Using Daily Steps to Identify Patients with Peripheral Artery Disease with High Sedentary Time and Low Physical Activity

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FUNDING: CNPq #409707/2016-3 and # 310508/2017-7, FAPESP #2016/16425-9, CAPES #01

DISCLOSURE: The authors declared no conflict of interest.

Patients with peripheral artery disease exhibit limitations in performing physical activities[1] In these patients, high sedentary time (ST) and/or low moderate-to-vigorous physical activity (MVPA) have been linked to adverse health outcomes[2] However, the identification of patients with an unhealthy combined profile of ST/MVPA (i.e., co-occurrence of physical inactivity and elevated ST) remains challenging in clinical practice Previous research has demonstrated that daily steps can be used to identify an unhealthy combined profile of ST/MVPA in older adults[3] However, the proposed cut-off point may not be suitable for patients with peripheral artery disease and claudication symptoms. Herein, our aim was to establish specific cut-off points for distinguishing between healthy and unhealthy combined profiles of ST/MVPA among patients with peripheral artery disease and claudication symptoms.

This cross-sectional study recruited patients with peripheral artery disease (ankle-brachial index ≤0.90), with practice of physical activity limited only by claudication symptoms at hospitals in Sao Paulo, Brazil. Patients were included according to the following criteria: a) ≥40 years; b) claudication symptoms in one or two legs; c) absence of critical limb ischemia or rest pain; d) absence of noncompressible vessels; e) no amputated limbs and/or ulcers. This study was approved by the institutional ethics committee.

Patients' characteristics was identified by clinician evaluation, medication use and/or by medical record review. Body weight and height were measured, and body mass index was calculated. Peripheral artery disease severity was verified by the ankle-brachial index, as the highest systolic blood pressure in the posterior tibial or dorsalis pedis artery divided by the highest systolic blood pressure in the brachial artery in both limbs using a vascular Doppler (Medmega DV160, Brazil). The six-minute walk test was performed using standardized procedures and the results were expressed in meters and relativized based on normative values of healthy individuals[4]

Daily steps, ST, and MVPA were assessed using the GT3X+ accelerometer (Actigraph, Pensacola, FL, USA) for seven consecutive days, following the standardized procedures[5]. The device was attached to an elastic belt and attached to the right side of the hip. Periods with consecutive values of zero for 60 min or longer were interpreted as "accelerometer not worn" and excluded from the analysis. Physical activity data were included only if the participant had accumulated a minimum of 10 hours/day of recording for at least four days, including one weekend day. ST and MVPA was calculated using cut-offs points for older adults (0-99 and ≥1952 cpm, respectively)[6] Daily steps were calculated by the amount of steps/day. Data analysis was adjusted for the time and number of days the device was worn. The combined profiles of ST/MVPA were defined as follows: i) unhealthy: highest tertile of ST and lowest tertile of MVPA; ii) healthy: lowest tertile of ST and highest tertile of MVPA[3]. The remaining combinations were classified as "neutral".

Receiver operating characteristic curves were constructed to assess the ability of daily steps to discriminate between patients with peripheral artery disease with healthy and unhealthy combined profiles of ST/MVPA. Cut-off points were obtained by minimizing the distance between points on the receiver operating characteristic curve and the upper left corner. Afterwards, the ankle-brachial index, absolute and relative six-minute walk test distances were compared between the healthy, neutral, and unhealthy profiles using generalized linear models adjusted by age, time of diagnosis, ST, MVPA, diabetes, stroke, use of vasodilator and antidiabetic medications. Data are presented in mean ± standard deviation, or relative frequency. $P \leq 0.05$ was accepted as significant.

Receiver operating characteristic curve analysis showed that daily steps discriminated between patients with PAD with healthy, neutral, and unhealthy combined profiles of ST/MVPA (Figure 1, Panel A and B). These findings support the use of daily steps as clinically useful metric to discriminate between patients with peripheral artery disease with healthy and unhealthy combined profiles of ST/MVPA. The identified cut-off points derived from the ROC curves for healthy (≥5,700 steps/day) and unhealthy (≤3,137 steps/day) combined profiles of ST/MVPA were lower than those previously reported in older adults free of cardiovascular diseases (≥7,134 and ≤5,263 steps/day, respectively)[3] This difference may be attributed to the walking impairment of patients with peripheral artery disease and claudication symptoms, which is a major barrier to physical activity for them[7]

Insert Figure 1

The patients' characteristics according to combined profiles of ST/MVPA are included in supplemental table 1. Out of 233 (66±9 years, 63% males, 27.4±5.3 kg/m^2; ankle-brachial index: 0.59±0.19 [0.17; 0.89]), 66 patients were identified with healthy and 76 with unhealthy combined profiles of ST/MVPA, with the remaining 91 patients identified with a "neutral" profile. Patients with an unhealthy profile were older compared to the neutral and healthy profiles ($p<0.05$), while also having a greater time of diagnosis compared to those with a healthy profile ($p<0.05$). Patients within the healthy profile spent more time in MVPA and less ST compared to both the neutral and unhealthy profile groups. Overall ST/MVPA results are in accordance with previous data investigating physical activity and ST in patients with peripheral artery disease[8,9].

Patients with healthy combined profile of ST/MVPA had greater relative (60±25% healthy vs. 46±24% unhealthy; p=0.004) six-minute walk test distance compared to the unhealthy profile, and greater absolute six-minute walk test distance compared to the neutral and unhealthy profiles (370±80 m healthy vs. 326±87 m neutral vs. 285±75 m unhealthy; $p<0.05$). Ankle-brachial index was higher in the neutral compared to the unhealthy profile (0.62±0.19 neutral vs. 0.55±0.18 unhealthy, p=0.023; Panel D). The six-minute walk test distance is strongly associated with mobility loss, adverse cardiovascular events, and mortality in patients with peripheral artery disease[10]. Patients with an unhealthy combined profile of ST/MVPA exhibited lower absolute and relative six-minute walk test distances, the latter considering sex, age, and body mass index when measuring walking distance. This demonstrates that the establishing of combined profiles of ST/MVPA seems to be more sensitive in detecting walking impairment in these patients. A previous study[11] has shown a positive association between MVPA and the six-minute walk test distance in patients with peripheral artery disease, and that reallocating 30 minutes per week from ST to MVPA was associated with higher six-minute walk test distance, highlighting the beneficial effect of increasing MVPA in this population. On the other hand, the ankle-brachial index, considered one of the best prognostic indexes in peripheral arterial disease has limited correlation with MVPA[12], which aligns with the ankle-brachial index values observed in our study.

A limitation that can be highlighted in this study is the use of a research-grade device instead of a commercially accessible one, which restricts its relevance in real-world settings, even though the accelerometer serves as the gold standard for physical activity and ST measurement and wearable devices are validated through accelerometer data.

In conclusion, our data derived from the receiver operating curves indicate that patients with peripheral artery disease who achieve ≥6,000 steps/day, which is an informative metric to facilitate clinician-patient communication, have the healthiest combined profile of ST/MVPA. Therefore, this number of steps could be a target for these patients. On the other hand, patients who take less than 3,000 steps per day are highly likely to present an unhealthy combined profile of ST/MVPA, requiring closer and more tailored care. Based on previous evidence[13] it is suggested that increasing daily step counts by ≥1,000 steps can provide health benefits and should be recommended for patients with an unhealthy combined profile of ST/MVPA. Considering the widespread availability of wearable technologies and smartphone apps that allow the assessment and monitoring of daily step counts, our findings have important and meaningful implications for various healthcare professionals in their daily practice, as any person in possession of a wearable device could monitor themselves and set step count goals in their daily lives.

References

1. Gerage AM, Correia M de A, de Oliveira PML, et al. Physical activity levels in peripheral artery disease patients. *Arq Bras Cardiol*. 2019;113(3):410-416. doi:10.5935/abc.20190142

2. Garg PK, Tian L, Criqui MH, et al. Physical activity during daily life and mortality in patients with peripheral arterial disease. *Circulation*. 2006;114(3). doi:10.1161/CIRCULATIONAHA.105.605246
3. Costa EC, Freire YA, Alves CPL, Cabral LLP, Barreira T V., Debra L. Waterse. Using Daily Steps to Identify Older Adults with (Un)healthy Joint Profiles of Sedentary Time and Physical Activity: A Starting Point. *PREPRINT (Version 1) available at Research Square* . Published online 2023. doi:https://doi.org/10.21203/rs.3.rs-3041511/v1
4. Ritti-Dias RM, Sant'anna F da S, Braghieri HA, et al. Expanding the Use of Six-Minute Walking Test in Patients with Intermittent Claudication. *Ann Vasc Surg*. 2021;70:258-262. doi:10.1016/j.avsg.2020.07.047
5. Copeland JL, Esliger DW. Accelerometer assessment of physical activity in active, healthy older adults. *J Aging Phys Act*. 2009;17(1). doi:10.1123/japa.17.1.17
6. Buman MP, Hekler EB, Haskell WL, et al. Objective light-intensity physical activity associations with rated health in older adults. *Am J Epidemiol*. 2010;172(10). doi:10.1093/aje/kwq249
7. Cavalcante BR, Farah BQ, Barbosa JPDA, et al. Are the barriers for physical activity practice equal for all peripheral artery disease patients? *Arch Phys Med Rehabil*. 2015;96(2):248-252. doi:10.1016/j.apmr.2014.09.009
8. Hernandez H, Myers SA, Schieber M, et al. Quantification of Daily Physical Activity and Sedentary Behavior of Claudicating Patients. *Ann Vasc Surg*. 2019;55. doi:10.1016/j.avsg.2018.06.017
9. Farah BQ, Ritti-Dias RM, Montgomery PS, Casanegra AI, Silva-Palacios F, Gardner AW. Sedentary behavior is associated with impaired biomarkers in claudicants. *J Vasc Surg*. 2016;63(3):657-663. doi:10.1016/j.jvs.2015.09.018
10. McDermott MM, Guralnik JM, Criqui MH, Liu K, Kibbe MR, Ferrucci L. Six-minute walk is a better outcome measure than treadmill walking tests in therapeutic trials of patients with peripheral artery disease. *Circulation*. 2014;130(1). doi:10.1161/CIRCULATIONAHA.114.007002
11. Germano-Soares AH, Tassitano RM, Farah BQ, et al. Reallocating time from sedentary behavior to physical activity in patients with peripheral artery disease: Analyzing the effects

on walking capacity using compositional data analysis. *J Phys Act Health*. 2021;18(4):426-432. doi:10.1123/JPAH.2020-0487

12. Gardner AW, Ritti-Dias RM, Khurana A, Parker DE. Daily ambulatory activity monitoring in patients with peripheral artery disease. *Physical Therapy Reviews*. 2010;15(3):212-223. doi:10.1179/174328810X12814016178917
13. Paluch AE, Bajpai S, Bassett DR, et al. Daily steps and all-cause mortality: a meta-analysis of 15 international cohorts. *Lancet Public Health*. 2022;7(3). doi:10.1016/S2468-2667(21)00302-9

Figure 1. ROC curve analysis using daily steps for identifying patients with peripheral artery disease with unhealthy (Panel A) and healthy (Panel B) combined profiles of sedentary time and moderate-to-vigorous physical activity (ST/MVPA). Six-minute walk test performance (Panel C) and ankle-brachial index (Panel D) of patients with unhealthy and healthy combined profiles of ST/MVPA.