Predictors of walking capacity in peripheral arterial disease patients

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OBJECTIVE: To estimate walking capacity in intermittent claudication patients through a prediction model based on clinical characteristics and the walking impairment questionnaire.

METHODS: The sample included 133 intermittent claudication patients of both genders aged between 30 and 80 years. Data regarding clinical characteristics, the walking impairment questionnaire and treadmill walking test performance were obtained. Multiple regression modeling was conducted to predict claudication onset distance and total walking distance using clinical characteristics (age, height, mass, body mass index, ankle brachial index lower, gender, history of smoking and co-morbid conditions) and walking impairment questionnaire responses. Comparisons of claudication onset distance and total walking distance measured during treadmill tests and estimated by a regression equation were performed using paired t-tests.

RESULTS: Co-morbid conditions (diabetes and coronary artery disease) and questions related to difficulty in walking short distances (walking indoors – such as around your house and walking 5 blocks) and at low speed (walking 1 block at average speed – usual pace) resulted in the development of new prediction models high significant for claudication onset distance and total walking distance ($p<0.001$). In addition, non-significant differences from the results obtained by the treadmill test and estimated by the current model ($p>0.05$) were observed.

CONCLUSION: The current study demonstrated that walking capacity can be adequately estimated based on co-morbid conditions and responses to the walking impairment questionnaire.

KEYWORDS: Intermittent Claudication; Peripheral Arterial Disease; Walking Prediction; Comorbidities.

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INTRODUCTION

Peripheral artery disease affects lower extremity arteries and reduces oxygen supply to peripheral tissues (1). Intermittent claudication, the most prevalent symptom of peripheral artery disease, leads to reduced walking capacity, which has been associated with all-cause and cardiovascular mortality (2,3), mobility loss (4) and lower extremity strength (5).

Walking capacity in intermittent claudication patients has been assessed in research settings with the standardized treadmill test, which provides the claudication onset distance and total walking distance (6). On the other hand, in clinical settings, the treadmill test is not feasible (7), and other tools to predict walking capacity have been used. Previous studies have proposed specific equations to predict walking capacity in intermittent claudication patients. Gardner et al. (8), validated an equation to predict walking capacity based on ankle-brachial index, body mass index and current smoking status. Recently, Leitch et al. (9), predicted walking capacity with better accuracy using general questions regarding quality of life in the equation.

The walking impairment questionnaire is a specific questionnaire for patients with intermittent claudication which has been used as an alternative tool to assess walking capacity (10,11). Previous studies have shown that the walking impairment questionnaire is more strongly correlated with

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walking capacity than the quality of life questionnaire (12,13). However, whether the walking impairment questionnaire accurately predicts claudication onset distance and total walking distance has not been not previously described.

Our hypothesis is that clinical status and walking impairment questionnaire responses are significant predictors of walking capacity. Therefore, the aim of this study was to estimate the walking capacity in intermittent claudication patients through a prediction model based on clinical characteristics and the walking impairment questionnaire.

MATERIAL AND METHODS

Patients

Four hundred forty consecutive patients were recruited at a tertiary care center that specializes in vascular disease. Patients with peripheral artery disease and claudication symptoms were included in this study if they had an ankle-brachial index $\leq$0.90 at rest, no pain at rest, and no evidence of mental disability identified by the Mini-Mental State Examination Questionnaire (14) and were willing to volunteer to participate in the study. A total of 133 intermittent claudication patients were deemed eligible for the study.

Assessments

Demographic information, height, weight, smoking history and comorbid conditions (hypertension, dyslipidemia, diabetes and coronary artery disease) were obtained through medical history and physical examination. Ankle and arm blood pressures were assessed, and the ankle-brachial index was calculated by the quotient of ankle systolic blood pressure over brachial systolic blood pressure (15).

Walking capacity on treadmill

The patients performed a graded maximal treadmill test (model 2200.1 Trimline; Hebb Industries Inc., Whitehouse, Texas) using a specific protocol for patients with IC as previously described (6). Briefly, the treadmill speed was maintained at 2.0 mph, and the treadmill grade was increased 2% every 2 minutes until the patients could no longer continue because of claudication symptoms. The claudication onset distance and the total walking distance were defined, respectively, as the distance walked when the patient first reported pain in the leg and the distance at which the patient was unable to continue to exercise due to leg pain.

Walking Impairment Questionnaire

The walking impairment questionnaire is composed of 14 items distributed in 4 domains, one including general information and three regarding walking capacity (distance, speed and using stairs). Each item is ranked from 0 to 4 on a Likert scale, in which 0 represents unable to perform and 4 represents no difficulty. These data were obtained through personal interviews. The Brazilian Portuguese version of the walking impairment questionnaire has previously been validated (11).

The distances that are assessed by the walking impairment questionnaire range from walking indoors around the home to walking 5 blocks outside. The speeds are assessed as the difficulty of walking 1 block at each of the following speeds: slowly, average speed, quickly and jogging or running. Stair use ability is assessed by the difficulty of climbing up one, two or three flights of stair. We analyzed the reliability of each question after seven days in a subsample of 25 patients, and the interclass correlation coefficient ranged from 0.76 to 0.98.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS version 10, SPSS Inc., Chicago, Illinois, USA). Normality was verified by the Kolgomorov-Sminorv test. Multiple regression modeling was conducted to predict claudication onset distance and total walking distance from the independent variables: age, height, mass, body mass index, the ankle-brachial index of the lower extremities, gender (male = 1, female = 0), smoking history (yes = 1, no = 0), co-morbid conditions (hypertension, diabetes, dyslipidemia and coronary artery disease; yes = 1, no = 0) and walking impairment questionnaire responses (0 to 4).

The claudication onset distance and total walking distance measured during the treadmill test were compared to the estimated values of claudication onset distance and total walking distance obtained by the regression model using paired t-tests. The accuracy of the regression model was further examined by the absolute error [(absolute difference between predicted and actual value)/actual value x 100] and the proportion of predicted values within 10%, 10-25% and >25% of the treadmill result (16). The significance level was set at $p<0.05$ for all analyses.

Ethics

The procedures used in this study were approved by the Institutional Review Board of the University of Pernambuco and by the Institutional Review Board of the Hospital of Clinics of University of São Paulo. Written informed consent was obtained from each patient prior to investigation.

RESULTS

The characteristics of the sample are shown in Table 1. Most of the patients were male (64.7%) and non-obese. The prevalence of co-morbid conditions ranged from 38.6% (diabetes) to 76.7% (hypertension).

Table 2 displays the responses for each question of the walking impairment questionnaire: 27.9% of patients reported being unable to walk 5 blocks, 85.7% reported that they are not able to jog or run, and 20.3% reported that they are not able to climb three flights of stairs.

Table 1 - General characteristics of intermittent claudication patients (n = 133).

Variables	Values
Age (years)	63.2 ± 8.8
Body mass index (kg.m^{-2})	26.4 ± 4.6
Ankle-brachial index	0.59 ± 0.15
Gender (% men)	64.7
Smoking history (% yes)	84.2
Hypertension (% yes)	76.7
Dyslipidemia (% yes)	70.7
Diabetes (% yes)	38.3
Coronary artery disease (% yes)	56.4

Values are presented in mean ± standard-deviation or frequency.

Table 2 - Frequency of responses on the Walking Impairment Questionnaire in intermittent claudication patients.

Questions	Degree of Difficulty				
	No (%)	Slight (%)	Some (%)	Much (%)	Unable (%)
Distance					
Q1. Walk indoors (such as around your house)	62.4	16.5	14.3	6.0	0.8
Q2. Walk 5 meters	71.3	12.8	9.8	5.3	0.8
Q3. Walk 45 meters	35.3	21.1	21.8	19.5	2.3
Q4. Walk 90 meters	22.6	15.8	18.0	36.8	6.8
Q5. Walk 180 meters	16.5	7.5	18.1	45.1	12.8
Q6. Walk 270 meters	9.8	10.5	10.5	53.4	15.8
Q7. Walk 450 meters	6.0	4.5	12.0	49.6	27.9
Speed					
Q8. Walk 1 block slowly (slower than usual)	38.4	36.8	13.5	10.5	0.8
Q9. Walk 1 block at average speed (usual pace)	11.3	32.3	16.5	33.1	6.8
Q10. Walk 1 block quickly (faster than usual)	4.5	7.5	11.3	40.6	36.1
Q11. Jog or run 1 block	1.5	1.5	1.5	9.8	85.7
Stairs					
Q12. Walk up one flights of stairs	38.3	24.8	9.8	25.6	1.5
Q13. Walk up two flights of stairs	23.3	12.0	18.8	37.6	8.3
Q14. Walk up three flights of stairs	12.0	12.0	11.3	44.4	20.3

Regression analyses indicated that Q1 (walking indoors – such as around your house), Q4 (walking 1 block) and Q9 (walking 1 block at average speed – usual pace) of the walking impairment questionnaire, as well as diabetes and coronary artery disease, were independent predictors of claudication onset distance and total walking distance (Table 3). Prediction models resulted in moderate correlation coefficients (claudication onset distance: $r = 0.52$; total walking distance: $r = 0.58$) and non-significant differences from the results obtained in treadmill test (Estimated by current model: claudication onset distance – 175 ± 81 m and total walking distance – 408 ± 173 m; Measured by the treadmill test: claudication onset distance – 175 ± 155 m and total walking distance – 408 ± 295 m; $p > 0.05$). In addition, absolute errors less than 25% were found for claudication onset distance (21%) and total walking distance (32%) (Figure 1).

DISCUSSION

The current study demonstrated that walking capacity may be adequately estimated based on co-morbid conditions and walking impairment questionnaire questions. Inclusion of co-morbid conditions, such as diabetes and coronary artery disease, as well as questions related to difficulty in walking short distances and at low speeds resulted in the development of new prediction models for walking capacity that are more accurate than previously published models for patients with intermittent claudication (8,9).

In the present study, diabetes and coronary artery disease were independent predictors of walking capacity. Previous studies have shown that diabetes and coronary artery disease are related to walking impairment in intermittent claudication patients (17-20), which has previously been attributed to respiratory, metabolic and vascular dysfunction (21,22). In addition, diabetes has been associated with endothelial dysfunction and increased oxidative stress, pro-inflammatory status and mitochondrial dysfunction (23). Coronary artery disease patients also have endothelial dysfunction and experience reduced cardiorespiratory fitness compared to non-coronary artery disease patients (21).

Although the walking impairment questionnaire has been widely used to assess walking impairment in intermittent claudication patients (13,24,25), whether this questionnaire is able to predict walking capacity has not been previously analyzed. The results of the present study indicate that the walking impairment questionnaire predicts walking capacity in intermittent claudication patients. Questions related to difficulty in walking short distances and walking at low speeds were significantly correlated to claudication onset distance and total walking distance. Thus, it seems that the best questions to predict walking capacity are those indicative of major limitations of the patient.

Interestingly, in the present study, walking impairment questionnaire questions regarding climbing stairs were not predictors of walking capacity in peripheral artery disease patients. Previous studies have observed that the climbing stairs domain of the walking impairment questionnaire was correlated with walking capacity (11-13). However, these studies were performed using bivariate analysis, which does not control for the relationships between the climbing stairs domain and walking capacity to potential confounders, such as clinical characteristics or other walking impairment questionnaire domains.

Poor walking capacity has been associated with increased risk for all-cause and cardiovascular mortality (2,3), mobility

Table 3 - Prediction model for claudication distance and total walking distance in intermittent claudication patients.

Variables	Prediction model	r (r^2)	SEE
CD (m)	= −21.535 + (Q4×25.351) + (Q1×31.484) + (Q9×27.146) - (diabetes presence x 47.909)[a]	0.52 (0.27)	134
TWD (m)	= 109.251 + (Q4×78.825) + (Q1×69.756) - (diabetes presence x 116.255) - (coronary artery disease presence x 98.725)[b]	0.58 (0.34)	242

CD – claudication distance; TWD – total walking distance; [a] $F_4 = 16.66$, $p < 0.001$; [b] $F_4 = 12.07$, $p < 0.001$; r - multiple correlation coefficient, r^2 - variance; SEE - standard estimate of the error; Q – question of Walking Impairment Questionnaire.

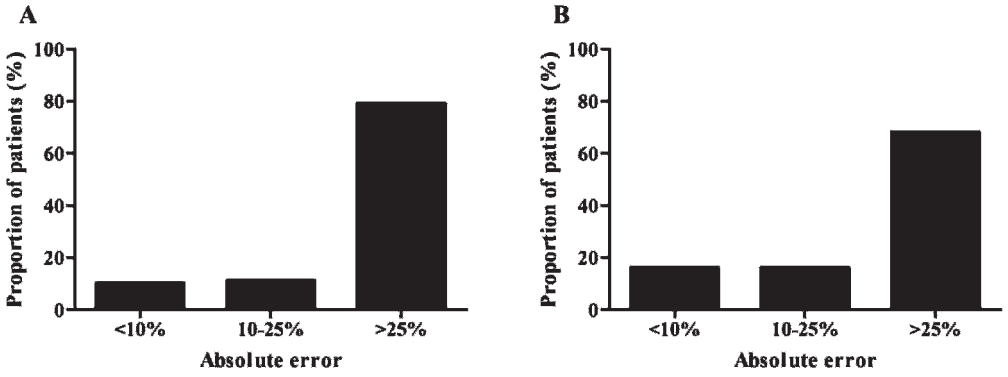

Figure 1 - Distribution of absolute error of the current prediction model for estimating claudication distance (Panel A) and total walking distance (Panel B).

loss (4) and reduced strength in the lower extremities (5). Thus, the assessment of walking capacity is clinically relevant. The results of this study showed that walking capacity is adequately estimated based on clinical characteristics and walking impairment questionnaire questions; this is useful for clinicians to quantify the walking capacity of intermittent claudication patients easily.

The present study has some limitations. Walking capacity was assessed in the graded treadmill test. Therefore, other ways of assessing walking capacity (e.g., the 6-minute test) cannot be predicted using the regression models proposed in this study. The equations for predicting the claudication onset distance and total walking distance were not cross-validated in an independent group of similar peripheral arterial disease patients. This study included only peripheral artery disease patients with claudication symptoms, and the predictive models cannot be extrapolated for patients with peripheral arterial disease in other stages.

In conclusion, the model based on walking impairment questionnaire and co-morbid conditions adequately predicted the walking capacity in intermittent claudication patients. This information is useful for clinicians to easily quantify the walking capacity of intermittent claudication patients.

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■ AUTHOR CONTRIBUTIONS

Farah BQ conceptualized and designed the study, carried out the analyses, drafted the initial manuscript, and approved the manuscript final version for submission. Gobbo LA carried out the analyses and approved the manuscript final version for submission. Barbosa JP, Cucato GG and Chehuen MR performed the data collection, and approved the manuscript final version for submission. Wolosker N and Forjaz CL coordinated and supervised data collection, critical evaluation of the manuscript, and approved the manuscript final version for submission. Ritti-Dias RM conceptualized and designed the study, coordinated and supervised data collection, reviewed the manuscript, and approved the manuscript final version for submission.

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