Minimally Important Difference of the Absolute and Functional Claudication Distance in Patients with Intermittent Claudication

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WHAT THIS PAPER ADDS
It is not clear what improvement or deterioration in walking performance constitutes a meaningful, clinically relevant, change for patients with intermittent claudication. Estimation of the minimally important difference for the absolute and functional claudication distance assessed with a standardized treadmill test is useful for further interpretation of these primary outcome measures.

Objective: Disease severity and treatment outcomes in patients with intermittent claudication (IC) are commonly assessed using walking distance measured with a standardized treadmill test. It is unclear what improvement or deterioration in walking distance constitutes a meaningful, clinically relevant, change from the patients' perspective. The purpose of the present study was to estimate the minimally important difference (MID) for the absolute claudication distance (ACD) and functional claudication distance (FCD) in patients with IC.
Method: The MIDs were estimated using an anchor based approach with a previously defined clinical anchor derived from scores of the walking impairment questionnaire (WIQ) in a similar IC population. Baseline and 3 month follow up data on WIQ scores and walking distances (ACD and FCD) were used from 202 patients receiving supervised exercise therapy from the 2010 EXITPAD randomized controlled trial. The external WIQ anchor was used to form three distinct categories: patients with "clinically relevant improvement," "clinically relevant deterioration," and "no clinically relevant change." The MIDs for improvement and deterioration were defined by the upper and lower limits of the 95% confidence interval of the mean change in ACD and FCD, for the group of IC patients that remained unchanged according to the WIQ anchor.
Results: For the estimation of the MID of the ACD and FCD, 102 and 101 patients were included, respectively. The MID for the ACD was 305 m for improvement, and 147 m for deterioration. The MID for the FCD was 250 m for improvement, and 120 m for deterioration.
Conclusion: The MIDs for the treadmill measured ACD and FCD can be used to interpret the clinical relevance of changes in walking distances after supervised exercise therapy and may be used in both research and individual care.

INTRODUCTION

Intermittent claudication (IC) is the most common symptom of peripheral arterial disease (PAD). Atherosclerosis in the major vessels supplying the lower extremities causes muscle discomfort provoked by exercise in IC patients. Exertional limitation of walking ability leads to functional disability in daily life.[1] Treatment of IC aims at reducing

symptoms and thereby improving walking capacity and health related quality of life (HRQoL).[1,2] Disease severity and treatment outcomes are commonly assessed by walking distance with standardized treadmill tests, and patient reported outcome measures reflecting HRQoL.[1,3]

However, the clinical value of different outcome parameters in IC is currently under debate. Treadmill measured walking distances have been disputed for being an inadequate reflection of walking capacity in daily life,[4,5] and for failing to address actual physical activity limitations.[6] Additionally, walking distances correlate moderately with HRQoL measures.[5] Notwithstanding these concerns, change in walking distance remains an important indicator of treatment effect in clinical decision making.[1,2] Moreover, it functions as the primary end point in most trials assessing

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IC.[1,3] Despite this important role, it is unclear what improvement or deterioration in walking performance constitutes a meaningful, clinically relevant, change from a patient's perspective.

The concept of the minimally important difference (MID) represents the smallest change on an outcome measure that patients value as important.[7] It was first described by Jaeschke et al.[8] in an attempt to elucidate what change in an asthma QoL questionnaire score would be meaningful. Recently, Conijn et al.[9] introduced the MID for an IC population. In their study, the MID was calculated for the Walking Impairment Questionnaire (WIQ); a patient reported assessment of walking impairment. The MID can be used to estimate clinically relevant improvement and deterioration, thus giving meaning to outcome measures such as walking distance. Hiatt et al.[10] postulated an established MID as a requirement for an optimal functional test in PAD. Determination of the MID of walking distance could facilitate clinicians and researchers in their interpretation of this widely used outcome measure.

The purpose of the present study was to estimate the MID for the absolute claudication distance (ACD) and functional claudication distance (FCD) in patients with IC.

MATERIALS AND METHODS

Study population

Data from the 2010 "Exercise Therapy in Peripheral Arterial Disease" (EXITPAD) trial were used. The EXITPAD study was a multicenter, randomized controlled trial of supervised exercise therapy (SET) versus verbal walking advice. Patients with Fontaine stage II peripheral arterial disease (PAD), an ankle brachial index (ABI) <0.9 and an ACD of <500 m were included from 11 outpatient vascular surgery clinics in the Netherlands. Their respective institutional review boards approved the trial and all patients gave written informed consent. Details on methodology were previously published[11]; a brief description of aspects relevant to the current study is given below.

In the present study, baseline and 3 month follow up data on WIQ scores and walking distances were used from the 202 patients receiving SET in the former EXITPAD study. Patients were referred to a local physical therapist and received a SET program according to recommendations in the guidelines of the Royal Dutch Society for Physical Therapy.[12] Prior to SET, all patients received cardiovascular risk management including cholesterol lowering medication, antiplatelet therapy, advice on stopping smoking, and modification of other atherosclerotic risk factors present.

Walking distances

The ACD is defined as the walking distance where intolerable claudication pain forces a patient to stop. An alternative term for ACD is maximal walking distance. The FCD is defined as the distance at which the patient preferred to stop walking because of pain.[13] Walking distances were determined by a standardized progressive treadmill test (i.e.

Gardner_Skinner protocol) with a constant speed of 3.2 km/h starting with 0% incline, increasing every 2 minutes by 2%.[14] The maximum incline was 10%, and the maximum duration of the test 30 minutes (1600 m).[11]

Walking impairment questionnaire

The WIQ is a patient reported outcome measure designed to assess the functional capacity of IC patients. It asks patients to rate their perceived difficulty regarding walking speed, distance and stair climbing. The total WIQ score constitutes a value ranging from 0 to 1. Lower scores represent more impairment. The validated Dutch version of the WIQ was used.[15,16]

Determination of the MID

As per current recommendations an anchor based approach as opposed to a distribution based approach was used in estimating the MID, using longitudinal prospective data.[17] An anchor is an external criterion for a meaningful change, and can be based on patient reported outcome measures that have demonstrated MID in the target population.[18] A previously defined MID for the WIQ was used as an anchor. A study by Conijn et al.[9] reported a MID of −0.03 for deterioration and 0.11 for improvement. Meaning a decrease in WIQ score of ≥0.03 is clinically relevant, as is an improvement of ≥0.11. Based on this anchor the current study population was divided into three categories: patients with "clinically relevant improvement," "clinically relevant deterioration," and "no clinically relevant change." Analogous to Conijn et al.,[9] the MID for improvement was determined using the upper limit of the 95% confidence interval (CI) of the mean change in walking distance of patients who experienced "no clinically relevant change" according to the WIQ anchor. The MID for deterioration was defined by the lower limit of the 95% CI in this "unchanged" category.

Statistical analysis

It is advised that the anchor (WIQ data) and the outcome measure (treadmill based walking distances) are correlated at ≥0.3 to ensure that an appropriate association exists between the two variables.[18] So, the Pearson correlation coefficient was calculated between the change in walking distance (between baseline and after 3 months of SET) and the anchor. Categorical variables were presented as numbers with percentages. Continuous variables were reported as means ± standard deviations if normally distributed, or as medians with interquartile ranges (IQR) in case of a skewed distribution. The methodology required the calculation of 95% CIs in the "no clinically relevant change" category. Thus, when changes in ACD or FCD for the "unchanged" patients demonstrated a distribution that was not normal, these variables were assessed for outliers. One patient who deviated approximately 4 standard deviations from the mean change in ACD, was excluded for this reason. Baseline characteristics were compared using a Pearson's chi-square test for categorical variables and a