Clinical Characteristics and Response to Supervised Exercise Therapy in People with Lower Extremity Peripheral Artery Disease

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Abstract

INTRODUCTION.—Among people with lower extremity peripheral artery disease (PAD), little is known about variation in response to supervised exercise therapy (SET). Clinical characteristics associated with greater responsiveness to SET have not been identified.

METHODS.—Data from participants with PAD in two randomized clinical trials comparing SET vs. non-exercising control were combined. The exercise intervention consisted of three times weekly supervised treadmill exercise. The control groups received lectures on health-related topics.

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RESULTS.—Of 309 unique participants randomized (mean age 67.9 (standard deviation (SD) =9.3), 132 (42.7%) women, 185 (59.9%) black), 285 (92%) completed six-month follow-up. Compared to control, those randomized to SET improved six-minute walk distance by 35.6 meters (95% confidence interval (CI) = +21.4,+49.8, P<0.001). In the 95 (62.1%) participants who attended at least 70% of SET sessions, change in six-minute walk distance varied from 149.4 to +356.0 meters. Thirty-four (35.8%) had no six-minute walk distance improvement. Among all participants, age, sex, race, body mass index, prior lower extremity revascularization and other clinical characteristics did not affect the degree of improvement in six-minute walk distance after SET, relative to the control group. Participants with six-minute walk distance less than the median of 334 meters at baseline had greater percent improvement in six-minute walk distance compared to those with baseline six-minute walk distance above the median (+20.5% vs. +5.3%, P for interaction= 0.0107).

CONCLUSIONS.—Among people with PAD, substantial variability exists in walking improvement after SET. Shorter 6-minute walk distance at baseline was associated with greater improvement after SET, but other clinical characteristics, including age, sex, prior lower extremity revascularization, and disease severity, did not affect responsiveness to exercise therapy.

TABLE OF CONTENTS SUMMARY.

In a randomized study of 309 patients with peripheral artery disease (PAD) shorter six-minute walk distance at baseline was associated with greater improvement after supervised exercise therapy (SET). Age, sex, history of revascularization and PAD severity did not affect response to SET, suggesting that no patients with PAD should be excluded from SET referral.

Supervised treadmill exercise therapy (SET) significantly improves walking distances in people with lower extremity peripheral artery disease (PAD) and is recommended by clinical practice guidelines as first line therapy to improve walking impairment in people with PAD (1-7). While SET consistently improves mean walking distance in people with PAD, little is known about the degree of variability in improved walking distance following SET or about the proportion of people with PAD who participate in SET but do not improve their walking distance. Little is known about characteristics of people with PAD, such as older age, sex, or disease severity, that are associated with better vs. poorer response to SET. Defining the degree of variability in response to SET and identifying clinical characteristics that are associated with poorer response to SET will help clinicians better counsel patients with PAD and select the most optimal therapy for patients with PAD.

In this study, data were combined from two randomized clinical trials of supervised treadmill exercise therapy in PAD (6,7) to address the following primary specific aims. First, to describe the degree of variability in improvement in walking distance in response to SET in people with PAD. Second, to identify clinical characteristics associated with greater or lesser response to a supervised treadmill exercise intervention, relative to a control group. Additional analyses limited to participants randomized to SET studied the effects of age, sex, race, and other clinical characteristics on the degree of walking improvement following SET.

METHODS

Overview

Data from two randomized clinical trials of SET in participants with PAD were combined for analyses. The two studies were the Study in Leg Circulation (SILC) and the PROgenitor cell release Plus Exercise to improve functional performance in PAD: (the PROPEL Trial) (6,7). All participants provided written informed consent.

Summary of included trials

Methods for each trial have been published (6,7) and are summarized here. In SILC, 156 participants with PAD were randomized to one of three groups: supervised treadmill exercise, supervised lower extremity resistance training, or attention control for six months. Participants randomized to supervised resistance training were excluded from analyses reported here, since the current analyses focused on supervised treadmill exercise training (6). In PROPEL, 210 participants with PAD were randomized to one of four groups: SET + granulocyte macrophage colony stimulating factor (GM-CSF), SET + placebo, GM-CSF + attention control, or placebo + attention control. For PROPEL, participants randomized to GM-CSF were included, since the effect of GM-CSF was found to be clinically insignificant (7).

Participant Identification

In both trials, participants were identified from Chicago-area medical centers, through newspaper or radio advertisements, or from mailings to older people living in the Chicago area (5,6). People with PAD who previously participated in research with the principal investigator (MMM) and expressed interest in future research were contacted.

Inclusion criteria

The two studies had an inclusion criterion of ankle brachial index (ABI)   0.90 and ABI   0.95, respectively (6–8). In PROPEL, potential participants with an ABI > 0.90 at the baseline visit were eligible, if a hospital-affiliated vascular laboratory report or angiogram demonstrated PAD (7). In PROPEL, participants with an ABI of 0.90–1.00 at baseline and those with a normal ABI and prior lower extremity revascularization were eligible if their ABI dropped by 20% after a heel-rise test, consisting of fifty heel rises at a rate of one per second followed by repeat ABI (9).

Exclusion criteria

Potential participants with a below or above-knee amputation, wheelchair confinement, walking impairment for a reason other than PAD, foot ulcer or critical limb ischemia, or significant visual or hearing impairment were excluded (6,7). Both trials excluded potential participants who used a walking aid other than a cane. Both trials included a run-in, in which participants were asked to attend an exercise session and a control group session within a three week period, to demonstrate willingness and ability to participate in the intervention. Those who did not complete the run-in successfully were excluded. The same run-in criteria were required for both trials. Potential participants with major surgery, revascularization, or

cardiac rehabilitation participation during the previous 3 months or planned during the next 6 months were excluded. People requiring oxygen with activity were excluded. Potential participants for whom exercise may be unsafe and those at risk for health deterioration were excluded. Those with a Mini-Mental Status Examination score < 23 were excluded (10).

MEASURES

The same methods were used in the two included trials for measurement of the ankle brachial index (ABI), six-minute walk distance, treadmill walking, questionnaire administration, and body mass index measurement and calculation.

Ankle-brachial index (ABI)

A handheld Doppler probe (Nicolet Vascular Pocket Dop II, Golden, CO) was used to measure systolic blood pressures in the right brachial, dorsalis pedis, and posterior tibial arteries and left dorsalis pedis, posterior tibial, and brachial arteries as previously described (8,11,12).

Six-Minute Walk Test

Six-minute walk distance is a well validated measure of walking endurance that predicts mortality, cardiovascular events, and mobility loss in people with PAD (13–17). Following a standardized protocol (6,7,13–17), participants walked up and down a 100-foot hallway for 6 minutes after instructions to cover as much distance as possible during the six-minutes. The distance completed after 6 minutes was recorded. Among participants with PAD, a small clinically meaningful change was defined as 12 meters and a large clinically meaningful change was defined as 34 meters (18).

Treadmill walking performance

Maximal treadmill walking distance was measured using the Gardner-Skinner protocol (6,7,19). Participants were not allowed to grip handrails. Participants began walking at 2.0 miles per hour at zero percent grade. Grade was increased two percent every two minutes. Participants unable to walk at 2.0 miles/hour began walking at 0.50 miles per hour (6,7,19), and treadmill speed was increased by 0.50 miles/hour every two minutes until 2.0 miles per hour was achieved. Subsequently, grade was increased two percent every two minutes. Protocols dictated that the same stress test (i.e. Gardner or modified Gardner) was performed at baseline and follow-up.

INTERVENTIONS

Supervised treadmill exercise therapy

The same SET protocol was used in both randomized trials. Participants attended exercise sessions three times weekly with an exercise physiologist for six months (6,7). Walking exercise time was increased during the intervention to 50 minutes/session, not including rest periods.

Control group

Participants in both trials randomized to the control group were asked to attend one-hour educational sessions led by Northwestern faculty and staff once per week for six months. Example topics in these sessions were nutrition, cancer screening, and immunizations.

Study injections in PROPEL

PROPEL participants were randomized to either granulocyte macrophage colony stimulating factor (GM-CSF) or placebo injected subcutaneously 3 times per week for the first 2 weeks after randomization, in a double-blinded manner (7).

Other Measures

Medical history, race, and demographics were obtained using patient report (6,7). Height and weight were measured. Body mass index (BMI) was calculated as weight (kg)/(height (meters))^2.

Statistical analyses

Characteristics of participants randomized to SET vs. control were compared using analysis of variance and statistical tests of trend. Generalized linear models were used to compare 6-month changes in six-minute walk distance and maximal treadmill walking time between PAD participants randomized to SET vs. control. Models adjusted for study and whether the intervention included GM-CSF. Analyses were repeated in the subset of participants who attended at least 70% of exercise or attention control sessions. Tests for interaction were performed to determine the effects of the following clinical characteristics: age, sex, race, ABI > 0.65 vs. ABI < 0.65, presence vs. absence of specific comorbidities, BMI > 30 vs. < 30 kg/M^2, current smoking status, prior lower extremity revascularization, adherence to study intervention sessions (both SET and attention control group sessions) and baseline walking performance (six-minute walk distance 334 vs. <334 meters and maximal treadmill walking time 6.3 vs. < 6.3 minutes) on change in six-minute walk distance and change in maximal treadmill walking time, respectively, relative to the control group. In analyses limited to participants randomized to exercise, the magnitude of improvement in six-minute walk distance and maximal treadmill walking time were evaluated according to the presence vs. absence of these baseline clinical characteristics, using linear and logistic regression models, adjusting for baseline six-minute walk distance and baseline maximal treadmill walking time, respectively. A p value of <0.05 was considered statistically significant, since the purpose of these post-hoc analyses was to increase sensitivity for identifying clinical characteristics that may influence responsiveness to SET in people with PAD.

RESULTS

361 unique people with PAD were randomized (205 in PROPEL and 156 in SILC). Of these, 52 participants randomized to resistance training in SILC were excluded, leaving 309 participants for analyses (153 randomized to exercise and 156 to control). Baseline characteristics of participants are shown in Table 1. Mean adherence to intervention sessions was 70.9% for participants randomized to SET and 69.7% for those randomized to control.

Participants who attended <70% of their study intervention sessions were younger (66.7 years (standard deviation (SD):9.3 vs. 68.7, SD: 9.2, P=0.049), had a higher prevalence of prior lower extremity revascularization (38.5% vs. 27.1%, P=0.037) and a higher baseline maximal treadmill walking time (6.7 minutes, SD:4.5 vs. 7.7 minutes, SD: 4.5, P=0.047), than those who attended 70% or more of their SET sessions. Of the 309 randomized, 285 (92.2%) completed 6-month follow-up testing.

Mean absolute changes in six-minute walk distance were +28.2 meters in the SET group vs. −7.4 meters in the control group (mean difference: +35.6 meters (95% Confidence Interval (CI) = 21.4, 49.8, P<0.001)). The mean percent change in six-minute walk distance was +12.4% in the SET group vs. −1.1% in the control group (mean difference: +13.5% (95% CI: 7.6%, 19.5%), P<0.001). Mean absolute changes in maximal treadmill walking time were +4.5 minutes in the SET group vs. +0.6 minutes in the control group (mean difference: +3.9 minutes (95% Confidence Interval (CI) = 3.1, 4.8, P<0.001)). Mean percent changes in maximal treadmill walking time were +101.4% in the SET group vs. 13.9% in the control group (mean difference: +87.5% (95% CI: 64.5%, 110.5%), P<0.001).

Change in six-minute walk distance and maximal treadmill walking time at 6-month follow-up varied substantially between participants (Table 2). For example, six-month change in six-minute walk distance ranged from −149.4 to +356.0 meters in the SET group and from −316.1 to +147.2 meters in the control group. Variability in change in maximal treadmill walking time ranged from –7.8 to +21.0 minutes in the SET group and from –7.8 to +12.6 minutes in the control group (Table 2). Results were similar when analyses were limited to participants who attended at least 70% of intervention sessions (Table 2).

Of 141 participants with PAD who were randomized to SET and had six-minute walk distance data at baseline and six-month follow-up, 47 (33.3%) declined in six-minute walk distance at six-month follow-up. PAD participants who declined in six-minute walk distance after SET had significantly higher baseline six-minute walk distance compared to those who did not decline after SET (375.4 meters (SD: 94.0) vs. 317.8 meters (SD: 91.0), P<0.01). Of 139 participants with PAD who were randomized to SET and had treadmill testing at baseline and six month follow-up, 12 (8.6%) declined in maximal treadmill walking time at six-month follow-up. Participants who declined in maximal treadmill walking time after SET had higher baseline treadmill walking time compared those who did not decline after SET (10.4 minutes (SD: 5.7) vs. 6.82 minutes (SD: 4.5)), P=0.01). There were no other baseline differences in characteristics of people who were randomized to SET and declined in six-minute walk distance or maximal treadmill walking time.

Based on statistical tests for interaction, relative to the control group, there were no significant differences in the degree of improvement in six-minute walk distance according to whether the participant was above or below the median age at baseline (67 vs. >67 years), or according to sex (male vs. female), race (black vs. white), median baseline ABI (0.65 vs. >0.65), median baseline BMI (30.0 kg/M^2 vs. >30 kg/M^2), presence vs. absence of specific comorbidities, smoking status (current smoker vs. not current smoker), leg symptoms (asymptomatic vs. not asymptomatic and classical intermittent claudication vs. not classical intermittent claudication), prior lower extremity revascularization vs. no

prior revascularization, adherence to study intervention sessions (<70% vs. 70%) or above vs. below baseline median treadmill walking distance (<6.3 minutes vs. 6.3 minutes) (Table 3, Figure 1). However, relative to the control group, participants with a baseline six-minute walk distance below the median (i.e. <334 meters at baseline) had significantly greater improvement in percent change in six-minute walk distance at 6-month follow-up, compared to those with baseline six-minute walk distance above the median (i.e. 334 meters at baseline) (20.5% improvement vs. 5.3% improvement, P for interaction = 0.0107) (Figure 1b). Within each defined subgroup, participants randomized to SET had significantly greater improvement in absolute and percent change in six-minute walk distance relative to the control group, except that the 14 participants who were asymptomatic (i.e. reported no exertional leg symptoms) and the 82 participants with history of coronary artery disease did not significantly improve absolute or percent change in six-minute walk distance following SET, relative to control (Table 3, Figure 1). The lack of improvement in six-minute walk distance among those with no exertional leg symptoms and among those with coronary artery disease may have been due to small sample size.

Based on statistical tests for interaction, relative to the control group, there were no significant differences in the degree of improvement in maximal treadmill walking distance by baseline age (<67 vs. 67 years), sex (male vs. female), race (black vs. white), baseline ABI (0.65 vs. >0.65), comorbidities, smoking status, leg symptoms, prior lower extremity revascularization, adherence to study interventions (<70% vs. 70%), or baseline six-minute walk distance (Table 3, Figure 2). However, participants with a baseline BMI below the median ($< 30 \text{ kg/M}^2$) had a significantly greater absolute improvement in maximal treadmill walking time at 6-month follow-up, compared to those with BMI above the median (30 kg/M^2) (4.95 vs. 3.09 minutes, P for interaction=0.036). In addition, participants with a baseline treadmill walking time below the median (i.e. < 6.3 minutes) had significantly greater improvement in percent change in maximal treadmill walking time at 6-month follow-up, compared to those with a higher maximal treadmill walking time at baseline (125.3% improvement in treadmill walking time vs. 32.7% improvement in treadmill walking time, P for interaction < 0.001) (Figure 2b). Within each defined subgroup, participants randomized to SET had significantly greater improvement in absolute and percent change in maximal treadmill walking time relative to the control group, except that the 14 participants who were asymptomatic did not significantly improve absolute or percent change in maximal treadmill walking time following SET, relative to the control group, perhaps due to small sample size (Table 3, Figure 1).

In analyses limited to participants randomized to SET, men had significantly greater improvement in six-minute walk distance than women (+36.4 vs. +14.8, P=0.036) (Table 4). However, because women randomized to the control group had twice the rate of decline in six-minute walk distance compared to men randomized to the control group (Table 4), there was no statistically significant interaction for sex on the response to SET. Women and men randomized to SET, respectively, had significant improvement in six-minute walk distance relative to the control group (Table 4, Figure 1).

DISCUSSION

Among 309 people with PAD randomized into a clinical trial of SET, there was wide variation in degree of change in six-minute walking distance and maximal treadmill walking time following SET. Despite this variability in response to SET, most clinical characteristics, including age, sex, race, PAD severity, comorbidities, presence of baseline leg symptoms, and prior lower extremity revascularization did not significantly affect the degree of improvement in six-minute walk distance or treadmill walking time following SET, relative to the control group. Compared to participants with baseline six-minute walk distance above the median value of 334 meters, baseline six-minute walk distance below the median of 334 meters value was associated with significantly greater percent change improvement but not with greater absolute improvement in six-minute walk distance following SET, relative to the control group. Compared to participants with maximal treadmill walking time above the median value at baseline (6.3 minutes), those with maximal treadmill walking time below the median had significantly greater improvement in percent change in treadmill walking time, relative to the control group. In addition, compared to participants with baseline BMI values above the median value of 30 kg/M^2 at baseline, participants with baseline BMI values below the median had greater improvement in maximal absolute treadmill walking time, relative to the control group. Despite these three statistical interactions, within each subgroup evaluated (i.e. those with baseline BMI above and below the median, those with baseline absolute treadmill walking time above and below the median, and those with six-minute walk distance above vs. below the median) there were statistically significant improvements in six-minute walk distance and treadmill walking time within each of these subgroups, relative to the control group.

The clinical implications of these results are as follows. First, clinicians should advise people with PAD that the degree of responsiveness to SET varies between individuals. Second, clinicians should monitor patients with PAD for responsiveness to exercise interventions since, in general, patient characteristics (such as age, sex, race, history of revascularization or severity of PAD) did not identify patients more likely to respond favorably. Clinicians can potentially monitor response to SET by performing a six-minute walk test at clinic visits, since a six-minute walk test can be performed in the clinician's office relatively easily and inexpensively. Patients with PAD who do not show improvement in six-minute walk distance after 6 months of SET could be evaluated for alternative therapies. Third, based on results reported here, clinicians could advise patients with PAD that people with higher baseline walking ability (i.e. a baseline six-minute walk distance > 333.8 meters or a baseline maximal treadmill walking time of > 6.3 minutes) may have a more modest response to SET than patients with poorer baseline walking performance. However, even participants within these higher categories of baseline walking performance significantly improved six-minute walk distance and maximal treadmill walking time in response to SET, relative to a control group.

Prior studies of older people without PAD also demonstrated variability in response to exercise interventions that was not explained by age, sex, or race (21–25). However, to our knowledge, no prior studies have evaluated the degree of change in six-minute walk

distance and treadmill walking distance according to baseline clinical characteristics in a large number of participants with PAD.

This study has limitations. First, individuals who were unable or unwilling to attend on-site supervised exercise sessions three times a week were excluded, thereby reducing the generalizability of the results. Second, this study focused on supervised treadmill exercise therapy. Further study is needed to determine whether these findings apply to home-based exercise therapy in PAD. However, prior trials of home exercise reported that baseline characteristics of study participants did not affect response to home-based exercise (25,26). Third, the exercise interventions in this study were six months duration. These results may not apply to exercise interventions of shorter or longer duration. Fourth, data were not available on effort expended during exercise activities. Fifth, multiple comparisons were made to evaluate the effects of multiple participant characteristics on response to SET. Analyses were not pre-specified and no adjustments were made for multiple comparisons. Further study is needed to confirm our findings regarding the effects of baseline walking performance on response to SET. Sixth, our analyses assessing whether prior history of lower extremity revascularization affected the degree of improvement in walking performance in response to SET is pertinent to individuals with lower extremity revascularization at least three months previously. However, these clinical trial data could not assess whether combining lower extremity revascularization with SET improves walking performance more than SET alone. This question has been evaluated in prior randomized trials (27,28). Seventh, we did not collect data on location of lower extremity atherosclerosis.

In conclusion, substantial variability in responsiveness to SET exists among people with PAD. However, clinical characteristics do not appear to identify which patients with PAD are more likely to respond to SET. Further research is needed to determine whether biologic markers can identify patients who are more likely to have a significant improvement in walking ability following an exercise intervention.

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ARTICLE HIGHLIGHTS

Type of data.

Combined data from two randomized clinical trials.

Key Findings.

Among 306 participants with peripheral artery disease (PAD), there was substantial variability in six-minute walk distance improvement following supervised exercise therapy (SET). While age, sex, race, PAD severity, and prior revascularization did not affect response to SET, shorter six-minute walk distances at baseline were associated with significantly greater percent improvement in six-minute walk.

Take home message.

Among people with PAD, substantial variability exists in walking improvement after SET. These analyses further suggest that no patients should be excluded from SET referrals.
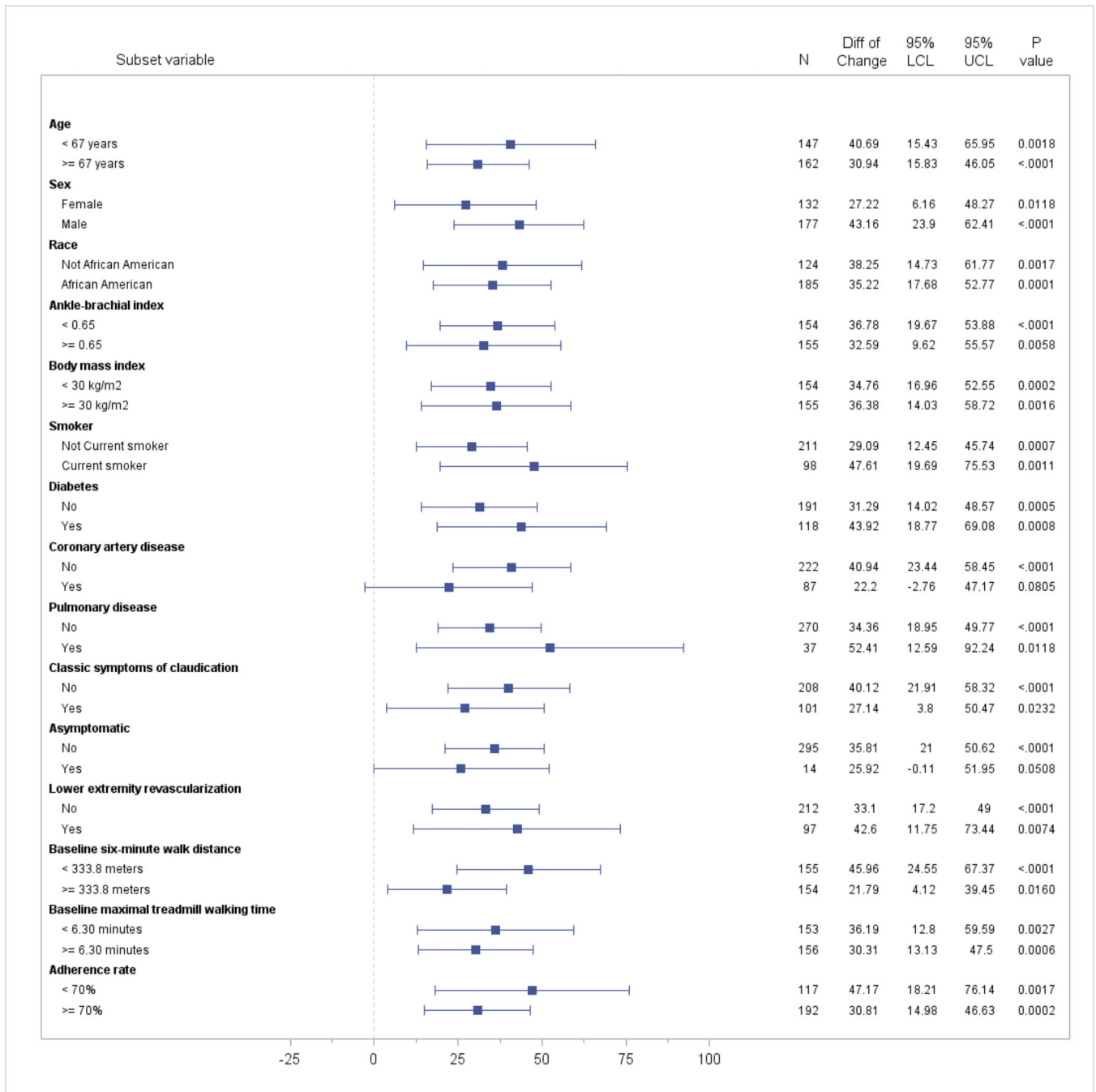
Figure 1a. Absolute change in six-minute walk distance between the supervised treadmill exercise vs. control groups, according to baseline characteristics.

*Groups for age, ankle brachial index, and body mass index were defined according to the baseline median value for each variable. P values shown represent the within-group statistical significance of change in the supervised exercise therapy group, relative to control.

Subset variable	N	Diff of Change	95% LCL	95% UCL	P value
Age					
< 67 years	147	15.84%	4.73%	26.96%	0.0055
>= 67 years	162	11.58%	5.90%	17.25%	<.0001
Sex					
Female	132	9.13%	1.67%	16.60%	0.0169
Male	177	17.36%	8.50%	26.23%	0.0002
Race					
Not African American	124	12.47%	4.31%	20.63%	0.0031
African American	185	14.75%	6.40%	23.09%	0.0006
Ankle-brachial index					
< 0.65	154	14.62%	7.39%	21.85%	0.0001
>= 0.65	155	12.09%	2.38%	21.80%	0.0151
Body mass index					
< 30 kg/m2	154	12.31%	6.20%	18.43%	0.0001
>= 30 kg/m2	155	14.38%	4.11%	24.65%	0.0064
Smoker					
Not Current smoker	211	12.49%	5.09%	19.89%	0.0010
Current smoker	98	15.75%	5.24%	26.27%	0.0038
Diabetes					
No	191	11.00%	4.75%	17.24%	0.0006
Yes	118	18.25%	5.90%	30.60%	0.0042
Coronary artery disease					
No	222	16.09%	8.63%	23.55%	<.0001
Yes	87	7.79%	-2.22%	17.80%	0.1255
Pulmonary disease					
No	270	13.06%	6.48%	19.64%	0.0001
Yes	37	19.54%	5.21%	33.88%	0.0094
Classic symptoms of claudication					
No	208	15.36%	7.28%	23.44%	0.0002
Yes	101	10.42%	2.00%	18.84%	0.0158
Asymptomatic					
No	295	13.75%	7.49%	20.02%	<.0001
Yes	14	8.50%	0.21%	16.79%	0.0454
Lower extremity revascularization					
No	212	13.38%	6.29%	20.47%	0.0003
Yes	97	14.68%	2.94%	26.42%	0.0149
Baseline six-minute walk distance					
< 333.8 meters	155	20.51%	9.51%	31.50%	0.0003
>= 333.8 meters	154	5.32%	0.94%	9.69%	0.0175
Baseline maximal treadmill walking time					
< 6.30 minutes	153	14.75%	3.77%	25.73%	0.0089
>= 6.30 minutes	156	10.15%	4.51%	15.79%	0.0005
Adherence rate					
< 70%	117	16.03%	5.71%	26.36%	0.0027
>= 70%	192	12.78%	5.32%	20.23%	0.0009

Figure 1b. Percent change in six-minute walk distance between the supervised treadmill exercise vs. control groups, according to baseline characteristics.

*Groups for age, ankle brachial index, and body mass index were defined according to the baseline median value for each variable. P values shown represent the within-group statistical significance of change in the supervised exercise therapy group, relative to control.

**Point estimates represent the difference in change in six-minute walk distance between the SET and control groups at 6-month follow-up. Groups for age, ankle brachial index, and body mass index were defined according to the baseline median value for each variable. P

values shown represent the within-group statistical significance of change in the supervised exercise therapy group, relative to control.

| Subset variable		N	Diff of Change	95% LCL	95% UCL	P value
Age						
< 67 years		147	3.15	1.87	4.43	<.0001
>= 67 years		162	4.79	3.59	5.98	<.0001
Sex						
Female		132	4.17	2.81	5.52	<.0001
Male		177	3.7	2.56	4.85	<.0001
Race						
Not African American		124	4.42	2.89	5.95	<.0001
African American		185	3.6	2.56	4.63	<.0001
Ankle-brachial index						
< 0.65		154	4.04	2.9	5.18	<.0001
>= 0.65		155	3.71	2.37	5.06	<.0001
Body mass index						
< 30 kg/m2		154	4.95	3.64	6.26	<.0001
>= 30 kg/m2		155	3.09	1.95	4.23	<.0001
Smoker						
Not Current smoker		211	4.02	2.92	5.11	<.0001
Current smoker		98	3.87	2.45	5.28	<.0001
Diabetes						
No		191	3.37	2.26	4.47	<.0001
Yes		118	4.79	3.37	6.21	<.0001
Coronary artery disease						
No		222	4.51	3.44	5.57	<.0001
Yes		87	2.95	1.45	4.44	0.0002
Pulmonary disease						
No		270	4.09	3.14	5.04	<.0001
Yes		37	2.85	0.84	4.86	0.0072
Classic symptoms of claudication						
No		208	3.42	2.38	4.46	<.0001
Yes		101	4.76	3.17	6.35	<.0001
Asymptomatic						
No		295	3.94	3.05	4.83	<.0001
Yes		14	3.26	-1.24	7.77	0.1360
Lower extremity revascularization						
No		212	3.96	2.89	5.03	<.0001
Yes		97	3.89	2.34	5.44	<.0001
Baseline six-minute walk distance						
< 333.8 meters		155	4.06	2.88	5.24	<.0001
>= 333.8 meters		154	3.9	2.62	5.19	<.0001
Baseline maximal treadmill walking time						
< 6.30 minutes		153	4.2	2.86	5.54	<.0001
>= 6.30 minutes		156	3.12	2.06	4.18	<.0001
Adherence rate						
< 70%		117	3	1.59	4.42	<.0001
>= 70%		192	4.4	3.29	5.51	<.0001

Figure 2a. Absolute change in treadmill walking time between the supervised treadmill exercise vs. control groups, according to baseline characteristics.
*Groups for age, ankle brachial index, and body mass index were defined according to the baseline median value for each variable. P values shown represent the within-group statistical significance of change in the supervised exercise therapy group, relative to control.
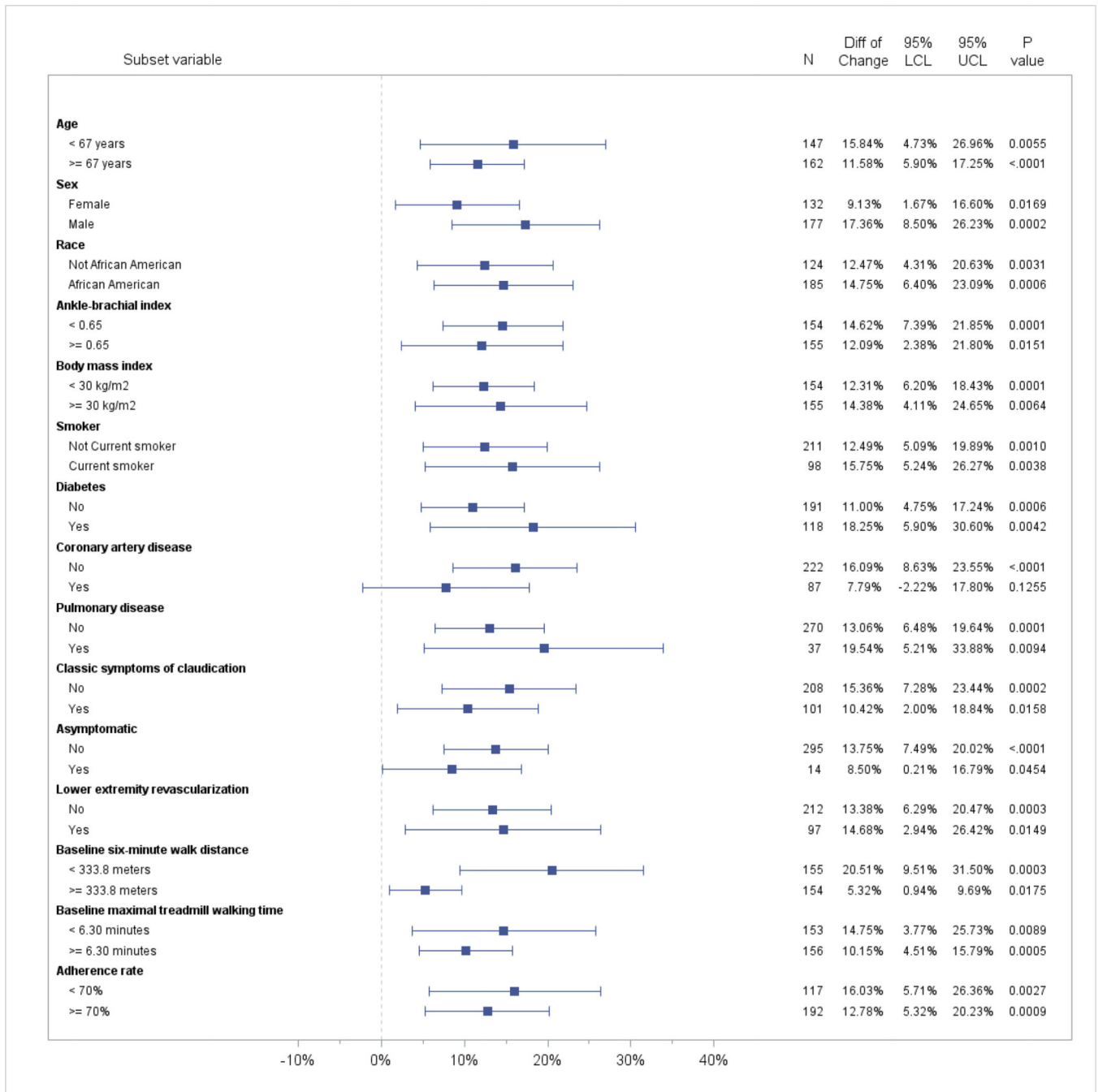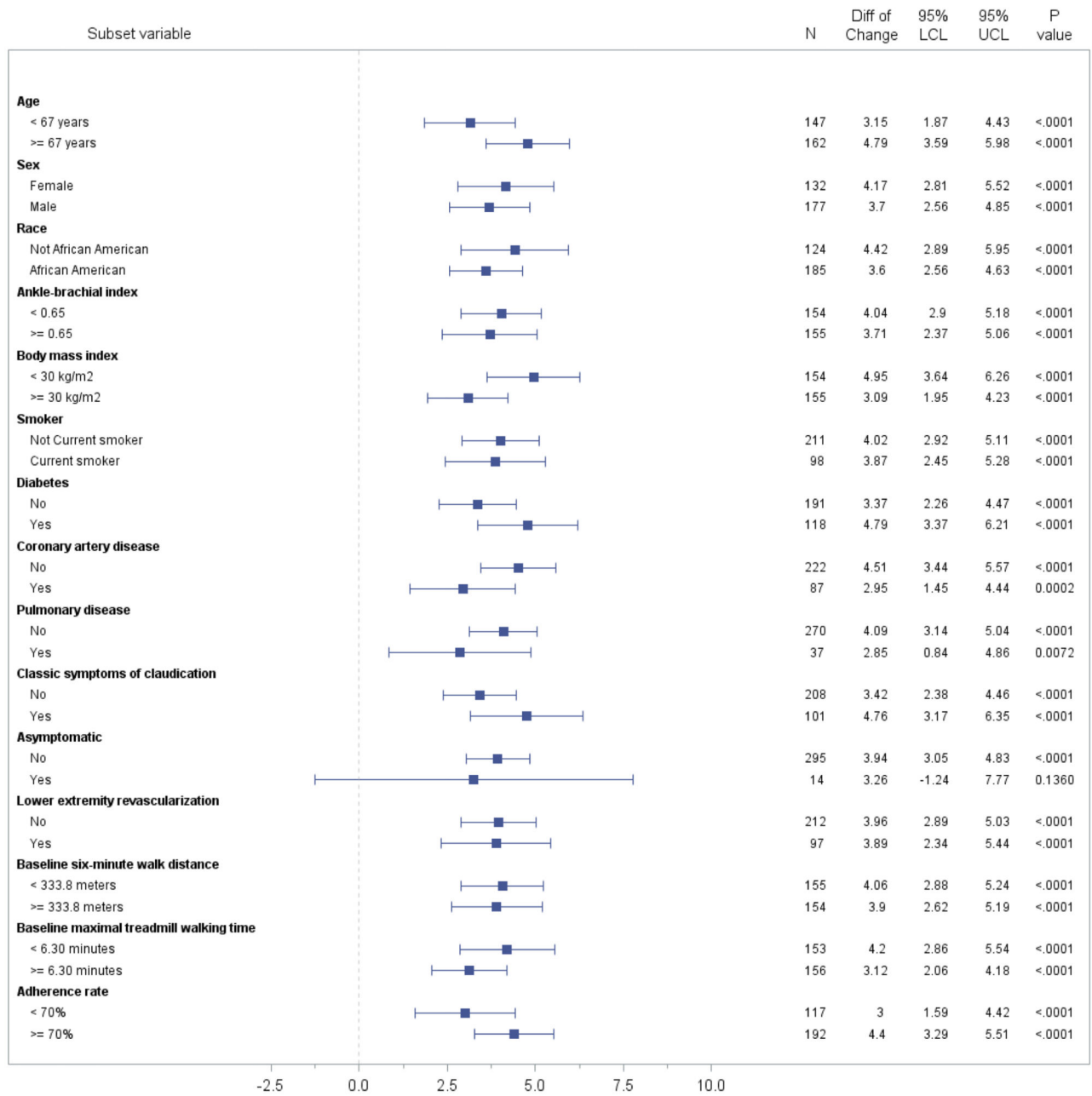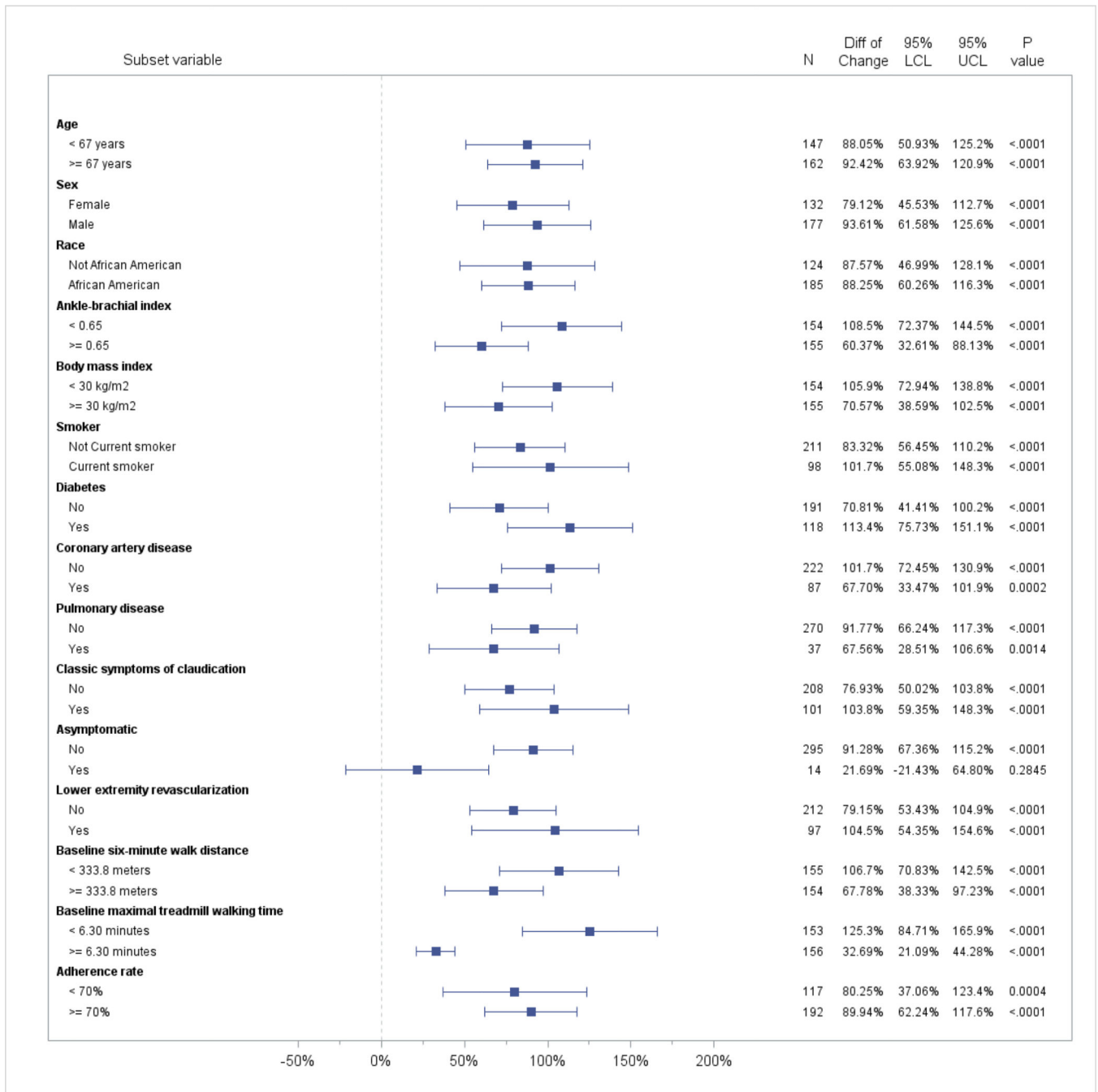
Figure 2b. Percent change in treadmill walking time between the supervised treadmill exercise vs. control groups, according to baseline characteristics.

*Groups for age, ankle brachial index, and body mass index were defined according to the baseline median value for each variable. P values shown represent the within-group statistical significance of change in the supervised exercise therapy group, relative to control.

* Point estimates represent the difference in change in treadmill walking time between the SET and control groups at 6-month follow-up. Groups for age, ankle brachial index, and body mass index were defined according to the baseline median value for each variable. P

values shown represent the within-group statistical significance of change in the supervised exercise therapy.

Table 1:

Baseline Characteristics of Participants with Peripheral Artery Disease

	Supervised Treadmill Exercise Therapy (SET) (N=153)	Attention Control (N=156)
Age (years)	68.31 (9.12)	67.56 (9.50)
Female sex, N (%)	66 (43.14)	66 (42.31)
Black race, N (%)	87 (56.86)	98 (62.82)
Ankle brachial index	0.66 (0.18)	0.66 (0.18)
Body mass index (kg/M^2)	30.46 (6.31)	30.33 (6.92)
Current smoker, N (%)	51 (33.33)	47 (30.13)
Diabetes mellitus, N (%)	56 (36.60)	62 (39.74)
Coronary artery disease, N (%)	48 (31.37)	39 (25.00)
Pulmonary disease, N (%) [*]	15 (9.80)	22 (14.29)
Heart failure, N (%) [*]	13 (8.61)	25 (16.03)
Classic Intermittent Claudication Symptoms, N (%)	54 (35.29)	47 (30.13)
Asymptomatic, N (%)	8 (5.23)	6 (3.85)
Prior lower extremity revascularization, N (%)	50 (32.68)	47 (30.13)
Baseline six minute walk distance (meters)	335.28 (96.47)	332.15 (92.58)
Baseline treadmill walking time (minutes)	7.22 (4.85)	7.46 (4.12)

Unless otherwise specified, data shown are means and (standard deviations).

[*] There are 2 participants in the Attention Control group missing baseline pulmonary disease data; there are 2 participants in the SET group missing baseline heart failure data.

Table 2.

Variation in change in six-minute walk distance and treadmill walking performance in people with PAD randomized to supervised treadmill exercise or control

Group	N	Range of 6-month change in six-minute walk	Range of 6-month change in maximal treadmill walking time	Number (%) of participants with any improvement in six-minute walk	Number (%) of participants with any improvement in maximal treadmill walking time
Entire Cohort					
Supervised exercise therapy	141	−149 to +356	−7.8 to 21.0	94 (66.7%)	127 (91.4%)
Control	142	−316 to +147	−7.8 to 12.6	67 (47.2%)	76 (55.5%)
Subset of participants adherent to at least 70% of intervention sessions					
Supervised exercise therapy	93	−149 to +356	−7.8 to +21.0	61 (65.6%)	86 (92.5%)
Control	95	−118 to +137	−7.8 to +12.6	49 (51.6%)	51 (54.8%)

Table 3:

Effects of clinical characteristics on change in six-minute walk distance and maximal treadmill walking time in response to supervised treadmill exercise vs. control in people with PAD*

Subgroup	Change in six minute walk distance (meters) in the exercise group relative to the control group (changes by subgroup)				Change in maximal treadmill walk time (minutes) in the exercise group relative to the control group (changes by subgroup)			
	Absolute change		Percentage change		Absolute change		Percentage change	
	Absolute change difference, (95% CI)	P value for interaction	Percentage change difference, (95% CI)	P value for interaction	Absolute change difference, (95% CI)	P value for interaction	Percentage change difference, (95% CI)	P value for interaction
Age 67 vs. <67 years	−10.3 (−38.9, 18.4)	0.48	−4.8% (−16.8%, 7.3%)	0.43	+1.5 (−0.2, 3.3)	0.084	2.0% (−44.2%, 48.2%)	0.93
Females vs. males	+15.8 (−12.8, 44.4)	0.28	8.1% (−3.9%, 20.1%)	0.18	−0.5 (−2.2, 1.3)	0.60	14.6% (−32.0%, 61.1%)	0.54
Blacks vs. whites	−1.1 (−30.3, 28.0)	0.94	2.9% (−9.4%, 15.2%)	0.64	−0.7 (−2.5, 1.1)	0.42	1.8% (−45.5%, 49.1%)	0.94
Ankle brachial index 0.65 vs. <0.65	−4.0 (−32.5, 24.4)	0.78	−2.6% (−14.6%, 9.5%)	0.68	−0.3 (−2.1, 1.4)	0.72	−47.6% (−92.8%, −2.3%)	0.039
Body mass index (30 vs. <30 kg/m^2)	+1.5 (−27.1, 30.0)	0.92	2.0% (−10.0%, 14.0%)	0.74	−1.8 (−3.5, −0.1)	0.036	−33.1% (−79.1%, 13.0%)	0.16
Current smoker	20.9 (−10.4, 52.2)	0.19	3.6% (−9.6%, 16.9%)	0.59	−0.2 (−2.1, 1.7)	0.86	16.4% (−34.5%, 67.3%)	0.53
Diabetes	12.6 (−16.8, 42.0)	0.40	7.2% (−5.2%, 19.6%)	0.25	1.4 (−0.4, 3.2)	0.12	42.4% (−5.0%, 89.9%)	0.080
Coronary artery disease	−18.0 (−49.9, 13.8)	0.27	−8.0% (−21.4%, 5.4%)	0.24	−1.7 (−3.6, 0.2)	0.082	−38.5% (−89.2%, 12.2%)	0.14
Pulmonary disease	19.3 (−26.8, 65.5)	0.41	7.0% (−12.5%, 26.5%)	0.48	−1.3 (−4.1, 1.4)	0.34	−31.4% (−105.4%, 42.6%)	0.40
Heart Failure	−43.2 (−91.8, 5.4)	0.081	−14.9% (−35.4%, 5.6%)	0.15	0.4 (−2.5, 3.2)	0.81	0.3% (−76.1%, 76.7%)	0.99
Classic symptoms of intermittent claudication	−13.1 (−43.4, 17.3)	0.40	−5.0% (−17.8%, 7.8%)	0.44	1.4 (−0.5, 3.2)	0.15	27.3% (−21.6%, 76.3%)	0.27
Asymptomatic (report of no exertional leg symptoms)	2.3 (−63.9, 68.6)	0.95	−1.8% (−29.8%, 26.1%)	0.90	−0.1 (−4.3, 4.1)	0.96	−63.9% (−175.0%, 47.1%)	0.26
History of lower extremity revascularization	9.1 (−22.2, 40.3)	0.57	1.0% (−12.1%, 14.2%)	0.88	−0.1 (−2.0, 1.8)	0.92	26.2% (−24.4%, 76.8%)	0.31

Table 3:

Clinical characteristics and effects on change in six-minute walk distance and maximal treadmill walking time in participants with PAD randomized to supervised treadmill exercise vs. control (continued)

Subgroup	Change in six minute walk distance (meters)				Maximal treadmill walk time (minutes)			
	Absolute change		Percentage change		Absolute change		Percentage change	
	Absolute change difference, (95% CI)	P value for interaction	Percentage change difference, (95% CI)	P value for interaction	Absolute change difference, (95% CI)	P value for interaction	Percentage change difference, (95% CI)	P value for interaction
Baseline six-minute walk distance (≥ 334 vs. <334 meters)	−24.0 (−51.4, 3.4)	0.086	−15.0% (−26.5%, −3.5%)	0.011	−0.1 (−1.9, 1.6)	0.88	−38.3% (−84.2%, 7.7%)	0.10
Baseline maximal treadmill walking time (≥ 6.3 vs. <6.3 minutes)	−5.1 (−33.6, 23.5)	0.73	−4.3% (−16.3%, 7.6%)	0.48	−1.0 (−2.7, 0.7)	0.24	−91.1% (−131.7%, −50.6)	<.001
Adherence to study intervention sessions (≥ 70% vs. ≥ 70%)	−15.8 (−45.8, 14.3)	0.30	−2.9% (−15.7%, 9.8%)	0.65	1.4 (−0.4, 3.3)	0.14	9.4% (−40.0%, 58.8%)	0.71

*
Data shown represent changes in six-minute walk distance or treadmill walking time in participants randomized to exercise relative to the control group by subgroup. For example, in the first row of data, participants age 67 and older randomized to supervised exercise therapy gained 10.3 meters less and 4.8% less on the six-minute walk test relative to control compared to participants less than age 67. However, these differences between those age 67 and older vs. those less than age 67 were not statistically significant, since the p value for interaction was not < 0.05.

Table 4.

Change in six-minute walk distance within groups of participants randomized to exercise and control, respectively

	N	Baseline six-minute walk, mean (STD)	6-month six-minute walk, mean (STD)	Within group change in six-minute walk distance, mean (95% CI)	Between group change in six-minute walk distance, mean (95% CI)	P value
Age						
Participants randomized to exercise						
67 years	64	345.84 (98.83)	379.52 (90.67)	33.69 (18.69, 48.68)	Reference	0.2154
> 67 years	77	329.63 (92.91)	350.54 (86.54)	20.91 (7.23, 34.58)	−12.78 (−33.07, 7.52)	
Participants randomized to control						
67 years	78	356.42 (85.57)	348.18 (102.30)	−8.24 (−21.87, 5.39)	Reference	0.9427
> 67 years	64	310.84 (95.24)	301.87 (94.66)	−8.98 (−24.02, 6.07)	−0.74 (−21.04, 19.56)	
Sex						
Participants randomized to exercise						
Female	63	336.95 (91.52)	351.71 (86.96)	14.76 (−0.20, 29.72)	Reference	0.0355
Male	78	337.01 (99.44)	373.37 (90.54)	36.36 (22.92, 49.81)	21.60 (1.49, 41.72)	
Participants randomized to control						
Female	59	301.72 (83.88)	289.27 (94.33)	−12.46 (−28.10, 3.20)	Reference	0.5225
Male	83	360.16 (91.22)	354.34 (97.76)	−5.81 (−19.01, 7.38)	6.64 (−13.83, 27.10)	
Race						
Participants randomized to exercise						
Not African American	61	349.32 (91.40)	373.48 (87.92)	24.17 (8.73, 39.61)	Reference	0.6667
African American	80	327.58 (98.28)	356.23 (90.17)	28.64 (15.16, 42.12)	4.47 (−16.02, 24.97)	
Participants randomized to control						
Not African American	52	331.12 (104.54)	319.61 (118.14)	−11.52 (−28.20, 5.16)	Reference	0.6615
African American	90	338.62 (85.39)	331.75 (90.51)	−6.87 (−19.55, 5.81)	4.65 (−16.30, 25.60)	
ABI						
Participants randomized to exercise						
0.65	76	303.09 (80.29)	336.46 (75.07)	33.36 (19.62, 47.11)	Reference	0.1607
> 0.65	65	376.62 (97.45)	395.54 (94.49)	18.93 (4.07, 33.79)	−14.44 (−34.68, 5.80)	
Participants randomized to control						
0.65	66	313.48 (84.31)	309.45 (91.50)	−4.03 (−18.81, 10.75)	Reference	0.4075
> 0.65	76	355.33 (95.52)	342.81 (107.22)	−12.52 (−26.29, 1.26)	−8.49 (−28.69, 11.71)	
BMI						
Participants randomized to exercise						
30 kg/m^2	64	359.93 (92.15)	384.13 (82.80)	24.20 (9.13, 39.27)	Reference	0.6567
> 30 kg/m^2	77	317.91 (94.86)	346.71 (91.44)	28.79 (15.05, 42.53)	4.60 (−15.80, 24.99)	
Participants randomized to control						

	N	Baseline six-minute walk, mean (STD)	6-month six-minute walk, mean (STD)	Within group change in six-minute walk distance, mean (95% CI)	Between group change in six-minute walk distance, mean (95% CI)	P value
30 kg/m^2	74	359.99 (88.60)	349.56 (100.67)	−10.42 (−24.41, 3.56)	Reference	0.7054
> 30 kg/m^2	68	309.64 (90.22)	303.09 (96.92)	−6.55 (−21.14, 8.04)	3.87 (−16.34, 24.08)	
Current smoker						
Participants randomized to exercise						
No	96	341.06 (101.56)	365.49 (92.59)	24.43 (12.13, 36.72)	Reference	0.5176
Yes	45	328.29 (81.99)	359.86 (82.71)	31.57 (13.61, 49.53)	7.14 (−14.62, 28.91)	
Participants randomized to control						
No	103	326.90 (92.82)	322.79 (102.68)	−4.11 (−15.88, 7.67)	Reference	0.1549
Yes	39	359.59 (88.74)	339.23 (97.71)	−20.36 (−39.49, −1.22)	−16.25 (−38.72, 6.22)	

Table 4.

Associations of clinical characteristics with change in six-minute walk among participants randomized to exercise and control, respectively (continued)

	N	Baseline six-minute walk, mean (STD)	6-month six-minute walk, mean (STD)	Change of six-minute walk within group, mean (95% CI)	Change of six-minute walk between groups, mean (95% CI)	P value
Diabetes						
Participants randomized to exercise						
No	90	344.64 (95.69)	369.88 (90.96)	25.24 (12.53, 37.95)	Reference	0.7043
Yes	51	323.48 (94.98)	352.78 (86.08)	29.30 (12.42, 46.19)	4.07 (−17.07, 25.20)	
Participants randomized to control						
No	87	345.48 (91.75)	340.77 (103.27)	−4.71 (−17.57, 8.16)	Reference	0.3414
Yes	55	320.69 (92.66)	306.01 (95.05)	−14.69 (−30.86, 1.49)	−9.98 (−30.65, 10.69)	
Coronary artery disease						
Participants randomized to exercise						
No	97	348.03 (95.13)	377.05 (80.97)	29.02 (16.79, 41.25)	Reference	0.5042
Yes	44	312.65 (93.27)	334.25 (100.18)	21.61 (3.45, 37.77)	−7.42 (−29.31, 14.48)	
Participants randomized to control						
No	106	338.60 (91.89)	327.44 (101.38)	−11.15 (−22.81, 0.51)	Reference	0.3858
Yes	36	327.86 (95.40)	326.90 (102.35)	−0.97 (−20.97, 19.04)	10.19 (−12.97, 33.35)	
Pulmonary disease						
Participants randomized to exercise						
No	128	340.13 (94.78)	364.15 (88.77)	24.02 (13.46, 34.59)	Reference	0.1003
Yes	13	306.07 (102.45)	359.20 (98.00)	53.13 (19.99, 86.27)	29.10 (−5.68, 63.89)	
Participants randomized to control						
No	122	339.19 (95.47)	329.47 (105.63)	−9.72 (−20.68, 1.23)	Reference	0.6458
Yes	18	315.01 (73.40)	312.40 (72.68)	−2.61 (−31.12, 25.91)	7.12 (−23.43, 37.66)	
Heart failure						
Participants randomized to exercise						
No	129	336.88 (95.07)	364.46 (89.73)	27.58 (16.98, 38.18)	Reference	0.2952
Yes	10	364.54 (95.46)	371.12 (86.85)	6.58 (−31.49, 44.65)	−21.00 (−60.52, 18.52)	
Participants randomized to control						
No	122	340.26 (94.36)	328.99 (104.40)	−11.27 (−22.10, −0.44)	Reference	0.1910
Yes	20	309.11 (77.51)	317.02 (80.93)	7.91 (−18.84, 34.66)	19.18 (−9.68, 48.04)	
Symptoms of classic intermittent claudication						
Participants randomized to exercise						
No	90	335.65 (96.76)	364.28 (87.69)	28.63 (15.92, 41.34)	Reference	0.6196
Yes	51	339.34 (94.54)	362.66 (92.94)	23.31 (6.43, 40.19)	−5.32 (−26.45, 15.81)	
Participants randomized to control						
No	98	337.71 (95.71)	327.62 (105.07)	−10.09 (−22.24, 2.06)	Reference	0.6584
Yes	44	331.80 (86.08)	326.61 (93.38)	−5.20 (−23.33, 12.94)	4.89 (−16.94, 26.72)	

	N	Baseline six-minute walk, mean (STD)	6-month six-minute walk, mean (STD)	Change of six-minute walk within group, mean (95% CI)	Change of six-minute walk between groups, mean (95% CI)	P value
Asymptomatic (no exertional leg symptoms)						
Participants randomized to exercise						
No	133	333.81 (94.36)	361.64 (88.79)	27.83 (17.40, 38.26)	Reference	0.3741
Yes	8	389.72 (108.00)	397.80 (96.95)	8.08 (−34.46, 50.62)	−19.75 (−63.55, 24.05)	
Participants randomized to control						
No	136	334.68 (93.15)	326.90 (102.42)	−7.78 (−18.08, 2.52)	Reference	0.4597
Yes	6	362.97 (80.33)	336.40 (76.34)	−26.57 (−75.61, 22.47)	−18.79 (−68.90, 31.32)	

Table 4.

Associations of clinical characteristics with change in six-minute walk among participants randomized to exercise and control, respectively (continued)

	N	Baseline six-minute walk, mean (STD)	6-month six-minute walk, mean (STD)	Change of six-minute walk within group, mean (95% CI)	Change of six-minute walk between groups, mean (95% CI)	P value
Lower extremity revascularization						
Participants randomized to exercise						
No	97	347.03 (89.77)	371.99 (78.87)	24.97 (12.73, 37.21)	Reference	0.6151
Yes	44	314.85 (105.17)	345.40 (107.60)	30.55 (12.38, 48.72)	5.58 (−16.33, 27.50)	
Participants randomized to control						
No	101	344.36 (93.43)	337.15 (99.11)	−7.21 (−19.18, 4.76)	Reference	0.6756
Yes	41	314.98 (88.06)	303.05 (103.64)	−11.93 (−30.72, 6.85)	−4.73 (−27.00, 17.55)	
Baseline six-minute walk						
Participants randomized to exercise						
333.8 meters	73	265.23 (57.68)	313.00 (72.66)	47.77 (34.60, 60.94)	Reference	<0.0001
> 333.8 meters	68	414.02 (62.51)	418.11 (72.00)	4.10 (−9.55, 17.75)	−43.67 (−62.64, −24.70)	
Participants randomized to control						
333.8 meters	64	255.02 (57.65)	257.23 (79.58)	2.21 (−12.64, 17.05)	Reference	0.0549
> 333.8 meters	78	402.22 (55.50)	384.81 (78.50)	−17.41 (−30.86, −3.96)	−19.62 (−39.65, 0.42)	
Baseline maximal treadmill walking time						
Participants randomized to exercise						
6.30 minutes	75	305.80 (84.70)	340.26 (83.37)	34.46 (20.66, 48.26)	Reference	0.1069
> 6.30 minutes	66	372.42 (95.59)	390.32 (88.93)	17.90 (3.19, 32.61)	−16.56 (−36.73, 3.62)	
Participants randomized to control						
6.30 minutes	62	297.74 (77.45)	294.29 (85.46)	−3.45 (−18.69, 11.80)	Reference	0.3774
> 6.30 minutes	80	365.44 (92.93)	352.89 (105.56)	−12.54 (−25.96, 0.88)	−9.10 (−29.41, 11.21)	

Table 5.

Associations of clinical characteristics with change in maximal treadmill walking time among participants randomized to exercise and control, respectively

	N	Baseline maximal treadmill walking time, mean (STD)	6-month maximal treadmill walking time, mean (STD)	Within group change in maximal treadmill walking time, mean (95% CI)	Between group change in maximal treadmill walking time, mean (95% CI)	P value
Age						
Participants randomized to exercise						
67 years	64	6.58 (4.74)	10.89 (5.14)	4.31 (3.26, 5.35)	Reference	0.6561
> 67 years	75	7.60 (4.58)	12.22 (5.78)	4.63 (3.66, 5.59)	0.32 (−1.10, 1.74)	
Participants randomized to control						
67 years	76	7.40 (3.69)	8.47 (4.34)	1.08 (0.42, 1.74)	Reference	0.0259
> 67 years	61	7.58 (4.08)	7.53 (4.14)	−0.05 (−0.79, 0.69)	−1.13 (−2.12, −0.14)	
Sex						
Participants randomized to exercise						
Female	65	6.82 (4.28)	11.54 (5.60)	4.72 (3.69, 5.76)	Reference	0.5234
Male	74	7.40 (5.00)	11.67 (5.48)	4.26 (3.29, 5.24)	−0.46 (−1.88, 0.96)	
Participants randomized to control						
Female	57	6.94 (4.04)	7.49 (4.41)	0.55 (−0.22, 1.33)	Reference	0.9453
Male	80	7.86 (3.70)	8.45 (4.14)	0.59 (−0.07, 1.25)	0.04 (−0.98, 1.05)	
Race						
Participants randomized to exercise						
Not African American	60	8.15 (4.98)	13.04 (6.30)	4.88 (3.81, 5.96)	Reference	0.3255
African American	79	6.35 (4.29)	10.52 (4.59)	4.17 (3.23, 5.11)	−0.71 (−2.14, 0.72)	
Participants randomized to control						
Not African American	50	8.46 (4.72)	9.05 (5.10)	0.59 (−0.33, 1.42)	Reference	0.9582
African American	87	6.92 (3.14)	7.48 (3.61)	0.56 (−0.07, 1.20)	−0.03 (−1.07, 1.02)	
ABI						
Participants randomized to exercise						
0.65	75	5.51 (3.25)	10.24 (4.15)	4.73 (3.77, 5.70)	Reference	0.4475
> 0.65	64	9.03 (5.34)	13.21 (6.45)	4.18 (3.14, 5.23)	−0.55 (−1.97, 0.87)	
Participants randomized to control						
0.65	64	6.44 (3.51)	7.11 (4.05)	0.67 (−0.06, 1.40)	Reference	0.7273
> 0.65	73	8.39 (3.94)	8.89 (4.30)	0.49 (−0.20, 1.18)	−0.18 (−1.18, 0.83)	
BMI						
Participants randomized to exercise						
30 kg/m^2	62	7.43 (5.00)	12.98 (5.97)	5.55 (4.52, 6.58)	Reference	0.0068
> 30 kg/m^2	77	6.89 (4.40)	10.50 (4.88)	3.62 (2.69, 4.55)	−1.93 (−3.32, −0.54)	

	N	Baseline maximal treadmill walking time, mean (STD)	6-month maximal treadmill walking time, mean (STD)	Within group change in maximal treadmill walking time, mean (95% CI)	Between group change in maximal treadmill walking time, mean (95% CI)	P value
Participants randomized to control						
30 kg/m²	70	8.16 (4.26)	8.78 (4.79)	0.62 (−0.08, 1.33)	Reference	0.8462
> 30 kg/m²	67	6.77 (3.27)	7.30 (3.52)	0.52 (−0.19, 1.24)	−0.10 (−1.10, 0.91)	
Current smoker						
Participants randomized to exercise						
No	95	7.72 (4.94)	12.27 (5.91)	4.55 (3.69, 5.40)	Reference	0.7881
Yes	44	5.84 (3.76)	10.18 (4.28)	4.34 (3.08, 5.60)	−0.21 (−1.73, 1.32)	
Participants randomized to control						
No	99	7.65 (3.99)	8.27 (4.39)	0.62 (0.03, 1.21)	Reference	0.7794
Yes	38	7.03 (3.50)	7.49 (3.93)	0.46 (−0.49, 1.41)	−0.16 (−1.28, 0.96)	

Table 5.

Associations of clinical characteristics with change in maximal treadmill walking time among participants randomized to exercise and control, respectively (continued)

	N	Baseline maximal treadmill walking time, mean (STD)	6-month maximal treadmill walking time, mean (STD)	Within group change in maximal treadmill walking time, mean (95% CI)	Between group change in maximal treadmill walking time, mean (95% CI)	P value
Diabetes						
Participants randomized to exercise						
No	87	7.47 (5.13)	11.83 (5.85)	4.36 (3.46, 5.25)	Reference	0.6591
Yes	52	6.56 (3.75)	11.25 (4.94)	4.68 (3.53, 5.84)	0.33 (−1.14, 1.79)	
Participants randomized to control						
No	85	7.69 (4.19)	8.70 (4.59)	1.01 (0.38, 1.63)	Reference	0.0286
Yes	52	7.13 (3.26)	7.00 (3.45)	−0.13 (−0.93, 0.67)	−1.14 (−2.15, −0.12)	
Coronary artery disease						
Participants randomized to exercise						
No	94	7.26 (5.15)	12.30 (5.83)	5.04 (4.19, 5.89)	Reference	0.0233
Yes	45	6.86 (3.50)	10.17 (4.53)	3.31 (2.09, 4.54)	−1.73 (−3.22, −0.24)	
Participants randomized to control						
No	102	7.59 (4.07)	8.17 (4.32)	0.58 (−0.003, 1.16)	Reference	0.9793
Yes	35	7.15 (3.18)	7.72 (4.13)	0.56 (−0.43, 1.56)	−0.02 (−1.17, 1.14)	
Pulmonary disease						
Participants randomized to exercise						
No	126	7.25 (4.77)	11.84 (5.53)	4.59 (3.85, 5.33)	Reference	0.3422
Yes	13	5.91 (3.48)	9.33 (5.01)	3.42 (1.10, 5.73)	−1.17 −3.60, 1.26)	
Participants randomized to control						
No	118	7.63 (3.93)	8.17 (4.37)	0.55 (0.007, 1.09)	Reference	0.9534
Yes	18	6.78 (3.33)	7.37 (3.63)	0.59 (−0.79, 1.98)	0.04 (−1.44, 1.53)	
Heart failure						
Participants randomized to exercise						
No	126	6.92 (4.53)	11.55 (5.51)	4.63 (3.90, 5.36)	Reference	0.6563
Yes	11	9.05 (6.06)	13.10 (5.81)	4.05 (1.59, 6.51)	−0.58 (−3.14, 1.98)	
Participants randomized to control						
No	118	7.70 (4.00)	8.41 (4.35)	0.71 (0.17, 1.25)	Reference	0.1823
Yes	19	6.12 (2.52)	5.85 (2.92)	−0.27 (−1.61, 1.07)	−0.98 −2.42, 0.47)	
Symptoms of classic intermittent claudication						
Participants randomized to exercise						
No	88	7.66 (4.88)	11.80 (5.49)	4.14 (3.25, 5.02)	Reference	0.2100
Yes	51	6.22 (4.16)	11.29 (5.60)	5.07 (3.90, 6.23)	0.93 (−0.53, 2.40)	
Participants randomized to control						
No	95	7.48 (3.71)	8.21 (4.22)	0.73 (0.13, 1.33)	Reference	0.3660

	N	Baseline maximal treadmill walking time, mean (STD)	6-month maximal treadmill walking time, mean (STD)	Within group change in maximal treadmill walking time, mean (95% CI)	Between group change in maximal treadmill walking time, mean (95% CI)	P value
Yes	42	7.48 (4.22)	7.71 (4.40)	0.23 (−0.67, 1.13)	−0.50 −1.58, 0.59)	
Asymptomatic (no exertional leg symptoms)						
Participants randomized to exercise						
No	131	6.72 (4.26)	11.21 (5.16)	4.50 (3.76, 5.23)	Reference	0.8544
Yes	8	13.86 (6.16)	18.07 (7.40)	4.21 (1.25, 7.17)	−0.28 (−3.33, 2.76)	
Participants randomized to control						
No	132	7.47 (3.87)	8.05 (4.30)	0.58 (0.07, 1.09)	Reference	0.9319
Yes	5	7.70 (3.89)	8.17 (3.45)	0.46 (−2.17, 3.09)	−0.12 (−2.79, 2.56)	

Table 5.

Associations of clinical characteristics with change in maximal treadmill walking time among participants randomized to exercise and control, respectively (continued)

	N	Baseline maximal treadmill walking time, mean (STD)	6-month maximal treadmill walking time, mean (STD)	Within group change in maximal treadmill walking time, mean (95% CI)	Between group change in maximal treadmill walking time, mean (95% CI)	P value
Lower extremity revascularization						
Participants randomized to exercise						
No	96	7.30 (4.73)	11.88 (5.71)	4.58 (3.73, 5.43)	Reference	0.6802
Yes	43	6.74 (4.57)	11.00 (5.07)	4.26 (2.98, 5.53)	−0.32 (−1.85, 1.21)	
Participants randomized to control						
No	97	8.05 (4.13)	8.70 (4.30)	0.65 (0.05, 1.24)	Reference	0.6607
Yes	40	6.09 (2.67)	6.49 (3.80)	0.40 (−0.53, 1.33)	−0.25 (−1.35, 0.86)	
Baseline six-minute walk						
Participants randomized to exercise						
333.8 meters	73	5.18 (3.01)	9.34 (4.09)	4.16 (3.19, 5.14)	Reference	0.3518
> 333.8 meters	66	9.28 (5.22)	14.11 (5.83)	4.83 (3.80, 5.86)	0.67 (−0.75, 2.09)	
Participants randomized to control						
333.8 meters	62	5.65 (2.83)	5.78 (3.16)	0.13 (−0.61, 0.87)	Reference	0.1094
> 333.8 meters	75	8.99 (3.95)	9.94 (4.16)	0.94 (0.27, 1.62)	0.81 (−0.19, 1.81)	
Baseline maximal treadmill walking time						
Participants randomized to exercise						
6.30 minutes	75	3.92 (1.46)	9.50 (4.67)	5.58 (4.66, 6.51)	Reference	0.0007
> 6.30 minutes	64	10.89 (4.32)	14.07 (5.44)	3.19 (2.18, 4.19)	−2.40 (−3.76, −1.03)	
Participants randomized to control						
6.30 minutes	59	4.17 (1.39)	5.47 (3.27)	1.30 (0.55, 2.05)	Reference	0.0120
> 6.30 minutes	78	9.98 (3.18)	10.01 (3.89)	0.03 (−0.62, 0.68)	−1.28 (−2.27, −0.28)	