Statistical Analysis Plan (SAP)

Supervised Exercise Therapy using Mobile Health Technology in Patients with Peripheral Arterial Disease

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Abbreviations

ABI	Ankle brachial index
PAD	Peripheral arterial disease
QoL	Quality of Life
SET	Supervised exercise training

1. Introduction

To support supervised exercise training (SET) in patients with peripheral arterial disease (PAD), a smartphone app called TrackPAD will be developed. Aim of this pilot study is to evaluate suitability, feasibility, and the impact on a prognosis relevant outcome measure for patients with PAD, the 6-minutes walking test, by using TrackPAD.

Within this statistical analysis plan (SAP), the study design as well as the statistical analysis will be explained in more detail.

2. Study Design

The pilot study is a two-armed, parallel randomized controlled trial with an intervention period of three months, only including patients with diagnosed and symptomatic PAD. A detailed overview of all inclusion criteria as well as exclusion criteria is given in Table 1.

Participants of the control group will continue to receive therapy without further indication. Participants of the intervention group will receive additional access to the TrackPAD-app, which will be considered as a complement to the patients' current treatment. The TrackPAD-app will be freely accessible to the intervention group. Beside the support during the installation procedure, the app will not require further technical maintenance.

The baseline and follow-up examinations will take place in the outpatient clinic of the vascular department and will include a 6-minutes walk test, measurement of the ankle brachial index (ABI) and a questionnaire package including self-reported physical activity, demographic characteristics and the PADQoL (quality of life) questionnaire.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	**Exclusion criteria**
Age ≥ 18 years	Wheelchair bound, use of walking aid or walking impairment due to another cause than PAD
Diagnosis of lower extremity PAD based on (and/or): • ABI ≤ 0.9 in at least one legs • Invasive or non-invasive imaging of stenotic lower extremity artery disease	• Below or above knee amputation • Acute or critical limb ischemia

• Endovascular or surgical revascularization of lower extremity artery	
PAD Fontaine Stage IIa/b	PAD Fontaine Stage I or III / IV
Smartphone with possibility to use TrackPAD: • Android ≥ 5.0 or IOS ≥ 11.0	
Written informed consent prior to any study procedures, including a specified follow-up evaluation	• No German knowledge • Severe cognitive dysfunction
Best-medical treatment in the last 2 months in accordance with standard guidelines	• Congestive heart failure with NYHA III-IV symptoms • Active congestive heart failure requiring the initiation or uptitration of diuretic therapy • Angina pectoris with CCS class 3-4 symptoms or myocardial infarction or stroke in the last 3 months • Active arrhythmia requiring the initiation or uptitration of anti-arrhythmic therapy • Severe valve disease

ABI, ankle-brachial index; CCS, Canadian Cardiovascular Society; NYHA, New York Heart Association; PAD, peripheral arterial disease

2.1. Randomization

All enrolled participants will be randomized by a clinical software (TenAlea) in standard care with or without smartphone-based self-tracking of their physical activity using TrackPAD. The participants will be stratified by their results during the six minutes walking test at baseline (distance less than 362 m, between 362 m and 430 m, more than 430 m).

3. Analysis

For statistical analyses R (version 3.6.0) will be used. In the following, a detailed description of the outcomes, the operationalization and the calculation will be given.

3.1 Primary Outcomes

The primary outcome is defined as the change in the 6-minutes walking distance and will be measured using a standardized protocol at baseline and after 3 months follow-up. The 6-minutes walking

distance test is objective, well-validated in terms of walking ability that predicts mobility loss and mortality in PAD, and has an excellent test-retest reliability.

To examine differences between the two study groups, a t-test will be performed with a significance level of p = 0.05 and a confidence interval (CI) of 95%.

3.2 Secondary Outcomes

The secondary outcome measures are changes in physical activity and the patient's PAD-related quality of life (QoL), as well as an evaluation of the used app TrackPAD.

Changes in physical activity

Changes in physical activity will be recorded by patient self-report and to analyze differences between the two study groups, a t-test will be performed with a significance level of p = 0.05 and a confidence interval (CI) of 95%.

Quality of Life

To measure PAD-related QoL, the PADQoL questionnaire will be used, which is a validated PAD-specific questionnaire. To examine differences in case of QoL, again a t-test will be performed with a significance level of p = 0.05 and a confidence interval (CI) of 95%.

Patient centered app evaluation

An evaluation of the TrackPAD app will be measured with the uMars questionnaire (User version of the Mobile Application Rating Scale). Therefore, the evaluation of the TrackPAD app will be measured by analyzing the questionnaire.