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EXERCISE REHABILITATION FOR PERIPHERAL ARTERY DISEASE: A REVIEW

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Abstract

PURPOSE—To summarize evidence regarding exercise therapy for people with lower extremity peripheral artery disease (PAD).

METHODS—Literature was reviewed regarding optimal strategies for delivering exercise interventions for people with PAD. Randomized trial evidence and recent studies were emphasized.

RESULTS—Randomized clinical trial evidence consistently demonstrates that supervised treadmill exercise improves treadmill walking performance in people with PAD. A meta-analysis of 25 randomized trials (1054 participants) concluded that supervised treadmill exercise was associated with 180 meters of improvement in maximal treadmill walking distance and 128 meters of improvement in pain-free walking distance compared to a control group. Three randomized trials of 493 patients with PAD demonstrated that home-based walking exercise interventions that incorporate behavioral change techniques improves walking ability in patients with PAD and improves the six-minute walk performance more than supervised treadmill exercise interventions (45-54 meters vs. 33-35 meters). Upper and lower extremity ergometry also significantly improved walking endurance in PAD. The Center for Medicare and Medicaid Services (CMS) recently determined that Medicare would cover 12 weeks (36 sessions) of supervised treadmill exercise for patients with PAD.

CONCLUSIONS—Supervised treadmill exercise and home-based walking exercise each improve walking ability in patients with PAD. The availability of insurance coverage for supervised treadmill exercise for patients with PAD will make supervised treadmill exercise more widely available and accessible. Home-based exercise that incorporates behavioral change technique is an effective alternative for patients unwilling or unable to attend three supervised exercise sessions per week.

Keywords

peripheral artery disease; exercise; intermittent claudication; home-based exercise; functional performance

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Lower extremity peripheral artery disease (PAD) affects 8.5 million men and women in the United States and more than 200 million people worldwide.[1,2] PAD is associated with a 2–3 fold increased rate of cardiovascular events and mortality, compared to people without PAD and this association is independent of established cardiovascular disease risk factors.[3,4] People with PAD also have greater functional impairment and faster functional decline than people without PAD.[5–10] While use of statins and other preventive medications are associated with reduced overall cardiovascular mortality in the U.S. population, only 2 medications, cilostazol and pentoxifylline, are approved by the Federal Drug Administration (FDA) for improving walking performance in people with PAD and neither is particularly effective.[11–17] Supervised treadmill exercise and home-based exercise that incorporates behavioral change techniques significantly improve pain-free and maximal walking distance in people with PAD.[18–23] In 2017, the Center for Medicaid and Medicare Services (CMS) announced plans to cover supervised treadmill exercise therapy for people with PAD, which is likely to increase availability of supervised treadmill exercise to the millions of patients with PAD in the U.S.[24] This review provides an overview of evidence regarding exercise therapy for people with PAD and provides practical information for implementing an exercise program for patients with PAD.

REVIEW OF LITERATURE

Epidemiology and Risk Factors for PAD

PAD is uncommon among people under age 50 and the prevalence increases markedly with older age.[1,2,4] Among community dwelling men and women age 65 and older, the prevalence of PAD is 10–15% and among community dwelling men and women age 80 and older, the prevalence is approximately 20%.[4,25] Older age, cigarette smoking, and diabetes mellitus are the strongest risk factors for PAD.[4] Current cigarette smoking is associated with a 2.0 to 3.4-fold increased risk of PAD compared to people who have never smoked.[4,26] Smoking cessation substantially reduces the risk of PAD, but smokers remain at increased risk for PAD for up to 10 years after quitting smoking.[4,26] Diabetes mellitus is associated with a 1.9 to 4.0 fold increased risk of PAD.[4] Hypertension and dyslipidemia are also independent risk factors for PAD.[4,26]

Diagnosing PAD

PAD can be non-invasively diagnosed with the ankle brachial index (ABI), a ratio of Doppler recorded systolic pressures in the lower and upper extremities. An ABI < 0.90 is highly sensitive and specific for a diagnosis of PAD.[27,28] Although intermittent claudication was traditionally considered the most classical symptom of PAD, it is now well established that most patients with PAD do not have classical symptoms of claudication.[8–10,25,29] Classical symptoms of intermittent claudication consist of exertional calf pain that do not begin at rest and that resolve within 10 min of rest.[29] In fact, most patients with PAD report exertional leg symptoms that do not meet the criteria for intermittent claudication and many report no exertional leg symptoms.[8–10,30]

Clinical Significance of PAD

PAD is associated with increased rates of all-cause mortality and cardiovascular events compared to people without PAD.[3,4] A meta-analysis of 16 population-based longitudinal studies involving 24 955 men and 23 339 women with 480 325 person years of follow-up summarized rates of acute coronary events, cardiovascular mortality, and all-cause mortality among people with PAD vs those with a normal ABI. In men, cardiovascular mortality rates at 10-y follow-up were 18.7% for men with ABI <0.90 vs 4.4% for men with a normal ABI value (1.10–1.40) (hazard ratio [HR] = 4.2; 95% confidence interval [CI], 3.3–5.4).[3] For women, cardiovascular mortality rates at 10-y follow-up were 12.6% among women with ABI <0.90 and 4.1% in women with a normal ABI (1.10–1.40) (HR = 3.5; 95% CI, 2.4–5.1).[3] When men and women were stratified by Framingham Risk Score (FRS), an ABI <0.90 was associated with an approximately 2-fold increased risk of 10-year all-cause mortality, cardiovascular mortality, and coronary event rate, compared to normal ABI values.

People with PAD also have greater functional impairment, lower physical activity, and higher rates of mobility loss than people without PAD.[5–10] Among 726 men and women age 55 y and older in the Walking and Leg Circulation Study (WALCS), those with an ABI <0.50 were 11.7 times more likely to be unable to walk for 6 min without stopping and those with an ABI of 0.70–0.90 were 2.7 times more likely to be unable to walk for 6 min without stopping, compared to individuals with a normal ABI value (5). At 5-year follow-up, participants with severe PAD in the WALCS cohort were 4.2 times more likely and those with mild PAD were 3.2 times more likely to become unable to walk one-quarter of a mile or walk up 1 flight of stairs without assistance compared to people without PAD, independently of age, comorbidities, and other confounders.[7] Functional impairment and functional decline in people with PAD is observed even among those who report no exertional leg symptoms.[8,9] For example, people with PAD in the WALCS who reported no exertional leg symptoms, even during the 6-min walk test at baseline, were significantly more likely to develop mobility loss compared to people with PAD who had classic claudication symptoms (HR=2.94; 95% CI,1.39–6.19).[8] Patients with PAD may restrict their activity or slow their walking speed to avoid exertional ischemic leg symptoms.[8]

Treatment Goals for Patients with PAD

Treatment goals should focus on reducing cardiovascular event rates, improving functional performance, and preventing functional decline. To prevent cardiovascular events, patients with PAD should be treated with anti-platelet therapy and high potency statin drugs. PAD patients who smoke should be advised to quit smoking at each clinical encounter and pharmacotherapy should be offered. Patients with PAD should have their blood pressure treated as per general guidelines regarding anti-hypertensive therapy.[11] Table 1 summarizes medical management to prevent cardiovascular risk in patients with PAD.

Just 2 medications, cilostazol and pentoxifylline, are FDA approved for treating PAD-associated ischemic symptoms. However, benefits from cilostazol are modest and recent evidence suggests that pentoxifylline does not improve walking performance meaningfully more than placebo. Cilostazol improves treadmill walking performance in people with PAD who have intermittent claudication symptoms by approximately 25% to 40%.[11,12] However,

side effects are common, including palpitations, dizziness, headaches, and diarrhea.[11] In 1 study, 20% of patients discontinued cilostazol within 3 mo.[31] Clinical practice guidelines recommend against pentoxifylline due to lack of efficacy.[11]

Supervised Treadmill Exercise for Peripheral Artery Disease

Randomized clinical trials have consistently demonstrated that supervised treadmill exercise significantly improves pain free and maximal treadmill walking distance in people with PAD. In 1995, a meta-analysis of 21 studies by Gardner et al concluded that supervised treadmill walking exercise improved maximum treadmill walking distance by 122% and pain-free treadmill walking distance by 179%.[32] However, only 3 of the 21 studies in the meta-analysis were randomized trials and the remainder were nonrandomized and uncontrolled studies. In a meta-regression analysis, Gardner et al concluded that the most effective exercise programs for patients with PAD had 3 supervised sessions/wk, asked the PAD patients to walk to maximal or near-maximal ischemic pain during exercise, had patients walking at least 30 min per session, and lasted for 6-mo duration or longer.[32] This meta-analysis has informed the design of supervised and home-based exercise programs for patients with PAD.[19–23] A typical supervised exercise program for patients with PAD consists of supervised treadmill exercise 3d/wk (ie, Monday, Wednesday, Friday), includes a minimum of 30 min of exercise, lasts for 6 mo duration, and asks participants to walk to maximum ischemic leg symptoms.[19,20,24]

Since the meta-analysis by Gardner et al was published in 1995, more than 25 randomized trials of supervised treadmill exercise in PAD have been completed. Most demonstrated that supervised treadmill exercise significantly improved treadmill walking performance in patients with PAD. A 2012 meta-analysis by Fakhry et al summarized results of 25 randomized clinical trials of supervised walking therapy in 1054 patients with PAD and claudication symptoms.[18] Trials ranged in duration from 4 to 104 wk and 60% had durations between 12 and 26 wk. Overall, supervised walking exercise was associated with 180 meters of improvement in maximal walking distance and 128 m of improvement in pain-free walking distance, compared to the control group that did not receive supervised walking exercise.[18] Furthermore, of 22 randomized trials in the meta-analysis by Fakhry et al that provided data on treadmill walking performance before and after supervised walking exercise, 15 (71%) reported between 50% and 99% improvement in maximal treadmill walking distance and 5 (21%) reported more than 100% improvement in maximal treadmill walking distance in response to supervised walking exercise.[33] While the meta-analysis by Fakhry et al demonstrated significant improvement in treadmill walking performance in PAD patients following supervised exercise, the magnitude of benefit was lower than in the meta-analysis reported by Gardner et al. The lower magnitude of benefit for supervised exercise reported by Fakhry et al is likely due to the fact that the meta-analysis by Fakhry et al included only randomized trials, while the meta-analysis by Gardner et al included mostly uncontrolled and non-randomized studies.[32,33]

Should Supervised Treadmill Exercise Programs Advise Patients with PAD to Exercise to Maximal Ischemic Leg Symptoms?

Despite consistent evidence from randomized trials regarding benefits of supervised exercise for patients with PAD, questions remain about some aspects of the most effective exercise interventions for people with PAD. Patients with PAD typically need to stop and rest during exercise, due to ischemic leg pain that increases during walking activity. It is currently unclear whether PAD patients who walk to maximal ischemic leg pain during exercise have greater gains from walking exercise activity than PAD patients who walk only to the initial onset of ischemic leg pain. In the 1995 meta-regression of walking exercise for PAD, Gardner et al reported that walking exercise to maximal ischemic leg pain was more effective than walking exercise to the onset of ischemic leg pain.[32] However, more recent randomized trial evidence showed no difference in the degree of improvement in treadmill walking time between randomized trials in which PAD patients were asked to walk to near maximal ischemic pain and those in which PAD walked for exercise only to the onset of ischemic pain.[18] To date, no adequately powered randomized trials have been conducted to determine whether high intensity is superior to low intensity exercise for patients with PAD.

What is the Optimal Program Duration of Supervised Treadmill Exercise?

Gardner et al reported that supervised exercise programs lasting 6 mo or longer were more effective than shorter programs for PAD patients with intermittent claudication.[32] However, the meta-analysis by Fakhry et al reported significant improvements in pain-free and maximal treadmill walking time regardless of whether the supervised exercise interventions were short duration (4–11 wk), medium duration (12–26 wk) or long duration (>26 wk).[18] Separate study showed that gains from treadmill exercise in PAD are realized somewhat gradually, with initial benefit observed only after about 4 wk of exercise and most of the treadmill walking benefit achieved by 8–12 wk after onset of treadmill exercise therapy.[20,34] In a supervised treadmill exercise program, improvement in treadmill walking performance occurs within 4–6 wk,[20,34] while improvement in 6-min walk performance is more gradual. [20] This is likely related to the fact that treadmill exercise trains the PAD patient to the treadmill walking outcome measurement.[35,36]

Is walking Exercise Beneficial for PAD Patients without Classic Claudication Symptoms?

Most patients with PAD do not have classical symptoms of intermittent claudication.[6,8–10] Two randomized trials of supervised treadmill exercise and 1 randomized trial of home-based exercise included PAD participants with and without classical symptoms of intermittent claudication, including PAD patients reporting no exertional leg symptoms. The trials reported that supervised and home-based walking exercise significantly improved treadmill walking performance and 6-min walk distance in PAD patients, including those without classical symptoms of intermittent claudication.[19,20,23]

Medicare Coverage for Supervised Exercise for Symptomatic PAD

In 2017, the Center for Medicare and Medicaid Services (CMS) published a decision memorandum in which they described their intention to cover supervised exercise therapy for symptomatic peripheral artery disease.[24] Medicare covers three exercise sessions per

week lasting 30–60 minutes per session for a duration of 12 weeks.[24] CMS requires that patients have a face-to-face meeting with a healthcare provider to obtain the referral. CMS also requires that the exercise facility be located in a hospital outpatient setting or physician's office; that the exercise intervention be delivered by qualified personnel trained in exercise therapy for patients with PAD; and that the exercise program must be carried out under direct supervision of physician, physician assistant, nurse practitioner/clinical nurse specialist. This policy change by CMS regarding coverage for supervised treadmill exercise is expected to increase access to supervised exercise for large numbers of patients with PAD. Table 2 summarizes components of supervised exercise covered by CMS.

Home-based Walking Exercise for Patents with PAD

Home-based exercise avoids the time, effort, and cost associated with travel to a medical center for supervised exercise. Therefore, home-based walking exercise has the potential to be more accessible and acceptable to patients with PAD than supervised exercise programs. Three randomized trials have demonstrated that walking exercise in a home setting significantly improves walking ability and improves the 6-min walk more than a supervised treadmill exercise program.[19–23] Out of 3 home-based exercise randomized trials that demonstrated benefit for patients with PAD, 2 were 12 wk in duration and 1 was 6 mo in duration. In the first, Gardner et al randomized 119 men and women with PAD and intermittent claudication to 1 of 3 groups (supervised treadmill exercise, home-based walking exercise, or a control group) for 12 wk.[21] Participants randomized to supervised treadmill exercise attended exercise sessions 3 times weekly and walked for 40 min/session at moderate to high intensity. Participants randomized to home-based exercise were instructed to walk 3 times/wk at a self-selected pace working up to 45 min of walking exercise/session. The control group did not exercise. Participants in the home-based exercise group wore activity monitors to track their exercise activity and returned to the medical center every 2 wk, where study staff reviewed their exercise progress and provided instructions for the next 2 wk. At a 12-wk follow-up, the groups randomized to supervised treadmill exercise and home-based walking exercise each significantly improved pain-free and maximal treadmill walking time, compared to the control group. There were no significant differences in the degree of improvement in pain-free or maximal treadmill walking time between the supervised and the home-based exercise groups. However, the trial had an overall 23% drop-out rate and a 28% drop-out rate in the home-based exercise group, suggesting difficulties with adherence to home-based exercise in people with PAD.

In a subsequent 12-wk randomized trial, Gardner et al randomized 180 participants with PAD and intermittent claudication to supervised treadmill exercise, home-based walking exercise, or a control group that received light resistance training focused on the upper extremities.[22] Participants randomized to home-based exercise returned to the exercise center at 1, 4, 8, and 12 wk after baseline so that study staff could review their walking exercise activity and provide instructions for exercise during the next 3–4 wk. At 12-wk follow-up, the supervised exercise group increased their maximal treadmill walking time by 192 sec, the home-based walking exercise group increased their maximal treadmill walking time by 110 sec, and the control group increased their maximal treadmill walking time by 22 sec. Six-minute walk distance increased by 15 m in the supervised exercise group, by 45 m

in the home-based exercise group, and by 4 m in the control group. The 45-m improvement in 6-min walk distance in the home-based exercise group represented a clinically meaningful improvement[37] and was statistically significantly greater than the 6-min walk test improvement in the supervised exercise group.

The third randomized trial demonstrating benefit of home-based exercise for patients with PAD, the Group Oriented Arterial Leg Study (GOALS), used a Group Mediated Cognitive Behavioral (GMCB) intervention to help patients with PAD adhere to a home-based walking exercise program and improve their walking endurance.[23] One-hundred ninety-two participants with PAD, with and without classical symptoms of intermittent claudication, were randomized to either the GMCB intervention or an attention control group for 6 mo. The GMCB intervention required weekly group meetings with other PAD patients and a facilitator (coach) and used social cognitive behavioral change theory and group support to help patients with PAD adhere to home-based exercise. Group meetings included discussions regarding goal setting, self-monitoring, and overcoming obstacles to exercise adherence. At 6-mo follow-up, compared to the control group, PAD participants randomized to the GMCB home-based exercise intervention significantly improved their 6-min walk distance, maximal and pain-free treadmill walking distance, physical activity level, and patient-perceived walking ability, measured by the Walking Impairment Questionnaire. Compared to the control group, the intervention group had a 53.5 m greater increase in 6-min walk distance, consistent with a large meaningful change.[37] These 3 trials demonstrating benefit of home-based exercise interventions improved 6-min walk distance by 45 to 54 m, relative to the control group, while supervised treadmill exercise improved 6-min walk distance by 15–35 m.[19–23] A fourth randomized trial of home-based exercise in 145 PAD patients with diabetes mellitus demonstrated no benefit of home-based walking exercise or treadmill walking in patients with PAD, but did not measure change in 6-min walk distance.[38]

Alternative Forms of Exercise for PAD

Most randomized trials of exercise for patients with PAD have focused on walking exercise. However, several randomized trials demonstrated that upper and lower limb ergometry also improve walking performance in people with PAD and intermittent claudication.[39–41] Zwierska et al randomized 104 participants with PAD into 1 of 3 groups: upper limb aerobic ergometry; lower limb aerobic ergometry; or a non-exercise control group for 6 mo.[39] Exercise sessions occurred twice/wk and consisted of 2 min of arm (or leg) ergometry cycling followed by 2 min of rest for a total of 10 cycles (ie, 20 min of exercise at each session).[39] After 6 mo, maximal walking distance, measured by a shuttle-walk protocol, increased by 29% in the upper limb ergometry group and by 31% in the lower limb ergometry group, but did not improve in the control group. Peak oxygen uptake improved in the groups randomized to ergometry, suggesting that improved walking endurance may have been due in part to improved cardiovascular fitness. Similar benefits of upper and lower extremity ergometry were reported in 2 additional trials in patients with PAD.[40,41]

Resistance Exercise Training for PAD

Several randomized trials have tested the ability of strength training to improve walking performance in patients with PAD.[19,42,43] Of these, 2 studies demonstrated that lower extremity strength training significantly improved maximal treadmill walking time compared to a control group that did not exercise and 1 reported an increase in lower extremity skeletal muscle capillary growth following resistance training.[42] However, the largest randomized trial of supervised exercise in patients with PAD reported no change in the primary outcome of 6-min walk distance, while supervised treadmill exercise significantly improved 6-min walk distance. Overall, evidence suggests that walking exercise is a more effective exercise intervention than strength training for PAD.[19,42,43]

DISCUSSION

PAD affects approximately 11% of adults in the U.S. overall and approximately 20% of those age 80 and older in the U.S.[44] People with PAD have greater functional impairment, faster functional decline, and increased rates of mobility loss compared to those without PAD. Functional impairment and decline occurs in PAD even among those who are asymptomatic and among those with atypical leg symptoms other than intermittent claudication that are than impairment.[5–10]

Few medical therapies are available to improve walking performance in people with PAD. Table 3 summarizes medical therapies available for PAD. Consistent evidence from randomized clinical trials demonstrates that supervised treadmill exercise and home-based exercise that incorporates behavioral techniques significantly improve treadmill walking and 6-min walk distance in people with PAD.[19–23] In the U.S., few patients with PAD have participated in formal exercise programs, in part because of lack of medical insurance coverage for this benefit. In 2017, the Centers for Medicare and Medicaid Services announced plans to cover supervised exercise for PAD, and this coverage should increase accessibility of supervised exercise for patients with PAD.

However, evidence suggests that many patients with PAD may decline participation due to the inconvenience or difficulty of traveling to an exercise center 3 times/wk to participate in supervised exercise.[45] In a systematic review of 1541 potential participants with PAD who were eligible for inclusion in supervised exercise studies, 769 (50%) either were not interested or refused participation in supervised exercise and an additional 295 (19%) reported that attending supervised exercise sessions was too inconvenient.[45] For patients who are unwilling or unable to attend supervised exercise sessions, home-based exercise programs are an effective alternative. Home-based exercise interventions improve the 6-min walk distance more than supervised exercise interventions in patients with PAD.[19–23] However, randomized trials demonstrating benefits of home-based exercise for patients with PAD have required infrequent but regular visits to the medical center as part of the home-based exercise intervention and all have used behavioral techniques to promote home-based exercise. Further research is needed to develop home-based exercise programs that are effective but also acceptable and accessible for most PAD patients.

Clinicians should counsel patients about what to expect from walking exercise interventions. Benefits of walking exercise are not immediate. Improvement in walking performance is measurable at 4–6 wk after the onset of supervised treadmill exercise and requires persistent walking exercise activity, from 3 to 5 times/wk. This contrasts with revascularization interventions, in which improvement in walking performance occurs immediately after the procedure and typically does not require an ongoing commitment. Data are mixed regarding the durability of supervised exercise programs.[46,47] Although the CLEVER trial reported that improvement in treadmill walking performance after a 6-mo supervised exercise intervention persisted for 12 mo after the supervised exercise intervention was completed, 29% of the 111 participants were lost to follow-up. A separate study showed that most patients with PAD do not continue to exercise after a supervised exercise program is completed, and those who do not continue exercising experience significant functional decline.[47] Multiple randomized trials show that combining supervised exercise with revascularization achieves greater benefit than either individual treatment.[48–50]

Application to Practice

The 2 treatment goals for patients with PAD are to prevent cardiovascular events and to improve lower extremity functional performance resulting in prevention of functional decline. To prevent cardiovascular events, all patients with PAD should be helped to quit smoking, including pharmacotherapy for smoking cessation. Patients with PAD should be prescribed high potency statins and anti-platelet therapy. Blood pressure should be treated as recommended by current hypertension guidelines. Low dose rivaroxaban (2.5 mg twice daily) combined with low dose aspirin was recently shown to prevent cardiovascular events and major lower extremity events (amputation, acute limb ischemia, and peripheral revascularization) in patients with PAD,[51] but a 2.5 mg dose of rivaroxaban is currently not available in the U.S., and the drug is not FDA-approved for this indication.

All patients with PAD should be considered for exercise therapy. Effective exercise therapies are summarized in Table 4. Prior to prescribing an exercise program, PAD patients should complete a baseline treadmill cardiac stress test to identify coronary ischemia that may develop during a new exercise program. For most patients with PAD, a regular treadmill exercise stress test is sufficient to identify coronary ischemia prior to initiating an exercise program.

Walking exercise programs for PAD should be tailored for the individual patient. Some patients with PAD may only be able accomplish 10 min of walking exercise at the initial exercise sessions. The duration of exercise should be increased by 5 min each week, until the PAD patient is walking at least 30 min/session. Participants able to walk more than 30 min/session should be encouraged to increase their walking exercise duration up to 45 to 50 min/session. Effective exercise interventions for patients with PAD have advised the patient to walk to near maximal leg pain,[19,20] although evidence suggests that walking to the onset of ischemic leg pain is also beneficial.[18] Patients with PAD should be told that stopping to rest during walking exercise is acceptable and typical in PAD. Once leg pain subsides during a rest period, the PAD patient should resume walking again.

Conclusions

Supervised treadmill exercise and home-based walking exercise each improve walking ability in patients with PAD. The availability of insurance coverage for supervised treadmill exercise for patients with PAD will make supervised treadmill exercise more widely available and accessible. Home-based exercise that incorporates behavioral change techniques and infrequent visits to the medical center is an important and effective alternative for patients unwilling or unable to attend 3 supervised exercise sessions/wk.

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Table 1

Preventing Cardiovascular Events in Peripheral Artery Disease

Prevention of Cardiovascular Events	Guideline Recommendations
Anti-platelet therapy	• Antiplatelet therapy with aspirin (dose range 75 mg to 325 mg). • Clopidogrel 75 mg daily. • Vorapaxar is of uncertain utility in PAD. It reduced rates of acute limb ischemia and revascularization, but was associated with increased bleeding. • Rivaroxaban 2.5 mg twice daily + low dose aspirin reduced cardiovascular event rates in people with stable atherosclerosis, including those with PAD.
Statin therapies	• All people with PAD should be treated with statin therapy. • Patients with PAD should be treated with potent statins.
Hypertension therapy	• Patients with PAD and hypertension should have blood pressure treated as recommended by hypertensive guidelines. • There is no definitive evidence that a particular class of anti-hypertensive drugs or strategy is more effective than others. However, ACE inhibitors may have advantages for patients with PAD.
Smoking cessation	• PAD patients who smoke cigarettes should be advised to quit at every clinical visit. • Patients with PAD who smoke cigarettes should be offered pharmacotherapy to assist with smoking cessation (including with varenicline, bupropion, and/or nicotine replacement therapy).

Abbreviations: ACE, angiotensin-converting enzyme; PAD, peripheral artery disease.

Table 2

Elements of Supervised Exercise Required for Coverage by the Center for Medicaid and Medicare Services[a]

- Exercise must be prescribed by a physician after a face-to-face meeting with the patient that includes counseling on cardiovascular disease prevention.
- Prescribed exercise must consist of 12 wk of exercise sessions that occur three times weekly.
- After completing 12 wk of supervised exercise, an additional 36 sessions may be prescribed, with written justification, after the first 12 wk are completed and may take place over a longer period of time.
- The exercise sessions must take place in a physician's office or outpatient hospital-affiliated setting.
- Exercise must be delivered by qualified personnel with training in basic and advanced life support and exercise therapy for PAD.
- Exercise must be supervised by a physician, physician's assistant or nurse practitioner/clinical nurse specialist.[b]

Abbreviation: PAD, peripheral artery disease.

[a]Adapted from McDermott MM. Supervised Treadmill Exercise Therapy for Peripheral Artery Disease. http://www.acc.org. August 3, 2017. http://www.acc.org/latest-in-cardiology/articles/2017/07/12/12/55/supervisedtreadmill-exercise-therapy-for-peripheral-artery-disease (last accessed December 9, 2017).[52]

Table 3

Medical Management of Walking Impairment in People with PAD

Medications	• Cilostazol improves treadmill walking performance by approximately 25%-40%. • Pentoxifylline is FDA approved for treating PAD-related ischemic leg symptoms, but recent evidence suggests that pentoxifylline is not effective for treating ischemic leg symptoms and current clinical practice guidelines recommend against its use.
Exercise therapy	• Supervised treadmill exercise improves treadmill walking performance in patients with PAD. Supervised treadmill exercise has greater benefit on treadmill walking performance than home-based walking exercise. • Home-based walking exercise interventions that involve behavioral techniques are effective for functional impairment in people with PAD and improve the 6-min walk distance more than supervised treadmill exercise. • Upper and lower extremity ergometry improve walking performance in patients with PAD and improve peak oxygen uptake. • Lower extremity resistance training can improve treadmill walking performance in PAD, but is not as effective as supervised treadmill exercise.

Abbreviation: PAD, peripheral artery disease.

Table 4

Recommended Exercise Programs for Peripheral Artery Disease

	Supervised Treadmill Exercise[a]	**Home-based Walking Exercise**	**Ergometry Exercise**
Overview of exercise characteristics	Treadmill walking in an exercise facility with an exercise physiologist	Unsupervised walking for exercise in or around home or in an exercise facility	Supervised arm or leg ergometry
Frequency	3 times/wk	3–5 times/wk	Twice/wk
Duration of each exercise session	Begin at 15 min/session increasing to 45–50 min/session	Begin at 10–15 min/session increasing gradually to 50 min/session	10 sets of 2 min of ergometry (total = 20 min/session)
Intensity	Walking to near maximal or maximal leg pain[b]	Walking at self-selected pace or to near maximal or maximal leg pain[c]	High intensity
Program duration	12 wk minimum	12 wk to 6 mo	12 wk to 6 mo
Benefit	180 m of treadmill walking[18] 30–35 m in 6-min walk distance.[19,20]	45–55 m in 6-min walk distance[23]	Improved shuttle corridor-walk test (walk) by about 30%[39]
Additional considerations	Medicare provides coverage as of 2017	Effective programs have incorporated behavioral change techniques	Effective ergometry interventions have been supervised
Class of recommendation; Level of evidence [11]	Class I; Level of evidence: A	Class IIa; Level of evidence: A	Class IIa; Level of evidence: A

[a] Center for Medicare and Medicaid Services (CMS) defines "supervision" as under the direct supervision of a physician (as defined in 1861(r)(1)), physician assistant, or nurse practitioner/clinical nurse specialist (as identified in 1861(aa)(5)) who must be trained in both basic and advanced life support techniques (https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=287&DocID=CAG-00449N&SearchType=Advanced&bc=IAAAABAAQAAA&). CMS further defines "direct supervision" as the physician or nonphysician practitioner must be immediately available to furnish assistance and direction through the performance of the procedure but does not mean the physician or nonphysician practitioner must be present in the room when the procedure is performed (Federal Register, vol. 74, no. 223, November 20, 2009: p. 74580)

[b] Most studies of supervised treadmill exercise have studied high intensity exercise. Several small trials have demonstrated that low intensity supervised exercise was effective. No adequately powered randomized trials have compared high vs low intensity exercise in PAD.

[c] Studies of home-based exercise that have shown benefit have advised participants to either walk at a self-selected pace or to walk to maximal ischemic leg pain.[21–23]