dt.$$

where T_1 to T_2 is the period in which the TA is working as an antagonist muscle, T_2 to T_3 is the period during which the GM is working as an antagonist muscle, and I_{total} is the integral of the sum of these two periods, as illustrated in Figure 1.

2.3. Statistical analysis

Statistical analysis was performed using Statistica Software 13.0 (Software, Inc., Tulsa, USA). Differences between groups were analyzed using Student t-test and prevalence of risk factors with a Chi-square test. Normality and homogeneity of variance were respectively determined using the Kolmogorov–Smirnov and Levene tests. When the parametric assumptions were met, a factorial ANOVA was applied with a post hoc Fisher's least significant difference (LSD multiple comparison procedure). For the controls, we applied a 2×3 factorial ANOVA [leg (right or left) × period (1st, 2nd and 3rd) (Leg × period)]. For the PAD-IC, we applied a 2×3 factorial ANOVA [leg (symptomatic or asymptomatic) × phase of pain (pain-free, pain and max-pain) (Leg × Pain)]. Comparison between controls and PAD-IC will not be presented in this study because the main objective is to analyze pain effects due to PAD-IC on the studied parameters. The control group is presented to show a model of coactivation under pain-free and healthy conditions. Relationships between the two peaks of the vertical ground reaction force and CI were evaluated using Pearson's correlations analysis. Values are expressed as means (± standard deviation (SD)). The level of significance was set at a 5% critical level ($p < 0.05$).

3. Results

3.1. Participants

17 patients constituted the PAD-IC group, 16 the Controls group. There was no significant difference between groups concerning anthropometric parameters (Table 1). The PAD-IC presented a more significant prevalence of cardiovascular risk factors (except for hypertension, which is corrected by medications). Logically, controls walked significantly longer than PAD-IC patients.

3.2. PAD-IC group

3.2.1. Index of coactivation

3.2.1.1. First double support

No significant pain or leg effects were revealed in first double support.

3.2.1.2. Single support

The two-way ANOVA showed a significant interaction of effects (Leg × Pain) on $CI_{(GM/TA)}$ ($F_{(2, 93)} = 4.84$, $p = 0.008$, $\alpha^2=0.10$, $\beta=0.78$). The $CI_{(GM/TA)}$ of the symptomatic leg was higher during the pain period compared to the pain-free period ($p = 0.015$). During the pain period, the $CI_{(GM/TA)}$ of the symptomatic leg was higher than that of the asymptomatic leg ($p = 0.021$). The $CI_{(GM/TA)}$ of the asymptomatic leg was higher during the max-pain period compared to the pain period ($p = 0.012$) (Figure 2).

3.2.1.3. Second double support

The two-way ANOVA showed a significant effect of leg ($F_{(1, 93)} = 12.51$, $p<0.001$, $\alpha^2=0.13$, $\beta=0.94$) and an interaction of effects (Leg × Pain) on $CI_{(GM/TA)}$ ($F_{(2, 93)} = 7.32$, $p<0.001$, $\alpha^2=0.15$, $\beta=0.92$). The $CI_{(GM/TA)}$ of the symptomatic leg was higher during the pain period compared to the pain-free period, and during the max-pain period compared to the pain-free period ($p = 0.024$). During the pain and max-pain periods, the $CI_{(GM/TA)}$ of the symptomatic leg was higher than that of the asymptomatic leg ($p = 0.016$) (Figure 2).

3.2.1.4. Swing phase

No significant pain or leg effects were revealed in the swing phase.

3.2.2. Vertical ground reaction force

The two-way ANOVA showed a significant effect of pain ($F_{(1, 93)} = 7.03$, $p=0.001$, $\alpha^2=0.13$, $\beta=0.92$) but no interaction of effects. For Peak 1, significant decreases were found between the pain-free and pain periods with the max-pain period in both legs ($p<0.001$, $p=0.023$ respectively for the symptomatic leg, and $p=0.036$, $p<0.001$ respectively for the asymptomatic leg). In the symptomatic leg, there was also a decrease between pain-free and pain periods ($p=0.033$). For Peak 2, the symptomatic leg presented a significant decrease between the pain-free and pain periods with the max-pain period ($p<0.001$, $p=0.038$ respectively). During the max-pain period, Peak 2 was lower in the symptomatic leg than in the asymptomatic one ($p=0.050$) (Figure 3).

3.2.3. Correlations

There was a significant negative correlation between CI and Peak 2 during the three periods of the gait during the second double support in the symptomatic leg (pain-free $r = -0.57$, pain $r = -0.76$, max-pain $r = -0.78$) (Figure 4).

3.3. Controls

No significant differences between legs nor between phases were revealed in gait parameters and muscle coactivation.

4. Discussion

Many studies previously highlighted changes in gait parameters in PAD-IC patients but there are few concerning the related neuromuscular adaptations. We highlighted here that the increase of pain during walking in PAD-IC patients induces the increase of the $CI_{(GM/TA)}$ during single support and second double support related to the decrease of the second peak force in the symptomatic leg. This suggests a compensatory strategy to reduce load in the painful limb.

The consequences of PAD-IC for muscles are widely described and some authors referred to “the myopathy of PAD” [18,19]. Indeed, PAD-IC induces not only muscular (e.g., muscle strength, fiber type, size, metabolism) but also neuromuscular consequences (e.g., partial denervation of legs muscles and loss in nerve conduction velocity) [11]. King et al. (2015) reported that PAD-IC patients present lower activation capacity [20]. In addition, GM and TA are two important muscles for locomotion [21]. In PAD-IC patients, the calf (and consequently, GM) is the most quoted site for pain location during walking. The GM is principally activated when a stabilization of the leg during the support phase and forward propulsion is required [22,23]. We demonstrate in this study that the onset of pain and the maximum pain increase the GM/TA coactivation pattern in PAD-IC patients, and principally in the symptomatic (painful and ischemic) leg (significant interaction effect of Leg x Pain). This phenomenon occurs only during the two phases of the gait where the GM is the most involved, i.e. single support and second double support. These results fit with the muscular pain adaptation theory [3,24] but they also reveal a particular motor adaptation to pain. Indeed, during single support, the symptomatic leg presents an increase of the CI between the pain-free and pain periods, but then, CI remains stable until the max-pain period. On the other hand, the asymptomatic leg presents an increase of the CI between the pain and max-pain periods. We hypothesize that the neuromuscular adaptations in response to pain onset occur

first in the symptomatic leg to reduce the activation of the GM and consequently its functional use. This would limit pain sensation and its development. Later, the asymptomatic (non-ischemic, non-painful) leg modifies the GM/TA coactivation modalities to adapt to the contralateral leg in order to limit gait alterations. This adaptation pattern between the two legs leads to a significant difference between legs in CI during the pain period. Moreover, the second double support is a propulsive phase during which the GM is highly involved (plantarflexion). This likely explains why we observed significant differences between the pain-free, pain and max-pain periods in the symptomatic leg only during this specific phase of the gait. As a result, significant differences were observed in CI between legs during pain and max-pain periods.

Theories about motor adaptations to pain suggest that they present short-term benefits (i.e., reduction of pain and reduced load on painful muscles) but also induce negative long-term consequences (i.e., increase of the biomechanical constraints at tendon and muscle levels in non-painful areas and then higher risk of injuries) [25]. By studying motor adaptations to locally induced muscle pain in knee extensor muscles, Brøchner Nielsen et al. (2017) confirmed that motor adaptations to pain occurred to decrease biomechanical constraint (i.e. load) within the painful tissue [26]. These studies showed that, when pain is induced in one limb during a plantarflexion task, force decreases in the painful limb while it increases in the contralateral non-painful limb, confirming that pain affects the distribution of force between limbs and triggers a compensatory mechanism. This is consistent with our results showing a different neuromuscular adaptation between legs involving coactivation mechanisms. When pain affects GM, its neuromuscular activity is reduced, likely in order to limit its solicitation and the ischemic pain development, leading to an increase of CI. At the same time, the asymptomatic (non-painful) limb implements a motor strategy to maintain the effort.

Increased coactivation is also correlated with the deterioration of gait parameters (such as the duration of stance phase) and of vertical ground reaction forces [8]. In our study, when analyzing vertical ground reaction forces, we observed a decrease of the two peak forces with the increase of pain intensity until maximum pain corresponded to the increase of the CI. Decrease in Peak 1 is found in both legs, whereas Peak 2 presents a significant decrease only in the symptomatic leg (leading to a difference between legs at max-pain). This suggests that changes in Peak 1 are more representative of the overall impact of pain in the lower limbs (weakness), whereas changes in Peak 2, which appear during the second double support where the GM is highly involved (propulsive phase), are more related to the onset of pain. This can explain the negative correlation found between the CI and the Peak 2 during the second double support (Figure 4). These results are in agreement with the decrease in Peak 2 during the pain period compared to the pain-free period in PAD-IC patients previously described [10]. In another study, the ischemic limb exhibited a decrease in propulsive forces in the forefoot during gait, but without any correlation with the onset of claudication pain [27]. In addition, PAD-IC patients showed a 40% higher energy cost of walking compared to a healthy control group, due to an altered mechanical locomotory pattern [28] and compensatory mechanisms [29]. Generally, a high level of energy cost is related to high muscle coactivation and fatigue during walking (i.e., simultaneous activity of an agonist and antagonist muscles) [8]. Therefore, in PAD-IC patients, the lower propulsive force and the probably higher level of energy cost could be partly the consequence of a high level of coactivation in lower limbs. This will warrant further investigations.

Describing the mechanisms by which gait changes occurred in PAD-IC patients could be helpful to adapt care. Indeed, the effectiveness of exercise therapy has been widely described in this population [30,31]. Schieber et al. (2020) observed that the second peak of vertical ground reaction force is decreased after supervised walking exercise therapy in PAD-

IC patients, unlike other parameters such as power generation at the ankle and hip [32]. In addition, an altered coactivation is known to induce walking balance disorders [33]. In our study, we found that a decrease of the second peak of VGRF is related to an increased coactivation. Therefore, it would be of interest to implement a physical rehabilitation program in PAD-IC patients focused on muscular strengthening of the plantar-flexor muscles to improve muscular functioning, reduce coactivation and increase the second peak of VGRF. In particular, it can be used to enhance vertical ground reaction force using real-time biofeedback [34,35]. Indeed, Awad et al. (2014) have shown that the development of the propulsive capacities in the paretic limb in stroke patients improves their functional balance [36]. Coyle et al. (2019) recently described that pain is related to an increased energy cost of walking in patients with chronic low back pain with radiculopathy compared to nonpainful subjects [37]. This confirms the “Pain-Energy Model” concept hypothesizing that pain enhances energy factors, leading to a decline in functional mobility [38]. In PAD-IC patients, the onset of pain induces a higher energy cost of walking [39]. Interestingly, energy cost also increased in level walking (0% slope) but not in uphill walking (7 or 12% slope) compared to controls [28]. This could be related to the deficiency in push-off in PAD-IC patients, inducing greater demand for work in other muscles and a higher energy cost; and to the fact that uphill walking is more energy efficient (reduced lift of the body mass center) [40]. Physical rehabilitation program allows to decrease pain sensation in PAD-IC patients [41]. Thus, in a future investigation, it would be relevant to determine if a physical activity program using uphill walking (allowing not to increase the energy cost [40]) and focused on strengthening of the plantarflexor muscles could be effective for PAD-IC patients to improve their walking capacities, reduce pain and therefore coactivation, energy cost and limit asymmetry.

Limitations

This study is part of a clinical project focusing on gait alterations in PAD-IC patients. Some limitations could be raised concerning the inclusion of patients with diabetes or the choice of the Strandness constant load walking test compared to other clinical test for gait evaluation in PAD-IC patients or ground test. We do believe that these different factors do not affect the conclusion of our study. For specific developments about these points, we invite the readers to consider the arguments developed in our last study [42].

5. Conclusion

This study provided information on coactivation patterns in PAD-IC patients related to pain development in lower limbs during walking. $CI_{(GM/TA)}$ increases during single support and second double support related to the increase of pain sensation during walking in PAD-IC patients, correlated with the decrease in the second peak force in the symptomatic leg. This indicates that pain sensation development in lower limbs leads to a compensatory strategy to reduce load in the painful limb.

These results provide additional insights into the underlying mechanisms by which gait changes occur in PAD-IC patients and also allows for the development of optimal prevention and rehabilitation strategies.

Conflict of interest: The authors declare that they have no competing (financial or personal) interest that could affect their work and objectivity.

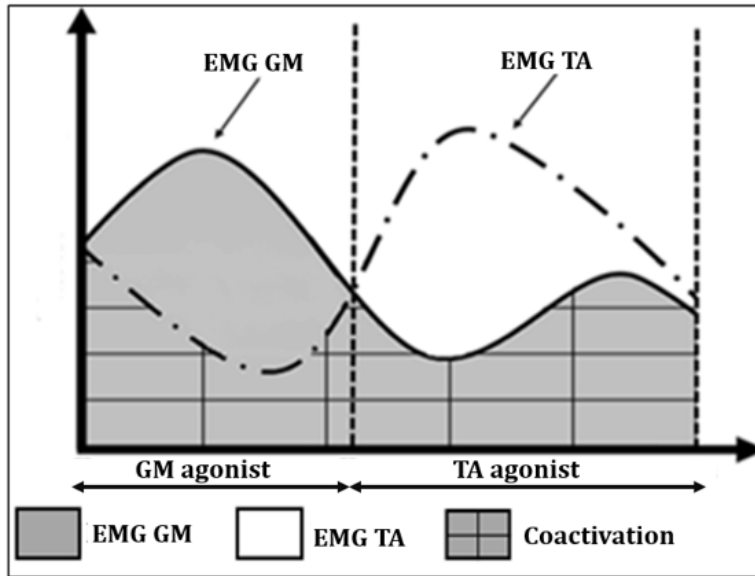
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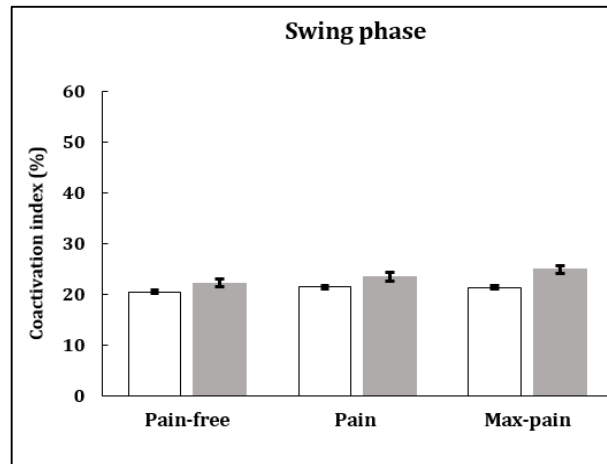
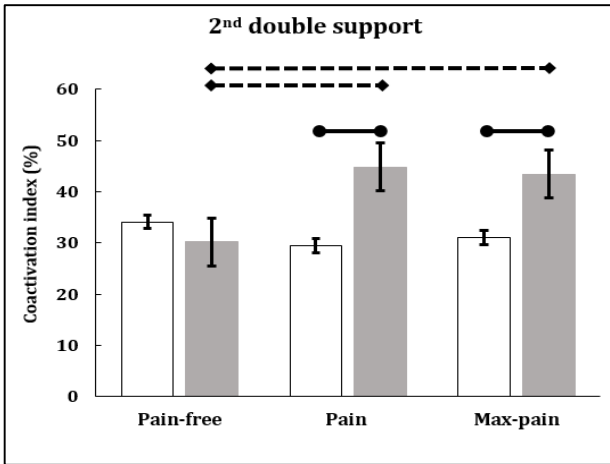
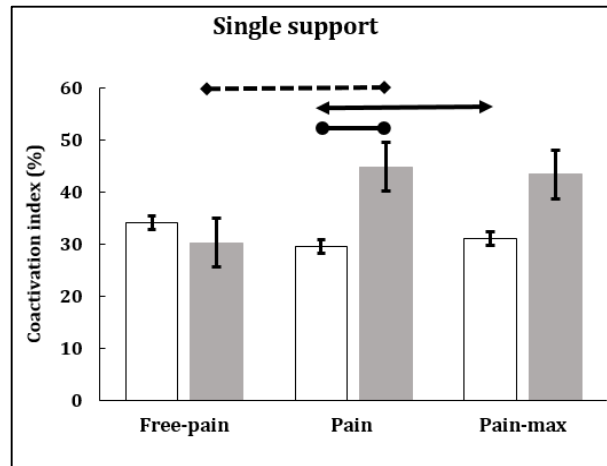
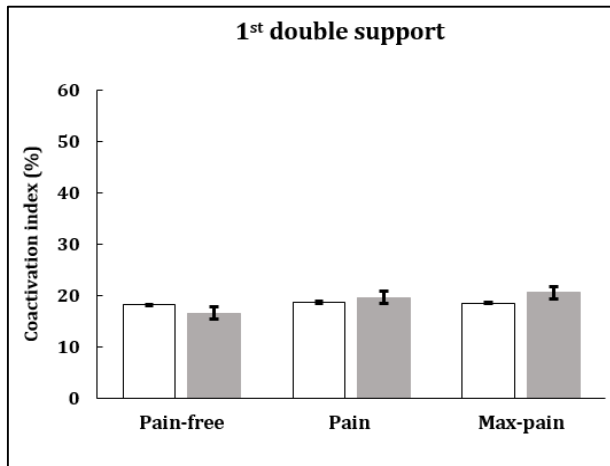
- [1] A.W. Gardner, P.S. Montgomery, R.M. Ritti-Dias, L. Forrester, The effect of claudication pain on temporal and spatial gait measures during self-paced ambulation., *Vasc. Med.* 15 (2010) 21–6. <https://doi.org/10.1177/1358863X09106836>.
- [2] Gardner, P.S. Montgomery, Impaired balance and higher prevalence of falls in subjects with intermittent claudication, *Journals Gerontol. A, Biol. Sci. Med. Sci.* 56 (2001) M454-8. <https://doi.org/10.1093/gerona/56.7.M454>.
- [3] J.P. Lund, R. Donga, C.G. Widmer, C.S. Stohler, The pain-adaptation model: a discussion of the relationship between chronic musculoskeletal pain and motor activity, *Can. J. Physiol. Pharmacol.* 69 (1991) 683–694. <https://doi.org/10.1139/y91-102>.
- [4] A.M. Smith, The coactivation of antagonist muscles, *Can. J. Physiol. Pharmacol.* 59 (1981) 733–747. <https://doi.org/10.1139/y81-110>.
- [5] Y. Iwamoto, M. Takahashi, K. Shinkoda, Differences of muscle co-contraction of the ankle joint between young and elderly adults during dynamic postural control at different speeds, *J. Physiol. Anthropol.* 36 (2017) 1–9. <https://doi.org/10.1186/s40101-017-0149-3>.
- [6] S. Cardarelli, A. Gentili, A. Mengarelli, F. Verdini, S. Fioretti, L. Burattini, F. Di Nardo, Ankle Muscles Co-Activation Patterns During Normal Gait : An Amplitude Evaluation, *IFMBE Proc.* 2 (2017) 1–4.
- [7] F. Di Nardo, A. Mengarelli, E. Maranesi, L. Burattini, S. Fioretti, Assessment of the ankle muscle co-contraction during normal gait : A surface electromyography study, *J. Electromyogr. Kinesiol.* 25 (2015) 347–354. <https://doi.org/10.1016/j.jelekin.2014.10.016>.
- [8] T. Varrecchia, M. Rinaldi, M. Serrao, F. Draicchio, C. Conte, S. Conforto, M. Schmid, Global lower limb muscle coactivation during walking at different speeds : Relationship between spatio-temporal, kinematic, kinetic , and energetic parameters, *J. Electromyogr. Kinesiol.* 43 (2018) 148–157. <https://doi.org/10.1016/j.jelekin.2018.09.012>.
- [9] L.N.M. Gommans, A.T. Smid, M.R.M. Scheltinga, F.A.M. Brooijmans, E.M.J. Van Disseldorp, F.T.P.M. Van Der Linden, K. Meijer, J.A.W. Tejjink, Altered joint kinematics and increased electromyographic muscle activity during walking in patients with intermittent claudication, *J. Vasc. Surg.* 63 (2016) 664–672. <https://doi.org/10.1016/j.jvs.2015.09.045>.
- [10] M.M. Scott-Pandorf, N. Stergiou, J.M. Johanning, L. Robinson, T.G. Lynch, I.I. Pipinos, Peripheral arterial disease affects ground reaction forces during walking, *J. Vasc. Surg.* 46 (2007) 491–499. <https://doi.org/10.1016/j.jvs.2007.05.029>.
- [11] A.E. Harwood, S. King, J. Totty, G.E. Smith, N. Vanicek, I.C. Chetter, A systematic review of muscle morphology and function in intermittent claudication, *J. Vasc. Surg.* 66 (2017) 1241–1257. <https://doi.org/10.1016/j.jvs.2017.05.106>.
- [12] P. Abraham, J. Picquet, B. Vielle, D. Sigauco-roussel, F. Paisant-thouveny, B. Enon, J. Saumet, Transcutaneous Oxygen Pressure Measurements on the Buttocks During Exercise to Detect Proximal Arterial Ischemia Comparison With Arteriography, *Circulation.* (2003) 1896–1900. <https://doi.org/10.1161/01.CIR.0000060500.60646.E0>.

- [13] D.E. Strandness, Exercise testing in the evaluation of patients undergoing direct arterial surgery., *J. Cardiovasc. Surg. (Torino)*. (1970).
- [14] H.J. Hermens, B. Freriks, Disstelhorst-Klug, G. Rau, Development of recommendations for SEMG sensors and sensor, *J. Electromyogr. Kinesiol.* 10 (2000) 361–374.
- [15] C.J. De Luca, L. Donald Gilmore, M. Kuznetsov, S.H. Roy, Filtering the surface EMG signal: Movement artifact and baseline noise contamination, *J. Biomech.* 43 (2010) 1573–1579. <https://doi.org/10.1016/j.jbiomech.2010.01.027>.
- [16] S. Dorel, A. Couturier, F. Hug, Intra-session repeatability of lower limb muscles activation pattern during pedaling, *J. Electromyogr. Kinesiol.* 18 (2008) 857–865. <https://doi.org/10.1016/j.jelekin.2007.03.002>.
- [17] K. Falconer, D.A. Winter, Quantitative assessment of co-contraction at the ankle joint in walking., *Electromyogr. Clin. Neurophysiol.* 25 (1985) 135–49. <http://www.ncbi.nlm.nih.gov/pubmed/3987606>.
- [18] I.I. Pipinos, A.R. Judge, J.T. Selsby, Zhen Zhu, S. a Swanson, A. a Nella, S.L. Dodd, The Myopathy of Peripheral Arterial Occlusive Disease: Part 1. Functional and Histomorphological Changes and Evidence for Mitochondrial Dysfunction, *Vasc. Endovascular Surg.* 41 (2008) 481–489. <https://doi.org/10.1177/1538574407311106>.
- [19] I.I. Pipinos, A.R. Judge, J.T. Selsby, Z. Zhu, S.A. Swanson, A.A. Nella, S.L. Dodd., The Myopathy of Peripheral Arterial Occlusive Disease: Part 2. Oxidative Stress, Neuropathy, and Shift in Muscle Fiber Type, *Vasc. Endovascular Surg.* 42; 101 (2008). <https://doi.org/10.1177/1538574408315995>.
- [20] S. King, N. Vanicek, T.D. O’Brien, Dynamic muscle quality of the plantar flexors is impaired in claudicant patients with peripheral arterial disease and associated with poorer walking endurance, *J. Vasc. Surg.* 62 (2015) 689–697. <https://doi.org/10.1016/j.jvs.2015.03.039>.
- [21] S.L. King, N. Vanicek, T.D. O’Brien, Dynamic muscle quality of the plantar flexors is impaired in claudicant patients with peripheral arterial disease and associated with poorer walking endurance, *J. Vasc. Surg.* (2015) 689–697. <https://doi.org/10.1016/j.jvs.2015.03.039>.
- [22] J.S. Gottschall, Energy cost and muscular activity required for leg swing during walking, *J. Appl. Physiol.* 99 (2005) 23–30. <https://doi.org/10.1152/japplphysiol.01190.2004>.
- [23] F.C. Anderson, M.G. Pandy, Individual muscle contributions to support in normal walking, *Gait Posture.* 17 (2003) 159–169. [https://doi.org/10.1016/S0966-6362\(02\)00073-5](https://doi.org/10.1016/S0966-6362(02)00073-5).
- [24] P.W. Hodges, K. Tucker, Moving differently in pain: A new theory to explain the adaptation to pain, *Pain.* 152 (2011) S90–S98. <https://doi.org/10.1016/j.pain.2010.10.020>.
- [25] F. Hug, P.W. Hodges, T.J. Carroll, E. De Martino, J. Magnard, K. Tucker, Motor adaptations to pain during a bilateral plantarflexion task: Does the cost of using the non-painful limb matter, *PLoS One.* 11 (2016) 1–17. <https://doi.org/10.1371/journal.pone.0154524>.

- [26] N.P. Brøchner Nielsen, K. Tucker, S. Dorel, A. Guével, F. Hug, Motor adaptations to local muscle pain during a bilateral cyclic task, *Exp. Brain Res.* 235 (2017) 607–614. <https://doi.org/10.1007/s00221-016-4826-y>.
- [27] R. Ayzin Rosoky, N. Wolosker, B. Muraco-Netto, P. Puech-Leão, Ground reaction force pattern in limbs with intermittent claudication, *Eur. J. Vasc. Endovasc. Surg.* 20 (2000) 254–259. <https://doi.org/10.1053/ejvs.2000.1146>.
- [28] C. Marconi, G. Ferretti, S. Anchisi, M. Catalano, G. Scandale, A. Antico, G. Iob, F. Peinetti, P. Cerretelli, Energetics of walking in patients with peripheral arterial disease : a proposed functional evaluation protocol, *Clin. Sci.* 111 (2003) 105–111. <https://doi.org/10.1042/CS20020310>.
- [29] R. Wang, E.M. Gutierrez-farewik, Compensatory strategies during walking in response to excessive muscle co-contraction at the ankle joint, *Gait Posture.* 39 (2014) 926–932. <https://doi.org/10.1016/j.gaitpost.2013.12.002>.
- [30] W.B. Baker, Z. Li, S.S. Schenkel, M. Chandra, D.R. Busch, E.K. Englund, K.H. Schmitz, A.G. Yodh, T.F. Floyd, E.R. Mohler, Effects of Exercise Training on Calf Muscle Oxygen Extraction and Blood Flow in Patients with Peripheral Artery Disease, *J. Appl. Physiol.* (2017) jap.00585.2017. <https://doi.org/10.1152/jappphysiol.00585.2017>.
- [31] D. Treat-Jacobson, M.M. McDermott, U.G. Bronas, U. Campia, T.C. Collins, M.H. Criqui, A.W. Gardner, W.R. Hiatt, J.G. Regensteiner, K. Rich, Optimal Exercise Programs for Patients with Peripheral Artery Disease: A Scientific Statement from the American Heart Association, *Circulation.* 139 (2019) E10–E33. <https://doi.org/10.1161/CIR.0000000000000623>.
- [32] M.N. Schieber, I.I. Pipinos, J.M. Johanning, G.P. Casale, M.A. Williams, H.K. DeSpiegelaere, B. Senderling, S.A. Myers, Supervised walking exercise therapy improves gait biomechanics in patients with peripheral artery disease, *J. Vasc. Surg.* 71 (2020) 575–583. <https://doi.org/10.1016/j.jvs.2019.05.044>.
- [33] J.D. Thompson, P. Plummer, J.R. Franz, Age and falls history effects on antagonist leg muscle coactivation during walking with balance perturbations, *Clin. Biomech.* 59 (2018) 94–100. <https://doi.org/10.1016/j.clinbiomech.2018.09.011>.
- [34] M.G. Browne, J.R. Franz, More push from your push-off: Joint-level modifications to modulate propulsive forces in old age, *PLoS One.* 13 (2018) 1–14. <https://doi.org/10.1371/journal.pone.0201407>.
- [35] B.A. Luc-Harkey, J.R. Franz, J.T. Blackburn, D.A. Padua, A.C. Hackney, B. Pietrosimone, Real-time biofeedback can increase and decrease vertical ground reaction force, knee flexion excursion, and knee extension moment during walking in individuals with anterior cruciate ligament reconstruction, *J. Biomech.* 76 (2018) 94–102. <https://doi.org/10.1016/j.jbiomech.2018.05.043>.
- [36] L.N. Awad, D.S. Reisman, T.M. Kesar, S.A. Binder-Macleod, Targeting paretic propulsion to improve poststroke walking function: A preliminary study, *Arch. Phys. Med. Rehabil.* 95 (2014) 840–848. <https://doi.org/10.1016/j.apmr.2013.12.012>.
- [37] P.C. Coyle, J.M. Pugliese, J.M. Sions, M.S. Eskander, J.A. Schrack, G.E. Hicks, Pain Provocation and the Energy Cost of Walking: A Matched Comparison Study of Older Adults With and Without Chronic Low Back Pain With Radiculopathy, *J. Geriatr.*

- Phys. Ther. 42 (2019) E97–E104. <https://doi.org/10.1519/JPT.0000000000000212>.
- [38] P.C. Coyle, J.A. Schrack, G.E. Hicks, Pain energy model of mobility limitation in the older adult, *Pain Med. (United States)*. 19 (2018) 1559–1569. <https://doi.org/10.1093/pm/pnx089>.
- [39] A.W. Gardner, R.M. Ritti-Dias, J.A. Stoner, P.S. Montgomery, K.J. Scott, S.M. Blevins, Walking economy before and after the onset of claudication pain in patients with peripheral arterial disease, *J. Vasc. Surg.* 51 (2010) 628–633. <https://doi.org/10.1016/j.jvs.2009.09.053>.
- [40] T.W.P. Huang, K.A. Shorter, P.G. Adamczyk, A.D. Kuo, Mechanical and energetic consequences of reduced ankle plantar-flexion in human walking, *J. Exp. Biol.* 218 (2015) 3541–3550. <https://doi.org/10.1242/jeb.113910>.
- [41] R. Lane, A. Harwood, L. Watson, L. Gc, Exercise for intermittent claudication (Review), (2017). <https://doi.org/10.1002/14651858.CD000990.pub4.www.cochranelibrary.com>.
- [42] C. Guilleron, S. Durand, W. Maktouf, S. Henni, P. Abraham, B. Beaune, Rearfoot-forefoot profile defined by vertical ground reaction forces during gait is altered in patients with unilateral intermittent claudication, *J. Biomech.* (2020) 109966. <https://doi.org/10.1016/j.jbiomech.2020.109966>.



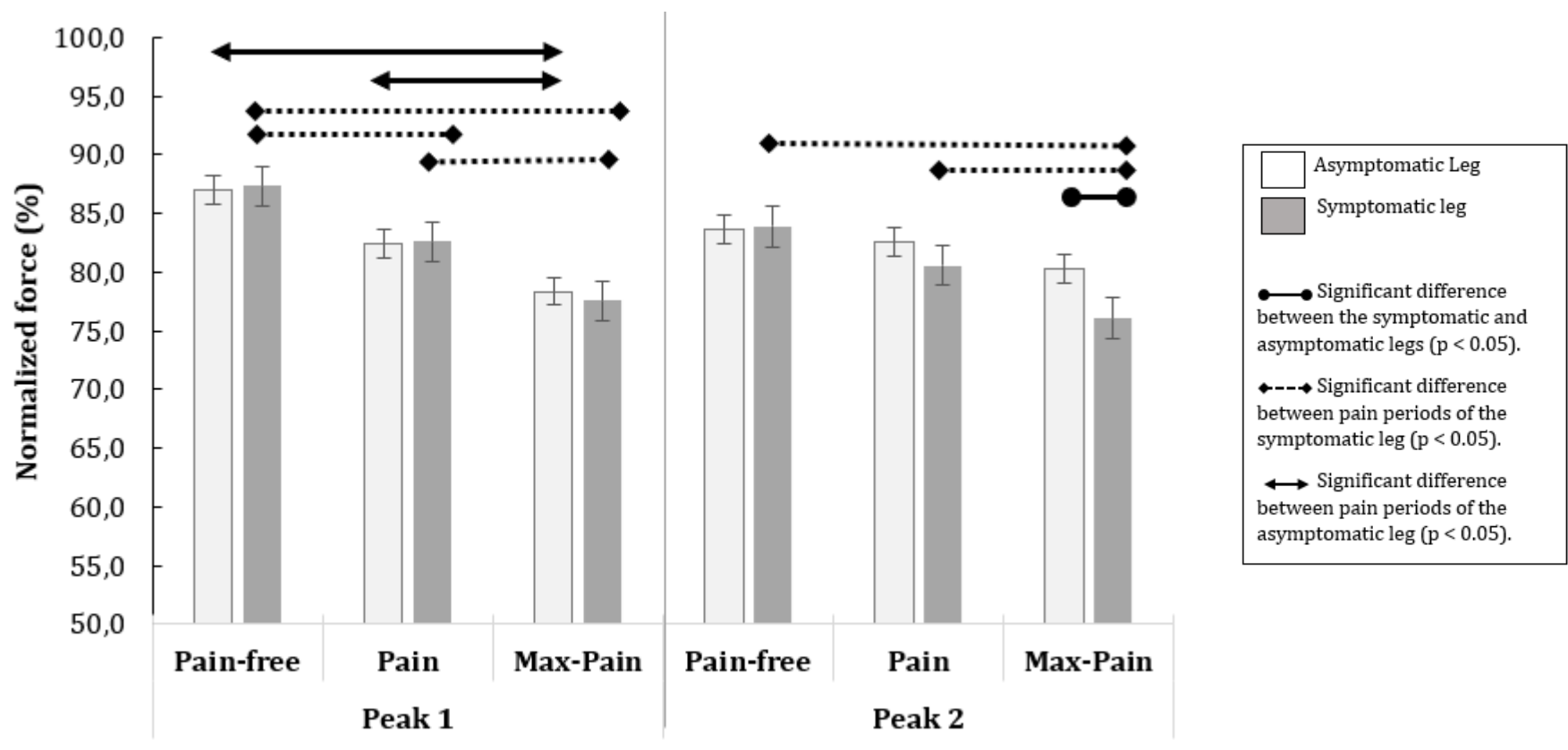


Asymptomatic Leg
 Symptomatic leg

Significant difference between the symptomatic and asymptomatic legs ($p < 0.05$).

Significant difference between the different periods of the symptomatic leg ($p < 0.05$).

Significant difference between the different periods of the asymptomatic leg ($p < 0.05$).



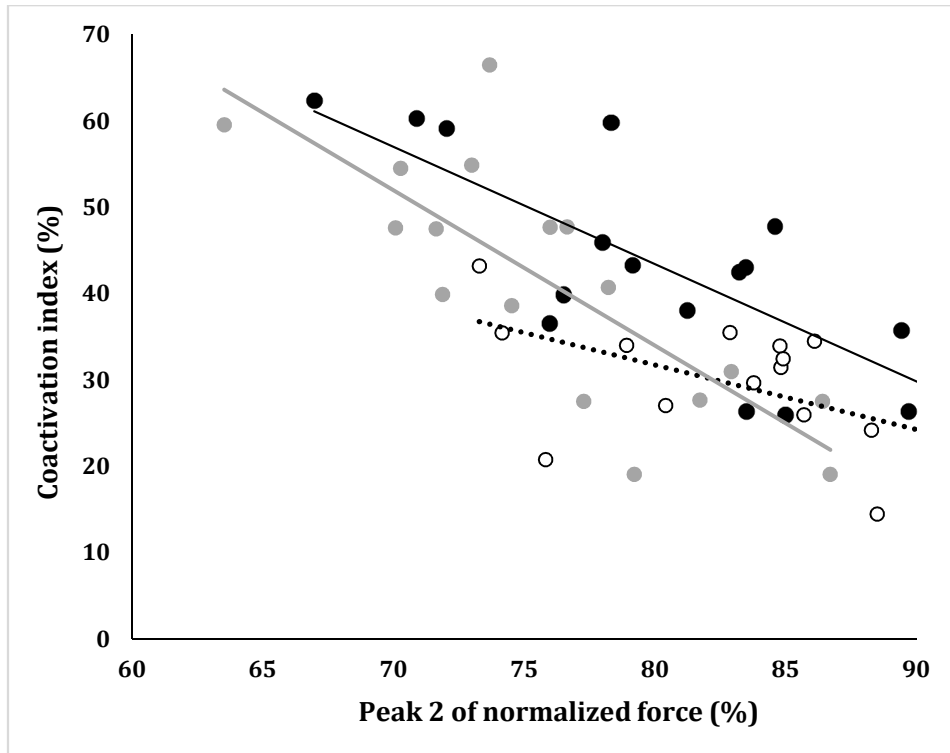


Table 1: Characteristics of the groups (*mean(SD)*)

Group / Characteristic	PAD-IC (n=17)	Controls (n=16)
Age (years)	66(7)	64(7)
Height (m)	1.71(0.07)	1.68(0.10)
Mass (kg)	76(14)	75(14)
Body Mass Index (kg/m ²)	25.8(4.4)	26.4(3.9)
ABI (Symptomatic or right leg) ‡	0.63(0.15)*	1.12(0.19)
ABI (Asymptomatic or left leg) ‡	0.95(0.13)*	1.16(0.19)
Maximal absolute DROP (mmHg) (Symptomatic or right leg) ‡	36.0(17.4)*	4.6(4.1)
Maximal absolute DROP (mmHg) (Asymptomatic or left leg) ‡	14.7(8.1)*	5.4(3.7)
Smoking (n)	14*	9
Active smoker	11*	3
Hypertension (n)	6	10
Diabetes (n)	5	2
Hypercholesterolemia (n)	5*	11
Distance for onset of pain (m)	107(62)	/
Maximal Walking Distance (m)	290(184)*	1074(259)

‡: Refers to the symptomatic and asymptomatic legs in PAD-IC, and to the right and left legs in controls

*: $P < 0.05$ between Peripheral Arterial Disease with Intermittent Claudication (PAD-IC) and controls groups
ABI: ankle brachial index, DROP: Delta from rest of Oxygen Pressure.