Don’t stop walking: an in-home rehabilitation program for peripheral artery disease patients during the COVID-19 pandemic.

Nicola Lamberti  
University of Ferrara  
https://orcid.org/0000-0001-5763-3069

Soa Straudi  
University hospital of Ferrara

Roberto Manfredini  
roberto.manfredini@unife.it  
University of Ferrara

Alfredo De Giorgi  
University Hospital of Ferrara

Vincenzo Gasbarro  
University of Ferrara

Paolo Zamboni  
University of Ferrara

Fabio Manfredini  
University of Ferrara

Research Article

Keywords: exercise, peripheral artery disease, cardiovascular diseases, rehabilitation, risk factors, mobility

Posted Date: October 6th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-86871/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Version of Record: A version of this preprint was published at Internal and Emergency Medicine on January 7th, 2021. See the published version at https://doi.org/10.1007/s11739-020-02598-4.
Abstract

Aims: We studied the outcomes of peripheral artery disease (PAD) patients enrolled in a structured in-home walking program before the lockdown due to the SARS-CoV-2 epidemic emergency, to determine whether this intervention ensured the maintenance of mobility in the case of strict movement restrictions.

Methods: We considered 83 patients (age 72±11, males n=65) enrolled in a rehabilitation program based on two daily 8-minute sessions of slow intermittent in-home walking at a prescribed cadence with circa-monthly hospital visits. During the lockdown period, the program was updated by phone. The 6-minute (6MWD) and pain-free walking distance (PFWD) were measured pre- and postlockdown. Body weight (BW), blood pressure (BP), and the ankle-brachial index (ABI) were also determined.

Results: Sixty-six patients were measured 117±23 days after their previous visit. A safe, pain-free execution the prescribed sessions, with a median distance covered of 74 km, was reported. Overall, the 6MWD was stable, while PFWD improved (p<0.001). Decreased BW with stable BP and ABI values were also recorded. When considering the outcome values according to the time of enrollment before the lockdown, new-entry subjects (≤3 months; n=35) obtained significant improvements, while those previously enrolled (>3 months; n= 31) were stable.

Conclusion: In PAD patients, a structured exercise program easily performed in a home corridor and guided with phone assistance was adhered to by patients and showed effectiveness in maintaining mobility and risk factor control during the COVID-19 pandemic. Safe structured exercise may involve frail subjects regardless of walking ability, type of home and external conditions.

Introduction

More than 202 million people are living with PAD, and of these, a high percentage includes elderly individuals [1]. PAD affects functional status by evoking classic claudication or atypical exertional leg symptoms and favoring functional impairment and decline in asymptomatic subjects [1,2].

Structured exercise, with supervised exercise being preferred and more effective [3], is part of a comprehensive program to manage disability and cardiovascular risk [4]; however, in recent years, various home-based structured programs have been proposed [2] based on indoor [5,6] or outdoor (guided or assisted by wearable technologic devices, etc.) walking [2,7-9].

Recently, the COVID-19 epidemic emergency has seriously limited the possibility of attending in-hospital supervised exercise, performing outdoor structured home-based programs and taking spontaneous walks [10], particularly in countries where strict movement restrictions have been imposed by the government in an attempt to slow virus transmission [11,12]. Italy was the first European country where, from March 9th to May 3rd (55 days), a series of restrictions on citizens’ mobility were adopted, including exercise and pet walking being allowed only around the home and a self-declaration form specifying the purpose of their movement and their destination being required [10,13].
The fear of contagion, particularly present among elderly people, due to the higher percentage of deaths among elderly individuals [14], limited their willingness to leave home to perform physical activity, e.g., to walk for claudication or medical reasons [15,16].

In addition to such dissuading factors, the reduced availability of non-strictly necessary outpatient services and the limited time of practitioners as well as delayed access to treatment [16,17] in a country where the National Healthcare Service offers free universal access to health care, may have triggered a subsequent wave of worsening of functional status and cardiovascular risk factors including glycemic or blood pressure control [18].

Ten years ago, to improve the mobility of PAD patients and to overcome most barriers to exercise in PAD patients, a structured in-home exercise program was developed for PAD and in an area of the Emilia Romagna Region with a very high aging index [19]. The program, regularly offered to patients with PAD as an outpatient program and successfully tested in stroke survivors and dialysis patients [20-23], is based on bouts of interval walking at progressively increasing speeds that are performed inside the home in a corridor. Only a few controls in the hospital are requested to update the program.

The present study aimed to evaluate the adherence to and the effects of the program in a cohort of elderly patients enrolled before the lockdown in Italy and assisted by phone during this period. The hypothesis was that a minimum but structured dose of exercise would guarantee functional stability in people deprived of the opportunity to walk freely.

**Methods**

*Study design*

This is an observational study that was carried out at the Department of Rehabilitation Medicine at the University Hospital of Ferrara. The Ethics Committee CE-AV approved the study (n. 539/2020) and written informed consent was obtained.

*Subjects and inclusion criteria*

All of the patients who were participating in the vascular rehabilitation program, which is part of the usual care for patients with claudication at University Hospital of Ferrara, at the time of lockdown (March 9th, 2020) were considered eligible for this study.

Males and females aged > 18 years with Leriche-Fontaine Stage II vascular claudication that was stable for at least 3 months are usually enrolled, whereas patients with conditions contraindicating safe training execution at home (e.g., unstable angina, severe heart failure, major amputation or clinical conditions limiting exercise testing) are usually excluded. The presence of PAD was previously diagnosed at the Vascular Surgery Unit of the Hospital of Ferrara by clinical and echo-color-Doppler examination [24].

In this study, all patients started the exercise program no more than 9 months before the lockdown date.
Exercise program

All the patients enrolled were executing the “Test in - Train out” (Ti-To), structured, pain-free home-based exercise program [5,6]. Ti-To program include a center-based phase and a home-based phase with walking exercises. The first phase is composed of circa-monthly visits at the hospital for clinical assessment, hemodynamic and performance measurements, an update of the home-based walking program prescription, and evaluation of patient adherence. The home-based phase includes the execution of training at home, preferably indoors (e.g., hallway, heated garage). The program is based on two daily 8-minute walking sessions per day (six days per week) of intermittent walking (1-minute work and 1-minute seated rest) at a prescribed speed. The training speed, converted into walking cadence (steps/minute), is maintained at home by a metronome as learned in a training session executed during the first visit. The exercise program increases weekly by 3 to 4 steps/min, from 60 to 92-100 steps/min according to the severity of claudication at baseline. Progressively, the length of each bout is amplified with a work:rest ratio from 1:1 to 2:1 and 3:1, while the whole duration of each session remains constant. Patients are asked to fill out a daily training diary, indicating completion of the exercise and any related symptoms. The exercise program ends when the patients reach a pain-free walking distance that is normal for their sex and age or when a stable satisfactory performance is attained. Additional details on the exercise program are reported elsewhere [5,25].

Outcome measures

At entry into the program, information regarding clinical status and functional impairment was collected by consulting patients’ medical documents, by means of physician examination or by specific tests. Body weight (BW) and height were measured for body mass index (BMI) calculation.

Hemodynamic assessment: After five minutes of rest, patients underwent ankle-brachial index (ABI) measurements according to a standard procedure using Doppler ultrasound (Dopplex SD2, Huntleigh Healthcare Ltd. Diagnostics, Cardiff, United Kingdom) and a standard blood pressure (BP) cuff. The leg with the lowest ABI value was considered the worst leg. The vessels were considered “not compressible” for ABI measurements > 1.31. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also collected.

Performance assessment: The 6-minute walking test was executed according to the published standard [26]. Patients were instructed to walk back and forth along a 21-m corridor alone at their own pace with the aim of covering as much distance as possible in 6 minutes. The total distance walked (6-minute walking distance, 6MWD) and the pain-free walking distance (PFWD) were recorded.

For this specific study, two time points of collection were considered: the last hospital visit before the lockdown (Pre) and the first return to the hospital after the lockdown (Post).

Program update during the lockdown period
Considering that the vascular rehabilitation program was closed from March 9th to May 18th 2020, the rehabilitation team remained available by phone during the entire period of closure. A team member called all the patients enrolled to check their health status and to update the exercise program. The scheduled training program progression [5,25], was confirmed if the patients reported regular program execution in the absence of general or peripheral symptoms. Otherwise, the progression was delayed in the presence of incomplete execution or limiting symptoms, with the patients being advised to repeat part of the previous program in the following weeks.

In addition, a quick telephone questionnaire was administered to the patients to examine factors related to exercise execution, clinical status and the characteristics of their home. The questionnaire was composed of nine Yes/No questions, which are reported in Table 1.

**Statistical analysis**

Data are expressed as the mean ± standard deviation for continuous data and as the percentage frequency for categorical data.

The entire enrolled PAD population was divided into two subgroups according to the time since they started the rehabilitation program. The “Rookies” subgroup included patients who started the program within the three months prior to the lockdown, whereas the “Veterans” subgroup included all the other patients who were enrolled more than three months before the lockdown. The cutoff was arbitrarily chosen considering an ideal duration of the program of 6 to 9 months [5] and a timeframe possibly associated with physiological adaptations to the program [25,27]. Pre versus Post comparisons of all outcomes were performed by paired samples t tests or Wilcoxon rank tests according to the data distribution. The between-subgroup comparisons were performed with chi-squared tests, independent samples t tests or Mann-Whitney tests, as appropriate.

Multiple and logistic regression models were employed to identify any factor potentially related to an increased walking ability by defining the performance variations (PFWD and 6MWD) in the Pre-Post period, properly dichotomized when needed, as dependent variables. Independent variables included patient characteristics (age, sex and marital status, cultural level), cardiovascular risk factors, comorbidities, hemodynamic severity and functional limitation (ABI, Pre-PFWD and 6MWD) and the items from the telephone questionnaire.

Statistical analyses were performed with MedCalc Statistical Software version 19.4.0 (MedCalc Software bvba, Ostend, Belgium).

**Results**

Sixty-six out of the 83 patients (80%) who were enrolled in the Ti-To exercise program completed the postlockdown visit and the outcome measurement session. Seventeen patients (20%) did not show up at the follow-up evaluation (Figure 1) for the following reasons: lack of availability (n=10, 12%), acute limb
ischemia (n=1, 1%), intercurrent disease such as low-back pain (n=3, 4%) or hip prosthesis (n=1, 1%), and death (neoplastic disease and COVID-19, n=2, 2%). At the control visit after the lockdown, 35 patients were categorized as “Rookies”, i.e., patients who enrolled less than 3 months before the lockdown, whereas the remaining 31 were categorized as “Veterans”. At baseline, the two subgroups did not present any differences (Table 2).

**Telephone questionnaire results and program update**

All patients answered the simple telephone questionnaire in a median time of 5 minutes. The answers provided by the patients to each question are reported in Table 1. Along with the questionnaire, patients were given the updated program by a team member. No adverse events were reported during execution of the program. Fifty-seven patients (86%) underwent the program progression as scheduled, whereas the remaining 9 patients (14%), due to an insufficient number of sessions performed or intercurrent problems, were advised to repeat the previous program. Six patients needed to contact the rehabilitation team again during the period for more information about the exercise training.

**Outcomes after lockdown**

Patients were subsequently called again starting from May 4\(^{th}\), 2020, to reschedule a hospital visit that occurred after 117 (95% CI 111-123) days after the previous visit.

Patients reported execution of a median of 85% (95% CI 77-100) of the prescribed exercise sessions, for a total of > 2100 minutes (35 hours). The training time considering a step length of 50 cm, and program execution 6 days/week corresponded to a median of 74 kilometers walked inside the house during the lockdown period. No adverse events related to execution of the training were reported, and the majority of the walking sessions were executed in the absence of claudication pain.

In the whole population, BW showed a significant decrease, while stable values were observed in BP (Table 3). The ABI of both limbs did not show significant variations in the Pre-Post period; otherwise, PFWD significantly improved (p<0.001) but not the 6MWD (p=0.13).

Considering the two groups, different responses were observed. The Rookies showed a significant improvement in the ABI of the less impaired limb, SBP, 6MWD, PFWD, and BW; the DPB and ABI of the more impaired limb also showed favorable variations approaching statistical significance (p<0.10).

The Veterans exhibited stable values for almost all outcomes, while positive variations were obtained for PFWD, though not reaching statistical significance. Data are reported in Table 3.

The between-group comparisons showed that significantly greater variations were observed for the 6MWD and PFWD in favor of the Rookies group (Table 3).

**Factors related to favorable performance variations during the lockdown period**
In the whole population, regression analyses were conducted to determine whether any health-related factor or “social” parameter examined through the telephone questionnaire could be related to a favorable performance.

Multiple regressions identified that in a weak model ($R^2 = 0.12; p=0.05$), only the Pre values of the 6MWD were inversely related to variations in the Pre-Post period. A similar model was observed for PFWD variations ($R^2 = 0.16; p=0.028$), including only PFWD-Pre values.

In the logistic regression models, the PFWD and 6MWD variations were dichotomized according to variation equal or greater to the MCID, which is 36 meters in the PAD population [28,29]. Seventeen patients achieved an MCID for PFWD during the lockdown period, and 6 achieved an MCID for 6MWD. No variables were retained in the model for 6MWD; otherwise, a significant model was observed for PFWD ($R^2 =0.10; p=0.039$) with the question “did your cohabitant exercise with you” showing a favorable odds ratio of 4.68 (95% CI: 1.09 to 20.20).

Finally, cardiovascular risk factors, other comorbidities, age, PAD severity by ABI, cultural level, sex and marital status were not included in any model.

**Discussion**

The study confirmed the sustainability and effectiveness of a structured in-home exercise program for PAD patients as well as the ability of patients to adhere to the program during the COVID-19 emergency.

Moreover, in the absence of significant further spontaneous physical activity, the study also highlighted the pure effect on mobility of a program carried out at low-moderate intensity (3-4 METS) that was able to guarantee a minimum of 1000 steps per day. A few minutes of activity performed inside the home in a corridor supported the walking ability of hypomobile patients and favored acceptable control of risk factors, including body weight, blood pressure and diabetes.

Further points of discussion are also offered by the study.

The program did not stop during the lockdown period, and adherence was high (85%), even without intermediate visits and with only remote control, as previously tested in a large randomized trial among dialysis patients [23].

The precise prescription allowed functional stability in the whole population, with functional improvement in PAD patients who started rehabilitation immediately before the lockdown (Rookies) and maintenance of the mobility level among those who previously achieved the benefits and were at the end of their program (Veterans). Interestingly, patients with more severe claudication prelockdown showed more favorable functional improvements, which may not regularly be observed following treadmill-based supervised programs.2.
Interestingly, the hemodynamic parameters also showed a similar pattern (slightly improved or stable), confirming previous observations [6,25,30].

The response was not different by sex, cultural level, marital status, type of house (flat or house with garden and courtyard), city or countryside living, or comorbidities. Interestingly, some family members (14%) also started the in-home walking program prescribed for their partners, and this proactive behavior was a factor correlated with functional improvements.

The characteristics of the program may also explain the outcomes. Unlike home-based programs where patients are generally advised to walk at a self-selected pace or to maximal ischemic leg pain [8,30,31], this program is performed at a lower speed for short bouts in the absence of ischemic pain [5,6,25]. These facts facilitate execution in limited spaces and favor adherence. Finally, only a metronome for maintaining the prescribed walking cadence, a stop-watch, a corridor and a chair to sit in during the resting phase are required.

**Conclusions**

The Ti-To program, designed to overcome the barriers to exercise in an area with a very high aging index [19,32] (almost double the Europe mean value), passed the test during the COVID-19 epidemic. Even if social frailty, i.e., reduced connections to society and little social activity, may be correlated with reduced physical function [33,34], the program was able to ensure stable or improved function in a population with disability that was exposed to strict movement restrictions.

Considering that resilient care systems should be identified to protect vulnerable patients [35], this program offers a facilitated way to carry out regular and safe structured exercise activities to frail subjects, even with telephone support only, regardless of the type of home, atmospheric conditions or epidemic limitations.

**Declarations**

**Funding**

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

**Conflicts of interest**

The authors declare that they have no conflict of interest.

**Ethics approval**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration
and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee CE-AV (n. 539/2020).

**Consent to participate**

Informed consent was obtained from all individual participants included in the study.

**Consent for publication**

Not applicable

**Availability of data and material**

The dataset analyzed during the current study is publicly available in the Mendeley repository, doi: 10.17632/kdgj4rrhdr.1

**Code availability (software application or custom code)**

Not applicable

**Authors' contributions**

FM, SS, RM, ADG, VG, PZ and NL contributed to the conception or design of the work. FM, RM and NL contributed to the acquisition, analysis, or interpretation of data for the work. FM, RM and NL drafted the manuscript. SS, ADG, VG, PZ critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

**References**


Tables

Table 1. The telephone questionnaire and the answers provided by the patients.
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes (%)</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did you exercise regularly at least once a day?</td>
<td>59 (90)</td>
<td>7 (00)</td>
</tr>
<tr>
<td>Did you executed more exercise sessions respect to the prescribed ones?</td>
<td>21 (32)</td>
<td>45 (68)</td>
</tr>
<tr>
<td>Did one of your cohabitant exercise with you?</td>
<td>9 (14)</td>
<td>57 (86)</td>
</tr>
<tr>
<td>Did you feel that your claudication is worsened?</td>
<td>5 (8)</td>
<td>61 (92)</td>
</tr>
<tr>
<td>Did you gain weight?</td>
<td>11 (17)</td>
<td>55 (83)</td>
</tr>
<tr>
<td>Did your blood glucose increase? †</td>
<td>6 (24)</td>
<td>19 (76)</td>
</tr>
<tr>
<td>Do you live in the city?</td>
<td>28 (42)</td>
<td>38 (58)</td>
</tr>
<tr>
<td>Does your house/building have a garden?</td>
<td>60 (91)</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Do you have a dog?</td>
<td>21 (32)</td>
<td>45 (68)</td>
</tr>
<tr>
<td>How big is your house? (m²)</td>
<td>86 ± 21</td>
<td></td>
</tr>
</tbody>
</table>

Legend: † collected only in the sample of diabetes patients.

**Table 2.** Baseline characteristics of the two subgroups of patients.
<table>
<thead>
<tr>
<th></th>
<th>Rookies (n=35)</th>
<th>Veterans (n=31)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73 ± 6</td>
<td>70 ± 14</td>
<td>0.20</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>87 ± 15</td>
<td>85 ± 18</td>
<td>0.66</td>
</tr>
<tr>
<td>BMI (kgm²)</td>
<td>30 ± 4</td>
<td>29 ± 5</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Education, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary school</td>
<td>16 (46)</td>
<td>10 (32)</td>
<td>0.18</td>
</tr>
<tr>
<td>Inferior middle school</td>
<td>15 (43)</td>
<td>9 (29)</td>
<td>0.21</td>
</tr>
<tr>
<td>Superior middle school</td>
<td>3 (9)</td>
<td>10 (32)</td>
<td>0.07</td>
</tr>
<tr>
<td>Degree</td>
<td>1 (3)</td>
<td>2 (7)</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>Risk factors, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>31 (89)</td>
<td>29 (94)</td>
<td>0.49</td>
</tr>
<tr>
<td>Hypertension</td>
<td>33 (94)</td>
<td>28 (91)</td>
<td>0.55</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>26 (74)</td>
<td>21 (68)</td>
<td>0.56</td>
</tr>
<tr>
<td>Diabetes</td>
<td>14 (40)</td>
<td>11 (36)</td>
<td>0.71</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>6 (17)</td>
<td>7 (23)</td>
<td>0.58</td>
</tr>
<tr>
<td>Family history for CVD</td>
<td>3 (9)</td>
<td>6 (19)</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Comorbidities, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>16 (45)</td>
<td>21 (68)</td>
<td>0.08</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>7 (20)</td>
<td>3 (10)</td>
<td>0.24</td>
</tr>
<tr>
<td>Osteoarticular disease</td>
<td>19 (54)</td>
<td>19 (61)</td>
<td>0.58</td>
</tr>
<tr>
<td>Rheumatic diseases</td>
<td>5 (14)</td>
<td>2 (7)</td>
<td>0.30</td>
</tr>
<tr>
<td>Age-adjusted Charlson Comorbidity Index</td>
<td>6 ± 2</td>
<td>6 ± 2</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>Peripheral arterial disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>5 ± 5</td>
<td>5 ± 5</td>
<td>0.89</td>
</tr>
<tr>
<td>Lower limb revascularization</td>
<td>10 (28)</td>
<td>8 (26)</td>
<td>0.80</td>
</tr>
<tr>
<td>Leriche-Fontaine Stage 2a</td>
<td>24 (69)</td>
<td>24 (77)</td>
<td>0.57</td>
</tr>
<tr>
<td>Leriche-Fontaine Stage 2b</td>
<td>9 (31)</td>
<td>9 (23)</td>
<td>0.57</td>
</tr>
<tr>
<td>ABI more affected limb</td>
<td>0.64 ± 0.17</td>
<td>0.65 ± 0.20</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>Whole population</td>
<td>Rookies</td>
<td>Veterans</td>
</tr>
<tr>
<td>--------------------------</td>
<td>------------------</td>
<td>---------</td>
<td>----------</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>86 (82-90)</td>
<td>87 (82-92)</td>
<td>85 (79-91)</td>
</tr>
<tr>
<td></td>
<td>85 * (81-89)</td>
<td>86 * (81-91)</td>
<td>84 (78-91)</td>
</tr>
<tr>
<td><strong>SBP (mmHg)</strong></td>
<td>147 (142-151)</td>
<td>151 (144-158)</td>
<td>147 * (141-153)</td>
</tr>
<tr>
<td></td>
<td>145 (141-149)</td>
<td>147 (141-153)</td>
<td>142 (136-147)</td>
</tr>
<tr>
<td><strong>DBP (mmHg)</strong></td>
<td>76 (74-78)</td>
<td>76 (73-80)</td>
<td>75 (73-78)</td>
</tr>
<tr>
<td></td>
<td>74 (72-76)</td>
<td>74 (71-77)</td>
<td>74 (71-77)</td>
</tr>
<tr>
<td><strong>ABI worst limb</strong></td>
<td>0.64 (0.59-0.69)</td>
<td>0.63 (0.57-0.70)</td>
<td>0.66 (0.59-0.73)</td>
</tr>
<tr>
<td></td>
<td>0.65 (0.60-0.70)</td>
<td>0.66 (0.59-0.73)</td>
<td>0.65 (0.58-0.63)</td>
</tr>
<tr>
<td><strong>ABI best limb</strong></td>
<td>0.85 (0.79-0.91)</td>
<td>0.81 (0.74-0.88)</td>
<td>0.86 * (0.78-0.94)</td>
</tr>
<tr>
<td></td>
<td>0.87 (0.80-0.94)</td>
<td>0.86 * (0.78-0.94)</td>
<td>0.90 (0.79-1.00)</td>
</tr>
<tr>
<td><strong>PFWD (m)</strong></td>
<td>200 (177-222)</td>
<td>192 (163-221)</td>
<td>230 * (199-262)</td>
</tr>
<tr>
<td></td>
<td>227 * (201-252)</td>
<td>230 * (199-262)</td>
<td>209 (171-246)</td>
</tr>
<tr>
<td><strong>6MWD (m)</strong></td>
<td>318 (298-338)</td>
<td>319 (299-338)</td>
<td>332 * (311-352)</td>
</tr>
<tr>
<td></td>
<td>323 (302-344)</td>
<td>332 * (311-352)</td>
<td>318 (281-355)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>319 (271-366)</td>
</tr>
</tbody>
</table>

Legend: data are expressed as mean and 95% Confidence Interval. * Within-group p value < 0.05.

Abbreviations: ABI: Ankle-Brachial Index; SBP: systolic blood pressure; DBP: diastolic blood pressure; PFWD: pain free walking distance; 6MWD: 6-minute walking distance.
**Figures**

**Figure 1**

Study flow diagram of participants enrolled in the period June 2019-March 2020