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Short interval or continuous training programs to improve walking distance for intermittent claudication: pilot study

Short title: Training with active recovery for intermittent claudication

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1 **Short interval or continuous training programs to improve walking distance for**
2 **intermittent claudication: pilot study**

3

4 **Abstract**

5 **Objective.** Supervised exercise training is part of first-line therapies for intermittent
6 claudication. Short periods of intensive treadmill training have been found efficient; however,
7 the optimal modalities remain to be determined, especially interval training with active recovery
8 (ITAR). In this prospective assessor-blinded single-centre pilot study, we assessed the feasibility
9 of a randomised controlled trial comparing parallel 4-week intensive rehabilitation programs
10 comprising treadmill training performed as ITAR or conventional training with constant slope
11 and speed interspersed with rest periods (CT).

12 **Methods.** A total of 38 in- or out-patients were randomised to the ITAR or CT program for 5
13 days/week for 4 weeks. The primary outcome was change in maximum walking distance
14 measured on a graded treadmill before and after the program.

15 **Results.** Adherence was high. All training sessions were completed in the ITAR program and
16 only a few were not completed in the CT program (median 100% [Q1–Q3 96–100]). Tolerance
17 was excellent (no adverse events). VO_{2peak} was low in both groups, corresponding to moderate to
18 severe exercise intolerance. The 2 groups did not differ in the primary outcome (median ITAR vs
19 CT 480 [135–715] vs 315 m [0–710]; $p=0.62$) or other walking distances (constant speed and
20 gradient treadmill test). For all 38 participants, both programs greatly increased maximum
21 walking distance in the graded treadmill test: median 415 [240–650] to 995 m [410–1490], with a
22 large effect size ($p<10^{-4}$).

1 **Conclusion.** A 4-week intensive rehabilitation program with ITAR or CT for intermittent
2 claudication showed high adherence, was well tolerated, and improved walking distance as much
3 as that reported for longer conventional programs. These findings prompt the design of a larger
4 multicenter randomised controlled trial.

5

6 **Key Words:** peripheral arterial disease; intermittent claudication; physical therapy; exercise
7 physiology; treadmill training with active recovery; supervised exercise

8

9 ClinicalTrials.gov registration: NCT01734603

10

11 **Introduction**

12 Peripheral artery disease (PAD) with intermittent claudication (IC) affects about 2% of the
13 general population, severely limiting walking ability and physical activity [1-5]. We now have
14 strong evidence that individuals with IC should receive management of cardiovascular risk
15 factors [1, 3, 6-9], therapeutic education [1, 3, 8-10], and medical treatment [1, 3, 8, 9] and
16 should perform supervised exercise therapy [1, 6, 7, 11-15] and home exercises [7, 14, 16, 17].

17 Since the 1970s [5], treadmill exercise therapy has become an important part of
18 rehabilitation programs for individuals with IC [6, 18, 19], although other training modalities
19 may also be efficient [7, 20]. The benefits are multifactorial, attributed to metabolic and
20 microcirculatory adaptations of the muscles and to improvements in cardiorespiratory fitness
21 [21-23]. However, the duration and frequency of sessions (number of hours per day and days per
22 week) is debated, as is the total length of rehabilitation programs. Programs may last from 6
23 weeks to 6 months, the frequency of sessions inversely proportional to the total length [24, 25].

1 The interest in short intensive programs of several days per week is increasing [6, 18, 26].
2 Such programs induce a rapid gain in walking abilities (within the first 2 months), maintained
3 with further training [27]. Relatively short rehabilitation programs (6-8 weeks) might have better
4 adherence than less intensive programs spread out over 6 months as well as less cost, thereby
5 allowing more individuals to be treated [26-28]. As well, the duration and frequency of
6 rehabilitation sessions might be reduced to reduce the total length of the program to 4 weeks
7 [28]. Hence, individuals living far from the rehabilitation centre might more easily benefit from
8 such programs [28].

9 Conventional training (CT) on a treadmill is often performed at an intensity close to the
10 maximum tolerated before the onset of claudication pain. When claudication pain occurs, the
11 pain imposes complete rest before continuing the exercise. During interval training with active
12 recovery (ITAR), exercise is at a level well below the pain threshold and is interspersed with
13 periods of low-level exercise but not rest. Such low-intensity active recovery facilitates lactate
14 removal [29] favouring better metabolic recovery of muscles [30]. Hence, ITAR is efficient and
15 safe for cardiac [31-33], respiratory [34], and metabolic [35] rehabilitation, with preliminary
16 evidence suggesting that it might provide benefits for patients with IC [26].

17 The results of our preliminary pilot study of individuals with PAD, involving 2 weeks of
18 the ITAR modality only, were encouraging, with walking distance clearly increased as compared
19 to baseline [28]. In the present study, we investigated the feasibility of a parallel-group
20 randomised study design, this time comparing two 4-week intensive treadmill exercise programs,
21 ITAR versus CT, at constant speed and slope with rest recovery if necessary.

22

1 **Methods**

2 *Study design and setting*

3 This study was a prospective assessor-blinded single-center randomised controlled trial that
4 compared 2 parallel rehabilitation interventions. It took place at Grenoble Alpes University
5 Hospital (France) from November 2012 to March 2014. The objectives were to assess the
6 feasibility of intensive 4-week treadmill exercise programs for PAD and compare 2 modes of
7 treadmill training: ITAR and CT. All physiotherapists and rehabilitation physicians involved had
8 received specific training and had at least 10 years of experience working with PAD patients in a
9 university hospital setting.

10 **Ethics**

11 The study protocol was approved by the regional medical research ethics committee (French
12 *Comité de Protection des Personnes CPP Sud-Est V*: no. 2011 A00969-32). The study was
13 financed by Grenoble Alpes University Hospital and registered at ClinicalTrials.gov
14 (NCT01734603). Written informed consent was obtained from all participants. The CONSORT
15 guidelines for reporting randomised trials of non-pharmacological treatments were followed.

16 **Inclusion and non-inclusion criteria**

17 Individuals, with or without prior revascularization, were referred by their vascular surgeon,
18 specialist in vascular medicine, or general practitioner. All eligible participants had been
19 examined by their cardiologist and vascular physician less than 3 months before inclusion. This
20 examination included evaluation of potential acute cardiac comorbidities, such as myocardial
21 ischemia, severe heart rhythm disorders or conduction disorders by exercise myocardial
22 perfusion scintigraphy, a graded maximal exercise test on an ergocycle or stress

1 echocardiography (exercise or dobutamine). The inclusion criteria were out-patient or
2 hospitalized patient 18 to 80 years old with claudication (in one or both lower limbs) due to PAD
3 diagnosed by a trained vascular physician based on a duplex scan, ankle–brachial index < 0.90 at
4 rest and a 20% decrease in ankle–brachial index after a constant speed (3 km/hr) and constant
5 gradient (10%) treadmill test (C-test, often called the “Strandness test”). Non-inclusion criteria
6 were exercise tolerance limited by factors other than claudication (poorly controlled blood
7 pressure, acute coronary artery disease, dyspnea, severe osteoarticular or neurological
8 deficiencies) or abdominal aortic aneurysm with diameter > 40 mm.

9

10 **Common therapeutic program**

11 All participants received therapeutic education on the management of cardiovascular risk factors.
12 Their regular medication remained unchanged during the study. They were advised on the need
13 to walk for at least 1 hr a day, at a pain-free level, if they wanted to maintain the benefits of
14 training. All participants followed a 4-week rehabilitation program (20 working days, 3 hr/day)
15 that combined supervised treadmill training (CT or ITAR) plus additional daily 2-hr supervised
16 physical therapy sessions. During this program, all individuals had a daily medical check-up to
17 detect any adverse events and ensure that the training was well tolerated.

18 Treadmill training was performed on a TechmedPhysio® treadmill (Auxerre, France) allowing
19 precise speed and slope adjustments (speed accuracy 0.1 km/hr [0.06 mph] and slope accuracy
20 0.5%). For each participant, training was adjusted according to their baseline maximal walking
21 speed, determined without slope but with a speed increased by 1 km/hr every 3 min to find the
22 speed at which maximum tolerable pain occurred. Then during the training period, the intensity

1 incremental was based on the achievement of the previous session. After each successfully
2 completed session, either the slope or the speed was increased (Fig. 1).

3 Additional supervised exercises combined 20 min of continuous arm-cycling (starting at 10 watts
4 and increased by 5 watts weekly, depending on upper-limb tolerance), 20 min of stationary
5 ergocycle (starting at 25 watts and increased by 5 watts weekly) and 45 min of soft floor
6 gymnastics. Each workshop was separated by about 5 min of passive recovery.

7 **Specific interventions**

8 The 2 arms differed in the modality of the treadmill training (Fig. 1). In the CT arm, individuals
9 walked at the predetermined constant speed, completely stopping if in pain and resting until the
10 pain ceased. In ITAR, individuals alternated 2 different walking speeds and slope, constituting
11 the exercise and recovery periods. Each session lasted 40 min, including warm-up.

12

13 *Conventional training (CT)*

14 This program, presented in Figure 1 (left side) was based on that proposed by Hiatt et al. [22].
15 Each treadmill session lasted 50 min, including a 5-min warm-up, 40 min of exercise at constant
16 speed and slope (including a 10-min run-in period), then 5 min of relaxation. The initial speed
17 was set at 3.2 km/hr (2 mph) with 0% slope, but 11 individuals unable to walk at this speed
18 started at 1.6 km/hr with 0% slope. If claudication pain occurred (≥ 3 on the 4-point claudication
19 pain rating scale of the American College of Sports Medicine) [22], individuals could stop
20 walking until all pain ceased, before restarting [10]. For this reason, the total duration of CT
21 sessions was set at 10 min longer than the ITAR program. The training intensity was increased
22 the next session if the individual was able to walk for at least 8 min.

23

1 *Interval training with active recovery (ITAR)*

2 This training program is also presented in Figure 1 (right side). Each session lasted 40 min
3 starting with 5-min warm up, then 5 cycles of 6 min: 3 min of walking at the targeted intensity
4 followed by 3 min of active recovery, and finally 5 min of relaxation.

5 At the first session, the walking speed was set at 70% and active recovery speed at 40%
6 of baseline walking speed. If no claudication pain occurred during the training session, the
7 intensity was increased at the next session.

8 **Randomisation and blinding**

9 The randomisation procedure was centralised, using a computer random-number generator with
10 random block size. Participants were included after screening for eligibility and randomised after
11 baseline assessments. Participants were aware of the type of training program (ITAR or CT) but
12 were assumed to have no idea as to which one was thought to be superior. Assessments were
13 performed by 2 physiotherapists and physicians who were blinded to treatment allocation.

14 **Assessments**

15 The battery of assessments was performed at baseline during the week before the start of training
16 and in the week after the end of the program, when walking distances and cardiovascular,
17 respiratory and psychological parameters were collected, in addition to general medical data.

18 Walking distance tests were performed with at least a 20-min rest between each test, in
19 the following order: 6-min walk test (6MWT) [36, 37], maximum distance at constant speed and
20 gradient before onset of claudication (C-test) [38], a graded treadmill test (G-test) derived from
21 the Gardner test [39], and finally a treadmill test of maximal walking speed before onset of
22 maximum tolerable pain with measurement of VO_{2peak} .

1 For the 6MWT, participants were instructed to walk at their fastest comfortable speed on
2 a flat surface (e.g., along a corridor) for 6 min, with or without stopping for rests. As
3 recommended for patients with PAD [40], the 6MWT was performed after 15 min of rest. The C-
4 test was performed at 3.2 km/hr (2 mph) on a 10% slope (TechmedPhysio® treadmill). The G-
5 test started at 3.2 km/hr and 0% slope. With speed remaining constant, the slope was increased
6 by 0.5% every 2 min until limited by pain (claudication). The slope increment was less than in
7 the original version (2%) for better feasibility for severely affected patients able to achieve only
8 very short walking distances [41]. For participants with the most severe disease and balance
9 disorders, handrail support was allowed during all treadmill tests. Running during treadmill tests
10 was not allowed.

11 Cardiopulmonary exercise testing was performed at baseline and during certain treadmill
12 tests to assess exercise tolerance and energy expenditure. Aerobic capacity and cardiovascular,
13 metabolic and respiratory parameters were measured during a graded exercise test on a Gymrol
14 Super 2500 treadmill (Tecmachine SA, Andrezieux-Boutheon, France). The initial speed was 2.4
15 km/hr with no slope. The speed or slope was increased every 2 min by 2% or 0.8-km/hr
16 increments, respectively, until pain limitation or exhaustion. Gas exchange was measured
17 continuously on an automated ergospirometer with a mixing chamber method (Metasys TRM,
18 Brainware, Toulon France), allowing for monitoring oxygen uptake (VO_2).

19 **Outcomes**

20 The primary outcome was the change in maximum walking distance (MWD) on the G-test.
21 Secondary outcomes were feasibility and safety of the program (adverse effects during the
22 sessions or reported at the daily medical check-up), adherence to rehabilitation (total number of

1 sessions attended*100/total number of sessions planned), and changes in other walking distances
2 (6MWT, C-test) and cardiorespiratory and exercise parameters.

3 **Sample size**

4 Taking into account the results of our previous non-randomised pilot study [28] we hypothesized
5 an improvement of 650 m (± 350) in the ITAR group and an improvement of 300 m (± 350) in the
6 CT group in a graded treadmill test. To show this clinically significant between-group difference
7 in walking distance of 350 m (Mann-Whitney test), with power of 80% and alpha risk of 5%, we
8 estimated that we needed 36 participants (18 in each group). We planned to include 10% more
9 participants (i.e., 40 individuals) in anticipation of potential dropouts.

10 **Statistical analysis**

11 The statistician was blinded to the intervention group. Statistical analysis was according to
12 intention to treat and by using Stata v13.0 (Stata Corp., College Station, TX). $P < 0.05$ was
13 considered statistically significant. Categorical variables are expressed with number (percentage)
14 and continuous variables with median (interquartile range [Q1–Q3]). For quantitative variables,
15 we used the Mann-Whitney (non-parametric) test to compare the 2 groups. The effect sizes of
16 significant differences were calculated with the z values of the Mann-Whitney test [$r = \frac{z}{\sqrt{N}}$] and
17 interpreted according to Cohen's guidelines (1988) as medium difference with $r > 0.29$ and large
18 difference with $r > 0.49$.

19

1 **Results**

2 **Participant characteristics**

3 Among the 60 individuals screened, 40 were enrolled between November 2012 and April 2014.
4 The flow chart of the study in Figure 2 respects the extension of the CONSORT statement for
5 randomised pilot and feasibility trials [42]. Characteristics of participants are in Table 1. Because
6 2 participants in the CT arm were included in error and were excluded soon after randomisation,
7 and given the relatively small sample size of the study, some variables differed between the 2
8 arms (Table 1). ITAR participants were older, tended to be diabetic, and had higher body mass
9 index and bilateral IC than CT participants. All received antiplatelet agents and statins; none was
10 on pentoxifylline or cilostazol.

11 **Adherence and safety**

12 No adverse event related to the training programs was reported. Adherence to the ITAR program
13 was excellent throughout the entire study; all 20 individuals successfully completed all daily
14 training sessions. Three participants in the CT program did not complete all training sessions.
15 One participated only sporadically in the study due to alcohol abuse; chronic heart failure was
16 discovered in a second participant, and the steering committee decided to stop this participant's
17 participation prematurely for safety reasons and delete the data from the database considering
18 that he/she had been wrongly included. A third individual missed a few training sessions but
19 finished the study. Finally in the CT arm, the median number of completed sessions was 100%
20 [Q1–Q3 96–100]. This procedure maintained intention to treat.

1 **Walking distances**

2 Table 2 and Figure 3 show maximum walking distances before and after the training programs.
3 The main outcome criterion (MWD measured with the G-test) improved in both arms ($p=0.007$
4 for CT and $p < 0.001$ for ITAR), but this improvement was not significantly different between the
5 groups ($p=0.62$). Likewise, the secondary outcome MWD was improved in both groups, with no
6 significant difference between the groups whatever the test used: C-test ($p=0.76$) or 6MWT
7 ($p=0.84$). Because of the lack of difference between the 2 groups, we compared the MWD for the
8 whole study population of 38 participants before and after the program. The improvement in
9 treadmill walking distances reached nearly 100% with very large effect sizes: median distance
10 before vs after was 415 [240-650] vs 995 m [410-1490], respectively, with $r=0.71$ and $p < 10^{-4}$ for
11 the G-test, and 150 [90-290] vs 290 m [140-530], respectively, with $r=0.84$ and $p < 10^{-4}$ for the C-
12 test. The before-after difference was less marked when walking along the floor at comfortable
13 speed (6MWT): median 355 [298-398] vs 378 m [338-428], respectively with $r=0.54$ and $p < 10^{-3}$.
14 For several participants, claudication was not reached until after 6 min.

15 **Exercise tolerance**

16 Table 2 shows that VO_{2peak} was low in both arms for participants' age, corresponding to about
17 65% to 70% of the predicted value. This finding corresponds to a moderate to severe exercise
18 intolerance. We found no significant difference in VO_2 change between the 2 groups after the
19 training.

20

21 **Discussion**

22 To our knowledge, this is the first randomised trial to assess the efficiency of a short exercise
23 program for PAD, lasting 4 weeks; almost all other reported programs lasted at least 6 weeks.

1 **A short program is feasible, safe and efficient**

2 Both programs, CT and ITAR, were safe, with no adverse events. Hence, individuals with severe
3 IC may follow an intensive rehabilitation program of 3 hr/day for 4 weeks, provided potential
4 cardiovascular complications have been previously identified. In our study, all individuals
5 underwent assessment by 2 specialists, in cardiology and vascular medicine, and eligibility to
6 participate in the program was carefully weighed for each participant. Our study exhibited one of
7 the highest rates of adherence to treatment ever reported in IC rehabilitation, but this is likely due
8 to the duration of the program, the shortest proposed so far. Indeed, a 6-month trial found that
9 adherence to exercise progressively declines [27]. This observation clearly argues in favour of
10 short programs, which seem more suitable for individuals who are still working, and also might
11 be less costly for both patients and the community. Future medico-economic studies need to
12 investigate this issue.

13 The major finding of this study was that individuals who completed an ITAR or CT
14 program improved their physical capabilities without any significant differences in the primary
15 or secondary criteria. Indeed, the increases in walking distance of 315 and 480 m in CT and
16 ITAR groups, respectively, along with doubling the MWD on the Gardner test with a very large
17 effect size, were greater than the minimally important improvement considered in the field (305
18 m) [43], and higher than that reported in most studies [7, 12, 15, 18, 26, 34, 44] .

19 The second finding was that a 4-week exercise training program increased the MWD by a
20 clinically relevant level in individuals with PAD, as shown by the main (G-test) and secondary
21 outcomes (6MWT, C-test), and the results were similar to those from previous trials with
22 exercise programs lasting 6 months [45].

1 **Differences between the 2 programs**

2 Similar improvements in walking distance were observed in both groups despite lower intensity
3 relative to the VO_{2peak} in the ITAR arm. This finding could be explained by both programs being
4 performed at relatively low intensities regarding percentage of VO_{2peak} (about 50%) because the
5 included participants had shown exercise intolerance. Also, we cannot exclude that the other
6 exercise activities that formed part of the rehabilitation along with the treadmill training may
7 have played a role in the improved physical functioning in both groups.

8 **Strengths and limitations**

9 The strengths of the study include the training being intensive (> 3 hr/day) with daily medical
10 check-ups to detect adverse events and assessments by 2 different physiotherapists and
11 physicians.

12 Although the results of this trial support the efficacy of both 4-week physical therapy
13 programs for individuals with PAD as compared with results obtained by previous published
14 studies, our study had several limitations. In retrospect, the study was underpowered to be able to
15 conclude for the main objective, and the comparison between the two groups featured a risk of
16 randomization in which participants of the control group were significantly younger. Also, the
17 relatively small sample size (calculated for the primary outcome) may explain why some results
18 for the secondary outcomes did not reach significance, although other studies have been able to
19 show improvements in basic cardiorespiratory parameters [12, 31]. Most assessments were
20 performed with blinding to treatment group, but there were some exceptions regarding walking
21 tests for some participants due to the unforeseen unavailability of physiotherapists. Treadmill
22 training made up only one-third of the daily rehabilitation. This situation may explain the lack of
23 significant difference between the 2 types of program. Indeed, the other exercises performed

1 during the common part of the rehabilitation have also been found effective in increasing aerobic
2 capacity and walking abilities in people with PAD [44]. Current smokers were included in the
3 study, which might have influenced response to training with altered muscular or
4 cardiorespiratory adaptations, but the number of current smokers did not differ significantly
5 between the 2 groups. The long-term maintenance of progress achieved during a course of
6 exercise training (long or short) remains a challenge, and a panel of strategies is needed to
7 encourage patients to continue exercising. This will require long-term patient follow-up, but for
8 logistic reasons the present study was not designed to do this. Long-term follow-up with regular
9 simple home-based exercises, possibly using information technology, should be included in
10 future trials of exercise strategies.

11 Exercise has multiple effects on the physiology of PAD, influencing quality of life,
12 morbidity and mortality. Analysing the neurovegetative and metabolic effects of the exercise
13 programs would have been of interest.

14 Concerning the tests used, because claudication was not reached in some participants
15 during the 6MWT, this test may not be well adapted to the context of this study. In addition, the
16 question of the most-effective intensity of effort to increase the walking distance remains (should
17 the pain of claudication be induced during walking?): for certain authors, the answer is no
18 [44,46,47], for others it is yes [7, 48].

19

20 **Conclusion**

21 This study showed the tolerance, high adherence, and efficacy of a 4-week supervised intensive
22 rehabilitation program based on ITAR or conventional treadmill training (3 hr/day except
23 weekends) designed for individuals with intermittent claudication. With both programs, walking

1 ability improved as much as with less-intensive (3 days/week) and longer (6-month) programs
2 described in the literature, with maximal walking distance on treadmill tests multiplied by 2 and
3 very large effect sizes. These results appeal for further studies with larger sample sizes and long-
4 term follow-up.

5

6 **Funding.** This work was supported by Grenoble Alpes University Hospital.

7

8 **Conflict of interest.** None declared.

9

10 **Figure legends**

11 **Figure 1.** Four-week treadmill training programs: left part, conventional training (CT) and right
12 part, interval training with active recovery (ITAR). Wk, week

13 **Figure 2.** Flow chart of the study, according the extension of the CONSORT statement for
14 randomised pilot and feasibility trials [44]. ITAR, interval training with active recovery; VO₂,
15 oxygen uptake

16 **Figure 3.** Maximum walking distance (m) before and after interval training with active recovery
17 (ITAR) or conventional training (CT) in a graded treadmill test (G-test). Maximum walking
18 distance improved in both arms (p=0.007 for CT and p<0.001 for ITAR), without significant
19 difference between gains in both arms (p=0.62).

20

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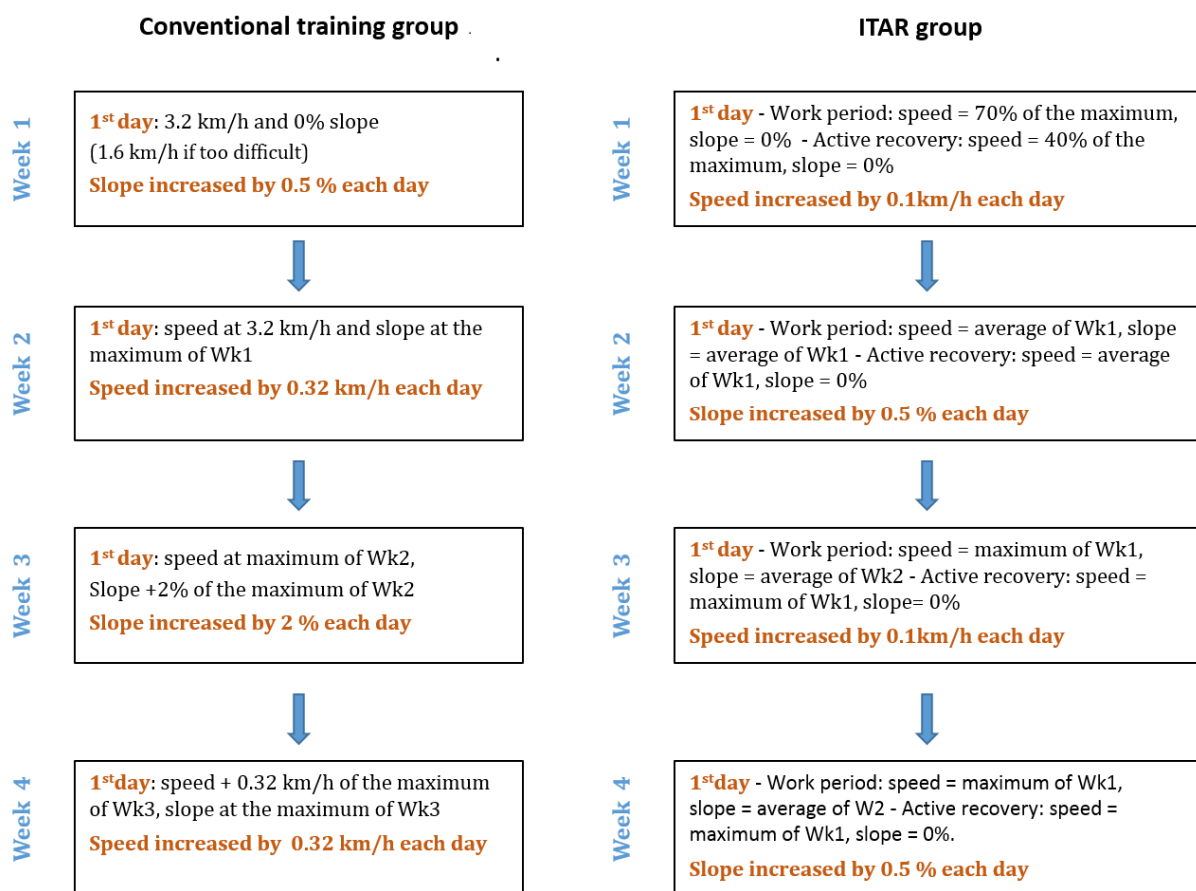
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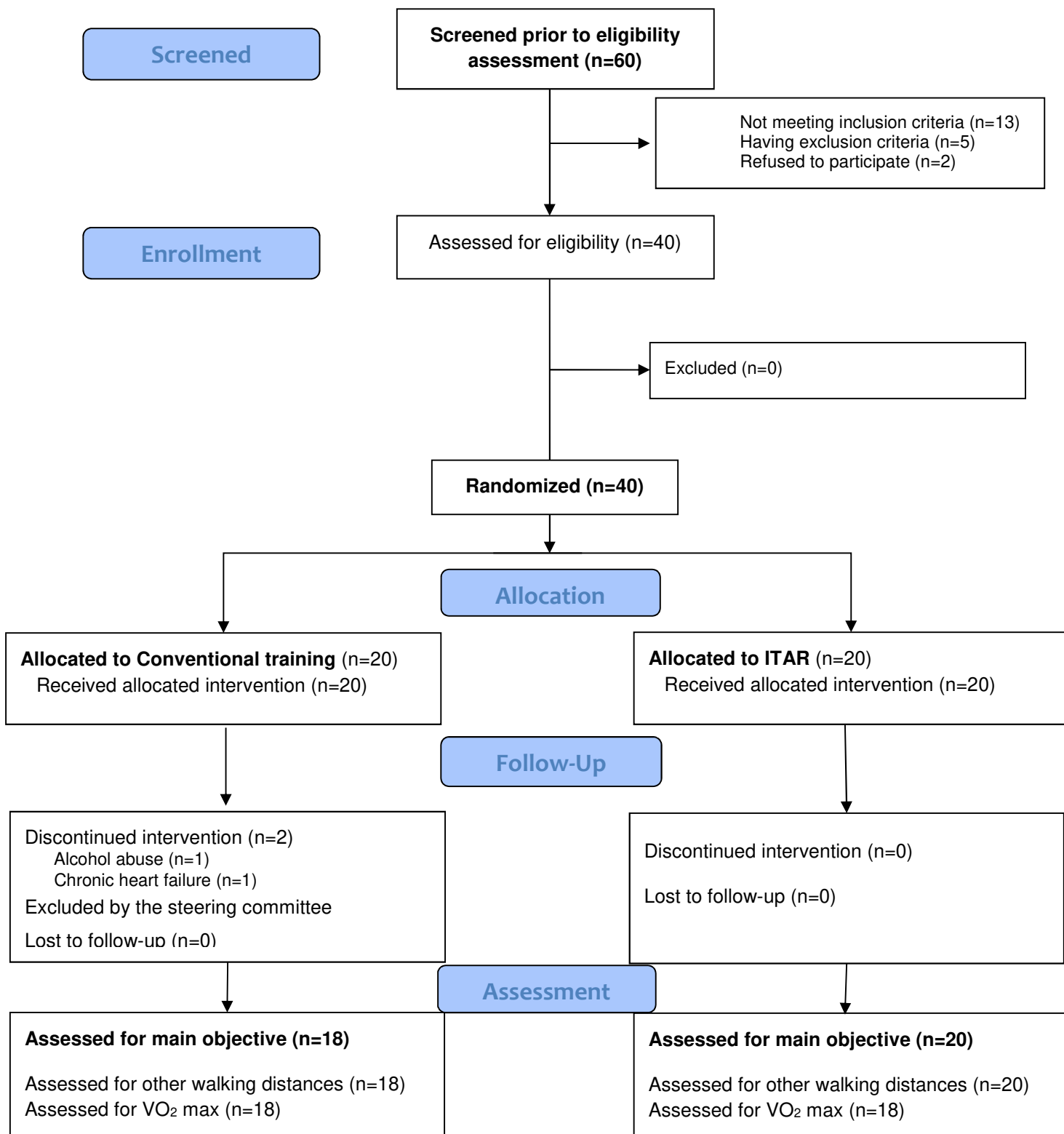
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4 week treadmill training program





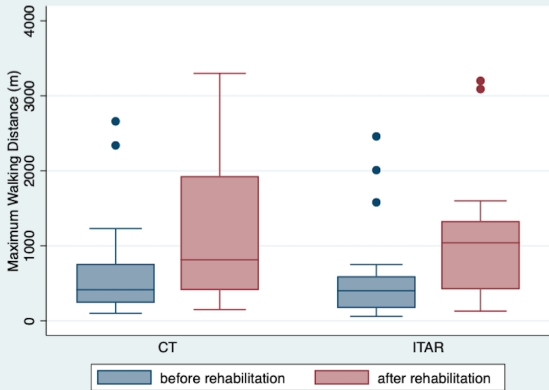


Table 1. Baseline clinical characteristics of participants undergoing conventional (treadmill) training (CT) and interval training with active recovery (ITAR).

	CT group (n=18)	ITAR group (n=20)	p-value
Age (years), median [Q1–Q3]	62 [51-64]	68 [63-70]	0.03
Male, n (%)	15 (83%)	16 (80%)	1.00
Body mass index, kg/m ²	27.2 [24.4-29.5]	29.8[27.9-32.1]	0.05
High blood pressure, n (%)	14 (78%)	18 (90%)	0.39
Diabetes, n (%)	6 (33%)	12 (60%)	0.10
Dyslipidemia, n (%)	15 (83%)	18 (90%)	0.65
Tobacco consumption (%)			
Never	0%	2 (10%)	
Former	11 (61%)	15 (75%)	0.13
Current	7 (39%)	3 (15%)	
Previous surgery of lower limb arteries, n (%)	6 (33%)	4 (20%)	0.47
Claudication side, n (%)			
Unilateral	9R+4L (72%)	5R+4L (45%)	0.09
Bilateral	5 (28%)	11 (55%)	
Arterial Doppler ultrasound Hemodynamically significant arterial stenosis, n (%)	13 (72%)	14 (70%)	0.88
Distal	2 (15%)	0%	
Proximal	10 (77%)	12 (86%)	
Both	1 (8%)	2 (14%)	
Artery occlusion, n (%)	14 (78%)	14 (70%)	0.72
Distal	2 (14%)	3 (21%)	
Proximal	11 (79%)	9 (64%)	
Both	1 (7%)	2 (14%)	

R, right; L, left

Table 2. Walking measurements. 415 [240-650] vs 995m [410-1490]

Variables	Pre-training (baseline)	Post-training	Change in score	P-value (CT vs ITAR)
Graded treadmill test:				
MWD (m)				
CT (n=18)	415 [240-760]	815 [410-1930]	315 [0-710]	0.62
ITAR (n=20)	400 [170-595]	1040 [420-1330]	480 [135-715]	
C-test: MWD (m)				
CT (n=18)	135 [100-270]	205 [140-500]	110 [20-230]	0.76
ITAR (n=20)	170 [85-295]	350 [165-620]	130 [35-325]	
6MWT (m)				
CT (n=18)	357 [245-398]	363 [330-403]	40 [-40-98]	0.84
ITAR (n=20)	356 [306-403]	390 [342-436]	37 [14-49]	
VO ₂ peak (mL/kg/min)				
CT (n=18)	18.2 [13.9-21.0]	17.7 [15.0-23.4]	1.1 [-2.2-4.6]	0.72
ITAR (n=20)	17.9 [15.7-21.8]	17.8 [14.7-25.1]*	0.7 [-0.5-3.0]*	

Mann-Whitney tests comparing gain after rehabilitation between ITAR and CT.

Data are median [Q1-Q3].

MWD, maximum walking distance; 6MWT, 6-min walk test.

* 2 missing values